1
A Randomized, Double-Blind, Placebo-Controlled Comparative Study to Evaluate the Efficacy of HiOra-SG gel in Stomatitis

6
Role of Hairzone Solution in Diffuse Hair Loss

10
Evaluation of Liv.52 DS and Ursodeoxycholic Acid in Nonalcoholic Steatohepatitis

14
Evaluation of Efficacy and Safety of Clarina cream in Acne Vulgaris

20
An Open Clinical Study to Evaluate the Efficacy and Safety of HiOra-K toothpaste in the Management of Sensitive Tooth
HiOra™
Setting High Standards in Oral Hygiene

HiOra™-K Toothpaste
For comprehensive management of sensitive teeth and gums

HiOra™-K Mouthwash
For sensitive teeth and halitosis

HiOra™ Mouthwash-Regular
Kills germs, tones gums & refreshes mouth

HiOra™-GA Gum astringent gel

HiOra™-Shine Herbal whitening toothpaste

HiOra™-SG The healing stoma gel
Dear doctor,

We are always interested in finding out whether the articles included in the magazine are useful in your practice. Please spend a few moments to fill the following questionnaire and send it to the address mentioned overleaf.

a) Rate this issue of Probe on the following aspects (on a scale of 1 to 5; 1 = Poor, 2 = Moderate, 3 = Good, 4 = Very good, 5 = Excellent).
   i) Quality of the selected articles
   ii) Layout and design
   iii) Overall content

b) Do the articles included in the magazine provide sufficient evidence to help you prescribe Himalaya’s products?
   Yes ☐ No ☐

c) Which section of the magazine you liked most?
   Clinical Insight ☐ Abstracts ☐ Wordsmith ☐
   Herbal Notes ☐ Other Please specify ________

d) In your opinion, which section of the magazine requires further improvement?
   Herbal Notes ☐ Drug Info ☐ Preclinical Evidence ☐
   Tech Bytes ☐ Other Please specify ________

e) Any other sections that you would like to be included in the forthcoming issues ________

f) Any other comments or suggestions ________

Name: __________________________ Qualification: __________________________ Phone: __________________________

Address: __________________________

E-mail: __________________________

---

Medical Crossword 4

Across

2. _________

4. _________

6. _________

8. _________

9. _________

10. _________

Down

1. _________

3. _________

5. _________

7. _________

*See page 81

Name: __________________________ Qualification: __________________________

Address: __________________________

Phone: __________________________

E-mail: __________________________

---

PIL Order Form

I wish to order for FREE reprints of the article published in the “Patient Education” section of this issue. Kindly send the requested number of copies (Patient Information Leaflets) to the below-mentioned address.

Name: __________________________ Qualification: __________________________

Institution/Clinic/Hospital: __________________________

Address: __________________________

No. of copies required

☐ 25
☐ 50
☐ 75
☐ 100

Phone: __________________________

E-mail: __________________________
<table>
<thead>
<tr>
<th>Contents</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drug Info</strong></td>
</tr>
<tr>
<td>Clarina® (ANTI-ACNE FACE WASH GEL) ................................................................. 53</td>
</tr>
<tr>
<td>Clarina® (ANTI-ACNE FACE MASK) ........................................................................... 54</td>
</tr>
<tr>
<td>Clarina® (ANTI-ACNE CREAM) .................................................................................. 55</td>
</tr>
<tr>
<td>Clearvital™ (ANTI-WRINKLE GEL) ........................................................................... 57</td>
</tr>
<tr>
<td>Bleminox® (ANTI-BLEMISH CREAM) .......................................................................... 58</td>
</tr>
<tr>
<td>Hairzone® (SOLUTION) ............................................................................................ 59</td>
</tr>
<tr>
<td>Talekt® (CAPSULE, SYRUP) .................................................................................... 61</td>
</tr>
<tr>
<td>HiOra®-K (Toothpaste) ............................................................................................ 63</td>
</tr>
<tr>
<td>HiOra®-Shine (Toothpaste) ....................................................................................... 64</td>
</tr>
<tr>
<td>HiOra®-K (Mouthwash) ............................................................................................. 65</td>
</tr>
<tr>
<td>HiOra® (Mouthwash–Regular) ................................................................................... 66</td>
</tr>
<tr>
<td>HiOra®-GA ................................................................................................................ 67</td>
</tr>
<tr>
<td>HiOra®-SG ................................................................................................................ 68</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient Education</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin Care .............................................................................................................. 69</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tech Bytes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ability of Optical Coherence Tomography to Detect Caries Beneath Commonly Used Dental Sealants ................................................................. 71</td>
</tr>
<tr>
<td>A Novel Fractional Microplasma Radio-frequency Technology for the Treatment of Facial Scars and Rhytids ............................................................... 71</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Liv.52 Update</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver Disorders during Pregnancy and Their Management ............................................... 72</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Wordsmith</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rare Skin Disorders .................................................................................................. 76</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Review</th>
</tr>
</thead>
<tbody>
<tr>
<td>Online ....................................................................................................................... 79</td>
</tr>
<tr>
<td>National Institute of Dental and Craniofacial Research</td>
</tr>
<tr>
<td>American Skin Association</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Book</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basic Guide to Oral Health Education and Promotion</td>
</tr>
<tr>
<td>Liver Cirrhosis: From Pathophysiology to Disease Management</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Quiz Corner</th>
</tr>
</thead>
<tbody>
<tr>
<td>Robert Willan and the French Willanists .............................................................. 83</td>
</tr>
<tr>
<td>Harry Sicher: Pioneer Dental Anatomist ............................................................... 83</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>From Other Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>An Essay on Desire ................................................................................................. 84</td>
</tr>
<tr>
<td>Colors ....................................................................................................................... 86</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Miscellaneous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laughter, the Best Medicine .................................................................................. 88</td>
</tr>
<tr>
<td>Think Wise ............................................................................................................... 88</td>
</tr>
</tbody>
</table>
Derma and Oral Care

The Himalaya Drug Company recently launched a range of derma care and oral health-care products. Products in the derma range are indicated for the treatment and management of blemishes, aging skin, age lines, skin wrinkles, acne, and hair loss. Products in the oral health-care range, aptly named as HiOra—setting high standards in oral hygiene, are indicated for the treatment and management of various dental and periodontal conditions.

The derma care products include Bleminor cream for hyperpigmentation and melasma; Clearvital gel for age lines, aging skin, and skin wrinkles; Clarina Anti acne cream, Clarina face wash gel, and Clarina face mask for acne vulgaris and acne rosacea; and Hairzone solution for hair loss due to varied etiology.

Dental caries, (affecting 60% to 90% of school children) and periodontal diseases (affecting up to 20% of the middle-aged adults) are the most common oral diseases reported worldwide. The burden of oral diseases can be reduced by avoiding common risk factors such as tobacco use and unhealthy diet.

HiOra products include HiOra mouthwash (regular), HiOra-K mouthwash, HiOra-K toothpaste, HiOra-Shine toothpaste, and HiOra GA and HiOra SG gel. These products are effective in the prevention and treatment of conditions such as tooth sensitivity, tooth discoloration, plaque, periodontitis, halitosis, postscaling periodontal pockets, tartar, gingivitis, bleeding gums, mouth ulcers, teething pain, and denture irritation.

This issue of Probe focuses on the dermal and oral health care. Also, it features an article on the efficacy of Liv.52 DS in the treatment of nonalcoholic steatohepatitis.

Apart from these, the issue also contains other regular features such as “Clinical Practice Pearls,” “Patient Education,” and “Wordsmith.” The “Patient Education” section of this issue provides information on the prevention and treatment of various skin disorders. Please use the patient information leaflet order form, enclosed in the issue, to avail the reprints of this information. Do write to us with your valuable feedback and suggestions at publication@himalayahealthcare.com.

Happy reading!

Dr Pralhad S Patki, MD
Editor-in-chief
Smile

A smile is a sign of love
A smile is a sign of care
A smile tells how much to others
You are important and also dear

A smile is a sign of cheer
A smile is a sign of trust
A smile shows how you can
Be happy even in hard crust

A smile is a sign of joy
A smile is a sign of hope
A smile teaches you how you can
Remove the clouds of mope

For nothing but only a smile
Takes away your pain and trial
And pick your troubles pile
And let you smile, smile and smile.

— Anonymous —
A Randomized, Double-Blind, Placebo-Controlled Comparative Study to Evaluate the Efficacy of HiOra-SG gel in Stomatitis

Sukumaran VG, et al.
Sree Balaji Dental College and Hospital, Velachery Main Road, Pallakaranai, Chennai, India


Abstract

Stomatitis, a relatively common oral disease, is defined as the inflammation of the soft tissues of the oral cavity. Present treatment options for stomatitis are associated with adverse effects and there is a need for novel therapies that are effective and cause decreased morbidity. The present study was conducted to evaluate the clinical efficacy and safety of polyherbal formulation (HiOra-SG gel) in the management of stomatitis. One hundred individuals of either sex, from the age group of 28 to 44 years, who were clinically diagnosed with stomatitis, were included in this randomized, double-blind, placebo-controlled clinical study. The individuals were randomized into Group A (HiOra-SG gel) or Group B (Placebo). All the individuals were advised to take HiOra-SG gel or similar-looking placebo on the tip of the index finger and apply it over their mouth ulcers four to five times daily for a period of 3 weeks. The individuals were evaluated for reduction in mouth ulcers, pain and swelling, and halitosis at weekly intervals for a period of 3 weeks by using a visual analog scale of 0 to 3. Statistical analysis was performed by repeated measures of ANOVA using Friedman test followed by Dunnett multiple comparison post hoc test. Of the 50 individuals treated with HiOra-SG gel, a significant reduction (P<.001) was observed in mouth ulcer and swelling and pain at the end of 3 weeks of treatment. In subjective evaluation, majority of the individuals experienced a remarkable overall improvement. There was no relief in individuals treated with placebo. No adverse drug effects were either reported or observed during the entire study period. The beneficial clinical efficacy of polyherbal formulation (HiOra-SG gel) in the management of stomatitis could be due to the synergistic actions of its potent herbs. Therefore, from the above findings it can be concluded that HiOra-SG gel is clinically effective and safe in the management of stomatitis.

Key Words

HiOra-SG gel, stomatitis, polyherbal formulation

Introduction

Stomatitis, one of the most commonly encountered oral complaints vexing for both physicians and patients, is defined as the inflammation of soft tissues of the oral cavity occurring as a result of mechanical, chemical, thermal, bacterial, viral, electrical, or radiation injury, or reactions to allergens, or as secondary manifestations of a systemic disease. Stomatitis can be the final common manifestation of a spectrum of conditions such as epithelial damage resulting from trauma; an immunological attack as in lichen planus, pemphigoid, or pemphigus; damage because of an immune defect as in acquired immunodeficiency syndrome (AIDS) and leukemia; infections such as herpes viruses, tuberculosis, and syphilis; cancer; nutritional defects such as vitamin deficiencies; and inflammatory bowel disease.1

Recurrent aphthous stomatitis (RAS) is a specific type of stomatitis that presents with shallow, painful ulcers usually located on the lips, cheeks, gums, or roof or floor of the mouth. The ulcers typically last from 7 to 14 days. The etiology of the disease is not known but appears to be multifactorial. Polymorphisms resulting in the increased production of interleukin-1β and tumor necrosis factor-α increase the risk for RAS.2 RAS can be classified according to the clinical characteristics into minor RAS, major RAS, and herpetiform aphthous stomatitis.3 Diagnosis is based on appearance and on exclusion, because
there are no definitive histologic features or laboratory tests. Immunofluorescence is useful in the differential diagnosis between RAS and bullous skin diseases. Behçet syndrome may also manifest with classical RAS and a range of systemic complications affecting the eyes, joints, neurological system, and skin.

Chronic ulcerative stomatitis (CUS), another type of stomatitis, is common in women in their late middle age. Patients with CUS are reported to have a clinical history of painful, exacerbating and remitting oral erosions, and ulcerations. The histologic features are nonspecific, with a chronic inflammatory infiltrate, often appearing similar to oral lichen planus. Diagnosis of CUS requires surgical biopsy with immunofluorescence microscopy examination.

Stomatitis venenata, an inflammation of the oral mucosa, is the result of contact allergy. The most common causative agents are volatile oils, iodides, dentifrices, mouthwashes, denture powders, and topical anesthetics. Possible manifestations include erythema, angioneurotic edema, burning sensations, ulcerations, and vesicles.

Infections causing stomatitis are mainly viral, especially the herpes, Coxsackie, and HIV viruses. Primary herpes simplex infection causes multiple vesicular lesions on the intraoral mucosa on both keratinized and nonkeratinized surfaces and always includes the gingiva. These lesions rapidly ulcerate. Clinical manifestation occurs most often in children. Subsequent reactivations (secondary herpes simplex, cold sore) usually appear starting in puberty on the lip at the vermilion border and, rarely, on the hard palate.

Bacterial causes of stomatitis are less common. Syphilis and tuberculosis are uncommon but increasing, especially in people infected with HIV. Fungal and protozoal causes of ulcers are also uncommon but increasingly seen in immunocompromised persons, and travelers from the developing world.

Lichen planus, an autoimmune skin condition, may have oral and genital involvements. Oral lichen planus may also occur as an isolated entity. The ulceration is typically superficial, often described as erosion, and blends with the surrounding inflamed tissue. The ulcer may be associated with desquamative full thickness gingivitis.

Drug-related stomatitis may mimic aphthous ulcers (aphthous-like ulceration) or oral lichenoid lesions. Many patients who present with an oral ulcer as the initial sign of malignancy would have had symptoms for more than 3 weeks. Oral squamous cell carcinoma is the most common epithelial malignancy within the oral cavity.

Location of oral lesions may help identify the cause. Interdental ulcers occur with primary herpes simplex or acute necrotizing ulcerative gingivitis. Lesions on keratinized surfaces suggest herpes simplex, RAS, or physical injury. Physical injury typically has an irregular appearance and occurs near projections of teeth, dental appliances, or where biting can injure the mucosa.

If stomatitis is recurrent, viral and bacterial cultures, complete hemogram, serum iron, ferritin, vitamin B12, folate, zinc, and endomysial antibody are done. Biopsy can be done for persistent lesions that do not have an obvious etiology.

Treatment of stomatitis is based on the underlying cause. Conditions that predispose to oral ulceration, such as iron deficiency anemia, vitamin B12 deficiency, and folate deficiency must be treated. Potential triggers such as oral hygiene products containing sodium lauryl sulfate, trauma, food and drink with a low pH, and offending medications and possible allergens need to be removed.

Treatment for recurrent stomatitis is usually palliative, because there is no known cure. Several therapies have been tried for recurrent stomatitis including topical and systemic corticosteroids, colchicine, thalidomide, and dapsone. Systemic immunomodulatory drugs (corticosteroids and thalidomide) have been the most effective at suppressing disease activity, presumably by modifying the underlying disease process. However, most of these drugs are associated with serious long-term adverse effects limiting their usage.

In the present study, a polyherbal formulation (HiOra-SG gel) was evaluated in the management of stomatitis. The principal ingredients of this formulation include Glycyrrhiza glabra, Jasminum grandiflorum, Azadirachta indica, Ocimum basilicum, Boerhaavia diffusa, Syzygium aromaticum, and Triphala.

Aim of the study

The present study was conducted to evaluate the clinical efficacy and safety of HiOra-SG gel in the management of stomatitis.

Study Design

A double-blind, randomized, placebo-controlled comparative clinical study was conducted at Sree
Clinical Insight

HiOra-SG gel in Stomatitis

Balaji Dental College and Hospital between November 2009 and August 2010. The study protocol, case report forms, regulatory clearance documents, product-related information, and informed consent form were submitted to the “Institutional Ethics Committee” and were approved by the same.

**Material and Methods**

**Inclusion criteria**

Individuals of either sex, aged more than 18 years, and who were clinically diagnosed with stomatitis, were included in the study provided they were able to attend the clinic on all assessment visits, willing to give the informed consent, and willing to comply with the study procedures.

**Exclusion criteria**

Individuals below 18 years of age, with other dental and oral disorders; with active skin infection; or with known history or present condition of allergic response to cosmetic/pharmaceutical products, toiletries, or their components or ingredients were excluded from the study. Pregnant and lactating women as well as individuals with genetic and endocrinial disorders and preexisting systemic disease necessitating long-term medications were also excluded from the study.

**Study procedure**

Hundred individuals (29 males and 71 females) in the age group of 28 to 44 years who were clinically diagnosed with stomatitis were included in the study. After obtaining the informed consent, baseline history (which included personal data, description of symptoms, details of past medical history, family history, and history of possible exacerbating factor/s) was obtained from each individual. The individuals were randomly divided into two groups—Group A (HiOra-SG gel) and Group B (placebo)—of 50 each. The mean ages (in years) of the individuals were 34.12 ± 4.8 in the HiOra-SG gel group and 33.84 ± 6.5 in the placebo group. There was no statistical difference between the two groups at entry (Table 1). All individuals were advised to take HiOra-SG gel or similar-looking placebo on the tip of their index finger and apply it over the mouth ulcers four to five times daily for a duration of 3 weeks. No other topical or systemic antibiotics were permitted during the trial. Individuals were evaluated for reduction in mouth ulcers, pain and swelling, and halitosis at weekly intervals for a period of 3 weeks. During each follow-up visit, local skin examination was done and observations were recorded in the case report form.

All adverse events, either reported or observed by patients, were recorded with information about severity, date of onset, duration, and action taken regarding the study drug. Relation of adverse events to the study medication was predefined as “Unrelated” (follows a reasonable temporal sequence from the administration of the drug), “Possible” (follows a known response pattern to the suspected drug, but could have been produced by the patient’s clinical state or other modes of therapy administered to the patient), and “Probable” (follows a known response pattern to the suspected drug that could not be reasonably explained by the known characteristics of the patient’s clinical state).

Patients were allowed to voluntarily withdraw from the study, if they so desired without assigning reasons. For those withdrawing from the study, efforts were made to ascertain the reason for dropout. Noncompliance (defined as failure to take less than 80% of the medication) was not regarded as treatment failure, and reasons for noncompliance were noted.

**Primary and secondary end points**

The predefined primary end points were rapid improvements in the symptoms of stomatitis, whereas the predefined secondary end points were incidence of adverse effects and patient compliance to the treatment.

**Follow-up**

The individuals were followed up at the end of first, second, and third weeks of the treatment for various clinical parameters such as reduction in mouth ulcers, pain and swelling, and halitosis. The symptoms were evaluated using a visual analog score of 0 to 3, where 0=nil, 1=mild, 2=moderate, and 3=severe.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>HiOra-SG gel</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of individuals</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>34.12 ± 4.8</td>
<td>33.84 ± 6.5</td>
</tr>
<tr>
<td>Male:Female</td>
<td>14:36</td>
<td>15:35</td>
</tr>
<tr>
<td>Smokers</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Alcohol</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>Diet (vegetarian)</td>
<td>17</td>
<td>19</td>
</tr>
</tbody>
</table>
Statistical analysis

Statistical analysis was performed by repeated measures of ANOVA using Friedman test followed by Dunnett multiple comparison post hoc test. The scores for symptomatic relief from various parameters were expressed as mean±SD. The minimum level of significance was fixed at P<.05. Statistical analysis was carried out using GraphPad Prism software version 4.03.

Results

Results of the study showed that most of the individuals treated with HiOra-SG gel started responding to the therapy at the end of the first week of treatment. The mouth ulcer score reduced from 2.64 ± 0.28 (at entry) to 2.35 ± 0.20 (at the end of first week), 1.45 ± 0.64 (at the end of second week; P<.05), and 0.23 ± 0.12 (at the end of third week) with a significance of P<.001. Pain score reduced from 2.75 ± 0.18 (at entry) to 2.33 ± 0.50 (at the end of first week), 1.54 ± 0.48 (at the end of second week; P<.05), and 0.32 ± 0.15 (at the end of third week) showing significant (P<.001) improvement. Swelling was reduced from 2.21 ± 0.62 (at entry) to 2.03± 0.41 (at the end of first week), 1.15 ± 0.22 (at the end of second week; P<.05), and 0.26 ± 0.04 (at the end of third week) showing significant reduction (P<.001). Halitosis was reduced from 2.30 ± 0.48 (at entry) to 2.00 ± 0.22 (at the end of first week), 1.80 ± 0.16 (at the end of second week), and 1.44 ± 0.56 (at the end of third week); however, the values were not statistically significant. In subjective evaluation, majority of the individuals experienced a remarkable improvement. The overall response to the treatment improved from 1.25 ± 0.50 (at the end of first week) to 2.50 ± 0.47 (at the end of second week; P<.05), which further improved to 2.84 ± 0.12 (at the end of third week; P<.001). A reduction in the symptoms of stomatitis in individuals treated with placebo was observed; however, the values were not statistically significant (Table 2). No adverse drug effects were reported during the entire study period.

Discussion

Stomatitis, observed in numerous systemic diseases, affects up to 25% of the population7 and may be induced by trauma, nutritional deficiency, stress, and allergens. Treatment is symptomatic, the goal being to lessen symptoms, reduce ulcer number and size, and increase disease-free periods. The best treatment is the one that will control ulcers for the longest period with minimal adverse effects. The treatment approach should be determined on the basis of disease severity (pain), the individual’s medical history, the frequency of flare-ups, and the individual’s ability to tolerate the medication. The currently available treatments for stomatitis are associated with adverse effects and therefore, there is a need for

<table>
<thead>
<tr>
<th>Table 2. Effect of Treatment on the Clinical Symptoms of Stomatitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical symptom score</td>
</tr>
<tr>
<td>------------------------</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Mouth ulcers</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Pain</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Swelling</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Halitosis</td>
</tr>
<tr>
<td>Overall impression</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

Values are expressed in mean ± SD.

a: significant as compared to initial versus 2 weeks; b: significant as compared to initial versus 3 weeks; NS: not significant.
novel therapies that are effective with less morbidity. In the present study, HiOra-SG gel (a polyherbal formulation) is evaluated for its efficacy and safety in the management of stomatitis.

Deglycyrrhizinated licorice from *G glabra*, an ingredient of HiOra-SG gel, has ulcer-healing as well as antiallergic effect on IgE, which is an important factor in triggering off the inflammatory process in the oral mucosa. Triphala, another ingredient of the gel, possesses antimicrobial, astringent, and ulcer-healing activities. *J grandiflorum* exhibits wound-healing activity. *S aromaticum* has analgesic and mild-anesthetizing effects on sensitive nerve endings and is thus helpful in the management of pain associated with mouth ulcers. *A indica*, *G glabra*, and the alkaloids from leaves of *J grandiflorum* are effective antimicrobials against certain bacteria, which are commonly found in denture-induced stomatitis. *O basilicum* is known to possess antimicrobial activity. *B diffusa* exhibits excellent immunomodulatory activity, which helps in correcting the immune dysregulation, an important cause for the formation of recurrent aphthous ulcers. Boerhaavia alkaloids are also known to possess anti-inflammatory and wound-healing activities.

The beneficial effects of HiOra-SG gel could be attributed to the synergistic actions (antimicrobial, antiallergic, anti-inflammatory, analgesic, anesthetizing, ulcer-healing, astringent, and immunomodulatory activities) of its ingredients.

**Conclusion**

Currently available treatment options for the management of stomatitis have various limitations and adverse effects. In the present study, of the 50 individuals treated with HiOra-SG gel, there was a significant reduction in the symptoms of stomatitis such as mouth ulcer, swelling, and pain at the end of the treatment. Majority of the individuals experienced a remarkable overall improvement. Also, there was a reduction in halitosis though values were not statistically significant. This clinical efficacy of the polyherbal formulation (HiOra-SG gel) could be attributed to the synergistic actions of its potent herbs. In addition, no adverse drug effects were reported or observed during the entire study period. Therefore, it may be concluded that HiOra-SG gel is clinically effective and safe in the management of stomatitis.

**References**

Role of Hairzone Solution in the Management of Diffuse Hair Loss: An Open Clinical Study

Rawal RC, et al.
NHL Medical College and Seth Vadilal Sarabhai General Hospital, Ellisbridge, Ahmedabad, India


Abstract

Hair loss has multiple causes and more loss can impact the psychological phenomenon of the person. The purpose of this study was to evaluate the safety and efficacy of Hairzone solution in diffuse hair loss. The cases were included in the study according to the subject selection criteria. All patients were advised to gently massage the solution into the scalp part by part, covering the whole area of the scalp and to rinse it in the morning. The response to therapy was evaluated at intervals of 2 weeks for 6 weeks. The changes in various parameters from baseline values and the values at each visit for 6 weeks were evaluated by paired t test. Criteria for evaluation were signs and symptoms such as reduction in hair fall, and associated symptoms like itching, dryness of scalp, pull test, one-minute comb test, and overall impression. This clinical study demonstrated the beneficial effects of Hairzone Solution in diffuse hair loss as evidenced by decrease in hair fall by hair pull test and one-minute combing test, improvement in moisturizing, and relief from itching. Further safety of the product was also substantiated by clinical parameters. Therefore, it can be concluded that Hairzone solution is safe and effective in diffuse hair loss.

Key Words

Hairzone solution, diffuse hair loss, alopecia

Introduction

Hair, one of the vital parts of the body derived from ectoderm of skin, is a protective appendage on the body and considered accessory structure of the integument along with sebaceous glands, sweat glands, and nails.1 The main component of hair fiber is keratin. Keratins are proteins—long chains (polymers) of amino acids. Hair has great social significance for human beings.

Each hair grows in three cyclic phases: anagen (growth), catagen (involution), and telogen (rest). The anagen phase can be as short as 2 to 6 years. In the catagen phase of 2 to 3 weeks, the growth activity increases and hair moves to the next phase. The telogen phase is a state at which the hairs move into resting state. This phase lasts for 2 to 3 months. In general, 50 to 100 hairs at random are shed everyday.2 Various factors contribute to hair fall or loss. Genetic predisposition and hormonal factors predominantly contribute to the above. Diseases such as typhoid, malaria, and jaundice also cause hair fall. The use of chemotherapeutic agents also causes hair fall.3

Hair loss has multiple causes and more loss may impact the psychological phenomenon of the person. There are several other kinds of hair loss such as:

- Traction alopecia is most commonly found in people with ponytails or cornrows who pull on their hair with excessive force.
- Trichotillomania is the loss of hair caused by compulsive pulling and bending of the hairs. It tends to occur more in children than in adults. In this condition the hairs are not absent from the scalp but are broken. Where they break near the scalp they cause typical, short, “exclamation mark” hairs.
- Traumas such as chemotherapy, childbirth, major surgery, poisoning, and severe stress may cause the hair loss condition known as telogen effluvium.
- Worrisome hair loss often follows childbirth without causing actual baldness. In this situation, the hair is
actually thicker during pregnancy due to increased circulating estrogens. After the baby is born, estrogen levels fall back to normal pre-pregnancy levels and the additional hair foliage drops out. A similar situation occurs in women taking the fertility-stimulating drug clomiphene.

- Iron deficiency is a common cause for the thinning of hair, though frank baldness is not usually seen.
- Exposure of radiation to the scalp, as happens when radiotherapy is applied to the head for the treatment of certain cancers, may cause baldness of the irradiated areas.
- Some mycotic infections may cause massive hair loss.
- Alopeia areata is an autoimmune disorder also known as “spot baldness” that may result in hair loss ranging from just one location (Alopecia areata monolocularis) to every hair on the entire body (Alopecia areata universalis).
- Localized or diffuse hair loss may also occur in cicatricial alopecia (lupus erythematosus, lichen planopilaris, folliculitis decalvans, central centrifugal cicatricial alopecia, postmenopausal frontal fibrosing alopecia). Tumors and skin outgrowths also induce localized baldness (sebaceous nevus, basal cell carcinoma, and squamous cell carcinoma).
- Hypothyroidism may cause hair loss, typically frontal, and is particularly associated with thinning of the outer third of the eyebrows (syphilis also can cause loss of the outer third of the eyebrows).
- Hyperthyroidism may also cause hair loss that is parietal rather than frontal.
- Temporary loss of hair may occur in areas where sebaceous cysts are present for considerable duration; normally one to several weeks in length.

Available treatment options for various forms of alopecia have limited success. Some individuals with hair loss make use of so-called “clinically proven treatments” in an attempt to prevent further loss and regrow hair. As a general rule, it is easier to maintain remaining hair than to regrow; however, the success rate is very less with unwanted adverse effects. Therefore, Hairzone solution—a polyherbal formulation—was evaluated for its safety and efficacy in diffuse hair loss. It consists of extracts of Butea monosperma and Butea parviflora.

**Aim of the study**

The purpose of this study was to evaluate the safety and efficacy of Hairzone solution in diffuse hair loss.

---

**Materials and Methods**

This study was an open clinical trial conducted at the Outpatient Department of Dermatology, STD, AIDS & Leprosy, NHL Medical College and Seth Vadilal Sarabhai General Hospital, Ellispbridge, Ahmedabad, India. The study protocol, case report forms, regulatory documents, product information, and informed consent forms were submitted to the Institutional Ethics Committee, and were approved by the same. A total of 100 patients of both sexes (in the age group of 18-40 years) with diffuse hair loss, and who were willing to give informed written consent were enrolled in the study. Patients on immunosuppressive drugs, applying other topical therapy for diffuse hair loss in the last 2 weeks prior to the initiation of the study, with evidence of skin infection, and pregnant and lactating women were excluded from the study. Also, those patients who were not willing to give informed written consent were excluded from the study.

**Study procedure**

Each patient’s demographic medical history (especially local fungal infection, dandruff, pediculosis, trichotillomania, stress, diet, past illness, and drugs) and treatment details were recorded. All the enrolled patients underwent a thorough clinical examination, and scalp skin examination, which included the assessment of number of hairs lost in one-minute combing test and presence of alopecic patches. All patients were advised to gently massage the solution into the scalp part by part, covering the whole area of the scalp and to rinse it in the morning. The response to therapy was evaluated at intervals of 2 weeks for 6 weeks. Criteria for evaluation were signs and symptoms such as reduction in hair fall and associated symptoms like itching, dryness of scalp or moisturizer effect, hair pull test, one-minute comb test, and overall impression. Response was evaluated on an analog scale of 0 to 3 (0—Nil, 1—Moderate, 2—Good, and 3—Excellent). The overall response was in turn correlated with response to the treatment as follows: Grade 0—no improvement, 1—Poor response (<25% reduction), 2—Moderate response (25%-49% reduction), 3—Good response (50%-74% reduction), 4—Excellent response (>75% reduction).

All the adverse events, either reported or observed by the patients, were recorded with information about severity, date of onset, duration, and action taken regarding the study drug. Relation of adverse events to study medication was predefined as “Unrelated” (a reaction that does not follow a reasonable temporal sequence
from the administration of the drug), “Possible” (follows a known response pattern to the suspected drug, but could have been produced by the patient’s clinical state or other modes of therapy administered to the patient), and “Probable” (follows a known response pattern to the suspected drug that could not be reasonably explained by the known characteristics of the patient’s clinical state).

Patients were allowed to voluntarily withdraw from the study, if they had experienced serious discomfort during the study or sustained serious clinical events requiring specific treatment. For patients withdrawing from the study, efforts were made to ascertain the reason for dropout. Noncompliance (defined as failure to take less than 80% of the medication) was not regarded as treatment failure and reasons for noncompliance were noted.

**Primary and secondary end points**

The predefined primary efficacy end point was a decrease in the symptom score for diffuse hair loss. The predefined secondary safety end points were acute and chronic safety, as assessed by the incidence of adverse events and patient compliance to the therapy.

**Statistical analysis**

Statistical analysis was done according to intention-to-treat principles. The changes in various parameters from baseline values and follow-up visits at once in 2 weeks for 6 weeks were evaluated by paired t-test. Statistical analysis was performed using GraphPad Prism Version 4.03 for Windows, GraphPad Software, San Diego, California, United States.

**Results**

The demographic details of subjects included in the study are listed in Table 1. The mean hair fall at entry was 123.4 ± 7.4, which significantly \(P<.05\) improved from second week onward, and which further improved with continued treatment with Hairzone solution until the end of treatment at 6 weeks. Itching was present in 40 cases at entry, which reduced significantly by second week onward, presenting in only 23 cases and continued to show improvement with only 2 cases presenting with itching \(P<.05\). Mean hair fall in one-minute comb test, which was 72.8 ± 8.6 decreased markedly at 2 months to 54.6 ± 2.8 and further decreased to 9.2 ± 1.5 with a significance of \(P<.05\). The hair fall in hair pull test also showed significant improvement from second week onward and further improvement till the end of 6 weeks with continued treatment. Moisturizing effect was appreciated by 25 cases at 2 weeks, 58 cases at 4 weeks, and 75 cases at 6 weeks of reatment, with a significance of \(P<.05\) (Table 2).

Assessment of overall response is listed in Table 3. At the end of the study, 16 cases reported excellent response, 47 cases reported good response, 25 cases reported
Hairzone Solution in Diffuse Hair Loss

moderate response, 10 cases reported poor response, and 2 cases reported no response to Hairzone Solution. The safety evaluation of the investigational product was also evaluated and found that there were no adverse effects on application of the product (Table 4).

Discussion

Management of hair fall is extremely complex. Hormone therapy, use of α-reductase inhibitors, vasodilators like minoxidil are widely used to reduce the hair fall or loss. Synthetic drug, minoxidil is a potent vasodilator that appears safe for long-term treatment. Available treatment options for various forms of alopecia have limited success with unwanted adverse effects.

The present study showed that Hairzone solution was beneficial in the management of diffuse hair loss. Hairzone Solution consists of potent herbs *B monosperma* and *B parviflora*.

*B monosperma* and *B parviflora* inhibit the hair follicular degeneration, extend the anagen phase of hair growth cycle, and enhance proliferation and maturation of precursor epithelial cells of the final hair strand. They prevent the massive apoptosis in the proximal hair bulb and stimulate the multiplication of hair fiber cells with the stimulation of anagenic phase, and reduction of catagenic and telogenic phases.2,4

*B monosperma* displays antifungal activity against *Cladosporium cladosporioides*.5 It also has a significant bactericidal effect.6 *B monosperma* has potential antiviral activities.7 *B monosperma* has astringent action.8,9 This action tends to shrink or constrict body tissues, usually locally after topical medicinal application. Externally applied astringents cause mild coagulation of skin proteins, dry, harden, and protect the skin. Mild astringent solutions are used in the relief of such minor skin irritations as those resulting from superficial cuts, allergies, insect bites, or fungal infections. *B monosperma* has potent free radical scavenging activity and proves to be effective in promoting the therapeutic activity of Hairzone solution.10 *B parviflora* has antimicrobial action.11

The efficacy of Hairzone solution can be attributed to the synergistic effects of both the herbs *B monosperma* and *B parviflora*.

Conclusion

This clinical study demonstrated the beneficial effects of Hairzone solution in diffuse hair loss as evidenced by decrease in hair fall by hair pull test, one-minute combing test, improvement in moisturizing, and relief from itching. Further safety of the product was also substantiated by clinical parameters. Therefore, it can be concluded that Hairzone solution is safe and effective in diffuse hair loss.

References


| Table 4. Dermal Safety Evaluation of Hairzone Solution (n = 100) |
|---------------------------------|------------------|------------------|------------------|------------------|
| Signs and Symptoms               | On application   |
|                                 | Initial          | After first application | Week 2          | Week 4          | Week 6          |
| Erythema                         | 0.00 ± 0.00      | 0.00 ± 0.00          | 0.00 ± 0.00      | 0.00 ± 0.00      | 0.00 ± 0.00      |
| Edema                            | 0.00 ± 0.00      | 0.00 ± 0.00          | 0.00 ± 0.00      | 0.00 ± 0.00      | 0.00 ± 0.00      |
| Pain                             | 0.00 ± 0.00      | 0.00 ± 0.00          | 0.00 ± 0.00      | 0.00 ± 0.00      | 0.00 ± 0.00      |
| Pruritus and urticaria            | 0.00 ± 0.00      | 0.00 ± 0.00          | 0.00 ± 0.00      | 0.00 ± 0.00      | 0.00 ± 0.00      |
| Burning sensation                | 0.00 ± 0.00      | 0.00 ± 0.00          | 0.00 ± 0.00      | 0.00 ± 0.00      | 0.00 ± 0.00      |

Values are expressed in mean ± SD.
Nonalcoholic steatohepatitis (NASH) is considered a particular type of a large spectrum of nonalcoholic fatty liver disease (NAFLD), which includes accumulation of fat alone and fat with nonspecific inflammation of liver. NAFLD is one of the frequent causes of abnormal liver dysfunction observed in clinical setup. It represents a spectrum of liver lesions that occur in individuals who either do not consume any alcohol or consume alcohol only in quantities, generally considered not harmful to liver (usually <20g/d). Several predisposing factors such as obesity and diabetes are related to NAFLD. The pathogenesis of NAFLD and its progression to fibrosis and chronic liver disease are still unclear. The prevalence of NAFLD has markedly increased with the change in lifestyle and dietary pattern. However, the mechanisms involved in the pathogenesis of NAFLD have not been thoroughly investigated.

Several hypotheses pertaining to the mechanism of hepatocyte injury in NASH is put forth. The most important is association of oxidative stress and lipid peroxidation resulting from the imbalance between pro-oxidant and antioxidant chemical species. The treatment of nonalcoholic steatohepatitis (NASH) is far from satisfactory, ursodeoxycholic acid (UDCA) has been suggested to give beneficial effect in an open label clinical study. Liv.52 DS is a hepatospecific formulation, which is reported to restore the metabolic efficacy of the liver by protecting the hepatic parenchyma and promoting hepatocellular regeneration. The antiperoxidative activity of Liv.52 DS prevents the loss of functional integrity of the cell membranes, maintains cytochrome P450 enzyme system, shortens the disease recovery period and ensures early restoration of hepatic functions in infective hepatitis. Liv.52 is also reported to offer protection against infective hepatic damage, and useful in the treatment of liver
pathologies associated with protein energy malnutrition and as a useful adjuvant with hepatotoxic drugs.

**Objective**

The purpose of the present study was to evaluate the use of Liv.52 DS in the management of NASH and to compare its activity with that of UDCA.

**Materials and Methods**

**Study design and compliance**

The study is a prospective, randomized, controlled, parallel, open multicenter clinical trial. The study was conducted as per the principles of “Declaration of Helsinki” and according to the Guidelines of Good Clinical Practice (GCP) as per Indian Council of Medical Research (ICMR) ethical Guidelines for Biomedical research on Human subjects. The study included 35 adult patients (either sex) with signs and symptoms of NASH attending the outpatient department. They were diagnosed clinically, biochemically, and ultrasonologically. The patients were then randomly allocated into two groups, Liv.52 DS group comprising 19 patients (mean age of 42.21 ± 11.22 years) and UDCA group comprising 16 patients (mean age of 38.63 ± 10.21 years). Informed written consent was obtained from all patients participating in the study.

**Inclusion criteria**

Patients with fatty liver, elevated liver enzyme levels, hepatomegaly, and conditions relating to NASH were included in the study.

**Exclusion criteria**

Patients with liver disease other than NASH, hypertriglyceridemia, malignant jaundice, diabetes mellitus, childhood cirrhosis, and congenital heart diseases were excluded from the study.

**Study drugs**

Liv.52 DS tablets (The Himalaya Drug Company) were administered to patients in the Liv.52 DS group at a dosage of two tablets twice a day orally for 12 weeks. UDCA (8–10 mg/kg body weight) was administered to patients in the UDCA group at a dosage of one tablet twice a day orally for 12 weeks.

**Study procedure**

Basic demographic information of all patients was recorded. Signs and symptoms such as jaundice, anorexia, nausea/vomiting, fever, and pruritus were also recorded and assessed on a four-point Lickert scale as: 0 = None, 1 = Mild, 2 = Moderate, and 3 = Severe.

Blood samples were collected for hematological and biochemical investigations. Hemoglobin content, total WBC count, differential WBC count, and levels of serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), serum bilirubin, serum albumin, serum globulin, and total proteins were estimated. Ultrasonography (USG) was also done for all the patients.

**Follow-up visits**

Follow-up visits were done at weeks 4, 8, and 12 of the assigned treatment. Signs and symptoms of the disease were assessed and scored as baseline. Investigators were asked to give their overall impression about therapy on a scale of –1 to 4, where 4 = symptom free (100% relief from symptoms), 3 = marked improvement in symptoms (75% to 99% relief from symptoms), 2 = moderate improvement (50% to 74% relief from symptoms), 1 = less than 50% relief from symptoms, 0 = no improvement, and –1 = symptoms became worse.

At the end of 12 weeks, signs and symptoms of the disease was assessed and scored as before. Blood was collected for hematological and biochemical investigations and USG/CT scan of liver was done. Monitoring of adverse drug reaction was done throughout the course of the study.

**End points**

Outcome measures were evaluated for all patients who participated in the study (intention-to-treat analysis) and also for those who continued the treatment till the end of the study. The last observation carried forward (LOCF) technique was used for intention-to-treat analysis. Primary end point was control of hepatitis symptom scores at the end of the study period as compared to baseline values and secondary end point was physician’s global assessment of efficacy and safety.

**Statistical analysis**

Baseline characteristics were compared using Fisher exact test, paired student t test, and Wilcoxon signed-rank test. Statistical analysis was done using GraphPad Prism software for Windows, version 4.03.

**Results**

Results of the study showed that there was a decrease in levels of serum markers such as SGPT, SGOT, and
alanine transaminase compared to baseline values in patients diagnosed with NASH and treated with Liv.52 DS and UDCA for 12 weeks. This decrease was found to be statistically significant in all the parameters in Liv.52 DS group. However, in case of UDCA group, only a decrease in SGPT was found to be statistically significant (Figures 1 to 3).

There was statistically significant improvement in the clinical signs and symptoms such as nausea/vomiting in Liv.52 DS group, whereas no such observations were made in UDCA group (Table 1).

Comparison of baseline USG of patients with that of posttreatment (12 weeks) in both the drug-treated groups exhibited significant improvement in hepatomegaly and liver lesions. The percentage improvement with respect to USG was found to be 37.39% in Liv.52 DS group and 23.56% in UDCA group (Table 2 and Figures 4 and 5).

The overall impression of investigators on the outcome of therapy with respect to signs and symptoms at the end of 12 weeks of treatment indicated that there was a 100% improvement in Liv.52 DS group and 87.5% improvement in UDCA group (Table 3).

**Conclusions**

NAFLD and NASH are distinct hepatic disorders observed in patients without a history of significant alcohol consumption. NASH is considered to be a more aggressive form of NAFLD. It is estimated that NAFLD affects up to 20% of adults and nearly 5% of children worldwide. Its widespread prevalence is mainly attributed to urbanization, increasing affluence, physical inactivity, high fat/energy excessive diet and type 2 diabetes.

---

**Table 1. Symptoms of Nausea/Vomiting at the Beginning and During the Progression of Study in Liv.52 DS and UDCA Groups**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>No. of patients</th>
<th>Signs/ Symptoms</th>
<th>Initial</th>
<th>Week 4</th>
<th>Week 8</th>
<th>Week 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liv.52 DS</td>
<td>19</td>
<td>Present</td>
<td>8</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Absent</td>
<td>11</td>
<td>19*</td>
<td>19*</td>
<td>19*</td>
</tr>
<tr>
<td>UDCA</td>
<td>16</td>
<td>Present</td>
<td>8</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Absent</td>
<td>8</td>
<td>12**</td>
<td>12**</td>
<td>12**</td>
</tr>
</tbody>
</table>

*P<.0031, **Not significant.
Statistical analysis: Fisher exact test.

**Table 2. Hepatomegaly Score at the Beginning and at the End of 12 Weeks in Liv.52 DS and UDCA Groups**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>No. of patients</th>
<th>Initial (Mean ± SD)</th>
<th>Week 12 (Mean ± SD)</th>
<th>Statistical significance</th>
<th>Percentage improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liv.52 DS</td>
<td>19</td>
<td>3.53 ± 0.84</td>
<td>2.21 ± 0.80</td>
<td>P&lt;.0003</td>
<td>37.39%</td>
</tr>
<tr>
<td>UDCA</td>
<td>16</td>
<td>3.44 ± 0.90</td>
<td>2.63 ± 0.89</td>
<td>P&lt;.001</td>
<td>23.56%</td>
</tr>
</tbody>
</table>

Hepatomegaly scores were based on a scale of 0 to 4. 4 = Hepatomegaly with fatty changes/infiltration, 3 = Mild to moderate hepatomegaly with fatty changes/infiltration, 2 = Improvement in hepatomegaly or no fatty changes, 1 = Improvement in hepatomegaly with no fatty changes/infiltration, 0 = Normal. Statistical analysis: Wilcoxon signed-rank test

**Table 3. Overall Impression of Investigators on the Outcome of Therapy at the End of 12 Weeks of Treatment Compared to Baseline Values in Liv.52 DS and UDCA groups**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>No. of patients</th>
<th>No. of patients showing improvement</th>
<th>No. of patients showing no change</th>
<th>Overall improvement in the signs and symptoms compared to baseline values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liv.52 DS</td>
<td>19</td>
<td>19</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>UDCA</td>
<td>16</td>
<td>14</td>
<td>2</td>
<td>87.5%</td>
</tr>
</tbody>
</table>
Liv.52 DS in NASH

Based on the above observations, it can be concluded that Liv.52 DS exhibits significant effect on patients with NASH, and its effect is comparably better than UDCA at tested dose levels. This beneficial effect of Liv.52 DS could be due to its direct or indirect favorable influence on the cellular and body metabolism in maintaining the integrity of liver and restoration of its function, as reported in several earlier studies.

**Figure 1.** Average serum levels of SGOT in patients at the beginning of study and after 12 weeks of treatment with Liv.52 and UDCA

**Figure 2.** Average serum levels of SGPT in patients at the beginning of study and after 12 weeks of treatment with Liv.52 and UDCA

**Figure 3.** Average serum levels of ALP in patients at the beginning of study and after 12 weeks of treatment with Liv.52 and UDCA

**Figure 4.** A representative USG of patient showing hepatomegaly with grade I fatty changes in liver (initial)

**Figure 5.** A representative USG of same patient in Liv.52 DS group (12 weeks posttreatment) showing more or less normal Liver
Evaluation of Efficacy and Safety of Clarina cream in Acne Vulgaris

Jerajani HR, et al.
LTMM College & LTMG Hospital, Sion, Mumbai, India


Abstract

Acne vulgaris is an extremely common skin disorder, affecting virtually all adolescents and adults at some time in their lives. An open noncomparative clinical trial was conducted to evaluate the clinical efficacy and short- and long-term safety of Clarina cream in newly diagnosed and previously treated cases of acne vulgaris.

The study included 50 patients in the age group of 14 to 32 years (23 males and 27 females). A baseline assessment of personal data, description of symptoms and details of past medical history (family history of acne, history of possible exacerbating factors, etc) was done. All patients underwent a clinical examination and a thorough skin examination for the presence of black and white heads, inflamed papules and pustules, cysts, and nodules.

Patients were advised to apply Clarina cream over the lesions, twice a day for a period of 6 weeks. All patients were followed up every two weeks and during each follow up visit, local skin examination was done and observations recorded in the structured case record sheet.

Results of the study showed that there was a significant reduction in erythema, telangiectasia, skin oiliness, hyperpigmentation, papules, pustules, black and white comedones, nodules, cysts, and scars after the treatment with Clarina cream. Based on the study findings, it was concluded that Clarina cream was safe and effective in the treatment of newly diagnosed and previously treated cases of acne vulgaris.

Key Words

Acne vulgaris, Clarina cream, black comedones, white comedones

Introduction

Acne vulgaris is an extremely common skin disorder, affecting virtually all adolescents and adults at some time in their lives. Although the overall health is not impaired, acne is not a trivial disease, as it can produce cutaneous and emotional scars that last a lifetime.1–3 Numerous psychological problems stem from acne, some even resulting in decreased employability in adulthood.4

The etiology of acne is multifactorial and according to the severity of inflammation, acne can be classified into purely comedonal (noninflammatory acne), mildly papular, scarring popular, and scarring nodular acne. Clinically, the peak incidence of acne is evident during the teen years, but a significant number of men and women aged between 20 and 40 years, also suffer from acne vulgaris.5,6

Topical therapy is advocated for the management of acne, especially for patients with noninflammatory comedones and mild to moderate inflammatory acne. Comedolytic and anti-inflammatory agents, along with antimicrobials, are generally preferred in topical treatment of acne.

Tretinoin is the most effective available topical comedolytic agent, but topical application may lead to erythema, peeling and burning of the skin. During the past few decades many reports have documented an emergence of antibiotic resistance by Propionibacterium acnes during treatment of acne.7–9 Furthermore, systemic antimicrobials used in the treatment of acne have been causally associated with various short- and long-term adverse effects.10

Clarina cream, a polyherbal formulation containing extracts of Aloe barbadensis (Aloe vera), Prunus amygdalus, Alternanthera sessilis, and Rubia cordifolia, was found to be beneficial in the topical treatment of acne vulgaris.11 The present study was conducted to evaluate the efficacy and safety of Clarina cream in the management of acne vulgaris.
Material and Methods

Aim of the study
This study was aimed to evaluate the clinical efficacy and short- and long-term safety of Clarina cream in newly diagnosed and previously treated cases of acne vulgaris.

Study design
This study was an open noncomparative clinical trial, conducted at the Department of Dermatology, approved by the Institutional Ethics Committee of LTMM College & LTMG Hospital, Sion, Mumbai, India.

Inclusion criteria
Fifty patients of both sexes, attending the outpatient clinic of the Department of Dermatology at LTMM College & LTMG Hospital, Sion, Mumbai, were included in the study. A written informed consent was obtained from all patients.

Exclusion criteria
Children below 18 years of age, patients with preexisting systemic disease necessitating long-term medications, genetic and endocrinal disorders, and those who refused to give informed consent, were excluded from the study. Pregnant and lactating women were also excluded from the study.

Study procedures
A baseline history was obtained in order to determine the patient’s eligibility for enrolment in the trial. The baseline assessment included personal data, a description of symptoms and details of past medical history (family history of acne, history of possible exacerbating factors, etc.). Thereafter, all patients underwent a clinical examination and a thorough skin examination for the presence of black and white heads, inflamed papules and pustules, cysts, and nodules.

All patients were advised to apply Clarina cream over the lesions, twice a day for a period of 6 weeks. All patients were followed up every two weeks and during each follow-up visit, local skin examination was done and observations recorded in the structured case record sheet. All patients were reviewed at the end of 6 weeks.

Primary and secondary outcome measures
The predefined primary outcome measures were the control of local inflammation (erythema and telangiectasia), reduction in facial oiliness, number of papules and pustules, new comedone (black and white) formation, and soothed skin (reduction in burning and itching sensation). The predefined secondary outcome measures were reduction in formation of nodules and cysts, healing without scar formation, incidence of adverse events, and compliance to the treatment.

Adverse events
All local and systemic adverse events regarding the study drug reported or observed by patients, were recorded with information about severity, time of onset, duration, and action taken. Patients were allowed to voluntarily withdraw from the study, if they had experienced serious discomfort during the study or sustained serious clinical events requiring specific treatment.

Statistical analysis
An analysis was done according to intention-to-treat principles. Changes in various parameters from baseline values to the values after 6 weeks were analyzed using paired t-test. The minimum level of significance was fixed at 95% confidence limit and a two-sided P value of <.05 was considered significant.

Results
The study included 50 patients in the age group of 14 to 32 years (mean ± SD: 19.55 ± 3.69 years). There were 23 (46%) males and 27 (54%) females in the study. There was excellent compliance for the treatment and no dropouts were recorded.

Thirty-one (62%) patients had a family history of acne and the mean duration of acne was 3.19 years. Forty-two (84%) patients had a history of topical treatment and 12 (24%) had a history of systemic medications for acne. Thirty-six patients in correlated sunlight as the exacerbating factor, whereas, 11 (40.7%) females had observed premenstrual flare of acne. Eight (16%) patients linked mental stress and 4 (8%) linked cosmetics as the exacerbating factors for acne. On clinical examination, it was observed that dandruff was a major common finding in 34 (68%) patients.

It was observed that from the second week onward, there was a significant improvement in the mean score of signs and symptoms as evaluated by erythema, telangiectasia, and oiliness of the facial skin. The mean baseline score for erythema significantly reduced from 1.26 ± 1.10 to 0.85 ± 0.78, 0.43 ± 0.58, and 0.30 ± 0.46 at the end of 2, 4, and 6 weeks, respectively. The mean baseline score for
telangiectasia significantly reduced from $0.36 \pm 0.70$ to $0.23 \pm 0.52$, $0.13 \pm 0.34$, and $0.19 \pm 0.45$ at the end of 2, 4, and 6 weeks, respectively. The mean baseline score for oiliness significantly reduced from $1.57 \pm 0.68$ to $1.02 \pm 0.57$, $0.57 \pm 0.50$, and $0.49 \pm 0.55$ at end of 2, 4, and 6 weeks, respectively (Figure 1).

The mean baseline score of hyperpigmentation $1.66 \pm 0.92$ significantly reduced to $1.23 \pm 0.67$, $0.72 \pm 0.58$, and $0.47 \pm 0.55$ at the end of 2, 4, and 6 weeks, respectively. There was no significant change in patients with hypopigmentation (Figure 2).

All included patients reported a significant symptomatic improvement. The burning sensation reduced significantly from the mean baseline score of $0.43 \pm 0.65$ to $0.19 \pm 0.45$, $0.17 \pm 0.38$, and $0.09 \pm 0.28$ at the end of 2, 4, and 6 weeks, respectively. The itching sensation reduced significantly from the mean baseline score of $0.49 \pm 0.59$ to $0.28 \pm 0.45$, $0.15 \pm 0.36$, and $0.02 \pm 0.15$ at the end of 2, 4, and 6 weeks, respectively (Figure 3).

There was a significant reduction in papules and pustules after the treatment. Papules reduced significantly from the mean baseline score of $18.73 \pm 7.29$ to $14.64 \pm 8.34$, $9.91 \pm 7.30$, and $5.80 \pm 6.50$ at the end of 2, 4, and 6 weeks, respectively. Pustules reduced significantly from the mean baseline score of $3.80 \pm 3.48$ to $1.84 \pm 1.91$, $1.04 \pm 1.54$, and $0.33 \pm 0.77$ at the end of 2, 4, and 6 weeks (Figure 4).

There was a significant reduction in black and white comedones after treatment. Black comedones reduced significantly from the mean baseline score of $11.91 \pm 8.01$ to $8.29 \pm 6.85$, $4.18 \pm 4.17$, and $2.02 \pm 3.16$ at the end of 2, 4, and 6 weeks, respectively. White comedones reduced significantly from the mean baseline score of $7.72 \pm 6.02$ to $5.07 \pm 5.19$, $2.56 \pm 3.82$, and $1.38 \pm 3.73$ at the end of 2, 4, and 6 weeks, respectively (Figure 5).

There was a significant reduction in nodules, cysts, and scars after treatment. Nodules reduced significantly...
from the mean baseline score of 0.60 ± 1.12 to 0.31 ± 0.76, 0.20 ± 0.59, and 0.07 ± 0.33 at the end of 2, 4, and 6 weeks, respectively. Scars reduced from the mean baseline score of 3.66 ± 7.19 to 3.40 ± 7.43 at the end of the study period. The study also observed total elimination of cysts at the end of the study period (Figure 6).

Figure 6. Mean scores of nodules and scars at baseline and 6 weeks

In the subjective evaluation of efficacy of the treatment, 4 (8%) patients rated the treatment as excellent, 32 (64%) as good, and 11 (22%) as fair. In the subjective evaluation of treatment tolerability, 40 (80%) patients rated the treatment as good and 10 (20%) as fair.

Discussion

Acne vulgaris has a multifactorial etiology and is influenced by keratinization, hormonal function, resident bacterial flora, and immune status of a person. The disease is limited to pilosebaceous follicles of the head and upper trunk because the sebaceous glands in these regions are comparatively more active. The sebum is composed of triglycerides, cholesterol esters, waxes, and fatty acids and its production is androgen-mediated. After puberty, androgen production is increased and it stimulates sebaceous follicles to secrete sebum. Paradoxically, androgen levels do not correlate with acne severity among people with acne.12 Sebum is an excellent growth medium for *P. acnes*.13 It has been documented that people with acne have a higher rate of sebum production than individuals without acne. Moreover, the severity of acne is generally proportional to the amount of sebum production.14

The primary acne lesion is the blackhead, also referred to as a microcomedo, which is an impaction formed in the distended pilosebaceous follicle by improperly desquamated keratinocytes and sebum. The stimulus for comedogenesis is uncertain. Melanin imparts black color to open comedones, commonly referred to as blackheads, which seldom become inflamed. Closed comedones commonly referred to as whiteheads block the pilosebaceous canal, which encourages anaerobic bacterial growth. *P. acnes* is a commensal of the normal dermal microbial resident flora and incapable of tissue invasion or serious infection. *P. acnes* fuels inflammatory process by lipase secretion, which leads to lysis of triglycerides and free fatty acids that in turn fuels local dermal irritation. *P. acnes* acts as inflammatory stimulus by producing neutrophil chemoattractants and activating the complement system. As a result, there is a formation of papules, pustules, nodules, or cysts.6,15

Non-inflammatory acne is one of the mildest forms of disease, but can be the hardest to treat. Topical retinoids, when applied daily, inhibit formation of comedones and are effective in clearing comedonal acne within few months. The major drawback of topical retinoids is dermal irritation and patients with atopic disease may not tolerate topical retinoids due to their inherently irritable skin. The most important adverse effect of topical retinoids is teratogenicity, and all fertile women taking the drug should take birth control measures to avoid pregnancy during the treatment period.6,16–18

Mild papulopustular acne rarely results in scarring and is responsive to aggressive topical treatment by an antibacterial and a comedolytic agent. Topical erythromycin and clindamycin are commonly used antibacterial agents. Benzoyl peroxide is the most commonly used comedolytic agent, but the major disadvantage is the resultant dermal irritation. Azelaic acid causes dermal hypopigmentation in few patients, but in dark skinned patients, it causes hyperpigmentation, which remains for weeks or months.6,19,20

Acne that is resistant to topical treatment or that manifests as scarring or nodular lesions typically requires oral antibiotics. Oral erythromycin used to be a common treatment for acne, but the emergence of antimicrobial resistance has greatly limited its utility. Although oral clindamycin improves inflammatory acne, its use has been virtually abandoned because of its association with pseudomembranous colitis.20–23 Hepatitis, reactions resembling serum sickness, lupus erythematosus, vestibular disturbances (dizziness, vertigo, and ataxia), and blue-gray discolorations of the skin have also been reported in association with the use of tetracyclines.24,25 Though co-trimoxazole is effective in the treatment of inflammatory acne, the potential for serious side effects (hypersensitivity reactions such as toxic epidermal necrolysis and bone marrow suppression) limits its use in patients who have responded inadequately to commonly used oral antimicrobials.24
Hormonal treatment improves acne by decreasing androgen-induced sebum production. Acne resistant to treatment (especially in women with irregular menses) should be investigated for total and free testosterone levels and dehydroepiandrosterone sulfate quantification.\textsuperscript{6,26} Hormonal therapy may be beneficial for women with significant hormonal influence (inadequate response to other acne treatments, acne that begins or worsens in adulthood, premenstrual flares of acne, excessive facial oiliness, and acne accompanied by mild to moderate hirsutism), however, long-term side effects have limited their use.\textsuperscript{6}

As mentioned above, the current available options in the management of acne are associated with various short- and long-term adverse events. This clinical trial was planned to evaluate the efficacy and safety of a polyherbal topical cream in acne. This study observed that from second week onward there were significant reductions in erythema, telangiectasia, skin oiliness, and hyperpigmentation and there was symptomatic improvement in all patients. There was also significant reduction in the mean number of papules, pustules, black and white comedones, nodules, cysts, and scars at the end of the study. The favorable improvement in acne by Clarina cream may be due to the synergistic actions of its ingredients.

\textit{A} \textit{vera} has been evaluated for its anti-inflammatory activity by various researchers. Heggers et al demonstrated that the extracts of \textit{A} \textit{vera} gel have anti-inflammatory activity and suggested its inhibitory action on the arachidonic acid pathway via cyclooxygenase.\textsuperscript{27} Davis et al demonstrated that \textit{A} \textit{vera} blocks wound healing suppression of hydrocortisone acetate and this response was due to growth factors in \textit{A} \textit{vera} that masked wound healing inhibitors such as sterols and certain amino acids.\textsuperscript{28,29}

When applied topically, \textit{A} \textit{vera} plays an important role in the wound healing process. Choi et al isolated and characterized a glycoprotein fraction (G1G1M1DI2) from \textit{A} \textit{vera}, which was demonstrated effective in wound healing and the proposed action was via cell proliferation and migration. This effect of G1G1M1DI2 on cell migration was confirmed on a monolayer of human keratinocytes, and when this fraction was tested on a raft culture, it stimulated the formation of epidermal tissue. Furthermore, proliferation markers (epidermal growth factor receptor, fibronectin receptor, fibronectin, keratin 5/14, and keratin 1/10) were markedly expressed at the immunohistochemical level.\textsuperscript{30} Chithra et al studied the influence of \textit{A} \textit{vera} on the glycosaminoglycan (GAG) components of the matrix in a healing wound. It was observed that levels of glycohydrolases were elevated on treatment with \textit{A} \textit{vera}, indicating increased turnover of the matrix. Both topical and oral treatments with \textit{A} \textit{vera} have a positive influence on the synthesis of GAGs to beneficially modulate wound healing.\textsuperscript{31,32} A basic peroxidase (EC 1.11.1.7) has been identified in \textit{A} \textit{vera} and it was observed that when applied topically, \textit{A} \textit{vera} peroxidase might scavenge \textit{H}2\textit{O}2 on the skin surface.\textsuperscript{33,34} Heggers et al observed that \textit{A} \textit{vera} expedites wound contraction and neutralizes wound retardant effect and this effect appears to be due to increased collagen activity, enhanced by a lectin, consequently improving the collagen matrix and enhancing breaking strength.\textsuperscript{27,35}

\textit{P} \textit{amygdalus} is known to exert a cooling action on inflamed wounds.\textsuperscript{36} A \textit{sessilis} contains very high amounts of carotene, a potent antioxidant.\textsuperscript{37} The extract of \textit{R} \textit{cordifolia} has been shown to possess significant inhibitory properties in experimentally-induced lipid peroxidation.\textsuperscript{38} There were no short- or long-term adverse events reported or observed during the study period and the study observed excellent compliance to Clarina cream.

**Conclusion**

Acne vulgaris, a common skin disorder, is not a trivial disease, as it can produce cutaneous and emotional scars that last for a lifetime. Topical therapy is advocated for patients with noninflammatory comedones and mild to moderate inflammatory acne. Comedolytic and anti-inflammatory agents, along with antimicrobials, are generally preferred in the topical treatment of acne. The emergence of antibiotic resistance and associated risk of short- and long-term adverse effects questions its advocacy in the management of acne.

In this study, it was observed that the use of Clarina cream was associated with significant reduction in erythema, telangiectasia, skin oiliness, hyperpigmentation, papules, pustules, black and white comedones, nodules, cysts, and scars, and there was excellent compliance for Clarina cream. Based on these observations, it can be concluded that Clarina cream is clinically effective and safe for long term usage in newly diagnosed and previously treated cases of acne vulgaris.

**References**

Clarina cream in Acne Vulgaris

An Open Clinical Study to Evaluate the Efficacy and Safety of HiOra-K toothpaste in the Management of Sensitive Tooth

Sukumaran VG, et al.
Sree Balaji Dental College & Hospital, Velachery Main Road, Pallikaranai, Chennai, India


**Abstract**

The purpose of this study was to evaluate the safety and efficacy of HiOra-K toothpaste in the management of sensitive tooth. This study was an open clinical trial conducted at Sree Balaji Dental College & Hospital, Chennai, India. After the initial examination and complete history about sensitive tooth, all patients were advised to brush twice daily with HiOra-K toothpaste for 6 weeks. All patients were followed up at once in 2 weeks for a period of 6 weeks and the symptom score evaluation was done during each follow-up visit. Of the 100 patients included in the trial, 96 completed the follow-up period of eight weeks. Four patients could not complete the scheduled follow-up. The efficacy parameters showed good improvement. In subjective evaluation, 92 out of 100 patients (92%) experienced remarkable overall improvement. No adverse effect was observed during the study. The above observations indicate that HiOra-K toothpaste is effective and safe in patients with sensitive tooth.

**Key Words**

Sensitive tooth, HiOra-K

**Introduction**

Sensitive teeth (dentin hypersensitivity) are characterized by a tingling sensation or sharp shooting pain that occurs when food or drink that is very cold, hot, or sweet is consumed. People are more likely to feel the sensitivity when the teeth come in contact with hot or cold foods or drinks and cold air. Some people experience sensitivity when they ingest sweet or acidic food and drink. The pain can appear at times, with some times being worse than others.

The part of tooth which is visible is covered by a layer of enamel that protects the softer dentine underneath. If the dentine is exposed, a tooth can become sensitive. This usually happens where the tooth and the gum meet and the enamel layer is much thinner.

Most commonly, the problem begins when the gums recede. Like a protective blanket, gums cover the roots of teeth and as gums recede, the underlying tooth roots are exposed. Gums commonly recede for one of two reasons:

**Improper heavy handed brushing of teeth**: It is estimated that 50% to 90% of people brush with too much pressure. Over weeks, months, and years of brushing they remove significant gum tissue exposing the tooth roots.

**Poor oral hygiene**: It can lead to plaque build-up around teeth and gums. Over time this plaque hardens into tartar. Bacteria in this tartar are responsible for gingivitis and periodontal diseases that cause gum recession.

The exposed roots contain small pores or tubules which lead directly to the nerve of the tooth. Pain, pressure, and cold stimuli can travel down the tubules and trigger the tooth nerve causing pain and discomfort. Normally, the gums cover the tooth root helping to prevent stimuli from reaching these pores.

**Symptoms of sensitive teeth**: Both dentinal and pulpal sensitivity usually involve reactions to temperature or pressure. Sensitivity to cold drinks or foods is the most
HiOra-K toothpaste in Sensitive Tooth

common symptom. Less often, the teeth are sensitive to hot temperatures.

There are several methods to prevent sensitivity, such as brushing teeth twice a day for two minutes with fluoride toothpaste, using small circular movements with a soft- to medium-bristled brush, avoiding brushing teeth from side to side, changing toothbrush every two to three months or sooner if it wears out. Keeping teeth clean by removing the plaque, the white gummy substance that forms on teeth, produces an acid that irritates teeth, especially if the choppers are naturally sensitive. Wage a daily attack against plaque by brushing at least twice, preferably right after eating and especially before bed and flossing at least once.

Other procedures of treatment include iontophoresis, usually used in conjunction with fluoride pastes or solutions. Another procedure is the use of low level laser therapy. A polyherbal formulation was evaluated for the safety and efficacy of HiOra-K in sensitive tooth.

Aim of the study
The purpose of this study was to evaluate the safety and efficacy of HiOra-K in the management of sensitive tooth.

Materials and Methods
This study was an open clinical trial, conducted at the outpatient department of Sree Balaji Dental College & Hospital, Chennai, India, including 100 patients with sensitive tooth. Healthy patients with a minimum of 20 permanent dentures presenting with sensitive tooth with symptoms such as feeling of pain and discomfort while eating or drinking hot and cold items, eating sweets, or touching with tongue were included in the study. Pregnant women, patients with orthodontic appliances or history or allergy to any medication were excluded from the study. All enrolled patients underwent a thorough clinical examination, with special emphasis on local dental examination. All subjects were advised to use HiOra-K toothpaste for brushing twice daily for a period of 6 weeks. Patients were told to restrict themselves to HiOra-K toothpaste as the only treatment for their sensitive tooth and resort to other active treatment intervention during the study period was not allowed. The investigator demonstrated proper technique of application of the investigational product. The efficacy and safety of HiOra-K toothpaste was evaluated during each visit for a period of 6 weeks. The patients underwent dental check-up at entry and second, fourth, and sixth week. The response to therapy was evaluated at intervals of two weeks for a period of 6 weeks. Criteria for evaluation were signs and symptoms such as reduction in toothache and sensitivity to cold, hot, and sweet, cleansing effect, and overall impression. Response was evaluated on an analog scale of 0 to 3 (0—Nil, 1—Moderate, 2—Good, and 3—Excellent). The overall response was in turn correlated with response to the treatment as follows: Grade 0—No improvement, 1—Poor response (<25% reduction), 2—Moderate response (25%–49% reduction), 3—Good response (50%–74% reduction), and 4—Excellent response (>75% reduction).

All adverse events, either reported or observed by the patients, were recorded with information about severity, date of onset, duration, and action taken regarding the study drug. Relation of adverse events to study medication was predefined as “Unrelated” (a reaction that does not follow a reasonable temporal sequence from the administration of the drug), “Possible” (follows a known response pattern to the suspected drug, but could have been produced by the patient’s clinical state or other modes of therapy administered to the patient), and “Probable” (follows a known response pattern to the suspected drug that could not be reasonably explained by the known characteristics of the patient’s clinical state). Patients were allowed to voluntarily withdraw from the study, if they had experienced serious discomfort during the study or sustained serious clinical events requiring specific treatment. For patients withdrawing from the study, efforts were made to ascertain the reason for dropout. Noncompliance (defined as failure to take less than 80% of the medication) was not regarded as treatment failure, and reasons for noncompliance were noted.

Primary and secondary end points
The predefined primary efficacy end point was a decrease in the symptom score for sensitive tooth. The predefined secondary safety end points were acute and chronic safety, as assessed by the incidence of adverse events and patient compliance to therapy.

Statistical analysis
Statistical analysis was done according to intention-to-treat principles. The changes in various parameters from baseline values and the values after 6 weeks were evaluated by paired t-test. Statistical analysis was carried out using GraphPad Prism software Version 4.01.
Results

Of the 100 patients included in the trial, 96 completed the 6 weeks of follow-up period. Four patients could not complete the scheduled follow-up due to their personal problems in visiting the dental unit within the stipulated time.

Demographic data including age, gender, history of previous medication and smoking, alcohol consumption, and diet were tabulated (Table 1).

The efficacy parameters showed good improvement. At entry, sensitivity to cold things was observed in 88 subjects and was reduced to 62 by second week and 8 by sixth week. At entry, sensitivity to hot things was observed in 64 patients and was reduced to 41 by second week and 12 by sixth week. Sensitivity to sweet was observed in 73 patients at entry, and was reduced to 23 by second week and 5 by sixth week. Toothache was observed in 48 patients at entry, which was reduced to 11 by second week and cured in all patients by sixth week (Table 2).

At the end of 6 weeks of treatment, cleansing effect was good in 78 patients and mouth freshening effect was good in 89 patients. Maintaining natural whiteness of the teeth was good in 67 patients (Table 2).

In subjective evaluation, 92 patients experienced remarkable overall improvement. The overall likeability for HiOra-K toothpaste was excellent in 22, good in 38, moderate in 17, poor in 11, and no response in 8 patients (Table 3).

<table>
<thead>
<tr>
<th>Table 1. Demographic Data of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameter</td>
</tr>
<tr>
<td>Age in years (mean ± SD)</td>
</tr>
<tr>
<td>Weight in kg (mean ± SD)</td>
</tr>
<tr>
<td>Sex ratio (M:F)</td>
</tr>
<tr>
<td>History of smoking (no. of patients)</td>
</tr>
<tr>
<td>History of alcohol consumption (no. of patients)</td>
</tr>
<tr>
<td>Diet (vegetarian/nonvegetarian)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2. Efficacy of HiOra-K toothpaste (n = 96)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameter</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Sensitivity to cold things</td>
</tr>
<tr>
<td>Sensitivity to hot things</td>
</tr>
<tr>
<td>Sensitivity to sweet</td>
</tr>
<tr>
<td>Toothache</td>
</tr>
<tr>
<td>Cleansing effect</td>
</tr>
<tr>
<td>Mouth freshening effect</td>
</tr>
<tr>
<td>Maintaining natural whiteness of the teeth</td>
</tr>
</tbody>
</table>

*P<.05 as compared to “At entry” values.

<table>
<thead>
<tr>
<th>Table 3. Overall Response to the Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Response score</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>No response</td>
</tr>
<tr>
<td>Poor</td>
</tr>
<tr>
<td>Moderate</td>
</tr>
<tr>
<td>Good</td>
</tr>
<tr>
<td>Excellent</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 4. Dermal Safety Evaluation of HiOra-K toothpaste</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days of application</td>
</tr>
<tr>
<td>Signs and symptoms</td>
</tr>
<tr>
<td>Erythema</td>
</tr>
<tr>
<td>Edema</td>
</tr>
<tr>
<td>Pain</td>
</tr>
<tr>
<td>Irritation</td>
</tr>
<tr>
<td>Burning sensation</td>
</tr>
</tbody>
</table>

Values are expressed in mean ± SD.
Thus, significant symptomatic relief was observed after 6 weeks of treatment with HiOra-K toothpaste. Results in this clinical trial indicate that HiOra-K toothpaste is effective in patients with sensitive tooth. There were no patients with a poor response by the end of the study period.

None of the patients reported any adverse effects during the entire period of the trial. All volunteers displayed an excellent acceptance to the trial medications. None of the patients complained of any side effects or untoward reactions (Table 4).

**Discussion**

Sensitive teeth (dentin hypersensitivity) are characterized by a tingling sensation or sharp shooting pain that occurs when food or drink that is very cold, hot, or sweet is consumed. Both dentinal and pulpal sensitivity usually involve reactions to temperature or pressure. Sensitivity to cold drinks or foods is the most common symptom. Less often, the teeth are sensitive to hot temperatures.

Keeping teeth clean by removing the plaque, the white gummy substance that forms on teeth, produces an acid that irritates teeth, especially if teeth are naturally sensitive. Brushing at least twice, preferably after eating and before bed, and flossing at least once protects from sensitive tooth.

HiOra-K contains herbs that act on tooth and have protective antimicrobial activities. It contains oils of *Syzygium aromaticum* and *Cinnamomum zeylanicum*; extracts of *Spinacia oleracea*, Triphala, and Trikatu; and powders of Yashada bhasma and Surya kshara.

*S. aromaticum* has antifungal, antiviral, analgesic/anesthetic, antiseptic, anticoagulant, and antioxidant properties. Dentists use clove oil as an oral anesthetic for toothaches. The antimicrobial activity is showed by volatile oil of clove.1

*C. zeylanicum* has antibacterial and antiseptic properties and can be safely used in all dental disorders. C *zeylanicum* has shown antibacterial and antioxidant properties in vitro.2 It also exhibited strong anti-inflammatory effect.3

*S. oleracea* is known for its antioxidant and antibacterial properties and can be used effectively for the treatment of periodontitis and other oral infections.4

Triphala is a compounded form of *Emblica officinalis*, *Terminalia bellerica*, and *Terminalia chebula* fruits. It exhibits wound healing property when applied externally on wounds.5 It resulted in complete wound healing and incorporated collagen sponge in fully infected dermal wounds.6 Hence, it can be safely used in mouth ulcers. Triphala has analgesic and anti-inflammatory properties7 and can be used for a better maintenance of oral hygiene. Trikatu, the preparation containing fruits of *Piper nigrum* and *Piper longum*, and rhizomes of *Zingiber officinalis* in equal proportion is widely used drug for many ailments. It has antibacterial, anti-inflammatory, and healing properties.8

Yashada bhasma contains processed zinc and possesses antiseptic and astringent properties.9

All these herbs in combination exhibit synergistic effect that helps to maintain good oral health and protect against dental diseases.

**Conclusion**

This study showed significant efficacy of HiOra-K toothpaste in sensitive tooth as evidenced by remarkable symptomatic relief in all patients. There was no adverse effect reported during the study. The above observations indicated that HiOra-K toothpaste is effective and safe in patients with sensitive tooth. It provides adequate relief from the symptoms of sensitivity and hence its acceptance by patients was excellent.

**References**

**Impaired Cardiovascular Function in Primary Biliary Cirrhosis**

Jones DE, et al.

*Am J Physiol Gastrointest Liver Physiol.*


Cardiovascular system dysregulation in the form of autonomic dysfunction is common at all stages of the disease process in the autoimmune liver disease primary biliary cirrhosis (PBC) and associates with the symptom of fatigue. The mechanisms underpinning autonomic dysfunction in PBC are, however, at present unclear. In this study the authors explore cardiac structure and function in PBC using impedance cardiography (ICG) and magnetic resonance methodologies. ICG was assessed beat to beat in response to orthostasis (by head-up tilt) in age and sex case-matched high-fatigue and low-fatigue PBC groups (assessed by Fatigue Impact Scale), normal control subjects (n = 15 each group) and a liver disease control cohort (primary sclerosing cholangitis). Cardiac structure and bioenergetics were examined in 15 of the PBC subjects and 8 of the normal control subjects by magnetic resonance spectroscopy and cine imaging. Capacity of the left ventricle to respond to orthostasis (left ventricular ejection time [LVET]) was impaired in PBC compared with matched normal control subjects (*P* = .05). This was a PBC-specific phenomenon unrelated to fatigue status. PBC patients exhibited significantly lower cardiac muscle phosphocreatine-to-ATP ratio (PCr/ATP ratio; measure of cardiac bioenergetic integrity) compared with control subjects (*P* < .01). PCr/ATP<1.6 (indicative of increased risk of death in cardiomyopathy) was present in 6/15 (40%) PBC patients (0/8 control subjects; *P* < .05). Cardiac structure and function were similar in all measures of left ventricular morphology between control subjects and PBC. The close relationship between PCr/ATP and LVET seen in normal subjects (*R*² = .6; *P* < .05) was lost in PBC patients, a finding compatible with myocardial dysfunction. Significant correlation was seen between fatigue severity in PBC and fall in cardiac output on orthostasis (*R*² = .25; *P* = .005). These findings suggest the presence of altered myocardial function in PBC. Autonomic dysfunction may, rather than being an abnormal process, represent a compensatory mechanism to increase cardiac return to mitigate these effects.

**Endothelial Function and Hemodynamics in Systemic Sclerosis**

Rossi P, et al.


Systemic sclerosis (SS) is characterized by the development of fibrosis of skin and internal organs and is associated with vascular damage. However, its related parameters have not been fully explored. The aim of this study was to investigate endothelial function in SS and its relationship with systolic pulmonary artery pressure and systemic arterial compliance (SAC). The study included 14 SS females (4 with diffuse and 10 with limited cutaneous form of the disease) and 14 healthy controls matched for age and cardiovascular risk factors. Endothelium-dependent (ie, flow-mediated) and endothelium-independent (ie, nitroglycerin-induced) dilations of the brachial artery were measured as the percentage of change from baseline. SAC, cardiac output (CO), systemic arterial resistance, and pulmonary artery pressure were estimated in patients with SS. Results of the study showed that heart rate, brachial artery pressure, and body mass index did not differ between patients with SS and controls. Flow-mediated vasodilation (FMD) and nitrate-mediated dilation (NMD) were significantly decreased in patients with SS (10.3% ± 8.6% vs 26.6% ± 7.4%, *P* < .001 and 24.2% ± 8.4% vs 33.3% ± 10.1%, *P* < .001, respectively). Postischemic reactive hyperemia was lower in patients with SS (275% ± 185% vs 618% ± 366%, *P* < .001). FMD and NMD were associated with CO, but not with SAC; moreover, FMD correlated with pulmonary artery pressure and peripheral arterial resistance conversely to NMD. From the above findings, it can be concluded that endothelium function in SS is impaired independent of SAC. Furthermore, the severity of both small artery and pulmonary artery involvement may impact on endothelium-dependant function.
Investigation of Reactions to Dental Materials

Gawkrodger DJ


Patients undergoing dental treatment can be exposed to a wide range of potential allergens, but adverse events seem infrequent. Patients with symptoms or signs of stomatitis, burning, tingling, cheilitis, oral lichenoid lesions, and lip and facial swelling may relate their problems to dental treatment or to the use of dental products. Investigation for immediate type or delayed type hypersensitivity is indicated using patch testing, prick testing and blood tests for allergen-specific IgE. The main allergic reactions found in patients include contact allergy to metals, cosmetics, food additives, flavors, and acrylates and immediate type allergy was found to latex. Adverse reactions following the administration of local anesthetics are seen in about 0.5% of cases, but immediate type allergy to these agents is rare. In dental staff, occupational-related problems are common and usually take the form of hand or facial dermatitis or respiratory disease. The most common allergic reactions in dental staff are immediate type allergy to latex and contact allergy to rubber additives, fragrances, acrylates, and formaldehyde. Occupational irritant problems causing hand dermatitis are probably more common in dental personnel than is dermatitis caused by contact allergy. Patch testing and tests for immediate type allergy are useful investigative methods in the investigation of patients who present with oral or facial symptoms possibly related to dental treatments and are also beneficial in dental personnel who present with hand or facial dermatitis or respiratory symptoms.

Effects of Skin Wrinkles, Age, and Wetness on Mechanical Loads in the Stratum Corneum as Related to Skin Lesions

Sopher R, Gefen A


Finite element models of skin were developed to determine the effects of wetness, age, and wrinkles on mechanical strains and stresses in the stratum corneum (SC) as related to skin lesions. The authors modeled two geometries, young (.12 mm deep wrinkles) and aged (.18 mm deep wrinkles), and for each geometry, three loading conditions were applied (compression in a dry environment, compression and shear in dryness, and compression with shear in wetness). Effects of skin wrinkling were studied independently or while coupled with age-related mechanical property changes. For each simulation, the peak maximal shear strain and stress in the SC, peak shear stress on the skin surface, and volumetric exposure of the SC to potentially injurious shear stresses (<70 kPa) were calculated. Compression and shear with wetness produced the highest skin surface loads. Volumetric exposure of aged skin to potentially injurious shear stresses was six times greater than in the young skin for these conditions. Deeper wrinkles caused elevated loads in the SC consistently for all outcome measures and independently of the age factor. Thinning and/or stiffening the SC increased both the surface and internal SC stresses. These findings indicate that theoretically, wetness, skin aging, and/or skin wrinkling are all risk factors for skin lesions such as superficial pressure ulcers.
**Helicobacter pylori Infection and Peptic Ulcer Disease in Patients with Liver Cirrhosis**

Kim DJ, et al.


**Objective**
The present study was conducted to investigate the prevalence and relationship of peptic ulcer disease and *Helicobacter pylori* infection with liver cirrhosis.

**Methods**
The study examined 288 patients with liver cirrhosis, 322 with nonulcer dyspepsia, and 339 with peptic ulcer disease. Rapid urease test and Wright-Giemsa staining were used for diagnosis of *H pylori* infection.

**Results**
The prevalence of peptic ulcer disease in patients with cirrhosis was 24.3%. The prevalence of peptic ulcer disease in patients with cirrhosis divided into Child-Pugh classes A, B, and C was 22.3%, 21.0%, and 31.3%, respectively (P > .05). The prevalence of *H pylori* infection in patients with cirrhosis, nonulcer dyspepsia, and peptic ulcer without chronic liver disease was 35.1%, 62.4%, and 73.7%, respectively (P < .001). The prevalence of *H pylori* infection did not differ depending on the presence (34.9%) or absence (35.6%) of peptic ulcer in patients with liver cirrhosis (P > .05). The prevalence of *H pylori* infection in patients with hepatitis virus-related liver cirrhosis and in those with alcohol-related liver cirrhosis was 42.5% and 22.0%, respectively (P < .001). The prevalence of *H pylori* infection in patients with Child-Pugh classes A, B, and C liver cirrhosis was 51.5%, 30.5%, and 20.0%, respectively (P < .001).

**Conclusions**
Factors other than *H pylori* may be involved in the pathogenesis of peptic ulcer disease in the setting of liver cirrhosis.

**Self-Reported Halitosis and Gastroesophageal Reflux Disease in the General Population**

Struch F, et al.


**Background and Objectives**
Patients with halitosis contact primary care practitioners, dentists, and gastroenterologists alike. The present study was conducted to investigate whether gastroesophageal reflux disease (GERD) is a risk factor for halitosis.

**Design and Patients/Participants**
The authors studied this possible relationship in the general population using the cross-sectional study of health in pomerania (SHIP). Employing structured interviews, self-reported halitosis was assessed among 417 edentulous (toothless) subjects aged 40 to 81 years and among 2,588 dentate subjects aged 20 to 59 years. The presence of heartburn or acid regurgitation (GERD-related symptoms) at 4 levels (absent, mild, moderate, severe) was taken as exposure and used for logistic regression. Analyses were adjusted for relevant confounders, such as age, sex, depressive symptoms, history of chronic gastritis and gastric or duodenal ulcer, smoking, school education, and dental status.

**Measurements and Main Results**
Results of the study showed a strong positive association between GERD-related symptoms and halitosis [odds ratio (OR) = 12.94; 95% confidence interval (CI), 2.66–63.09; P = .002 for severe compared to no GERD-related symptoms] in denture-wearing subjects and a moderate, positive association between GERD-related symptoms and halitosis (OR = 2.24; 95% CI, 1.27–3.92; P = .005) in dentate subjects with a clear dose-effect relationship.

**Conclusions**
The present study provided clear evidence for an association between GERD and halitosis. As there are effective treatments for GERD, these results suggest treatment options, such as proton pump inhibitors, for halitosis. These should be studied in randomized controlled trials.
Premenstrual Syndrome and Associated Skin Diseases Related to Hypersensitivity to Female Sex Hormones

Itsekson A, et al.


**Objective**

To study skin diseases and hypersensitivity related to female sex hormones in patients with premenstrual syndrome (PMS).

**Study Design**

Thirty women answered a questionnaire related to PMS and underwent gynecologic, dermatologic, and laboratory examinations. Intradermal testing was performed with estradiol valerate, progesterone, and placebo. Desensitization treatment was instituted in 15 patients.

**Results**

Ten patients were diagnosed with PMS and concomitant skin disease, including pruritus vulvae, hyperpigmentation, papular eruption, and acne vulgaris (group A). Ten patients diagnosed with PMS but without skin disease served as the first control group (group B). The second control group consisted of 10 healthy women (group C). Immediate and delayed hypersensitivity reactions to sex hormones were observed in all patients with PMS and PMS-related skin diseases (groups A and B) but not in healthy women (group C). Desensitization produced a decrease in PMS symptoms and improvement in the skin disease related to PMS.

**Conclusion**

Skin diseases may be a part of PMS. Demonstration of a delayed allergic reaction to female sex hormones may uncover a significant pathogenetic mechanism in patients with recurrent skin disease and PMS.

Maternal Hepatitis B Virus or Hepatitis C Virus Carrier Status as an Independent Risk Factor for Adverse Perinatal Outcome

Safir A, et al.


**Objective**

To examine the impact of maternal hepatitis B virus (HBV) or hepatitis C virus (HCV) carrier status on pregnancy outcomes.

**Methods**

A population-based study was performed by comparing all pregnancies of HBsAg and/or anti-HCV seropositive women who delivered during the years 1988 to 2007 with all other pregnant women who delivered in the same period. Multivariable logistic regression models were constructed to control for confounders.

**Results**

Seven hundred and forty-nine hepatitis seropositive pregnancies were identified out of 186,619 deliveries (0.4%). Maternal characteristics and perinatal outcomes were comparable between the HBV and HCV carriers. HBV/HCV carriers had higher rates of preterm deliveries (<37 weeks of gestation; 11.5% vs 7.9%, \(P<.001\)), premature rupture of membranes (8.9% vs 6.9%, \(P = .026\)), placental abruption (1.5% vs 0.7%, \(P = .018\)), labor induction (33.9% vs 28.1%, \(P <.001\)) and cesarean deliveries (19.0% vs 13.2%, \(P <.001\)). Higher rates of perinatal mortality (2.3% vs 1.3%, \(P = .016\)), congenital malformations (7.2% vs 5.1%, \(P = .01\)) and low birth weight (<2500 kg; 10.4% vs 7.8%, \(P = .009\)) were noted in newborns of hepatitis carriers compared with the control group. Controlling for possible confounders such as maternal age and parity by using multivariable analyses, the significant association between HBV or HCV carrier status and perinatal mortality, congenital malformations and low birth weight remained significant.

**Conclusions**

Maternal HBV or HCV carrier status is an independent risk factor for adverse perinatal outcome and careful surveillance is warranted.
Role of Acute Viral Hepatitis as a Confounding Factor in Antituberculosis Treatment-Induced Hepatotoxicity
Sarda P, et al.

Background and Objective
Drug-induced hepatotoxicity (DIH) is an important and commonly encountered adverse effect with antituberculosis (anti-TB) treatment. Acute viral hepatitis (AVH) is an important confounding reason which clinically, biochemically, and histologically mimics DIH.

Methods
The contributory role of acute viral hepatitis as a confounding factor in patients with normal baseline liver functions who developed acute hepatitis while receiving short-course anti-TB treatment was prospectively studied. The sera of all the patients who developed acute hepatitis were analyzed for markers of hepatitis A, B, C, and E viruses.

Results
Viral hepatitis was present in 15 of the 102 (14.7%) patients who developed acute hepatitis while receiving anti-TB treatment with hepatitis E virus being the most common cause. Later onset of acute hepatitis (58 [5–133] vs 26 [3–221] days; \( P = .04 \)), large elevations in aspartate aminotransferase (AST) (371 [30–2643] vs 212 [63–1990 IU/L]; \( P = .03 \)) and alanine aminotransferase (ALT) (388 [31–2997] vs 225 [52–1670 IU/L]; \( P = .002 \)) and a longer time for normalization of deranged liver functions (36.7 ± 13.3 vs 24.5 ± 19.3 days; \( P = .02 \)) indicated acute viral hepatitis as the cause of liver function derangement.

Interpretation and Conclusion
These findings showed that acute viral hepatitis occurred in 14.7% of the patients who developed hepatotoxicity while receiving anti-TB treatment. Therefore, in endemic areas, viral hepatitis should be sought after and excluded in all patients suspected to have drug-induced hepatitis before attributing the hepatotoxic effects to anti-TB drugs.

Prevalence, Characteristics, and Severity of Nonalcoholic Fatty Liver Disease in Patients with Chronic Plaque Psoriasis
Miele L, et al.

Background and Aims
The association between nonalcoholic fatty liver disease (NAFLD) and psoriasis has never been explored in prospective epidemiological studies. The aim of this two-phase study was to investigate the clinical features of NAFLD in patients with psoriasis.

Methods
Phase 1: Investigation of prevalence and characteristics of NAFLD in an unselected cohort of 142 adult Italian outpatients with psoriasis vulgaris. Phase 2: Comparison of the psoriasis cohort subgroup with NAFLD and an age- and body mass index-matched retrospective cohort of 125 nonpsoriatic patients with biopsy proven NAFLD.

Results
Based on histories, laboratory tests, and ultrasound studies, 84 (59.2%) patients received clinical diagnosis of NAFLD; 30 had factors potentially associated with liver disease other than NAFLD (eg, viral hepatitis, significant ethanol, and methotrexate use); and 28 (19.7%) had normal livers. Comparison of the normal liver and NAFLD subgroups revealed that NAFLD in psoriasis patients (Ps-NAFLD) was significantly correlated with metabolic syndrome (\( P < .05 \)); obesity (\( P = .043 \)); hypercholesterolemia (\( P = .029 \)); hypertriglyceridemia (\( P < .001 \)); AST/ALT ratio >1 (\( P = .019 \)), and psoriatic arthritis (PsA) (\( P = .036 \)). The association with PsA remained significant after logistic regression analysis (OR = 3.94 [CI, 1.07–14.46]). Compared with the retrospective nonpsoriatic NAFLD cohort (controls), Ps-NAFLD patients (cases) were likely to have severe NAFLD reflected by noninvasive NAFLD Fibrosis Scores and AST/ALT >1.

Conclusions
NAFLD is highly prevalent among patients with psoriasis, where it is closely associated with obesity (overall and abdominal), metabolic syndrome, and PsA and is more likely to cause severe liver fibrosis (compared with non–Ps-NAFLD). Routine work-up for NAFLD may be warranted in patients with psoriasis, especially when potentially hepatotoxic drug therapy is being considered.
Receptor for Advanced Glycation End Products Mediates Pro-Atherogenic Responses to Periodontal Infection in Vascular Endothelial Cells

Pollreisz A, et al.
Atherosclerosis. 2010.

Objective
A link between periodontal infections and an increased risk for vascular disease has been demonstrated. Porphyromonas gingivalis, a major periodontal pathogen, localizes in human atherosclerotic plaques, accelerates atherosclerosis in animal models, and modulates vascular cell function. The receptor for advanced glycation endproducts (RAGE) regulates vascular inflammation and atherogenesis. In this study, the authors hypothesized that RAGE is involved in the contribution of P gingivalis to proatherogenic responses in vascular endothelial cells.

Methods and Results
Murine aortic endothelial cells (MAEC) were isolated from wild-type C57BL/6 or RAGE/-/- mice and were infected with P gingivalis strain 381. P gingivalis 381 infection significantly enhanced expression of RAGE in wild-type MAEC. Levels of proatherogenic advanced glycation endproducts (AGEs) and monocyte chemoattractant protein 1 (MCP-1) were significantly increased in wild-type MAEC following P gingivalis 381 infection, but were unaffected in MAEC from RAGE/-/- mice or in MAEC infected with DPG3, a fimbriae-deficient mutant of P gingivalis 381. Consistent with a role for oxidative stress and an AGE-dependent activation of RAGE in this setting, both antioxidant treatment and AGE blockade significantly suppressed RAGE gene expression and RAGE and MCP-1 protein levels in P gingivalis 381-infected human aortic endothelial cells (HAEC).

Conclusion
The present findings implicate for the first time the AGE-RAGE axis in the amplification of proatherogenic responses triggered by P gingivalis in vascular endothelial cells.

Heat-Killed Propionibacterium acnes Is Capable of Inducing Inflammatory Responses in Skin

Lyte P, et al.

The etiology of acne is a complex process, and acne is one of the most common skin disorders affecting millions of people. The pathogenesis of acne is closely associated with the bacterium, Propionibacterium acnes (previously known as Corynebacterium parvum). Both viable and nonviable P acnes/C parvum have been shown to induce an immunostimulatory effect in vivo, suggesting that even dead bacteria continue to activate an inflammatory response. Acne treatments with lasers or devices induce a bactericidal effect through heat generation which may not address the immunogenic activity of P acnes and the resulting acne inflammation. Therefore, the authors sought to determine whether killed P acnes is capable of inducing an inflammatory response and therefore could be a contributing factor in acne. Direct heat treatment of P acnes cultures with temperatures ranging from 50ºC to 80ºC reduced P acnes viability. Both viable and heat-killed P acnes activated the p38 MAP kinase and its downstream substrate Hsp27. Stimulating keratinocytes with normal and heat-inactivated P acnes resulted in an induction of proinflammatory nitric oxide and IL-8 production. Thus killed P acnes is capable of inducing inflammation in skin suggesting that therapies that have both bactericidal and anti-inflammatory effects may result in a more effective treatment of patients with acne than treatments that are bactericidal alone.
Sensory Neuropathy in Patients with Cryoglobulin Negative Hepatitis C Infection

Yoon MS, et al.

J Neurol. 2010.

There is a growing evidence that hepatitis C virus (HCV) infection might cause peripheral neuropathy. This study was conducted to investigate the prevalence and clinical and electrophysiological features of sensory neuropathy in patients with cryoglobulin negative HCV infection. The study included 46 consecutive cryoglobulin negative HCV positive patients (24 with and 22 without neuropathic symptoms, NS) and compared with 28 age- and gender-matched controls. In all patients, clinical neuropathy symptom (NSS) and neuropathy deficit scores (NDS) were assessed and standard nerve conduction velocity (SNCV) and pain related-evoked potentials (PREP) were recorded. Both, SNCV and PREP were abnormal in 13 of the NS-positive patients (28%). Abnormal PREP but normal SNCV were found in 5 (11%) of the NS-positive and 2 of the NS negative patients (4%). PREP abnormalities correlated positively with both clinical neuropathy scores (NSS: $r = 0.62$; $P<.001$; NDS: $r = 0.57$; $P<.001$), but not with the duration of the disease, current viral load, or the virus subtype. PREP abnormalities were more frequent (48.5%) in HCV patients treated with interferon than in therapy naive patients (30.8%); however, the difference was not significant. Results of the study showed that all virus subtypes were capable of inducing neuropathy, there were no differences between interferon therapy and treatment naive patients, the prevalence of peripheral sensory neuropathy including small sensory fibers (43.5%) was higher than previously reported, and the detection of HCV associated neuropathy was dependent on the evaluation method.

Vasodilatation of Human Gingiva and Neurogenic Inflammation

Scardina GA, et al.


Background and Aim

Neurogenic inflammation (NI) is the consequence of amylolinger-sensitive neuron activation. Recent studies on rats proved that NI could be experimentally induced by topical capsaicin application. The aim of this study was to evaluate the effects of topical capsaicin application on human periodontal mucosa and to assess if NI might have a role in the pathogenesis of periodontal diseases.

Methods

The study included 15 patients. NI was experimentally induced in the gingival mucosa close to: (1) the interdental papilla corresponding to the upper central incisors; and (2) the interdental papilla corresponding to the lower left lateral incisor and canine after ipsilateral nerve trunk anesthesia. The characteristics of gingival microcirculation were observed using computerized videocapillaroscopic techniques.

Results

Axon-reflected vasodilatation was observed close to the papilla corresponding to the upper central incisors. An important correlation was observed between capsaicin application and capillary tortuosity. No significant modifications in vascular diameter and tortuosity were observed after capsaicin application close to the interdental papilla corresponding to the lower left lateral incisor and canine.

Conclusions

The study showed that NI can be induced in human gingiva, and such evidence could be extremely important in the pathogenesis and treatment of periodontal diseases.
Evaluation of Ocular Surface Damage and Dry Eye Status in Chronic Hepatitis C at Different Stages of Hepatic Fibrosis

Gumus K, et al.
Cornea. 2009;28(9):997-1002.

Aim
The purpose of this study was to explore changes in ocular surface and tear function parameters in chronic hepatitis C at different stages of hepatic fibrosis.

Methods
Fifty-four patients with biopsy-proven chronic hepatitis C and 54 age- and sex-matched healthy control subjects without systemic hepatitis C infection were examined with the Ocular Surface Disease Index questionnaire, Schirmer with and without anesthesia, tear film breakup time, and scoring of ocular surface Lissamine green staining using modified Oxford and van Bijsterveld scoring systems and corneal fluorescein staining.

Results
Patients with chronic hepatitis C scored significantly worse than the control subjects on all parameters: modified Oxford scores of Lissamine green staining (5.5/3.0; P<.001), Oxford and van Bijsterveld scores (4.0/2.0; P<.001), and corneal fluorescein staining (1.5/0.0; P=.001). Also, the chronic hepatitis C group had higher Ocular Surface Disease Index scores than the control subjects (22.3/13.7; P=.001). Schirmer with and without anesthesia and tear film breakup time scores were found to be lower in patients with chronic hepatitis C (P<.001). Moreover, patients with advanced stages of hepatic fibrosis (stages 4–6) had significantly lower values of tear film breakup time and worse Ocular Surface Disease Index scores and ocular surface vital dye staining than those with initial stages of hepatic fibrosis (stages 0–3).

Conclusion
Patients with chronic hepatitis C, especially those with advanced stages of hepatic fibrosis, were more likely to exhibit severe ocular surface damage and signs of dry eye.

Ocular Abnormalities in Indian Patients with Atopic Dermatitis

Kaujalgi R, et al.
Indian J Dermatol Venereol Leprol. 2009;75(2):148-151.

Background and Aims
Atopic dermatitis (AD) is a common skin disease. Long-standing, severe AD with repeated scratching and rubbing of the face, which requires continuous dermatologic care, predisposes the patient to various ocular complications. The knowledge of the frequency and significance of these ocular complications may allow their early diagnosis and treatment. The present study assesses the ocular complications in Indian children suffering from AD.

Methods
In order to study the ocular complications in AD, 100 patients (61 male and 39 female) between the ages of 1 and 14 years were recruited. All the patients had complete dilated fundus examination with indirect ophthalmoscopy. The lid, conjunctiva, and cornea were examined. Also, any evidence of cataract formation and retinal disorders were recorded.

Results
Mean age of the children was 5.4 years. Forty-three (43.0%) patients with AD showed ocular abnormalities in the form of lid and conjunctival changes. Of these, 18 (41.9%) patients showed only lid involvement, 16 (37.2%) only conjunctival involvement and 9 (20.9%) both conjunctival and lid changes. Conjunctival changes were mostly in the form of a cobblestone appearance of the papillae, with mild to moderate papillary reaction and papillary hypertrophy. Variables observed to have a significant impact on the development of ocular abnormalities were age >5 years, duration of illness >12 months, positive family history of atopy, presence of palmar hyperlinearity, and a combination of both xerosis and Dennie-Morgan fold.

Conclusions
The present study is the first of its kind from India to document an association between AD in children and various ocular manifestations. The ocular manifestations observed in this cohort were not associated with significant ocular morbidity or visual impairment possibly because of a less-severe disease in Indians.
Bone Mineral Density, Bone Turnover Markers, and Cytokines in Alcohol-Induced Cirrhosis

Díez-Ruiz A, et al.

Aims
Liver cirrhosis is a risk factor for osteoporosis. However, the pathogenesis of the bone mass loss in patients with alcohol-induced cirrhosis (AC) is not well understood. Serum concentrations of soluble tumor necrosis factor receptor (sTNF-R55), neopterin, soluble interleukin 2 receptor (sIL-2R), and activation markers of cellular immunity correlate with clinical activity and severity of AC. The aim of this study was to evaluate the association of these soluble markers with the development of osteoporosis in patients with AC.

Methods
The study included 33 consecutive patients with AC and 24 healthy volunteers. Bone mineral density (BMD) was measured by X-ray absorptiometry in the lumbar spine (LS) and femoral neck (FN). Neopterin was measured by radioimmunoassay. Serum concentrations of sTNF-R55 and sIL-2R were measured by enzyme immunoassay. Also, serum levels of osteocalcin and bone alkaline phosphatase were determined as biochemical markers of bone formation, and deoxypyridinoline urinary excretion (D-Pyr) as marker of bone resorption.

Results
 Patients with AC had reduced BMD (expressed as z-score) in all sites (LS: \( P < .001 \) and FN: \( P < .05 \)). Serum concentrations of sTNF-R55 were significantly higher in patients with both AC and osteoporosis than in those with only AC (\( P < .001 \)). Serum levels of sTNF-R55 positively correlated with D-Pyr urinary excretion (\( r = 0.354; P = .01 \)). Serum levels of sIL-2R were significantly higher in patients with both AC and osteoporosis than in those with only AC (\( P < .05 \)).

Conclusions
There is a relation between activation of the cellular immunity and osteoporosis in AC. Bone mass loss could be related to the increased bone resorption found in these patients.

The Association between Periodontal Disease and Osteoporosis in Postmenopausal Women in Jordan

Al Habashneh R, et al.

Background
Some studies suggest that females with osteoporosis are at increased risk for periodontal attachment loss and tooth loss, however results have varied. The aim of this study was to determine the relationship between periodontitis and osteoporosis among postmenopausal Jordanian women.

Methods
This cross sectional study included 400 Jordanian postmenopausal women with a mean (SD) age of 62.5 (6.4) years. These subjects were recruited from patients who had received a routine dual energy X-ray absorptiometry (DXA) examination in the Radiology Clinics in King Abdullah Hospital between June 2008 and February 2009. The relationship between skeletal bone mineral density (BMD) and radiographic and clinical parameters of periodontal status, including loss of alveolar crestal height (ACH), clinical attachment level (CAL), probing depth (PD), and percentage of sites with bleeding on probing (% BOP) was evaluated after controlling for known confounders.

Results
Bivariate analyses revealed no significant differences in the severity and extent of clinical attachment and ACH loss among women with normal BMD, osteopenia, and osteoporosis. However, in the multivariate analysis, women with osteoporosis were more likely to have severe ACH loss (OR = 4.20 [95% CI, 1.57-11.22]) and periodontitis (OR = 2.45 [95% CI, 1.38-4.34]).

Conclusions
Osteoporosis was significantly associated with severe alveolar crestal bone loss and the prevalence of periodontitis cases in postmenopausal Jordanian women.
Quantitative Estimation of AgNORs in Inflammatory Gingival Overgrowth in Pediatric Patients and its Correlation with the Dental Plaque Status

Mukhopadhyay S

Background and Objectives
Nucleolar organizer regions (NORs) are situated within the nucleolus of a cell. The proteins are selectively stained by the silver colloid technique that is known as the AgNOR technique. AgNOR stain can be visualized as a black dot under the optical microscope. The present study aimed to evaluate the cases for quantitative estimation of AgNORs in the epithelial cells in various grades of gingival overgrowth to that of normal gingival tissues.

Materials and Methods
Only preadolescent and adolescent groups aged up to 14 years were selected. Twenty normal and 31 disease cases of gingival overgrowth were selected. The tissue sections were stained by the hematoxylin and eosin (H&E) technique for the routine histological evaluation, while the AgNOR counts were performed through the improved one-step method of Ploton et al.

Results
H&E staining revealed five different types of gingival overgrowth. The plaque index (PI), gingival index (GI), and AgNOR count were not significantly (P > .05) higher than that of control cases in pyogenic granuloma, puberty gingivitis, and drug-induced gingival overgrowth. In gingival fibromatosis cases, for comparison of different indices t-tests were done. The PI, when compared with AgNOR count, was found significant at 5% level and 0.1% level for mixed and permanent dentition, respectively. The GI when compared with AgNOR count was found significant at 1% level and 0.1% level in mixed and permanent dentitions, respectively.

Predisposing Factors and Outcomes of Malignant Skin Tumors in Children

Tatiana KSC, et al.

Although benign and metastatic tumors occur in children, primary malignant skin tumors are uncommon in the pediatric population. In this study, the authors aimed to determine the incidence, risk factors, treatment, reconstruction details, and outcome of malignant skin tumors occurring in pediatric patients at the Hospital for Sick Children, Canada.

The electronic database (CoPath) of the pathology department was searched for all cases of malignant skin tumors treated surgically between January of 2000 and September of 2008. Eighteen patients had been diagnosed and treated surgically for malignant skin tumors. The mean age was 10.4 years. Malignant melanoma was diagnosed in 14 patients, basal cell carcinoma diagnosed in 4 patients, and squamous cell carcinoma was diagnosed in one patient. The most common sites of occurrence were lower limbs (33%) and face (28%). Gorlin syndrome was an underlying predisposing condition in three patients with basal cell carcinoma. All cases of basal cell carcinoma and squamous cell carcinoma underwent surgical resection and primary closure or skin graft. Among the patients with malignant melanoma, seven underwent surgical excision and primary closure and five had excision and skin graft. Eleven patients underwent sentinel node biopsy (Breslow thickness ≥0.75 mm). Interferon was used as an adjuvant therapy in patients with positive regional lymph nodes. One patient with melanoma suffered a recurrence.

These findings suggested that malignant skin tumors are rare in children. In accordance with previously published data, malignant melanoma was the most frequent tumor in our study. Epithelial tumors were less common and were all associated with an underlying predisposing condition.
Hepatic Disease as the First Manifestation of Progressive Myoclonus Epilepsy of Lafora

Gómez-Garre P, et al.


Background

Lafora disease (LD; progressive myoclonus epilepsy type 2; EPM2) is an autosomal recessive disorder caused by mutations in the EPM2A and EPM2B genes. LD is characterized by the presence of strongly PAS-positive intracellular inclusions (Lafora bodies) in several tissues. Glycogen storage disease type IV (GSD-IV; Andersen disease) is an autosomal recessive disorder characterized by cirrhosis leading to severe liver failure. GSD-IV has been associated with mutations in the glycogen branching enzyme gene (GBE). Histopathologic changes of the liver in both diseases show an identical appearance, although cirrhosis has never been described in patients with LD. This study reports an LD family in which the proband presented severe liver failure at onset of the disease.

Methods

Clinical histories, physical and neurologic examination, laboratory tests, EEGs, MRI of the brain, and liver or axillary skin biopsies were performed in the two affected siblings. The diagnosis was confirmed by molecular genetic analysis of the EPM2A, EPM2B, and GBE genes and loci.

Results

During the first decade of life, abnormalities in liver function tests were detected in the two affected siblings. The proband’s liver dysfunction was severe enough to require liver transplantation. Subsequently, both siblings developed LD. Mutation analysis of EPM2A revealed a homozygous Arg241stop mutation in both patients.

Conclusions

This is the first description of severe hepatic dysfunction as the initial clinical manifestation of LD. The phenotypic differences between the two affected siblings suggest that modifier genes must condition clinical expression of the disease outside the CNS.

Psychocutaneous Disorders: A Survey Study of Psychiatrists’ Awareness and Treatment Patterns

Jafferany M, et al.


Objective

To assess the level of training, awareness and attitude about psychocutaneous disorders among psychiatrists.

Methods

A mail-in survey was sent to all members of the Washington State Psychiatric Association and the Washington State Council on Child and Adolescent Psychiatry. Survey respondents were asked about demographic variables, level of training, skills, and degree of comfort in managing psychodermatological disorders, referral patterns, knowledge of patient and family resources on psychodermatology, and interest in continuing medical education on psychocutaneous disorders.

Results

A total of 632 surveys were mailed and 223 were returned for analysis. Only 21% of psychiatrists reported a clear understanding of psychodermatology in terms of the interface between skin and the psyche. Twenty-two percent of the respondents reported being very comfortable in diagnosing and treating psychocutaneous disorders. Self-inflicted cutaneous lesions were reported as the most common psychiatric condition associated with a dermatologic component. Medication-related cutaneous rash was the most common diagnosis necessitating referral to dermatologists. About 90% of survey respondents were not aware of any patient or family resources on psychodermatology. Eighty-five percent of psychiatrists expressed interest in attending continuing medical education activities.

Conclusion

Results of this survey suggest that knowledge about the diagnosis, treatment and/or appropriate referrals of psychocutaneous disorders is lacking. Significant information gaps were also identified about the knowledge of patient or family resources on psychodermatological disorders. Incorporating formal training and didactics on psychodermatology in psychiatry residency programs and regularly occurring CME events are recommended. Psychiatry-dermatology liaison services will prove helpful in the management of these patients.
Liv.52 Attenuates Copper-Induced Toxicity by Inhibiting Glutathione Depletion and Increases Antioxidant Enzyme Activity in HepG2 Cells

Vidyashankar S, Patki PS
R&D Center, The Himalaya Drug Company, Bangalore, India


**Abstract**

Altered copper metabolism plays a pivotal role in the onset of several hepatic disorders and glutathione (GSH) plays an important role in its homeostasis. Hepatic diseases are often implicated with decreased content of intracellular GSH. GSH depleted cells are prone to increased oxidative damage eventually leading to its death. The present study was conducted to evaluate the potential cytoprotective effect of Liv.52 against toxicity induced by copper in HepG2 cells. Copper (750 μM)-induced cytotoxicity to HepG2 cells as determined by MTT assay. The toxicity was brought about by increased lipid peroxidation, DNA fragmentation, and decreased GSH content. However, treatment with Liv.52 significantly abrogated copper-induced cell death through inhibition of lipid peroxidation by 58% and DNA fragmentation by 37%. Liv.52 increased the GSH content by 74%. In Liv.52 treated cells, activities of the antioxidant enzymes catalase, glutathione peroxidase, and superoxide dismutase were increased by 46%, 22%, and 81%, respectively. Thus, it is apparent from these results that Liv.52 abrogates copper-induced cytotoxicity in HepG2 cells by inhibiting lipid peroxidation and increased GSH content and antioxidant enzyme activity.

**Key Words**

HepG2 cells, Liv.52, lipid peroxidation, glutathione, copper, antioxidant enzymes

**Introduction**

Copper (Cu²⁺) is an essential trace element in human nutrition. Physiologically, it is controlled by well-established homeostatic mechanisms. However, such mechanisms can be altered under certain environmental or genetic conditions, leading to accumulation of toxic concentration of Cu²⁺ in cells. Cu²⁺-induced toxicity involves its ability to catalyze the generation of free radicals and/or directly interact with essential biomolecules, hence Cu²⁺ sequestering is of vital importance for maintaining cellular integrity. Reduced glutathione (GSH) plays a pivotal role in maintaining the intracellular Cu²⁺ homeostasis. It is due to the fact that cysteine residues constitute one-third of GSH and are responsible for its ability to bind with Cu²⁺. GSH is likely to be one of the first molecules with which Cu²⁺ ions interact upon entering cells. During such interaction, the tripeptide reduces Cu²⁺ ions as a Cu-GSH adduct. This adduct forms the principle carrier of Cu²⁺ to several metalloproteins. On the other hand, GSH is also considered to play a role in defining the susceptibility of the cells to excess Cu²⁺ via its interaction with Cu²⁺ ions. To the extent that GSH sequesters redox-active Cu²⁺ ions, it would prevent these from catalyzing free radical generation, thus serving as a mechanism that protects cells against the deleterious consequences of excessive Cu²⁺ accumulation. GSH is a potent antioxidant molecule and protects cells by acting directly as a scavenger of free radicals generated during cellular metabolism and serves as cofactor in the GSH-peroxidase-
dependent removal of peroxides generated in Cu^{2+}-overloaded cells.\textsuperscript{7–9}

The liver is particularly susceptible to metal-induced toxicity as it is the site for diverse biochemical reactions. The absorbed metal ions in a concentrated form can cause ROS- and free radical-mediated damage that may result in inflammatory and fibrotic processes.\textsuperscript{10}

Liv.52, used since long time to combat liver disorders, is claimed for its potential hepatoprotective effects. Several epidemiological and toxicological studies suggest that Liv.52 plays a pivotal role in detoxification of xenobiotics from liver.\textsuperscript{11–13} It is shown that diets rich in fruit and vegetables and other plant foods (including tea and wine) are associated with a decreased risk of chronic diseases such as cardiovascular diseases and some types of cancer.\textsuperscript{14,15} Polyphenols, have immense beneficial effects on certain diseases through their potential to scavenge the free radicals and neutralize the reactive oxygen species and act as metal ion chelators.\textsuperscript{16} Liv.52 is rich in phenolic compounds, especially polyphenols, that are believed to be partly responsible for such effects.\textsuperscript{17} However, few studies address the biological effects of Liv.52 and the ones performed using cellular and in vivo models indicate a poor correlation between the antioxidant potency and biological activity.

HepG2 cells are considered as good model to study in vitro xenobiotic metabolism and toxicity to the liver, as they retain many of the specialized functions that characterize normal human hepatocytes. HepG2 cells retain the activity of many phase I and phase II antioxidant enzymes ensuring that they help to study cytoprotective, genotoxic, and antigenotoxic effects of compounds.\textsuperscript{17,18} Therefore, it was postulated that Liv.52 may rescue liver from metal-induced toxicity and its hepatoprotective effect against Cu^{2+}-induced toxicity was evaluated in HepG2 cells.

### Materials and Methods

#### Chemicals

Bradford reagent, bathocuproine disulfonate (BCS), bathionine sulfoximine (BSO), copper sulfate (CuSO\textsubscript{4}·7H\textsubscript{2}O), cytochrome-C, 2,2-Diphenyl-1-picrylhydrazyl (DPPH), diphenylamine (DPA), Dulbecco’s minimum essential medium (DMEM), ferric chloride (anhydrous), fetal bovine serum (FBS), GSH, hydrogen peroxide, 3(4,5-dimethyl thiazol-2-yl) 2,5-diphenyl tetrazolium bromide (MTT), β-nicotinamide adenine dinucleotide phosphate (β-NADPH), perchloric acid, thiobarbituric acid, xanthine and xanthine oxidase were purchased from Sigma-Aldrich (St. Louis, MO, USA). All other reagents were of analytical grade.

#### Cell culture

All the experiments were performed using HepG2 cells (hepatocellular carcinoma cell lines) on 10 passages after thawing. Continuous cultures were maintained by subculturing every 4 days at 2.2×10\textsuperscript{6} cells/25 cm\textsuperscript{2} flask by trypsination.

#### Cu^{2+}-induced cytotoxicity and protection by Liv.52

HepG2 cells were plated in 96-multiwell culture plates at 1×10\textsuperscript{5} cells per well. To study Cu^{2+} cytotoxicity, the medium was discarded after 24 hours of plating and fresh media containing Cu^{2+} at various concentrations were added. Cellular viability was determined using MTT assay at different time points.\textsuperscript{19} Cells were incubated with Cu^{2+} for 24 hours to induce significant cell death to determine the concentration of Liv.52 that protects 50% (IC\textsubscript{50}) of the cells from the toxicant-induced damage. Based on the dose–response curves of cell death protection by Liv.52 against the Cu^{2+}-induced oxidative damage in HepG2 cells, the IC\textsubscript{50} concentrations were determined and used in the following experiments to evaluate the protective potential of Liv.52 on several cellular parameters.

#### Effect of Cu^{2+} and Liv.52 on lipid peroxidation, GSH levels, DNA fragmentation, and antioxidant enzyme activities in HepG2 cells

HepG2 cells were plated in 60 mm culture plates at a concentration of 7.5×10\textsuperscript{5} cells per well. The medium was discarded after 40 hours of plating and fresh medium containing Cu^{2+} and Liv.52 was added. After 24 hours, cell culture medium and cell scrapings were harvested and kept at –80°C for following quantification of several parameters. Cell scrapings were harvested in lysis buffer (25 mM KH\textsubscript{2}PO\textsubscript{4}, 2 mM MgCl\textsubscript{2}, 5 mM KCl, 1 mM EDTA, 1 mM EGTA, and 100 mM PMSF; pH = 7.5) after rinsing the cells with PBS (pH = 7.4).

#### Lipid peroxidation

The extent of lipid peroxidation was estimated by the levels of malondialdehyde measured using the thiobarbituric acid reactive substances (TBARS) assay at 535 nm.\textsuperscript{20} Results were expressed as nmol/mg of protein using a molar extinction coefficient of 1.56×10\textsuperscript{5} M/cm.
Liv.52 in Copper-Induced Toxicity

Diphenylamine assay for DNA fragmentation
Perchloric acid (0.5 M) was added to the cell pellets containing uncut DNA (resuspended in 200 mL of hypotonic lysis buffer) and to the other half of the supernatant containing DNA fragments. Then two volumes of a solution consisting of 0.088 M diphenylamine (DPA), 98% (v/v) glacial acetic acid, 1.5% (v/v) sulfuric acid, and 0.5% (v/v) concentration of 1.6% acetaldehyde solution were added.\textsuperscript{21} Samples were stored at 4°C for 48 hours. The reaction was quantified spectrophotometrically at 575 nm. The percentage of fragmentation was calculated as the ratio of DNA in the supernatants to the total DNA.

Nonenzymatic antioxidants
Cells were homogenized in trichloroacetic acid (5% w/v), and deproteinized supernatant was used for GSH assay. The GSH levels from the cell homogenates was determined using DTNB-GSSG reductase recycling assay as previously described with some modifications.\textsuperscript{22} Results were expressed as nmol GSH/mg protein.

Antioxidant enzymes
The activity of antioxidant enzymes such as superoxide dismutase, catalase, and glutathione peroxidase (GPx) were assayed in 1000 xg supernatants of cell homogenates. Total SOD activity was determined by monitoring the inhibition of the reduction of ferricytochrome C at 550 nm, using the xanthine-xanthine oxidase system as the source of superoxide. One unit of the SOD was defined as the amount of the enzyme required to inhibit 50% of the rate of cytochrome C reduction.\textsuperscript{23} Catalase activity was measured spectrophotometrically at 240 nm by evaluating the rate of H$_2$O$_2$ consumption and expressed as mmol H$_2$O$_2$ oxidized/min/mg protein.\textsuperscript{24} GPx activity was determined by following the enzymatic NADPH oxidation at 340 nm.\textsuperscript{25}

Statistical analysis
Results were expressed as mean ± SEM. Statistical significances were determined by one- way ANOVA using Tukey-Kramer test using GraphPad Prism 4. Results were considered to be significant at $P<.05$.

Results

Cytotoxicity
Cytotoxicity of Cu$^{2+}$ and Liv.52 in HepG2 cells was evaluated using MTT assay. Liv.52 did not show any cytotoxic effect at concentration ranging from 1% to 5%.

On the other hand, Cu$^{2+}$ was tested for its cytotoxicity with wide range of concentration for 24 hours. Results showed that Cu$^{2+}$ (>750 mM) caused significant cytotoxicity to HepG2 cells. Therefore, 750 mM concentration of Cu$^{2+}$ was used in all the subsequent experiments for testing hepatoprotective effect of Liv.52.

Effect of Liv.52 on Cu$^{2+}$-induced toxicity on HepG2 cell viability
Liv.52 effectively protected 62% of the cells against Cu$^{2+}$-induced toxicity at a concentration of 1%. BSO (an inhibitor of GSH synthesis) induced significant toxicity to HepG2 cells at a concentration of 250 mM. On the other hand, BCS (Cu$^{2+}$ chelating agent) had no effect on the cell viability. BCS significantly decreased cytotoxicity by 52% when added along with Cu$^{2+}$.

Effect of Liv.52 on GSH depletion in Cu$^{2+}$-induced toxicity
The effect of Cu$^{2+}$ on GSH and GSSG levels in the HepG2 cell was evaluated and the results showed that Cu$^{2+}$ significantly depleted the GSH levels by 86% in the cells. The BSO treated cells resulted in 78% lowered GSH content and the cells were found to be more vulnerable for Cu$^{2+}$-induced toxicity. On the other hand, when cells were exposed to Cu$^{2+}$ along with BCS (Cu$^{2+}$ chelating agent) the GSH level was significantly increased by 42%. Liv.52 significantly replenished the GSH levels by 74% in Cu$^{2+}$-induced toxic conditions.

Cu$^{2+}$ significantly increased the GSSG content but the increase in the GSSG content was not proportionate with the depleted GSH. However, Liv.52 effectively reduced the GSSG content in the cells treated with Cu$^{2+}$.

Effect of Liv.52 on lipid peroxidation and DNA fragmentation
The lipid peroxidation was significantly increased by 5.6 folds after addition of Cu$^{2+}$ in HepG2 cells. The cells treated with Cu$^{2+}$ along with BSO showed 5.5 folds higher MDA levels. Addition of Liv.52 significantly reduced the lipid peroxidation by 58% as compared to toxicant group. Similarly, BCS significantly inhibited lipid peroxidation by 76% in Cu$^{2+}$-treated cells.

Cu$^{2+}$ significantly increased the DNA fragmentation by 48% as compared to control cells. Results showed that there was no significant DNA damage in cells with BSO alone; however, DNA damage was significantly increased by 49% in cells incubated with Cu$^{2+}$. Liv.52
resulted in a n inhibition of DNA damage by 37% in cells treated with Cu²⁺. Similarly, the cells treated with Cu²⁺ and BCS showed reduced DNA damage as compared to toxicant group.

**Effect of Liv.52 on antioxidant enzyme activity in Cu²⁺-induced toxicity**

The activities of antioxidant enzymes catalase, GPx, and SOD were evaluated and the results showed that Cu²⁺ inhibited the catalase activity by 47%, GPx activity by 23% and SOD activity by 34% in Cu²⁺-induced toxic conditions. Catalase, GPx, and SOD activities were increased after addition of Liv.52 by 46%, 22%, and 81%, respectively, as compared to toxicant group.

**Discussion and Conclusion**

The present study showed the antioxidant and cytoprotective effects of Liv.52 against Cu²⁺-induced toxicity in HepG2 cells, which is attributed to the inhibition of GSH depletion. Liv.52 liquid concentrate was used in the study as the biological activity of the drug depends on its association and permeability. The antioxidant and biological activity of biologically active compounds depend more on the extent to which they associate, interact, and permeate cell membranes. Existing evidence supports the participation of GSH and metallothionein (MT) as two of the major molecules involved in the intracellular sequestering and storing of Cu²⁺. Earlier, it was shown that Liv.52, rich in polyphenols, act as hepatoprotective agent by modulating the antioxidant molecules and xenobiotic enzymes in cells. It was also reported that phenolic compounds activates enzymes involved in the biodegradation of xenobiotics.

Results showed that cytotoxicity of Cu²⁺ is mediated by increased lipid peroxidation (5.6 folds) and GSSG levels (3.7 folds) as well as decreased GSH levels (86%) and glutathione-related enzyme activity in HepG2 cells. However, Liv.52 attenuated the cytotoxicity in HepG2 cells when co-incubated with Cu²⁺ by increased GSH content and activity of glutathione-related enzymes.

Previous studies showed that different origins of HepG2, culture medium composition, and cultivation time (age of cells) may affect the experimental outcome through differences in sensitivity toward drugs. Therefore, it becomes imperative to characterize the cells response to the toxicant and experimental conditions used for the detection of protective effects of test compounds. In an attempt to explain the observed cytoprotective effects of Liv.52, its effects at IC₅₀ concentration on markers of cellular oxidative stress such as lipid peroxidation DNA fragmentation, and GSH levels were studied.

The susceptibility of HepG2 cells toward Cu²⁺-induced cytotoxicity shows good correlation between initial cell viability and lipid peroxidation compared to control in the present study (P<.05). But Liv.52 significantly increased the cell viability (67%) and decreased the lipid peroxidation (58%) along with elevated GSH levels. Thus, showing that hepatoprotection by Liv.52 is brought about by preventing excessive lipid peroxidation. The ability of Liv.52 to chelate metal ions and/or to act as chain breaking antioxidants by scavenging (as hydrogen donors) lipid alkoxy and peroxy radicals could provide an explanation for the observed reduction in lipid peroxidation. Hence, from these findings it is speculated that besides inhibiting lipid peroxidation Liv.52 may have also involved in other mechanisms in abrogating the cytotoxicity in HepG2 cells.

Earlier, it was shown that cytotoxicity induced by tertiary butyl hydroperoxide in HepG2 cells was proportional to the depletion of GSH. Therefore, low GSH levels in Cu²⁺- loaded cells could be considered a major intracellular determinant of their susceptibility to cytotoxicity. Another report also demonstrated that Cu²⁺-induced toxicity is modulated by depleted amounts of GSH content and increased lipid peroxidation. Concurrent to these, GSH levels were significantly depleted by Cu²⁺ in the present study causing cytotoxicity in HepG2 cells. But upon treatment with Liv.52 the GSH level was replenished and the cell viability was increased.

Increase in GSSG levels was not in the same range as the decrease in GSH levels as observed and part of the GSSG generated by the HepG2 cells is likely to be continuously pumped out, but to establish the exact contribution of such mechanisms to the loss of GSH is difficult to measure. Thus, it is inferred that Cu²⁺ reduced GSH levels mainly through formation of GSH conjugates rather than oxidation to GSSG. These findings were in accordance with studies reported earlier in liver cells. If the adduct was assumed to have been formed within the scope of this study, it was likely to have compromised the GSH pool to an extent comparable to that of Cu²⁺ needed to be intracellularly sequestered. Considering the role that GSH plays in sequestering copper and carrying the metal into MT, the results addressed the possible changes in the GSH pool associated with Cu²⁺-induced toxicity.

The lower GSH levels observed in cells were in line with
Liv.52 in Copper-Induced Toxicity

the low GSH levels occurring in the livers of individuals with Wilson disease. It is known that GSH plays an important role in hepatocyte defense against ROS, free radicals, and electrophilic metabolites. Hence, severe GSH depletion leaves cells more vulnerable to oxidative damage by radicals and increases protein thiolation or oxidation of SH groups that may lead to alterations in cellular calcium homeostasis. A sustained increase in cytosolic calcium levels results in activation of enzymes (phospholipases, non-lysosomal proteases, endonucleases) and cytoskeletal damage, which ultimately causes cell death. The decrease of GSH levels has indeed been suggested as one of the primary mechanisms of Cu²⁺-induced toxicity in liver cells, which is generally followed by an increase in the intracellular levels of calcium. Thus, the potential of Liv.52 to maintain GSH at reasonably high levels is of importance against Cu²⁺-induced toxicity. Therefore, the ability of Liv.52 to prevent Cu²⁺-induced GSH depletion by about 74% was very significant in restoring the cell viability. The GSSG formation was inhibited by Liv.52 and this may be attributed to the formation of GSH conjugates rather than oxidation to GSSG in Cu²⁺-induced toxic conditions. In addition to these, the activities of antioxidant enzymes such as SOD, catalase, and GPx were increased and DNA fragmentation was decreased by Liv.52 during Cu²⁺-induced toxicity.

In conclusion, Liv.52 abrogated the Cu²⁺-induced toxicity in HepG2 cells by inhibiting GSH depletion, lipid peroxidation, and DNA fragmentation and increased antioxidant enzyme activity. Therefore, Liv.52 may be beneficial in the treatment of Wilson disease and other liver disorders in which Cu²⁺-induced oxidative stress and homeostasis play a crucial role.

References
Liv.52 Protects HepG2 Cells from Oxidative Damage Induced by Tertiary-Butyl Hydroperoxide

Vidyashankar S, et al.
R&D Center, The Himalaya Drug Company, Bangalore, India


The potential hepatoprotective effect of Liv.52 against tert-butyl hydroperoxide (t-BHP)-induced oxidative damage was evaluated in HepG2 cells in order to relate in vitro antioxidant activity to cytoprotective effects. Liv.52 was tested at concentrations of 1% to 5% for total phenolic content (TPC) and antioxidant activity (AOA). AOA included 1,1-diphenyl-2-picrylhyrazyl (DPPH) free radical scavenging ability and ferric-reducing antioxidant power (FRAP) ability of Liv.52. The TPC content increased linearly from 83 to 260 mg/mL but AOA was not increased linearly with increasing Liv.52 content. The t-BHP induced considerable cell damage in HepG2 cells, as shown by significant increased lipid peroxidation by 5 folds and decreased reduced glutathione (GSH) by 4 folds. Cell death induced by t-BHP was significantly reduced after Liv.52 treatment. Liv.52 was found to significantly decrease lipid peroxidation and prevent GSH depletion induced by t-BHP by 40%. Therefore, Liv.52 appeared to be of greater importance for cell survival during t-BHP-induced toxicity. The protective potential against cell death was achieved mainly by preventing intracellular GSH depletion and lipid peroxidation. Liv.52 showed protective potential against oxidative damage induced in HepG2 cells. This could be beneficial against liver diseases in which oxidative stress plays a crucial role.

Key Words
Liv.52, liver, oxidative stress, HepG2 cells, tert-butyl hydroperoxide, t-BHP

Oxidative stress has been recognized to be involved in the etiology of several age-related and chronic diseases such as cancer, diabetes, and neurodegenerative and cardiovascular diseases. In liver diseases such as hepatocellular carcinoma, viral and alcoholic hepatitis, and nonalcoholic steatosis, reactive oxygen species (ROS) and reactive nitrogen species have been found to play a crucial role in disease induction and progression. The liver is particularly susceptible to toxicants since the portal vein brings blood to this organ after intestinal absorption. The absorbed drugs and xenobiotics in a concentrated form can cause ROS- and free radical-mediated damage that may result in inflammatory and fibrotic processes. Because oxidative stress plays a central role in liver diseases pathology, herbal therapeutic agents are of great importance to counteract liver damage and other oxidative stress-based chronic diseases. Several epidemiological and toxicological studies suggest that Liv.52, an Ayurvedic herbal formulation, plays a pivotal role in detoxification of xenobiotics from liver. Several epidemiological studies have shown that diets rich in plant foods are associated with a reduced risk of premature death and mortality from chronic diseases such as cardiovascular diseases and some types of cancer. The biological effect of active constituents of Liv.52 and their in vivo circulating metabolites ultimately depend on their cellular uptake and/or the extent to which they associate with cell membranes.

HepG2 cells, a human hepatoma cell line, are considered as good model to study in vitro xenobiotic metabolism and toxicity to the liver, as they retain many of the specialized functions that characterize normal human hepatocytes. HepG2 cells retain the activity of many phase I and phase II antioxidant enzymes ensuring that they help to study cytoprotective, genotoxic, and antigenotoxic effects of compounds.

This study evaluated the hepatoprotective effects of Liv.52 against t-BHP-induced oxidative damage in HepG2 cells...
and related in vitro antioxidant activity with cytoprotective effects. The concentrations of Liv.52 that protected 50% (IC\text{50}) against t-BHP-induced cell death were determined. Based on the IC\text{50} values for Liv.52, biological activity was related to antiradical efficiency. Subsequently, IC\text{50} values were used to evaluate the effects of Liv.52 at different concentration on several markers of oxidative damage such as intracellular glutathione, lipid peroxidation, and glutathione-related enzyme such as glutathione peroxidase (GPx).

**Materials and Methods**

**Chemicals**

Bradford reagent, cytochrome-C, DPPH, Dulbecco’s Minimum Essential Medium Eagle (DMEM), ferric chloride (anhydrous), Fetal bovine serum (FBS), glutathione, hydrogen peroxide, MTT, NADPH, tert-butyl hydroperoxide, thiobarbituric acid, xanthine and xanthine oxidase were purchased from Sigma-Aldrich (St. Louis, MO, USA). All other reagents were of analytical grade. Liv.52 liquid concentrate was obtained from the Himalaya Drug Company, Bangalore, India.

**Determination of total phenolic content**

Total phenolic content (TPC) was determined by Folin-Ciocalteu method. TPC was expressed as gallic acid equivalents (GAE). The calibration equation for gallic acid was $y = 0.0111x - 0.0148$ ($R^2 = 0.9998$).

**Determination of antioxidant activity**

Free radical scavenging activity of Liv.52 was studied with stable free radical DPPH. For DPPH scavenging activity, after addition of Liv.52 to DPPH (90 μM), the percentage of remaining DPPH was determined at different times from the absorbance at 515 nm using a plate reader spectrophotometer. As suggested by Sanchez- Moreno and collaborators, the amount of antioxidant necessary to decrease by 50% the initial DPPH concentration (IC\text{50}) was expressed in terms of initial concentration of DPPH.

**Ferric-reducing antioxidant power assay**

The ferric-reducing antioxidant power assay (FRAP) of Liv.52 was determined, as previously described with minor modifications. Samples often have to be diluted because precipitation occurs upon color development when the reducing power is too high. Different dilutions of extracts (up to 1 mL) were added to 2.5 mL PBS and 2.5 mL of potassium ferriyanide (1% w/v). The mixture was incubated at 50°C for 20 minutes. Total 2.5 mL trichloroacetic acid solution (10% w/v) was added to the mixture. The mixture was then separated into aliquots of 2.5 mL and each was diluted with 2.5 mL of water. To each diluted aliquot, 500 mL of ferric chloride solution (0.1% w/v) was added and they were allowed to stand for 30 minutes for color development. Absorbance measured at 700 nm in triplicate was used to calculate the gallic acid equivalents. Results of the FRAP assay were expressed as mg GAE.

**Cell culture**

HepG2 cells, obtained from the National Center for Cell Science (NCCS) Pune, India, were maintained in culture in 25 cm$^2$ polystyrene flasks (Tarsons) with DMEM containing 10% FBS, 1% antibiotic-antimycotic solution, and 3.7 g/L sodium bicarbonate under an atmosphere of 5% CO$_2$ at 37°C with 95% humidity.

**ASSay for t-BHP cytotoxicity and protection by Liv.52**

HepG2 cells were plated in 96-multiwell culture plates at 1×10$^5$ cells per well. To study t-BHP cytotoxicity, the medium was discarded after 24 hours of plating and fresh medium containing t-BHP at various concentrations was added. Cellular viability was determined by the MTT assay at different time points. Cells were incubated with 200 mM t-BHP for 24 hours to induce significant cell death to determine the concentration of Liv.52 that protects 50% (IC\text{50}) of the cells from toxicant-induced damage. Based on the dose–response curves of cell death protection by Liv.52 against the t-BHP-induced oxidative damage in HepG2 cells, the IC\text{50} concentrations were determined and used in the following experiments to evaluate the protective potential of Liv.52 on several cellular parameters.

**Evaluation of the effects of t-BHP and Liv.52 on lipid peroxidation, glutathione levels, and antioxidant enzyme activities in HepG2 cells**

HepG2 cells were plated in 60 mm culture plates at 7.5×10$^5$ cells per well. The medium was discarded after 40 hours of plating and fresh medium containing 200 mM t-BHP and Liv.52 was added. Cell culture medium and cell scrapings were harvested after 24 hours and kept at −80°C for following quantification of several parameters. Cell scrapings were harvested in lysis buffer (25 mM KH$_2$PO$_4$, 2 mM MgCl$_2$, 5 mM KCl, 1 mM EDTA, 1 mM EGTA, and 100 μM PMSF; pH = 7.5) after rinsing the cells with PBS (pH = 7.4).
Biochemical analysis

Lipid peroxidation

The extent of lipid peroxidation was estimated by the levels of malondialdehyde measured using the thiobarbituric acid reactive substances (TBARS) assay at 535 nm. Results were expressed as nmol/mg of protein using a molar extinction coefficient of 1.56×10^5 M/cm.

Measurement of nonenzymatic antioxidants

Cells were homogenized in trichloroacetic acid (5% w/v) and deproteinized supernatant was used for GSH assay. The glutathione levels from the cell homogenates were determined by DTNB-GSSG reductase recycling assay as previously described with some modifications. Results were expressed as nmol GSH/mg of protein.

Measurement of enzymic antioxidants

The activity of antioxidant enzymes such as superoxide dismutase (SOD), catalase, and glutathione peroxidase (GPx) were assayed in 1000× g supernatants of cell homogenates. Total SOD activity was determined by monitoring the inhibition of the reduction of ferricytochrome C at 550 nm, using the xanthine-xanthine oxidase system as the source of superoxide. One unit of the SOD was defined as the amount of the enzyme required to inhibit 50% of the rate of cytochrome C reduction. Catalase activity was measured spectrophotometrically at 240 nm using the rate of H₂O₂ consumption and expressed as mmol H₂O₂ oxidized/min/mg protein. GPx activity was determined by following the enzymatic NADPH oxidation at 340 nm.

Statistical analysis

Results were expressed as mean ± SEM. Statistical significances were determined by one-way ANOVA using Tukey-Kramer test using graph pad prism 4. Results were considered to be significant at P<.05.

Results

Total phenolic content and antioxidant activity

The TPC and antioxidant activity of Liv.52 liquid concentrate was determined and the results showed that phenolic content was linear with the tested concentration of Liv.52. The FRAP assay showed that there was no significant difference in the antioxidant activity at lower concentrations of Liv.52. But at higher concentration the activity was increased by 2 folds. Results of the free radical scavenging activity (DPPH) showed that antiradical activity followed linearity at the lower concentration of Liv.52 (1% and 2%) and did not follow linearity at higher concentration. Results also showed that Liv.52 could effectively scavenge 50% of the original DPPH content at a concentration of 2% and the same concentration was effective to show cytoprotective effect on HepG2 cells.

Cytotoxicity

Cytotoxicity of t-BHP and Liv.52 was evaluated using MTT assay. Liv.52 did not present any cytotoxic effect at concentration ranging from 1% to 5%. On the other hand, t-BHP was tested for its cytotoxicity with wide range of concentrations for 24 hours and the results showed that at 200 mM t-BHP showed >95% cytotoxicity to HepG2 cells. Liv.52 effectively protected 50% of the cells against (200 mM) t-BHP at all the tested concentrations. Thus, 200 mM of t-BHP was used for all subsequent experiments for testing hepatoprotective effect of Liv.52.

Cell growth suppression

The possible protection by Liv.52 against t-BHP induced loss of cell viability was evaluated by preincubating the cells with Liv.52 for 30 minutes, followed by addition of 200 mM of t-BHP for 24 hours. Similarly, the Liv.52 was co-incubated with t-BHP for 24 hours. Results showed that pre-incubation with Liv.52 for 30 minutes was less effective than co-incubation in rescuing the cell death. Similar observations were made when cells were treated with Vitamin C (50mM) although the cytoprotection rendered was higher compared to Liv.52.

Lipid peroxidation and glutathione content

The addition of t-BHP resulted in 5-fold increase in lipid peroxidation in HepG2 cells. Liv.52 restored the increased level of MDA at all the tested concentrations through inhibition of lipid peroxidation. Vitamin C significantly reduced the lipid peroxide content as compared to t-BHP group. However, Liv.52 was more effective in inhibiting the formation of lipid peroxides as compared to vitamin C. Similarly, t-BHP significantly reduced the GSH level by 4 folds, which was restored by Liv.52. On the other hand, t-BHP increased the GSSG content by 4.8 folds, but Liv.52 effectively reduced the GSSH levels in cells.

Antioxidant enzymes

The effect of Liv.52 on antioxidant enzymes in t-BHP treated cells was evaluated and the results showed that t-BHP increased the activities of catalase and SOD by 1.6- and 12.6-folds, respectively. Liv.52 effectively countered
the increased activity of these enzymes and brought down the activity by >50%. The GPx activity was decreased by 15.5% in t-BHP group. Liv.52 treatment partially increased the GPx activity and was effective in counteracting the toxicity, but the results were not statistically significant.

Discussion

The present study demonstrated that Liv.52 possesses protective effects against t-BHP-induced cell death in HepG2 cells. Cell viability assay showed that the conferred protection decreased in the order of 5% > 4% > 3% > 2% > 1% concentration of Liv.52. Considering the solubility and free radical scavenging activity of Liv.52, the drug was evaluated for both DPPH and superoxide radical scavenging activities. Results showed that the hepatoprotective potential of Liv.52 correlated primarily with the degree of hydrophilicity and secondarily with its antioxidant capacity. Rice-Evans suggested that the antioxidant biological activity of biologically active compounds depend more on the extent to which they associate, interact, and permeate cell membranes than on its antiradical activity alone. In agreement with this, Liv.52 liquid concentrate had a direct correlation between biological and antioxidant activity.

Results observed for Liv.52 (liquid concentrate) implicated hydrophilicity as an important factor for this cytoprotective and antioxidant effect. Results revealed that co-incubation of HepG2 cells with t-BHP and Liv.52 showed better protection than pre-incubation. This discrepancy could be due to varied action of Liv.52 on several cellular components involved in mediating cytotoxicity. One of these could be the ability of Liv.52 to chelate metal ions, which was previously described by Rice-Evans while quoting antioxidant properties of phenolic compounds. Iron chelation could indeed be important for the protection against t-BHP toxicity by Liv.52, as intracellular iron is known to be toxic. Liv.52 may also indirectly act as antioxidant in cells by modulating the activity of antioxidant, detoxifying and repairing enzymes, and enzymes involved in the bioactivation of xenobiotics as reported earlier with other compounds. In the present study, Liv.52 protection through increased activity of glutathione-related enzymes was evident. On the other hand, longer term pre-incubations would help in the induction of proteins and enzymes, such as antioxidant enzymes, by interaction with antioxidant response elements. t-BHP-induced cell death was accompanied by increased lipid peroxidation and GSSG levels and decreased GSH levels and glutathione-related enzyme activity. The increase in GSSG levels was not in the same range as the decrease in GSH levels. This indicated that t-BHP reduced GSH levels mainly through formation of GSH conjugates rather than oxidation to GSSG. These findings were in accordance with findings in liver cells reported earlier. However, t-BHP exposure conditions are different among different studies published so far, particularly in HepG2 cells.

Previous studies showed that different origins of HepG2 clones, culture medium composition, and cultivation time (age of cells) may affect the experimental outcome through differences in sensitivity toward drugs. Therefore, it becomes imperative to characterize the response of cells to the toxicant and the experimental conditions used for the detection of protective effects of test compounds. In an attempt to explain the observed cytoprotective effects of Liv.52, its effects at IC50 concentration on markers of cellular oxidative stress such as lipid peroxidation and glutathione levels were studied. It was observed from the present study that, t-BHP-induced lipid peroxidation in HepG2 cells was attenuated by Liv.52 at all concentrations on par with vitamin C. A good correlation seemed to exist between hepatoprotective effects and the prevention of lipid peroxidation. Therefore from these findings, it was speculated that Liv.52 mediated protection of HepG2 cells against t-BHP was brought about by other factors besides the inhibition of lipid peroxidation. In agreement with this, previous reports indicated that t-BHP-induced toxicity was not mediated by lipid peroxidation. Therefore, cell viability seemed to depend on other cellular defense mechanisms. In this regard, Liv.52 treatment significantly replenished GSH levels depleted by t-BHP. GSH plays an important role in hepatocyte defence against ROS, free radicals, and electrophilic metabolites. Hence, severe GSH depletion made cells more vulnerable to oxidative damage by radicals and increased protein thiolation or oxidation of SH groups that may lead to alterations in cellular calcium homeostasis. A sustained increase in cytosolic calcium levels results in activation of enzymes (phospholipases, non-lysosomal proteases, and endonucleases) and cytoskeletal damage that ultimately causes cell death.

The decrease of GSH levels has been suggested as one of the primary mechanisms of t-BHP-induced toxicity in liver cells that is generally followed by an increase in the intracellular levels of calcium. Thus, the potential of Liv.52 to maintain GSH at reasonably high levels is important against t-BHP-induced toxicity. Therefore, the ability of Liv.52 to prevent t-BHP-induced GSH depletion
by about 40% was probably a major contribution to its cytoprotective effect. The protection by Liv.52 against increased GSSG levels induced by t-BHP was effective and Liv.52 protected GSH levels in cells mainly by preventing the formation of GSH conjugates rather than oxidation to GSSG.

In conclusion, Liv.52 showed protective effects against oxidative damages induced in HepG2 cells that could be of use against liver diseases in which oxidative stress plays a crucial role. Moreover, the protective potential seems to be dependent on the nature of compounds present in Liv.52 in conjunction with its antioxidant activity. The effect of Liv.52 against t-BHP-induced GSH depletion seemed to be an important factor for preserving cell viability.

References
Systemic Disease Manifestations of Oral Infection

Background
Infections in the oral cavity may significantly contribute to the course and pathogenesis of several systemic diseases such as diabetes mellitus, malignancies, and cardiovascular and respiratory diseases. There is a strong epidemiological and mechanistic association between chronic periodontitis (the most prevalent oral infection) and systemic diseases.

Three mechanisms have been proposed to explain the link between oral infections and systemic diseases.

Metastatic spread of oral infection as a result of transient bacteremia
Close anatomical proximity of oral pathogens to bloodstream facilitates the spread of these pathogens leading to secondary systemic infections. Poor oral hygiene and sometimes dental procedures such as tooth extraction, endodontic treatment, periodontal surgery, and root scaling can significantly increase the prevalence of bacteremia.

Metastatic inflammation caused by immunological injury from oral pathogens
Soluble antigens may enter the bloodstream and react with specific circulating antibodies to form a macromolecular complex. These macromolecular immunocomplexes give rise to several acute and chronic inflammatory reactions at the location of deposition.

Metastatic injury resulting from circulation of certain oral microbial products
Exotoxins, such as cytolytic enzymes and dimeric toxins, are mostly lethal and exhibit specific pharmacological actions causing various pathological manifestations.

The following table gives a summary of the possible pathways of nonoral systemic diseases caused by oral infections.

<table>
<thead>
<tr>
<th>Pathways</th>
<th>Probable nonoral systemic diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metastatic spread of oral infection as a result of transient bacteremia</td>
<td>Acute bacterial myocarditis, subacute infective endocarditis, cavernous sinus thrombosis, brain or lung abscess, sinusitis, Ludwig’s angina, skin ulcer, prosthetic joint infection, osteomyelitis, and orbital cellulitis</td>
</tr>
<tr>
<td>Metastatic inflammation caused by immunological injury from oral pathogens</td>
<td>Crohn’s disease, chronic urticaria, Behcet’s syndrome, inflammatory bowel disease, and uveitis</td>
</tr>
<tr>
<td>Metastatic injury resulting from circulation of oral microbial products (proteins, toxins)</td>
<td>Acute myocardial and cerebral infarction, persistent pyrexia, abnormal pregnancy outcome, idiopathic trigeminal neuralgia, systemic granulocytic cell defects, toxic shock syndrome, and chronic meningitis</td>
</tr>
</tbody>
</table>

Major Systemic Manifestations and Their Association with Oral Infections

Cardiovascular disease
Periodontal pathogens such as Porphyromonas gingivalis, Bacteroides forsythus, and Actinobacillus actinomycetemcomitans may enter the bloodstream and infect the walls of blood vessels. The infection is mainly asymptomatic but may cause local vascular inflammation that further contributes to the development of lipid-rich plaques and atherosclerosis. These pathogens and their products can also stimulate the production of proinflammatory and procoagulant molecules (such as C-reactive protein and fibrinogen) and expression of tissue factor that activates coagulation. Coagulation results in thrombus formation—one of the key factors in the development of atherosclerotic plaques.
Respiratory infections

Respiratory infections such as bacterial pneumonia and bronchitis partially occur due to aspiration of oropharyngeal microbes into the lower respiratory tract and failure of host defense mechanisms to eliminate the respiratory pathogens that multiply to cause infection. Dental plaque acts as a reservoir of respiratory pathogens, especially in patients with periodontal disease. Oral infection can contribute to the pathogenesis of respiratory diseases by one of the following mechanisms.

- Aspiration of oral pathogens such as *P. gingivalis* and *A. actinomycetemcomitans* may result in lung infection.
- Modification of mucosal surfaces by periodontal disease-associated salivary enzymes may promote adhesion and colonization of respiratory pathogens and facilitate infection.
- Cytokines originating from periodontal tissues may modify respiratory epithelium to promote infection by respiratory pathogens.

Diabetes mellitus

Severe periodontal disease can alter the systemic physiology and complicate metabolic control in patients with diabetes mellitus, further aggravating the condition. Studies suggest that periodontopathic organisms or their products (such as lipopolysaccharide [LPS]) stimulate the upregulation of cytokine synthesis and induce a state of insulin resistance. Chronic insulin resistance affects glucose-utilizing pathways that in turn contribute to the cycle of hyperglycemia and nonenzymatic irreversible glycation.

Some of the oral manifestations and possible associated systemic indications are listed in the adjacent table.

<table>
<thead>
<tr>
<th>Oral manifestation</th>
<th>Possible indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrophic glossitis</td>
<td>Iron deficiency</td>
</tr>
<tr>
<td>Candidiasis</td>
<td>AIDS, diabetes, immunosuppression disorders (neutropenia, agranulocytosis, leukemia, and leukocyte dysfunction), and use of antibiotics</td>
</tr>
<tr>
<td>Magenta tongue</td>
<td>Vitamin B12 deficiency</td>
</tr>
<tr>
<td>Painful atrophy of oral mucosa or surface of tongue</td>
<td>Megaloblastic anemia</td>
</tr>
<tr>
<td>Dark pigmentation, especially the lining of the mouth</td>
<td>Addison’s disease, Peutz-Jeghers syndrome, smoker’s melanosis, and hemochromatosis</td>
</tr>
<tr>
<td>Linear, grayish discoloration in the gingiva adjacent to teeth</td>
<td>Bismuth, lead, or silver poisoning</td>
</tr>
<tr>
<td>Reddish discoloration of teeth</td>
<td>Congenital erythropoietic porphyria</td>
</tr>
<tr>
<td>Violaceous patches</td>
<td>AIDS, Kaposi sarcoma</td>
</tr>
<tr>
<td>Red to reddish purple collections of oral telangiectases</td>
<td>Osler-Weber-Rendu syndrome, also known as hereditary hemorrhagic telangiectasia</td>
</tr>
<tr>
<td>High, arched soft palate</td>
<td>Marfan syndrome</td>
</tr>
<tr>
<td>Hairy leukoplakia (white, vertical folds on the lateral edge of tongue)</td>
<td>HIV transforming to AIDS</td>
</tr>
<tr>
<td>Multiple impacted supernumerary teeth and osteomas</td>
<td>Gardner’s syndrome</td>
</tr>
<tr>
<td>Keratotic lichenoid patches often with painful mucosal atrophy (observed in the mouth of a transplant recipient)</td>
<td>Graft versus host disease</td>
</tr>
<tr>
<td>Notched incisors, domed or mulberry molars</td>
<td>Congenital syphilis</td>
</tr>
</tbody>
</table>

Oral infection and premature labor during pregnancy

During the second trimester of pregnancy, the ratio of anaerobic gram-negative bacteria to aerobic bacteria in dental plaques is increased significantly. These gram-negative bacteria produce bioactive molecules such as LPS that activate macrophages and other immune cells to synthesize and secrete a wide array of immune molecules such as tumor necrosis factor (TNF), interleukin-1 (IL-1), and PGE2. These immune molecules may enter maternal circulation, cross the placental barrier that augments the physiologic levels of PGE2 in the amniotic fluid, and induce premature labor.

Oral health is integral to overall health and well-being of an individual; hence, it is imperative that physicians educate their patients regarding the importance of oral hygiene. Early identification of problems associated with oral cavity helps physicians in early diagnosis as well as management of systemic diseases.
**Chronic Hepatitis Caused by Persistent Parvovirus B19 Infection**

Mogensen TH, et al.

*BMC Infect Dis.* 2010;10:246.

**Background**

Human infection with parvovirus B19 may lead to a diverse spectrum of clinical manifestations, including benign erythema infectiosum in children, transient aplastic crisis in patients with haemolytic anemia, and congenital hydrops fetalis. These different diseases represent direct consequences of the ability of parvovirus B19 to target the erythroid cell lineage. However, accumulating evidence suggests that this virus can also infect other cell types resulting in diverse clinical manifestations, of which the pathogenesis remains to be fully elucidated. This has prompted important questions regarding the tropism of the virus and its possible involvement in a broad range of infectious and autoimmune medical conditions.

**Case Presentation**

The study presents an unusual case of persistent parvovirus B19 infection as a cause of chronic hepatitis. This patient had persistent parvovirus B19 viremia over a period of more than four years and displayed signs of chronic hepatitis evidenced by fluctuating elevated levels of ALAT and a liver biopsy demonstrating chronic hepatitis. Other known causes of hepatitis and liver damage were excluded. In addition, the patient was evaluated for immunodeficiency, since she had lymphopenia both prior to and following clearance of parvovirus B19 infection.

**Conclusions**

This case report described the current knowledge on the natural history and pathogenesis of parvovirus B19 infection, and discussed the existing evidence of parvovirus B19 as a cause of acute and chronic hepatitis. The results suggested that parvovirus B19 was the direct cause of this patient’s chronic hepatitis, and that she had an idiopathic lymphopenia, which may have predisposed her to persistent infection, rather than bone marrow depression secondary to infection. Additionally, the results also proposed that her liver involvement may have represented a viral reservoir. Finally, the findings suggest that clinicians should be aware of parvovirus B19 as an unusual etiology of chronic hepatitis, when other causes have been ruled out.

---

**Gingival Abscess due to an Unusual Nail-Biting Habit: A Case Report**

Sousa D, et al.


**Aim**

Nail-biting is one of the most frequent deleterious oral habits in children. It can result in systemic diseases or oral traumatic lesion. This report describes a case of gingival abscess in a child due to a fingernail-biting habit.

**Case Description**

A 5-year, 6-month-old female child presented gingival swelling and fistula in the primary maxillary left central and right lateral incisors as an unusual sequelae to the periodontal tissues from fingernail-biting. A periodontal curette was used to remove the fragments and to curette the area. After the curettage, an exudate of blood and pus was drained. Then the area was irrigated with 0.12% chlorhexidine solution; applying finger pressure controlled the secretion. After one week, the patient returned with gingival swelling present in the same teeth. The same curettage procedure was performed. It was suggested that the deleterious habit was related to emotional tension and anxiety behaviors and the patient was referred for psychological treatment. When the patient returned one month later, she was still biting her fingernails, but had stopped placing fragments into the gingival crevice. No more gingival inflammation or swelling was observed.

**Clinical Significance**

The fingernail-biting habit can induce a periodontal traumatic injury yielding more serious complications such as gingival abscess.
A Case of Anaphylaxis to Oral Minocycline

Jang JW, et al.

Minocycline is a semisynthetic tetracycline derivative that is often used in the treatment of acne vulgaris. To date, there has been only one case report of anaphylaxis to minocycline. Here a case of anaphylaxis to oral minocycline has been reported. A 56-year-old woman visited the hospital after three episodes of recurrent anaphylaxis. An oral challenge test (the standard method for diagnosing drug allergies) was performed with minocycline, which was one of the drugs the patient had taken previously. The patient developed urticaria, angioedema, nausea, vomiting, hypotension, and dyspnea within 4 minutes and was treated with intramuscular epinephrine, intravenous antihistamine, and systemic corticosteroid. However, she presented similar symptoms at 50 and 110 minutes. In prescribing oral minocycline, physicians should consider the possibility of serious adverse reactions, such as anaphylaxis.

Amiodarone-Induced Liver Cirrhosis and Parkinsonism: A Case Report

Ishida S, et al.

Background and Objective
Amiodarone-induced hepatotoxicity consists of mild liver test abnormalities and rare cases of acute hepatitis and chronic hepatic lesions, and histologically resembles the whole spectrum of alcoholic liver disease, that is non-alcoholic steatohepatitis. Amiodarone-induced neurotoxicity, including tremor, ataxia and peripheral neuropathy, is known, and some cases of parkinsonism following amiodarone use have also been reported. The objective of this study was to determine the pathology of amiodarone-associated parkinsonism.

Results
On postmortem examination, the liver showed micronodular cirrhosis. Striking steatosis and frequent Mallory bodies were present on light microscopy. There were lysosomal inclusion bodies on electron microscopy. From these findings, amiodarone-induced liver cirrhosis was diagnosed. Brain atrophy and infarcts were not observed, and pigmentation in the substantia nigra was preserved. Histologically, there was a slightly lesser degree of neuronal loss with astrocitosis in the substantia nigra, locus ceruleus, and dorsal vagal nucleus. Lewy bodies were not found. In the cerebral white matter and basal ganglia, Alzheimer Type II astrocytes, which are abundant in hepatic encephalopathy, had deposition of electron-dense materials within the lysosomes and mitochondrial matrices. The materials were compatible with the accelerated amiodarone.

Conclusion
This is the first case in which the accumulation of amiodarone in the brain was morphologically observed. Amiodarone accumulation in the brain may play a role in neurotoxicity inducing parkinsonism.
**Bacopa monnieri**

**Sanskrit name/Indian name:** Brahmi; **English name:** Thyme-leaved gratiola

**Cognitive Enhancement and Neuroprotective Effects of Bacopa monnieri in Alzheimer Disease Model**

Uabundit N, et al.


**Ethnopharmacological Relevance**

*Bacopa monnieri* (L.) Wettst., a plant belonging to the family Scrophulariaceae, has been used in the traditional system of Ayurvedic medicine to improve intelligence and memory for a long time. Therefore, the potential of this plant to protect against Alzheimer disease has been raised but less supported document is available.

**Aim**

To determine the effect of alcoholic extract of *B. monnieri* on cognitive function and neurodegeneration in animal models with ethylcholine aziridinium ion (AF64A)-induced Alzheimer disease.

**Materials and Methods**

Male Wistar rats were orally given the alcoholic extract of *B. monnieri* at doses of 20, 40 and 80 mg/kg body weight two weeks before and one week after the intracerebroventricular administration of AF64A bilaterally. Rats were tested for spatial memory using Morris water maze test and the density of neurons and cholinergic neurons were determined using histological techniques seven days after AF64A administration.

**Results**

*B. monnieri* extract improved the escape latency time (*P*<.01) in Morris water maze test. Moreover, the reduction of neurons and cholinergic neuron densities were also mitigated.

**Conclusion**

These findings suggest that *B. monnieri* is a potential cognitive enhancer and neuroprotectant against Alzheimer disease.
Terminalia bellirica/Terminalia chebula/Emblica officinalis

Sanskrit name/Indian name: Triphala (Vibhitaki, Haritaki, and Amalaki); English name: Bellirica Myrobalan, Chebulic Myrobalan, and Indian Gooseberry

Comparison of Enteroprotective Efficacy of Triphala Formulations (Indian Herbal Drug) on Methotrexate-Induced Small Intestinal Damage in Rats

Nariya M, et al.


Triphala is categorized as a rejuvenator and antioxidant-rich Ayurvedic herbal formulation and has traditionally been used in various gastric problems including intestinal inflammation. The aim of the present study was to examine the comparative enteroprotective effect of Triphala formulations against methotrexate-induced intestinal damage in rats. Triphala formulations were prepared by mixing equal (1:1:1) and unequal (1:2:4) proportions of *Terminalia chebula* Retz., *Terminalia belerica* (Gaertn.) Roxb., and *Emblica officinalis* Gaertn. Intestinal damage was induced by administering methotrexate (MTX) in a dose of 12 mg/kg, orally for 4 days to albino rats. The intestinal damage response was assessed by gross and microscopical injury, measuring the intestinal permeability to phenol red and tissue biochemical parameters. Triphala equal and unequal formulations at the dose of 540 mg/kg significantly restored the depleted protein level in brush border membrane of intestine, phospholipid and glutathione content and decreased the myeloperoxidase and xanthine oxidase level in intestinal mucosa of methotrexate-treated rats. In addition, *Triphala* unequal formulation showed significant decrease in permeation clearance of phenol red with significant attenuation in the histopathological changes, level of disaccharidase in brush border membrane vesicles, and lipid peroxidation content of intestinal mucosa. Based on the data generated, it is suggested that Triphala unequal formulation provides significantly more protection than Triphala equal formulation against methotrexate-induced damage in rat intestine.
Syzygium aromaticum

Sanskrit name/Indian name: Lavangaha; English name: Clove

Compounds from Syzygium aromaticum Possess Growth Inhibitory Activity Against Oral Pathogens

Cai L, Wu CD


A crude MeOH extract of Syzygium aromaticum (clove) exhibited preferential growth-inhibitory activity against gram-negative anaerobic periodontal oral pathogens, including Porphyromonas gingivalis and Prevotella intermedia. By means of bioassay-directed chromatographic fractionation, eight active compounds were isolated from this extract and were identified as 5,7-dihydroxy-2-methylchromone 8-C-γ-d-glucopyranoside, biflorin, kaempferol, rhamnocitrin, myricetin, gallic acid, ellagic acid, and oleanolic acid, based on spectroscopic evidence.

The antibacterial activity of these pure compounds was determined against Streptococcus mutans, Actinomyces viscosus, P gingivalis, and P intermedia. The flavones, kaempferol and myricetin, demonstrated potent growth-inhibitory activity against the periodontal pathogens P gingivalis and P intermedia.
Aloe barbadensis

Sanskrit name/Indian name: Ghrita-kumari/Kanya/Kumari; English name: Barbados Aloe

Moisturizing Effect of Cosmetic Formulations Containing Aloe vera Extract in Different Concentrations Assessed by Skin Bioengineering Techniques

Dal’Belo SE, et al.


**Background and Aim**

The polysaccharide-rich composition of Aloe vera extracts (*Aloe barbadensis* Miller), often used in cosmetic formulations, may impart moisturizing properties to the product. The aim of this study was to evaluate the effect of cosmetic formulations containing different concentrations of freeze-dried *A* vera extract on skin hydration, after a single and a 1- and 2-week period of application, by using skin bioengineering techniques.

**Methods**

Stable formulations containing 5% (w/w) of a trilaureth-4 phosphate-based blend were supplemented with 0.10%, 0.25% or 0.50% (w/w) of freeze-dried *A* vera extract and applied to the volar forearm of 20 female subjects. Skin conditions in terms of the water content of the stratum corneum and of transepidermal water loss (TEWL) (Corneometer CM 825 and Tewameter TM 210) were analyzed before and after a single and 1- and 2-week period of daily application.

**Results**

After a single application, only formulations supplemented with 0.25% and 0.50% (w/w) of *A* vera extract increased the water content of the stratum corneum, while after the 2-week period application, all formulations containing the extract (0.10%, 0.25% and 0.50%) had the same effect, in both cases as compared with the vehicle. TEWL was not modified after a single and after 1- and 2-week periods of application, when compared with the vehicle.

**Conclusion**

The results show that freeze-dried *A* vera extract is a natural effective ingredient for improving skin hydration, possibly through a humectant mechanism. Consequently, it may be used in moisturizing cosmetic formulations and also as a complement in the treatment of dry skin.
Clarina® (ANTI-ACNE FACE WASH GEL)

Cleanses skin. Controls acne

Introduction

Clarina anti-acne face wash gel, a topical phytopharmaceutical formulation, is recommended for the management of acne vulgaris.

Composition

Each gram of Clarina anti-acne face wash gel contains:

Exts.

Kumari (Aloe barbadensis) 1.0 mg, Nimba (Azadirachta indica) 0.5 mg, Haridra (Curcuma longa) 0.5 mg, Jalavetasa (Salix tetrasperma) 0.1 mg

Clinical Pharmacology

Clarina anti-acne face wash gel has anti-inflammatory, wound-healing, antiseborrheic, keratolytic, and antibacterial activities. Clarina anti-acne face wash gel inhibits the production of reactive oxygen species (ROS) by its antioxidant activity, thus reducing inflammation mediated by acne-causing bacteria. Clarina anti-acne face wash gel improves general skin health.

Indications

Acne vulgaris

Directions for Use

Required quantity of Clarina anti-acne face wash gel should be applied on moist face in gentle circular motions to work up a lather and then washed off, after which the face should be patted dry. Recommended twice daily.

Route of Administration

Topical

Side Effects

No known side effects.

Adverse Reactions

No clinically significant adverse reactions have been reported.

Warning

None

Special Precautions

To be used exclusively for external application. Contact with eyes or open wounds to be avoided.

Precautions

Application should be limited to area no larger than face and neck.

Contraindications

No known contraindications.

Presentation

Seamless tube of 60 mL.

Pharmacological Actions of Principal Ingredients

Haridra (C longa) and Nimba (A indica) have shown in vitro inhibition of ROS and pro-inflammatory cytokines, two important mediators of Propionibacterium acnes-induced inflammation. Nimba (A indica) has also shown encouraging activity on skin-renewal rate in vitro studies.

Kumari (A barbadensis) exhibits anti-inflammatory activity by suppressing bacteria-induced pro-inflammatory cytokines. It is also an excellent wound-healing agent. Studies have demonstrated the antiseborrheic activity of Kumari (A barbadensis).

Jalavetasa (S tetrasperma) exhibits keratolytic activity, which helps in controlling the excessive follicular hyperproliferation and hyperkeratinization involved in acne.
Clarina® (ANTI-ACNE FACE MASK)

Controls oil. Cleanses pores. Clears acne

**Introduction**

Clarina anti-acne face mask, a topical phytopharmaceutical formulation, is recommended for the management of acne vulgaris.

**Composition**

Each gram of Clarina anti-acne face mask contains:

Exts.

Haridra (*Curcuma longa*) 1.0 mg, Kumari (*Aloe barbadensis*) 0.5 mg, Jalavetasa (*Salix tetrasperma*) 0.1 mg

**Clinical Pharmacology**

Clarina anti-acne face mask has anti-inflammatory, wound-healing, antiseborrheic, keratolytic, and antibacterial activities. Clarina anti-acne face mask inhibits the production of reactive oxygen species (ROS) by its antioxidant activity, thus reducing inflammation mediated by acne-causing bacteria. Clarina anti-acne face mask improves general skin health.

**Indications**

Acne vulgaris

**Directions for Use**

Sufficient quantity of Clarina anti-acne face mask to be applied evenly over cleansed face and neck, avoiding the area around eyes. The mask should be allowed to dry for 10 to 15 minutes and then removed with a wet sponge, after which the skin is to be washed with cool water. To be used twice a week.

**Route of Administration**

Topical

**Side Effects**

No known side effects.

**Adverse Reactions**

No clinically significant adverse reactions have been reported.

**Warning**

None

**Special Precautions**

- To be used exclusively for external application.
- Contact with eyes or open wounds to be avoided.

**Precautions**

Application should be limited to area no larger than face and neck.

**Contraindications**

No known contraindications.

**Presentation**

Seamless tube of 75 mL.

**Pharmacological Actions of Principal Ingredients**

Haridra (*C longa*) has shown in vitro inhibition of ROS and pro-inflammatory cytokines, two important mediators of *Propionibacterium acnes*-induced inflammation.

Kumari (*A barbadensis*) exhibits anti-inflammatory activity by suppressing bacteria-induced pro-inflammatory cytokines. It is also an excellent wound-healing agent. Studies have demonstrated the antiseborrheic activity of Kumari (*A barbadensis*).

Jalavetasa (*S tetrasperma*) exhibits keratolytic activity, which helps in controlling the excessive follicular hyperproliferation and hyperkeratinization involved in acne.
Clarina® 
(ANTI-ACNE CREAM)

Clears acne effectively and safely

Introduction

Clarina, a phytopharmaceutical formulation, is recommended for topical treatment of acne. Clarina causes significant reduction in the formation of blackheads and whiteheads, number of inflamed pustules, and overall inflammation. Clarina offers moisturizing and soothing effects, and significantly heals acne lesions without scar formation. Thus, Clarina clears acne effectively and safely.

Composition

Each gram of Clarina cream contains:

Exts.
Kumari (Aloe barbadensis) 200 mg, Vatada* (Prunus amygdalus) 10 mg, Matsuks (Alternanthera sessilis) 10 mg, Manjishtha (Rubia cordifolia) 5 mg

Pdrs.
Tankana 12.5 mg, Yashada bhasma 12.5 mg, Base q.s. ad 750 mg

*Also known as Badama.

Clinical Pharmacology

Clarina has antimicrobial, anti-inflammatory, wound-healing, antioxidant, astringent, and emollient and soothing effects, which act synergistically in the management of acne. The antimicrobial and anti-inflammatory properties of Clarina help control infection and inflammation in acne lesions. The cooling, soothing, and emollient properties of Clarina are useful in relieving burning sensation and pruritus, and make the skin soft and supple. Clarina’s astringent properties relieve inflammatory pain in acne lesions. Clarina also accelerates the wound-healing process.

Indications

- Acne vulgaris
- Acne rosacea

Directions for Use

After cleansing the face with Clarina anti-acne face wash gel, Clarina cream should be applied twice daily on acne lesions and inflamed surfaces until the lesions heal completely.

Adverse Effects

No adverse effects have been reported.

Contraindications

No absolute contraindications.

Special Precautions

- To be used exclusively for external application on acne lesions.
- It is advisable to confirm safety of topical application in individuals with a history of allergy. If any allergic or hypersensitivity reaction occurs, Clarina cream should be discontinued.
- Severe reaction may require conventional treatment.

Drug Interactions

No clinically significant drug interactions with commonly used drugs.

Presentation

Lamitube of 30 g packed in monocarton.

Pharmacological Actions of Principal Ingredients

Antimicrobial activity
Matsuks (A sessilis) and Kumari (A barbadensis) have potent antibacterial activities.

Manjishtha (R cordifolia) has potent antibacterial activity that helps control infection in acne lesions.

Tankana is an effective antimicrobial agent, useful in treating superficial dermal infections.

Yashada bhasma possesses antiseptic property.

Anti-inflammatory activity
Clarina has significant anti-inflammatory action that helps reduce inflammation associated with acne.

**Wound-healing activity**

Kumari (*A. barbadensis*) has wound-healing property. Yashada bhasma accelerates wound-healing and has beneficial effects in treating acne.

**Antioxidant activity**

Kumari (*A. barbadensis*) has potent antioxidant action. Matsyakshi (*A. sessilis*) contains high amounts of carotene, a known potent antioxidant. The phenolic constituents of Manjishtha (*R. cordifolia*) have potent free radical scavenging activity and inhibit lipid peroxidation.

**Astringent activity**

Manjishtha (*R. cordifolia*), Tankana, and Yashada bhasma possess significant astringent actions that cause shrinkage of mucous membranes or exposed tissues, and check discharge of blood serum or pus-like secretions of acne mass.

**Emollient and soothing effects**

Kumari (*A. barbadensis*) has a natural sunscreen effect that moisturizes skin. It is useful in burns, dermatitis, and other skin troubles. Vatada (*P. amygdalus*) has cooling, soothing, and emollient effects that relieve burning sensation and pruritus. Matsyakshi (*A. sessilis*) is applied externally for acne and pimplles. Tankana is useful in prickly heat, acne, and ulcers. Yashada bhasma helps in keeping the skin soft and supple.
Clearvital™ (ANTI-WRINKLE GEL)

Clears wrinkles, vitalizes skin

Introduction

Clearvital (anti-wrinkle gel), a topical phytopharmaceutical formulation, is recommended for the management of premature skin wrinkles that appear due to diverse causes including excessive exposure to sun, smoking, poor hydration, and hereditary factors.

Composition

Each gram of Clearvital (anti-wrinkle gel) contains:

Exts.

Rosemyrtle (Rhodomyrtus tomentosa) 0.15%
Fire-flame Bush (Woodfordia fruticosa) 0.15%

Clinical Pharmacology

Clearvital (anti-wrinkle gel) helps in the management of skin wrinkles through its elastase- and collagenase-inhibitory, collagen synthesis-enhancing, and antioxidant activities. Clearvital (anti-wrinkle gel) protects collagen and elastin, the fibers that determine the mechanical properties and structure of the skin. Clearvital (anti-wrinkle gel) prevents aging of the skin by its antioxidant activity and protects skin from oxidative damage such as photodamage, a leading cause of skin wrinkles.

Indications

- Age lines – Fine lines and aging spots
- Aging skin – Premature aging due to diverse causes
- Skin wrinkles

Directions for Use

A pea-size amount of Clearvital (anti-wrinkle gel) should be applied on cleansed skin and spread evenly over the face and neck in upward strokes until the gel is fully absorbed. Should be used twice daily.

Route of Administration

Topical

Side Effects

No known side effects.

Adverse Reactions

No clinically significant adverse reactions have been reported.

Drug interactions

No clinically significant drug interactions have been reported.

Special Precautions

To be used exclusively for external application.
Application to be limited to an area no larger than face and neck, or hands and arms.

Contraindications

No absolute contraindications.

Presentation

Seamless tube of 30 mL packed in monocarton.

Pharmacological Actions of Principal Ingredients

*R tomentosa* (Rosemyrtle) has shown excellent in vitro elastase-inhibitory activity. It also stimulates collagen synthesis.

*W fruticosa* (Fire-flame Bush) has shown in vitro collagenase-inhibitory activity. It also has antioxidant activity, which helps in the management of skin aging.
Bleminor™ (ANTI-BLEMISH CREAM)

For blemish-free skin

Introduction
Bleminor, a phytopharmaceutical formulation, is recommended for the management of blemishes or skin hyperpigmentation, characterized by dark discoloration of the skin, occurring due to various causes including excessive sun exposure, inflammatory conditions such as acne, injuries, and hormonal disturbances. Bleminor has good tolerability and is safe for long-term use.

Composition
Each gram of Bleminor cream contains:
Exts.
Yashtimadhu (Glycyrrhiza glabra) 1.70 mg, Sarja (Vateria indica) 0.80 mg, Shalmali (Bombax malabaricum) 0.10 mg, Amlaparni (Rheum emodi) 0.10 mg
Oil
Vatada (Prunus amygdalus) 10 mg

Clinical Pharmacology
Bleminor inhibits melanin synthesis and has anti-inflammatory and antioxidant activities. Bleminor has tyrosinase-inhibitory activity without causing cytotoxicity. Due to its anti-inflammatory activity, Bleminor helps in the prevention of hyperpigmentation occurring due to recurrent inflammation. Bleminor soothes and nourishes the skin and improves general skin health.

Indications
- Hyperpigmentation due to varied etiologies like sun & UV exposure, age, etc.
- Melasma
- Post-injury and post-inflammatory hyperpigmentation

Directions for Use
After cleansing the face and neck with Clarina anti-acne face wash gel, sufficient quantity of Bleminor cream should be applied over the affected areas at least twice daily. Areas around eyes, nostrils, mouth, and ears should be avoided.

Route of Administration
Topical.

Side Effects
No known side effects.

Adverse Reactions
No clinically significant adverse reactions have been reported.

Drug Interactions
No clinically significant drug interactions have been reported.

Special Precautions
- To be used exclusively for external application.
- Contact with eyes or open wounds to be avoided.

Precautions
Application should be limited to an area no larger than face and neck, or hands and arms.

Contraindications
No absolute contraindications.

Presentation
Seamless tube of 30 mL packed in monocarton.

Pharmacological Actions of Principal Ingredients
Glabridin in Yashtimadhu (G glabra) has inhibitory effect on pigmentation by inhibiting melanocyte tyrosinase activity without causing cytotoxicity. The anti-inflammatory property of glycyrrhizin in the herb helps in the management of hyperpigmentation due to recurrent inflammatory conditions such as acne. Gallic acid in Shalmali (B malabaricum) and Amlaparni (R emodi) has excellent tyrosinase-inhibitory and antioxidant activities, which inhibit melanin production. Phenols of Sarja (V indica) and oil of Vatada (P amygdalus) are natural antioxidants that help in decreasing melanin synthesis. They have proven activity in inhibiting melanogenesis. The oil from Vatada smoothens and rejuvenates the skin and is effective in improving complexion and skin tone.
Hairzone® (SOLUTION)

Prevents hair fall, promotes hair growth

Introduction

Hairzone, a phytopharmaceutical topical preparation, is recommended to treat hair loss. Hairzone reduces hair fall, improves hair growth, and enhances the tensile strength of hair. Hairzone helps enhance the hair follicle density and hair follicle count. Hairzone provides relief from symptoms of itching, dryness, and dandruff.

Composition

Each milliliter of Hairzone solution contains:

Exts.

Palasha (*Butea monosperma*) 2.5 mg, Palashabheda (*Butea parviflora*) 2.5 mg. Processed in Prasanna q.s.

Clinical Pharmacology

Hairzone has hair follicular degeneration-inhibitory, hair growth cycle-stimulatory, antimicrobial, astringent, and antioxidant actions. The two herbs present in Hairzone act synergistically to reduce inflammation and itching of the scalp, stimulate hair growth cycle, and increase hair density. They reduce the negative ratio between hair fall and hair regrowth, thus reducing hair loss.

Indications

- Hair loss of varied etiology:
  - Telogen effluvium (temporary hair loss in the resting phase of hair growth cycle)
  - Anagen effluvium (hair loss on scalp in the growth phase of hair growth cycle)
  - Alopecia areata
  - Drug-induced alopecia including chemotherapy and radiotherapy
  - Diffuse hair loss
- Hair fall due to dry and itchy scalp

Directions for Use

Adequate quantity of Hairzone solution to be sprayed over affected areas, followed by a gentle massage for 5 to 10 minutes. Best if left overnight and rinsed next morning. In severe cases, should be applied twice daily.

Adverse Reactions

None reported.

Drug Interactions

No clinically significant drug interactions have been reported.

Special Precautions

- Inflammable. Keep away from fire and children.
- Should not be applied on sensitive areas of the scalp, and fissured or injured scalp. If skin irritation persists or if swallowed accidentally, appropriate treatment to be given.
- In the event of accidental contact with eyes, advise the patient to rinse the eyes thoroughly with water.
- To be used exclusively for external application.
- May cause light staining on clothes, but can be easily rinsed off with water.

Contraindications

No absolute contraindications.

Presentation

HDPE container of 60 mL with calibrated spray packed in monocarton.

Pharmacological Actions of Principal Ingredients

Hair follicular degeneration-inhibitory and hair growth cycle-stimulatory actions

The hair growth cycle undergoes three phases: anagen, catagen and telogen, and finally, the hair sheds.

Palasha (*B monosperma*) and Palashabheda (*B parviflora*) inhibit hair follicular degeneration and extend the anagen phase. They enhance proliferation and maturation of precursor epithelial cells of the final hair strand.

Hairzone prevents chemotherapy-induced dystrophic changes in the growing follicles, and also premature regression of severely damaged follicles. Thus, it prevents massive apoptosis in the proximal hair bulb.
Antimicrobial action
Palasha (B. monosperma) exhibits antifungal and antiviral activities, and also has significant bactericidal effect. Palashabheda (B. parviflora) has antimicrobial action.

Astringent action
Astringent solutions are used for the relief of minor skin irritations such as those resulting from superficial cuts, allergies, insect bites, or fungal infections. Palasha (B. monosperma) has astringent action.

Antioxidant action
Palasha (B. monosperma) has potent free radical scavenging action, and is proven effective in promoting the therapeutic activity of Hairzone solution.
**Introduction**

Talekt, a phytopharmaceutical formulation, is recommended for various skin disorders such as disorders of sebaceous glands, bacterial infections of skin, infective and allergic dermatitis, systemic mycoses, parasitic infections, and psoriasis. Talekt enhances the immune response to prevent repeated relapses. Talekt is safe for short- and long-term treatment.

**Composition**

Each Talekt capsule contains:

**Pdrs.**
Haridra (*Curcuma longa*) 36 mg
Aragvadha (*Cassia fistula*) 36 mg

**Exts.**
Nimba (*Azadirachta indica*) 32 mg, Guduchi (*Tinospora cordifolia*) 32 mg, Triphala 31 mg, Vidanga (*Embelia ribes*) 31 mg, Bhringaraja (*Eclipta alba*) 31 mg, Yavatikt*a* (*Andrographis paniculata*) 31 mg

Each 5 mL of Talekt syrup contains:

**Exts.**
Aragvadha (*C fistula*) 18 mg, Nimba (*A indica*) 16 mg, Guduchi (*T cordifolia*) 16 mg, Triphala 15.5 mg, Vidanga (*E ribes*) 15.5 mg, Bhringaraja (*E alba*) 15.5 mg, Yavatikt*a* (*A paniculata*) 15.5 mg

*a*Also known as Kalamegha.

**Clinical Pharmacology**

Talekt has antimicrobial, antiallergic, wound-healing, anti-inflammatory, antioxidant, detoxifying, hepatoprotective and immunostimulatory actions, which synergistically complement the renormalization of disturbed physiological metabolic processes.

Talekt’s antimicrobial actions combat the dermal infections due to gram-positive and gram-negative bacteria. The anti-allergic property of Talekt helps to control pruritus associated with dermal infections and allergies. The detoxifying property of Talekt helps in the removal of toxic metabolic products, thus providing additional therapeutic effect. Talekt also enhances the immune response, thus preventing repeated relapses.

**Indications**

- Disorders of sebaceous glands
  - Infective and non-infective acne vulgaris
  - Seborrhea
  - Rosacea
- Bacterial infections of skin
  - Furuncles, carbuncles, and boils
  - Paronychia
- Dermatitis
  - Infective
  - Allergic
- Systemic mycoses
  - Ringworm
  - Candidiasis
- Parasitic infections of skin
  - Scabies
  - Pediculosis
- Papulosquamous disorders
  - Psoriasis

**Dosage**

Capsule: Two capsules twice daily.

Syrup:
- Children: One teaspoonful twice daily.
- Adults: Two teaspoonfuls twice daily.

**Adverse Effects**

No adverse effects have been reported.

**Contraindications**

No absolute contraindications.

**Drug Interactions**

No clinically significant drug interactions have been reported.
Presentation
Capsule: Sealed packs of 60 capsules.
Syrup: Pilfer-proof bottles of 120 mL.

Pharmacological Actions of Principal Ingredients

Antimicrobial action
Haridra (C longa), Nimba (A indica), Vidanga (E ribes), Yavatikta (A paniculata), and Guduchi (T cordifolia) have remarkable antimicrobial activities against common bacteria.
Haridra (C longa) and Nimba (A indica) have antiviral properties.

Anti-allergic action
Haridra (C longa) significantly inhibits OVA-induced allergy that extends antiallergic action.
Guduchi (T cordifolia) also has potent antiallergic activity.

Wound-healing action
Haridra (C longa) and Aragvadha (C fistula) help in the wound-healing process.
In an experiment, Vidanga (E ribes) showed increase in cross-linking of collagen fibers and absence of monocytes, which proves its wound-healing effect.

Anti-inflammatory action
Haridra (C longa), Nimba (A indica), Bhringaraja (E alba), and Yavatikta (A paniculata) have remarkable systemic anti-inflammatory activities, useful in various dermatological disorders.

Antioxidant action
Haridra (C longa), Nimba (A indica), Guduchi (T cordifolia), and Yavatikta (A paniculata) have potent antioxidant activities.

Detoxifying action
Haridra (C longa), Nimba (A indica), Triphala, and Yavatikta (A paniculata) are used as detoxifiers, and are beneficial in different skin diseases.

Hepatoprotective action
Bhringaraja (E alba) is enriched with hepatoprotective action and is useful in various skin diseases.

Immunostimulatory action
Haridra (C longa), Nimba (A indica), Guduchi (T cordifolia), Bhringaraja (E alba), and Yavatikta (A paniculata) have immunostimulatory activities.
HiOra-K (Toothpaste)
For comprehensive management of sensitive teeth and gums

Introduction
HiOra-K toothpaste, a herbomineral dental formulation, is recommended for use in cases of sensitive teeth. HiOra-K toothpaste brings about an enhanced desensitizing effect on sensitive teeth. HiOra-K toothpaste helps in remineralization of tooth surfaces and reduces the perception of pain. HiOra-K toothpaste contributes to the maintenance of overall oral health and hygiene.

Composition
Each gram of HiOra-K toothpaste contains:

Oils
Tvak (Cinnamomum zeylanicum) 2.5 mg, Lavanga (Syzygium aromaticum) 2.5 mg

Exts.
Palakya (Spinacia oleracea) 10.0 mg, Triphala 6.0 mg, Trikatu 4.0 mg

Pdrs.
Suryakshara* 30.0 mg, Yashada bhasma** 10.0 mg
*Potassium nitrate, ** Zinc oxide

Clinical Pharmacology
HiOra-K toothpaste has remineralizing, protective, anti-inflammatory, analgesic, anaesthetizing, and antimicrobial activities. HiOra-K toothpaste treats the sensitive teeth by forming a protective layer over them and by remineralization of teeth. It also has a desensitizing activity which reduces tooth pain.

HiOra-K toothpaste helps control oral bacterial population and maintains good oral health and hygiene.

Pharmacological Actions of Principal Ingredients
Suryakshara and Yashada bhasma are known for their ability to remineralize tooth surfaces.

S oleracea contains natural oxalate compounds which help in forming phytocomplexes that occlude dentinal tubules and block the transmission of pain from the tooth surface to the tooth nerve. These oxalate compounds produce protective films on the molars, thus helping to prevent tooth destruction.

Triphala contains polyphenols that have a strong inhibitory activity against PMN-induced matrix metalloproteinase, involved in severe gum disease (periodontitis).

Trikatu contains piperine which has anti-inflammatory activity and helps in reducing gingivitis (gum inflammation).

S aromaticum has eugenol that has analgesic and mild anaesthetizing effect on sensitive nerve endings. It also has antibacterial activity.

C zeylanicum has cinnamaldehyde which has antimicrobial effect on oral bacteria that helps in reducing caries and gum disease, the causes of sensitive teeth.

Indications
• Dentinal hypersensitivity
• Periodontitis
• Receding gums
• Post scaling periodontal pockets

Directions for Use
Brush twice daily till symptoms subside or as directed by the doctor.

Side Effects
No known side effects.

Adverse Reactions
No clinically significant adverse reactions have been reported.

Warning
None

Precautions
For dental use only.

Contraindications
No known contraindications.

Presentation
Lamitubes of 50 g and 100 g.
HiOra™-Shine (Toothpaste)

Herbal whitening toothpaste

Introduction
HiOra-Shine toothpaste is a phytopharmaceutical dental formulation, which helps in reducing tooth discoloration and enhances tooth whitening. HiOra-Shine toothpaste acts through multiple approaches which ensure tangible results without damaging the enamel.

Composition
Each gram of HiOra-Shine toothpaste contains:

Exts.
Lodhra (Symplocos racemosa) 5.0 mg, Draksha (Vitis viniíera) 5.0 mg

Oils
Tvak (Cinnamomum zeylanicum) 1.25 mg, Lavanga (Syzygium aromaticum) 1.25 mg

Pdrs
Anannasa (Ananas comosus) 12.5 mg, Erandakarkati (Carica papaya) 1.7 mg

Clinical Pharmacology
HiOra-Shine toothpaste has antiplaque, antibacterial, astringent, and teeth whitening properties. It effectively fights plaque with the help of phyto enzymes. HiOra-Shine toothpaste ensures whiter and shinier teeth without causing any damage to the enamel.

Pharmacological Actions of Principal Ingredients
C papaya and A comosus have proteolytic enzymes which help in removal of plaque, the leading cause of tooth discoloration and thereby act as nonabrasive whiteners. Oleanolic acid in V viníera inhibits the growth of the oral bacteria Streptococcus mutans which leads to dental caries, another common cause of tooth discoloration. Cinnamaldehyde present in C zeylanicum and Eugenol present in S aromaticum exhibit antibacterial activity against oral bacteria. S racemosa has an excellent astringent activity.

Indications
• Tooth discoloration
• Plaque

Directions for Use
Brush twice daily or as directed by the doctor.

Side Effects
No known side effects.

Adverse Reactions
No clinically significant adverse reactions have been reported.

Warning
None

Precautions
For dental use only.

Contraindications
No known contraindications.

Presentation
Lamitubes of 50 g and 100 g.
HiOra-K (Mouthwash)

For sensitive teeth and halitosis

Introduction
HiOra-K mouthwash, a herbomineral dental formulation, is recommended for use in cases of sensitive teeth. It helps in reducing the pain associated with sensitive teeth.

HiOra-K mouthwash also helps in the remineralization of teeth and acts against various strains of oral pathogens, which can cause gum and tooth disease. It maintains oral hygiene and ensures strong and healthy teeth and gums.

Composition
Each gram of HiOra-K mouthwash contains:

Exts.
Tulasi (*Ocimum sanctum*) 0.3 mg, Lavanga (*Syzygium aromaticum*) 0.1 mg

Oils
Jatiphal (Myristica fragrans) 0.5 mg, Misreya (*Foeniculum vulgare*) 0.5 mg

Pdrs.
Suryakshara* 50.0 mg (*Potassium nitrate), Peppermint satva (*Mentha spp.*) 1.0 mg

Clinical Pharmacology
HiOra-K mouthwash has remineralizing, desensitizing, antimicrobial, analgesic, and mouth freshening activities. It protects teeth against various strains of bacteria which cause periodontitis leading to sensitive teeth.

HiOra-K mouthwash also helps in restoring the mineral composition of the teeth and strengthens them. HiOra-K mouthwash helps in maintaining optimum health of the gums and teeth.

Pharmacological Actions of Principal Ingredients
Suryakshara helps in remineralization of enamel. *Mentha sylvestris* and *M fragrans* have antimicrobial activity against certain oral pathogens, which can lead to gum disease, a major cause of sensitive teeth. *F vulgar* is the source of an essential oil, which has anticandidal activity and antimicrobial activity against gram positive bacteria such as *Staphylococcus aureus* that cause periodontitis which lead to sensitive teeth. *O sanctum* has antimicrobial activity against microorganisms like *S aureus*. *S aromaticum* has eugenol, which has excellent pain relieving activity and mild anaesthetizing effect.

Indications
- Dental hypersensitivity
- Periodontitis
- Receding gums
- Post scaling periodontal pockets
- Halitosis

Directions for Use
Rinse mouth thoroughly for 30 seconds with 15 mL (3 teaspoonfuls/one capful) and expel. Use twice daily or as directed by the doctor.

Side Effects
No known side effects

Adverse Reactions
No clinically significant adverse reactions have been reported.

Warning
None

Precautions
For dental use only. Not to be swallowed.

Contraindications
No known contraindications.

Presentation
Bottles of 215 mL.
**Introduction**

HiOra (Mouthwash–Regular), a phytopharmaceutical dental preparation, is formulated to maintain and enhance oral health and hygiene, by providing antiseptic, refreshing, and antimicrobial activities. The polyherbal composition provides anti-plaque activity, which is helpful in the management of common oral conditions like caries, gingivitis, and halitosis (bad breath), which generally manifest subsequent to plaque formation.

**Composition**

Each gram of HiOra (Mouthwash–Regular) contains:

**Exts.**

Bibhitaka (*Terminalia bellirica*) 10.0 mg, Nagavalli (*Piper betle*) 10.0 mg, Pilu (*Salvadora persica*) 5.0 mg

**Oils**

Gandhapura Taila (*Gaultheria fragrantissima*) 1.2 mg, Ela (*Elettaria cardamomum*) 0.2 mg

**Pdrs.**

Peppermint satva (*Mentha spp.*) 1.6 mg, Yavani satva (*Trachyspermum ammi*) 0.4 mg

**Clinical Pharmacology**

HiOra (Mouthwash–Regular) has antimicrobial, antiplaque, antiseptic, analgesic, and refreshing properties. It has active herbal ingredients that act against several strains of oral bacteria and fungi and prevent gum and tooth disease. It also helps relieve pain associated with caries and gingivitis. HiOra (Mouthwash–Regular) gives a refreshing feeling in the mouth and helps overcome the embarrassing problem of halitosis.

**Pharmacological Actions of Principal Ingredients**

*S. persica* exhibits excellent antimicrobial activity against oral pathogens such as *Staphylococcus aureus*, *Streptococcus mutans*, *Streptococcus faecalis*, *S pyogenes*, *Lactobacillus acidophilus*, *Pseudomonas aeruginosa*, and *Candida albicans*, thus helpful in minimizing the plaque formation. *T. bellirica* has encouraging activity against *S. aureus*.

*P. betle* inhibits common oral bacteria like *Streptococcus sanguinis*, *S. mitis*, and *Actinomyces* species. Aqueous extract of *P. betle* has shown plaque inhibitory activity in vitro studies. *G. fragrantissima* is the source of an essential oil, which is used for its antimicrobial activity. *E. cardamomum* has inhibitory activity on oral microbial population in vitro. *T. ammi* gives an essential oil, which has significant analgesic action which may be attributed to the presence of thymol. This is helpful in the management of pain associated with common oral conditions like caries and gingivitis. *G. fragrantissima*, *E. cardamomum*, and *T. ammi* impart a fragrant, refreshing effect and help in the management of halitosis.

**Indications**

- Plaque
- Tartar
- Gingivitis
- Halitosis

**Directions for Use**

Rinse mouth thoroughly for 30 seconds with 15 mL (3 teaspoonfuls/one capful) and expel. Use twice daily or as directed by the doctor.

**Side Effects**

No known side effects.

**Adverse Reactions**

None reported.

**Warning**

None

**Precautions**

For dental use only. Not to be swallowed.

**Contraindications**

No known contraindications.

**Presentation**

Bottles of 215 mL.
HiOra-GA
Gum astringent gel

Introduction
HiOra-GA gel, a phytopharmaceutical dental formulation, is recommended for strengthening gums and for the prevention and management of painful gum disorders, gingivitis and periodontitis. It arrests bleeding of gums, reduces inflammation and pain associated with gum disease, and promotes wound healing. HiOra-GA also helps overcome the embarrassing problem of halitosis or bad breath. It has antibacterial properties and helps maintain healthy gums and teeth.

Composition
Each gram of HiOra-GA gel contains:

Oils
Jatipala (Myristica fragrans) 1.5 mg

Exts.
Triphala 20.0 mg, Asana (Pterocarpus marsupium) 12.0 mg, Arjuna (Terminalia arjuna) 8.0 mg

Clinical Pharmacology
HiOra-GA gel has hemostatic, astringent, antibacterial, anti-inflammatory, analgesic, mouth-freshening, and wound healing actions. It inhibits the action of PMN-induced matrix metalloproteinases involved in adult periodontitis. HiOra-GA strengthens gums, heals wounds, arrests bleeding, reduces bad breath, and works against bacteria growing in the oral cavity. It is responsible for maintaining healthy and strong gums and teeth.

Pharmacological Actions of Principal Ingredients
Triphala contains polyphenols, which have a strong inhibitory activity against PMN-induced matrix metalloproteinase, involved in adult periodontitis. P marsupium is known for its astringent action on gums, which strengthens gums and arrests bleeding. It also exhibits antibacterial activity against bacterial strains such as Staphylococcus aureus and Pseudomonas aeruginosa which predispose to periodontitis. T arjuna contains tannins, which have excellent wound healing and antibacterial activity against gram positive bacteria such as S aureus and P aeruginosa, causes of periodontitis. M fragrans has eugenol, which shows significant antibacterial activity against oral bacteria and reduces bad breath.

Indications
- Bleeding, spongy and painful gums (gingivitis)
- Halitosis

Directions for Use
Massage gently a sufficient quantity over the affected areas of gums or as directed by the doctor.

Side Effects
No known side effects.

Adverse Reactions
No clinically significant adverse reactions have been reported.

Warning
None

Precautions
For dental use only.

Contraindications
No known contraindications.

Presentation
Pilfer-proof pack of 15 mL.
HiOra-SG
The healing stoma gel

Introduction
HiOra-SG gel is a phytopharmaceutical dental formulation, which helps in the management of painful mouth ulcers. It has wound healing and immunity enhancing activities, which help in healing mouth ulcers and in preventing their recurrence. HiOra-SG gel also acts against oral pathogens, which damage oral mucosa and relieves pain and inflammation associated with the ulcers.

Composition
Each gram of HiOra-SG gel contains:

Exts.
Jati (Jasminum grandiflorum) 20.0 mg, Yashtimadhu (Glycyrrhiza glabra) 8.0 mg, Triphala 6.0 mg, Punarnava (Boerhavia diffusa) 6.0 mg

Oils
Lavanga (Syzygium aromaticum) 5.0 mg, Vanatulasi (Ocimum basilicum) 3.3 mg, Nimba (Azadirachta indica) 1.7 mg

Clinical Pharmacology
HiOra-SG gel has ulcer-healing, anti-allergic, antibacterial, analgesic, and anti-inflammatory properties. It relieves inflammation and pain associated with mouth ulcers and heals the damaged mucosal lining of the oral cavity.

HiOra-SG gel also prevents oral pathogenic bacteria from proliferating and causing mucosal damage. It enhances the immune system and provides protection against recurrence of mouth ulcers.

In addition, HiOra-SG gel inhibits IgE production by lymphocytes and thus providing relief from allergic manifestations.

Pharmacological Actions of Principal Ingredients
Deglycyrrhizinated licorice from G glabra has both ulcer-healing effect as well as antiallergic effect on IgE, which is an important factor in triggering off the inflammatory process in the oral mucosa. Triphala is rich in tannins and phenolic constituents, which have ulcer healing activity. J grandiflorum also exhibits excellent wound healing activity. Eugenol present in S aromaticum and O basilicum has an analgesic and mild anaesthetizing effect on sensitive nerve endings and is thus helpful in the management of pain associated with mouth ulcers.

O basilicum, A indica, G glabra, and alkaloids from the leaves of J grandiflorum have antibacterial action against certain bacteria which are commonly found in denture induced stomatitis. Alkaloids from B diffusa have anti-inflammatory activity. B diffusa also exhibits excellent immunomodulatory activity, which helps in correcting immune dysregulation, an important cause in the formation of recurrent aphthous ulcers.

Indications
• Mouth ulcers
• Pain due to teething
• Denture irritation

Directions for Use
Take sufficient quantity of the gel on the tip of the clean finger and apply gently over the affected areas. Repeat application three to five times or as directed by the doctor.

Side Effects
No known side effects.

Adverse Reactions
No clinically significant adverse reactions have been reported.

Warning
None

Precautions
For local application in the mouth only.

Contraindications
No known contraindications.

Presentation
Lamitubes of 10 g.
Skin Care

The skin as the largest organ of the body performs multiple functions. Consisting of three layers, the skin acts as a barrier against harmful elements of the external environment like dirt, bacteria, and other germs entering your body. It plays a vital role in regulating the body temperature. Its millions of nerve endings help us identify hot, cold, hard, sharp, or dull sensations.

What are the most common types of skin infections?

There are various skin infections and diseases that range from mild to dangerous, some of which include:

- Acne
- Dermatitis
- Eczema
- Pigmentation
- Psoriasis
- Rosacea
- Vitiligo
- Warts
- Melanoma

Can I prevent skin infections?

Yes. Adopting clean habits and a regular skin care regime can definitely prevent skin infections and contribute to good and healthy skin.

- Maintain good hygiene and keep your hands clean at all times. Always wash your hands before and after meals, after using toilet and before and after attending to any wounds. Take special care to keep your feet clean too, as germs tend to have an easy access into your body through them.
- Educate yourself about the type of skin you have. Take extra care to keep your skin moisturized if it is dry or cracked, more so during winters.
- Try to include a good portion of fruits and vegetables in your diet. Keep yourself well hydrated by drinking at least 8 glasses of water/ fluids during the day.

Skin infections and diseases have seen a rapid increase during the past years, and become a subject of major health concern.

What factors trigger a skin infection?

Most common skin problems occur due to bacterial, yeast, or fungal infections, and other causes like allergies or sunburn. At times, the cause could also be an autoimmune response.

Skin diseases usually occur in mild form, the most common being pimples and acne, which threaten the aesthetic look more rather than the health, at least in the early stages. Some skin infections may even take a serious form if left untreated, and become difficult to treat at a later stage.

What symptoms indicate a skin infection?

The initial signs that may indicate a skin infection are warmth, tenderness, pain, discoloration, itchiness followed by a rash, drainage of pus, or other discharge from wounds on the skin surface.
• Keep cuts, abrasions, and burns clean and covered with a bandage until they are healed. Watch carefully for any signs of infection.
• Avoid sharing personal items such as clothes, towels, hairbrush, and razors through which an infection can be easily contacted.
• Avoid too much use of cosmetic products on your skin as the chemicals in them may cause a reaction, rash, or an infection. Natural and mild products will be much safer.
• Avoid excessive exposure to the sun, especially during peak hours of the day. If going out, apply sunscreen of a high SPF (25 to 30) on the exposed areas of the skin.

How can skin infections be treated?
Skin problems should not be neglected, as treatment and cure may become difficult at a later stage. The best option always is to act as soon as possible.
Though there are innumerable methods and remedies available today for different skin conditions, natural methods of treatment, especially pertaining to skin, are accepted in a big way today.

Dear Doctor,
We hope you found this article useful for your patients. You can order for FREE reprints of this article (25, 50, 75, or 100 nos.), by using the tear-out card enclosed in this issue, and use them as patient information leaflets in your clinic.

– Editor
Ability of Optical Coherence Tomography to Detect Caries Beneath Commonly Used Dental Sealants

Holtzman JS, et al.

Background and objective
The onset and progression of early tooth decay is often preventable with dental sealants. However, occasionally decay progresses underneath the sealant. Current technology does not permit monitoring of potential lesion progression or arrest. Dental sealants themselves mask the visual cues that identify early tooth decay, and radiographs are not sufficiently sensitive. Therefore, clinicians can be reluctant to use dental sealant. The objective of this ex vivo study was to evaluate the ability of dentists to detect decay beneath commonly used dental sealants using optical coherence tomography (OCT) imaging.

Study Design
Forty extracted teeth were divided into equal groups of carious and non-carious teeth, as determined by visual inspection. After radiographs and OCT imaging, teeth were randomly assigned for sealant placement with one of four commonly purchased dental sealants: Clinpro™, Fuji Triage™, Embrace Wet Bond™, and Delton™. Following sealant placement, teeth were radiographed, imaged with OCT, sectioned, examined histologically, and scored as healthy/not healthy. OCT and radiographic images were scored separately. The gold standard was histopathological diagnosis from the serial sections. Cohen’s kappa, sensitivity, negative predictive value, and positive predictive value were computed for all measures.

Results
After 90 minutes training, pre-standardized dentists were able to detect tooth decay more accurately using OCT than with visual or radiographic examination. Detection using OCT was somewhat better prior to sealant placement than afterwards. This effect varied in size depending on the type of sealant used. Radiographic diagnosis was also less accurate after sealant placement. Of the four dental sealants, Delton provided excellent positive predictive value and the best post-sealant negative predictive values.

Conclusion
In this ex vivo study, dentists were able to detect tooth decay beneath four commonly used dental sealants based on OCT images. Clinical investigations are now underway to determine the usefulness of this approach in vivo.

A Novel Fractional Microplasma Radio-frequency Technology for the Treatment of Facial Scars and Rhytids

Halachmi S, et al.

Introduction
Fractional ablative and non-ablative lasers have gained popularity in the treatment of acne scars and rhytids due to their efficacy and improved tolerability. Plasma and radio-frequency (RF) have also emerged as methods for ablative or non-ablative energy delivery. We report preliminary experience with a novel fractional microplasma RF device for the treatment of facial acne scars and rhytids.

Methods
Sixteen patients with facial acne scars or rhytids were treated at 4-week intervals. Treatment parameters were titrated to an immediate end point of moderate erythema. The clinical end point for cessation of treatment was the attainment of satisfactory clinical results. Results were monitored photographically up to 3 months after treatment.

Results
Acne scars showed marked improvement after two to four treatments. Facial rhytids demonstrated reduced depth after two treatments and marked improvement after four treatments. Treatment was well-tolerated by all participants, with transient erythema and short downtime. These results provide initial evidence for the safety and effectiveness of fractional microplasma RF as a low-downtime and well-tolerated modality for the treatment of acne scars and facial rhytids.
Liver Disorders During Pregnancy and Their Management

Mitra AK, et al.


**Introduction**

During pregnancy, human body undergoes several changes in the process of its adaptation to the growing fetus. Although these changes are physiological, there is potential for morbidity and mortality to both the mother and the fetus. Liver is the site of many important metabolic and synthetic functions of the body. In normal pregnancy, the liver is not palpable. Due to hemodilution, biochemical tests may reveal mild increase in liver function tests. Abnormal liver tests occur in 3% to 5% of pregnancies, with many potential causes, including coincidental liver disease (most commonly viral hepatitis or gallstones) and underlying chronic liver disease (Table 1). Wide multitudes of liver diseases are encountered during pregnancy. For example, liver could be the target of diseases specific to pregnancy, such as intrahepatic cholestasis of pregnancy and acute fatty liver of pregnancy, and there are no available means to predict with certainty how and when such illnesses may occur. In tropical countries like India, morbidity and mortality due to liver diseases during pregnancy is very high. In addition, morbidity is more likely in the presence of a preexisting liver disease as in autoimmune hepatitis or when a new onset liver disease occurs during pregnancy as in herpes simplex hepatitis. Several physiologic changes occur during pregnancy and could pose difficulty in evaluating hepatobiliary function because they may be misinterpreted as pathological. For example, the blood volume expands during pregnancy due to retention of salt and water. This induces a state of hemodilution, an increase in cardiac output, and a reduction in systemic vascular resistance and systemic blood pressure. These changes are highest during the second trimester and reduce until delivery. Consequently serum levels of uric acid, albumin, total protein, and hematocrit are decreased. On the other hand, serum alkaline phosphatase levels may be elevated three to four folds due to placentation and serum levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), \( \gamma \)-glutamyl transpeptidase (GGT),

<table>
<thead>
<tr>
<th>Increase</th>
<th>Blood volume, heart rate, and cardiac output increase by 35% to 50% and are highest at 32 weeks. Further increase by 20% occurs during twin pregnancies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Alkaline phosphatase levels increase 3 to 4 folds</td>
</tr>
<tr>
<td></td>
<td>Clotting factors</td>
</tr>
<tr>
<td></td>
<td>Ceruloplasmin</td>
</tr>
<tr>
<td></td>
<td>Transferrin</td>
</tr>
<tr>
<td></td>
<td>ESR, CRP, C3 and C4</td>
</tr>
<tr>
<td>Decrease</td>
<td>Gallbladder contractility</td>
</tr>
<tr>
<td></td>
<td>Hemoglobin</td>
</tr>
<tr>
<td></td>
<td>Uric Acid</td>
</tr>
<tr>
<td></td>
<td>Albumin and total protein</td>
</tr>
<tr>
<td></td>
<td>Antithrombin III and protein S</td>
</tr>
<tr>
<td></td>
<td>Systemic vascular resistance</td>
</tr>
<tr>
<td></td>
<td>Modest decline in blood pressure</td>
</tr>
<tr>
<td></td>
<td>Modest or no decline in platelet levels</td>
</tr>
<tr>
<td>No Change</td>
<td>Liver transaminase levels (AST, ALT)</td>
</tr>
<tr>
<td></td>
<td>GGT</td>
</tr>
<tr>
<td></td>
<td>Bilirubin level</td>
</tr>
<tr>
<td></td>
<td>Prothrombin time</td>
</tr>
<tr>
<td></td>
<td>Blood flow to the liver</td>
</tr>
</tbody>
</table>
Liver Disorders During Pregnancy and Their Management

Liver Disorders During Pregnancy

Liver dysfunction can appear at any point of pregnancy and causes great anxiety to patients, their family, and sometimes their medical attendants. Many of these diseases have been identified to be responsible for morbidity and mortality (Figure 1).

Viral Hepatitis

Acute viral hepatitis is the most common cause of jaundice during pregnancy. The outcome is usually, but not always, benign except in viral hepatitis E and herpes simplex hepatitis. Infections with viral hepatitis during pregnancy may not always affect the outcome of the pregnancy; however, transmission to the newborn is always a concern. Diagnosis of viral hepatitis during pregnancy is not different from the diagnosis in nonpregnant state. Viral hepatitis during pregnancy has been a subject of continuing interest and controversy. Reports from Europe and US have shown the course of viral hepatitis during pregnancy to be in no way different from nonpregnant women. However, studies conducted in India, Iran, and Africa have found the incidence of fulminate hepatitis to be higher during pregnancy. Malnutrition superimposed on the normal demands of pregnancy and inversion of T and B lymphocytes in early pregnancy have been postulated to be the contributing factors. In a study of 97 consecutive pregnant patients with acute viral hepatitis, mortality was observed in 18 patients. Mortality rate due to viral hepatitis during pregnancy ranges between 30% and 45% and it may be as high as 70%. Majority of cases die undelivered. Besides, greater mortality and morbidity has been noted during epidemics of viral hepatitis, especially in developing countries. This may indicate that malnutrition is involved. About 6% of women with hepatitis may develop gallstones during their pregnancy. The problem of liver diseases during pregnancy is more in women from low socioeconomic group living in unhygienic surroundings and drinking unfiltered water.

Hepatitis A virus infection

Acute hepatitis A during pregnancy is self limited and maternal fetal transmission is very rare and reported in only few cases. Transmission may occur if delivery takes place during the incubation period because of viral shedding and contamination during vaginal delivery. The risk of premature labor may be increased in women who are seriously ill during the third trimester. Treatment of hepatitis A is supportive. IgG antibodies to HAV infection are passively transmitted to the newborn, which may lead to protection of the infant in the first several months of life. A recent study evaluating the impact of acute hepatitis A on pregnancy over consecutive admission of 79,000 patients over a period of 25 years, reported that acute Hepatitis A infection during pregnancy was associated with high risk of maternal complication and preterm labor. Generally, safety of Hepatitis A vaccine during pregnancy has not been determined.

Hepatitis B virus infection

If acute hepatitis B occurs during pregnancy, the outcome of the pregnancy is similar to that of the nonpregnant state. A major concern is the transmission of hepatitis B to the fetus. The risk of transmission is greatest (90%) when the mother is positive for hepatitis B envelope antigen (HBeAg) and has high viral deoxyribonucleic acid (DNA) levels and when maternal infection occurs in the third trimester. Average rate of transmission is 10% when HBeAg is negative or maternal infection occurs in the first trimester. Perinatal and early childhood contaminations as a result of the stability of hepatitis B virus (HBV) in the environment could result in an estimated 30% to 40% of chronic infections. HBV is viable for more than 7 days at room temperature on environmental surfaces and at concentrations as low as 10^2 to 10^3 virions/mL even in the absence of visible blood.

Hepatitis C infection

It is a rare problem during pregnancy. The rate of vertical transmission is less than 5%. Spontaneous resolution of infection may occur. Sometimes, complications may be severe.
Hepatitis delta virus infection
This is the smallest hepatotropic RNA virus that is dependent on HBV for its replication. Coinfection of HBV and hepatitis D virus (HDV) together can lead to fulminant hepatic failure. The risk for HDV transmission via breastfeeding is unknown.

Hepatitis E virus infection
This is a nonenvelope RNA virus responsible for large epidemics in Asia, Middle East, Mexico, and Africa. It spreads via the fecal–oral route, and has an incubation period of 8 to 10 weeks. The infection is usually self-limited and does not result in chronic disease. The incidence of acute viral hepatitis E is similar in pregnant and nonpregnant women. However, pregnant women are at high risk for acute and fulminant hepatitis. Mortality rate due to hepatitis E in nonpregnant women is 0.65%, whereas it may reach up to 25% in pregnant women.

The mortality rate is highest when HEV infection occurs in the late stages of pregnancy. Vertical transmission to the newborn occurs in 50% of the cases if mothers are positive for HEV PCR at the time of delivery. Premature deliveries, miscarriages, and stillbirths have been reported in patients with HEV infection during pregnancy.

Acute Fatty Liver of Pregnancy
Acute fatty liver of pregnancy (AFLP) is a potentially fatal condition of the third trimester with an estimated incidence of one case per 13,000 pregnancies. AFLD may affect pregnant women of any age but is most commonly reported in primiparous women aged >30 years and in women with multiple fetal gestations and/or a male fetus.

Initial symptoms are typically nonspecific and include nausea, vomiting, epigastric, or right upper quadrant abdominal pain mimicking biliary tract disease or acute pancreatitis. Jaundice is a late sign and typically occurs one to two weeks after the onset of symptoms. Pruritus is uncommon and suggests an alternative diagnosis such as intrahepatic cholestasis of pregnancy. Moderate elevations in the levels of liver enzymes (ALT, AST), bilirubin, serum creatinine, and uric acid are common. The modest abnormality of aminotransferase can be misleading and may not accurately reflect the degree of liver injury. Frank liver failure associated with hepatic encephalopathy, jaundice, renal failure, hypoglycemia, and coagulopathy may present as early as 2 weeks after the onset of symptoms. The etiology and pathogenesis of AFLP are not clearly understood. It is proposed that the underlying mechanism of AFLP consists of a fatty acid oxidation disorder. Fatty acid oxidation disorders are autosomal recessive disorders involved in the transport and oxidation of fatty acids in the mitochondrion. Byproducts of fatty acid oxidation provide the energy necessary for the growth of the fetus. AFLP occurs in women who have fatty acid oxidation disorder, of which the most common is the inherited deficiency of the enzyme long chain 3-hydroxyacyl-coA dehydrogenase (LCHAD). This enzyme is involved in the final step of beta-oxidation of fatty acids in the mitochondrion of the hepatocyte. Deficiency of this enzyme is associated with the accumulation of fatty acids in the cell with a resultant lack of energy fuel necessary for the growth of the fetus. In the last trimester of pregnancy, the metabolic demands of the fetus increase, and when affected mothers with one defective allele for LCHAD are pregnant with an affected baby (with 2 alleles, one allele inherited from each parent), acute fatty liver of pregnancy will ensue. Although it is not proven, additional triggering factors such as drugs (aspirin and nonsteroidal medications) may further impair beta-oxidation.

Autoimmune Hepatitis
Autoimmune hepatitis (AIH) is a progressive liver disease that predominantly affects women of all ages. Women with AIH can become pregnant and carry successful pregnancies to term with the expectation of delivering a normal baby. However the disease activity is unpredictable during pregnancy. Attenuation of disease activity and spontaneous remissions have been reported due to the immune tolerance induced by pregnancy. Flares of the disease have also been described in 11% of cases during pregnancy and up to 50% in the postpartum period. Maternal deaths due to liver decompensation, variceal bleeding, and portopulmonary hypertension have been reported especially when treatment is withdrawn. Preterm delivery and fetal loss occur in 24% of the cases.

Primary Biliary Cirrhosis and Primary Sclerosing Cholangitis
Few cases of pregnancy have been described in women with primary biliary cirrhosis (PBC). This is partly due to the later age at presentation of the disease. Although reports suggest an increased risk for premature delivery, stillbirths, and liver failure, there are no good data on the outcome of pregnancy in women with PBC. When pregnancy occurs, PBC may induce pruritus. Diagnosis and management are similar to the nonpregnant state.
Liver Disorders During Pregnancy and Their Management

There is no indication for termination of pregnancy in these patients.

**Gallstone Disease During Pregnancy**

The risk for sludge and gallstone formation doubles by the end of gestation in comparison with the first trimester (10% vs 5%), and it is further increased with parity. Gallstones are found in 6.5% to 8.4% of nulliparous women, and 18.4% to 19.3% of women with two or more pregnancies. Most of the sludge and one-third of gallstones disappear spontaneously after delivery without resulting in any symptoms. Acute cholecystitis and gallstone pancreatitis rarely occur during pregnancy (<1/8000) but they require immediate attention. Medical intervention is often effective.

Liver disease during pregnancy may manifest as a benign entity that resolves with delivery of the fetus without any consequences, or a more serious disease that could adversely affect the overall well-being of both the mother and the baby potentially resulting in liver failure and death. Although there are no available clinical markers to predict with certainty how and when such situations may be encountered, prior history of liver disease, knowledge of the patient’s risk factors for liver disease, and the gestational age of the pregnancy are the best guides to a differential diagnosis.

**Drug-Induced Hepatitis**

Although pregnancy is not reported to increase the susceptibility to drug-induced liver disease, drug hepatotoxicity should always be considered in pregnant women taking prescription or nonprescription medications.

Pregnant women can react to drug causing jaundice in an exaggerated way as manifested with the use of tetracycline, anesthetic agents, and sulfonamides. Antitubercular drugs are also known to induce drug related hepatitis. Therefore, selection of drug therapy during pregnancy needs to be carefully made.

**Management**

Liver disease changes a normal pregnancy to a high-risk pregnancy. Extreme vigilance is needed to detect early signs and symptoms of liver dysfunction and to distinguish these from the anticipated benign hepatic changes of pregnancy. Prompt management can save life of the mother and the baby. Management of liver disease during pregnancy requires a concerted effort between the primary care physician, liver specialist, and obstetrician.

Acute liver failure (ALF) during pregnancy is a common challenging clinical problem both in terms of correct diagnosis and management. Acute viral hepatitis is the most common cause of jaundice during pregnancy. The course of acute viral hepatitis is unaffected by pregnancy, except in patients with hepatitis E (HEV), especially from endemic countries like India, where ALF carries a high mortality rate. In both HEV and herpes simplex infections, maternal and fetal mortality rates are significantly increased. ALF specific to pregnancy including preeclampsia (associated with hemolysis, elevated liver enzymes, and low platelet count [HELLP] syndrome), acute fatty liver of pregnancy, and hepatic infarction result in increased maternal and fetal mortality if not recognized and acted on early. Early recognition of possible causes and prompt treatment are crucial for successful outcome of ALF during pregnancy. Treatment involves prompt delivery, whereupon the liver disease quickly reverses.

**Indigenous Drugs**

The efficacy and safety of Liv.52 was studied in the management of liver disorders during pregnancy. The study was conducted (1974-1975) to evaluate the efficacy and safety of Liv.52 in the treatment of jaundice during pregnancy and consisted of 84 cases of liver disorder during pregnancy.

In this study population of 84 patients, there were 9 pregnant women who were down with severe viral hepatitis. Of these 84 patients, 21 had undergone liver biopsy after written informed consent. Histopathological examinations of these patients with viral hepatitis indicated extensive periportal round cell infiltration, fibrosis, and scarring. All these patients recovered completely after 6 weeks of treatment except one patient (19 years, second trimester of pregnancy). This patient had undergone liver biopsy and the histopathology revealed severe round cell infiltration, fibrosis, and nodule suggestive of cirrhosis. Further, Liv.52 did not produce any adverse effects in any of the 84 patients who underwent Liv.52 therapy. Therapy with Liv.52 brought down the earlier reported mortality rate from 26.7% to 1.1% in patients with jaundice during pregnancy. However, a larger trial will be needed to confirm these findings. Liv.52 is a well studied herbal formulation in various diseases. Liv.52 is a safe and effective formulation for the management of liver diseases during pregnancy.
Rare Skin Disorders

Rare skin disorders, unlike the common disorders, are usually associated with aggravating cosmetic symptoms and can be life threatening. Although their etiologies are ambiguous, studies suggest that sensitivity to allergic substances or genetic abnormalities are the common causative factors. Some of the rare skin diseases and their associated manifestations are described below.

Acute Febrile Neutrophilic Dermatosis

Acute febrile neutrophilic dermatosis (AFND), also known as Sweet syndrome, is a hypersensitivity reaction characterized by abrupt onset of tender, indurated, red-to-purple colored papules and nodules that together form plaques. These plaques appear in the upper dermis of face, neck, and upper extremities, especially the dorsum of hands, and are usually associated with fever and peripheral neutrophilia. Although the etiology is not well known, studies suggest that type 1 helper T-cell cytokines, including interferon-γ and interleukin-2, may play a role in the formation of lesions. AFND occurs frequently with hematologic cancers, acute respiratory illness, gastrointestinal infection, vaccination, exposure to allergic substances and certain drugs, and autoimmune disorders. The condition is more predominant in females (15:1), especially in those aged between 30 and 50 years. AFND is curable in most cases, however, it could persist indefinitely if associated with disease conditions such as cancer. The prognosis of the disease depends on the underlying cause.

Harlequin Ichthyosis

Harlequin ichthyosis, an autosomal recessive disorder, occurs due to mutation in ABCA12 gene (adenosine triphosphate [ATP]-binding cassette transporter, subfamily A member 12). ABCA12, present in chromosome 2, encodes a transmembrane protein that is crucial for transporting lipids in epidermal cells and normal development of skin. The disease manifests at birth and is characterized by thickening and hardening of the skin, which appear as large, diamond-shaped plates separated by deep cracks. These skin deformities affect the motility of arms and legs and the appearance of eyelids, ears, nose, and lips. Thickening of skin restricts chest wall expansion that could result in respiratory distress, hypoventilation, and respiratory failure. It also causes dysregulation of body temperature and dehydration and renders the individuals susceptible to life-threatening infections.

Hailey-Hailey Disease

Hailey-Hailey disease or familial benign pemphigus is an autosomal dominant disorder occurring due to mutation in ATP2C1 gene localized in chromosome 3. The gene codes for secretory pathway Ca²⁺/Mn²⁺ ATPase (hSPCA1), a calcium/manganese pump, essential for transporting Ca²⁺.
and Mn2+ ions. Hailey-Hailey disease is characterized by painful erosive skin rashes on skinfolds, usually in armpits, neck, groin, between buttocks, and under the breasts. Keratinocytes appear as layers of detached skin cells due to improper assembling of desmosomes in the absence of sufficient Ca2+ ions. The disease usually manifests in late teenage years or adulthood (30–40 years) and causes severe discomfort. Heat, sweat, bacterial infection, and friction may worsen the symptoms further.

**Morgellons Disease**

Morgellons disease is referred to as unexplained dermopathy by the Centers for Disease Control and Prevention (CDC). Although the cause of this disease is not well understood, studies suggest that the condition could be a manifestation of certain known medical conditions such as delusional parasitosis, Lyme disease, schizophrenia, liver or kidney disease, and drug/alcohol abuse. The disease is characterized by symptoms such as crawling, biting, and stinging sensations on or under the skin, persistent skin rashes or sores, behavioral changes, joint pain, vision problems, fatigue, and short-term memory loss.

Focal dermal hypoplasia, also known as Goltz syndrome or Goltz-Gorlin syndrome, is an X-linked disorder characterized by skin abnormalities that primarily affect the eyes, teeth, and skeletal, urinary, gastrointestinal, cardiovascular, and central nervous systems. The disease occurs due to mutations in PORCN gene (Xp11.23), which codes for transmembrane endoplasmic reticulum proteins that target Wnt signaling proteins (primary regulators of embryonic development). Streaks of very thin skin, yellowish-pink fat nodules, and telangiectasia are some of the commonly observed skin abnormalities. Hand and foot abnormalities include missing fingers or toes, deep split in the hands or feet, and webbed fingers or toes. The affected individuals also have distinctive facial features such as small or severely underdeveloped eyes, notched nostrils, pointed chin, small ears, facial asymmetry, cleft lip with or without cleft palate, and papillomas of gums, palate, tongue, and buccal mucosa. The kidneys could be fused, predisposing the individuals to kidney infections. Focal dermal hypoplasia is predominant more in females than males (5:1).

**Dystrophic Epidermolysis Bullosa**

Dystrophic epidermolysis bullosa (DEB), one of the major forms of epidermolysis bullosa, is characterized by skin erosions and blister formation in response to mechanical trauma such as itching and scratching. The disorder occurs due to mutations in COL7A1 gene, which disrupts the production and alters the structure of type VII collagen that is crucial for maintaining the structure of the skin. One of the most common forms of DEB is autosomal recessive dystrophic epidermolysis bullosa, in which the affected infants are born with blisters and areas of missing skin due to trauma during birth. Blisters are present in most parts of the body and affect mainly the mucous membranes of mouth and digestive tract. Blisters heal with time but result
in severe scarring. Scarring in the mouth and esophagus makes the individual difficult to swallow food, resulting in chronic malnutrition. Some of the other complications associated with scarring include fusion of fingers and toes, joint deformities, loss of fingernails and toenails, and inflammation of the eyes.

Xeroderma Pigmentosum

Xeroderma pigmentosum is an autosomal-recessive inherited disorder characterized by extreme sensitivity to ultraviolet light. The condition is caused by mutations of genes such as XPC, ERCC2, and POLH involved in repairing DNA damage. It mainly affects the eyes and the portions of skin exposed to sunlight. The affected individuals develop severe skin burns that causes long-lasting redness and blistering, freckling of the skin, xeroderma, and pigmentation. These individuals are also at an increased risk of skin cancer and progressive neurological abnormalities.
Online

National Institute of Dental and Craniofacial Research

National Institute of Dental and Craniofacial Research (NIDCR) is the federal government’s lead agency for scientific research on oral, dental, and craniofacial health and disease. NIDCR is one of the National Institutes of Health (NIH) in the US Department of Health and Human Services.

The mission of NIDCR is to improve oral, dental, and craniofacial health through research, research training, and the dissemination of health information. The official website of NIDCR provides vital information on various oral health-related topics and research work being conducted in the field of oral health care.

American Skin Association

American Skin Association (ASA) is one of the leading organizations fighting against melanoma and other serious forms of skin cancer and disease. The mission of ASA is to

- Advance research
- Raise public awareness about skin disease and its often devastating impact
- Champion good skin health - particularly among children

The official website of the ASA provides information on various skin-related diseases and their management. Also, the organization, in partnership with The New York Academy of Medicine (NYAM), has developed a free program that provides schools with a comprehensive skin health education curriculum, onsite professional development training workshops, student materials, ongoing consultation, and technical assistance.
Books

Basic Guide to Oral Health Education and Promotion
Felton A, et al.
Publisher: Wiley-Blackwell, 2009
ISBN-10: 1405161620
Price: US $44.99
Paperback: 296 pages

The Basic Guide to Oral Health Education and Promotion is a step by step course companion for dental nurses studying for the Certificate in Oral Health Education. In addition, it is an invaluable resource for other members of the dental team and health professionals involved in educating and promoting oral health to patients and the wider general public.

Each chapter focuses on different aspects of oral health education and promotion in line with the NEBDN syllabus, yet is written in logical sequence for the benefit of those not studying the exam and those in professions other than dental nursing. Topics covered include dental structures, anatomy and physiology, oral diseases and prevention, the principles of education, oral health and society, promoting oral health in the 21st century, patient communication, project planning and workplace assignments.

Liver Cirrhosis: From Pathophysiology to Disease Management
Bosch J
Publisher: Springer, 2008
ISBN-10: 1402086555
Price: € 199.95
Paperback: 334 pages

Liver cirrhosis, a leading cause of morbidity and mortality worldwide, is the fifth most common cause of death in individuals between the ages of 25 and 45 years. This book, the proceedings of Falk Symposium No.162 entitled “Liver Cirrhosis: From Pathophysiology to Disease Management,” held in Dresden, Germany, October 13 and 14, 2007, focuses on the pathogenetic mechanisms of liver cirrhosis and clinical management of the complications. The first part of the book discusses liver fibrogenesis and the cellular responses to chronic liver injury as well as new non-invasive techniques for assessment of fibrosis in patients. The remainder focuses on preprimary and primary prophylaxis of variceal bleeding and therapy of other complications of cirrhosis.
Dear doctor,
Welcome to the Quiz Corner! This issue features the fourth Medical Crossword. You can win exciting prizes by sending in correct answers using the Answer card enclosed in this issue. Please let us know your feedbacks and suggestions on the same.
Wish you the very best!

Medical Crossword 4

Across
2. It is the hardest and most highly mineralized substance in the human body. (5, 6)
4. Infection of the oral cavity by Candida is known as ___. (6)
6. Inflammation of the dental pulp as a result of untreated caries, trauma, or multiple restorations. (8)
8. It is a melanin-producing cell. (10)
9. Lack of melanin pigment in the skin is called ___. (8)
10. The condition of having stale or foul-smelling breath is ___. (9)

Down
1. Inflammation of the gum surrounding the teeth is known as ___. (10)
3. Redness of the skin accompanied by inflammation is known as ___. (8)
5. The most common form of hepatitis in children is ___. (9, 1)
7. An intense itching sensation that creates an urge to rub or scratch the skin to obtain relief. (8)

Answers to Medical Crossword 2 (Vol. XLIX • No. 4 • Jul–Sep 2010)

Across : 1) Oligouria 3) Tooth 4) Cirrhosis 8) Stapedius 9) Splenectomy
Down : 2) Lithotripsy 5) Parotid 6) Osseous 7) Amenorrhea 10) Liver
Picture Quiz 18

A 42-year-old man presented with a life-long history of an asymptomatic white patch on the left side of his back (see the accompanying figure). He stated that the patch was more prominent after exercise. On physical examination, a large, nonscaly, pale patch on his back was apparent. When a glass slide was applied to the border of the lesion, the border became inapparent.

Question

Given the patient’s history and results of a physical examination, which one of the following is the correct diagnosis for the disorder shown above?

A. Hansen disease
B. Nevus anemicus
C. Nevus depigmentosus
D. Tinea versicolor
E. Vitiligo

Answer (Picture Quiz 18)

B. Nevus anemicus

Nevus anemicus is a congenital patch manifested by skin pallor. It most commonly occurs on the trunk. Several studies have shown that nevus anemicus is caused by a localized vascular hyporesponsivity to the skin. B. Nevus anemicus is a congenital patch manifested by skin pallor. It most commonly occurs on the trunk.
Robert Willan and the French Willanists

Tilles G, Wallach D

In 1798, Robert Willan published the founding textbook of British dermatology. To adopt the elementary lesion principle previously described by Josef Plenck and improve the nomenclature of the skin diseases, Willan established a method for the diagnosis and a doctrine for the nosology of cutaneous diseases. Introduced into France by Biett in the 1810s, the Willanist method, which allowed diagnosis on the basis of objective criteria, was adopted by a majority of the dermatological community. However, as a doctrine, Willanism, which is the use of elementary lesions as a framework for classifying diseases, became the subject of lasting debate. In fact, apart from a few, most leading French dermatologists did not accept Willan’s doctrine and preferred classifications according to systems which were supposed to reflect the best understanding of the cutaneous diseases: physiological, aetiological and pathological. Willanism is still used by every dermatologist as a method for recognizing skin diseases. It constitutes a firm link to the founding period of modern dermatology and remains a bastion against uncertain hypotheses.

Harry Sicher: Pioneer Dental Anatomist

Christen AG, Christen JA

Harry Sicher, MD, DSc (1889-1974), a world-renowned and highly respected head, neck, and dental anatomist, received his MD from the University of Vienna Medical School, Austria, in 1913. Studying under the famed Dr Julius Tandler, Sicher received a broad and solid foundation in all aspects of anatomy. He clearly understood that anatomic structure was closely related to body function. After graduating from medical school, Dr Sicher specialized in dentistry and worked in clinical practice, teaching, and research areas. He remained associated with the University of Vienna until 1938, when Hitler’s annexation of Austria forced Jewish intellectuals to flee from Europe. Sicher immigrated to Chicago in 1939 where he became a professor and chairman of the anatomy department at the Loyola Dental School until his retirement as professor emeritus in 1960. The extent of Harry Sicher’s knowledge and scientific productivity was staggering. He studied and understood the complexities of many scientific disciplines, including anthropology, applied head, neck and oral anatomy, biology, bone metabolism, comparative anatomy, embryology, endocrinology, entomology, evolutionary biology, histology, occlusion, pathology and physiology. His collaborations with Dr Balint J Orban and Dr Joseph P Weinmann were especially productive. In the classroom, his teaching skills were legendary. As a roving lecturer, he spoke to dental, medical, and specialty audiences worldwide for decades. He had the rare ability to make a description of the human body come vibrantly alive. Several of his books such as Oral Anatomy (1949), Bone and Bones (1944), and Orban’s Oral Histology and Embryology (1962, 1966, 1972) became authoritative textbooks for dentists throughout the world.
The fall and winter of 1993 were among the best times of my life. I was 62 years old and working on a book about Native American animal rituals; my wife, Annemarie, was preparing a paper in environmental sociology. Our intellectual lives were full. And since we were living in a remote area near the Canadian border and Glacier National Park, spectacular beauty surrounded us. During the fall, we laid in firewood, took long hikes, and fed our souls on the gorgeous crispness and solitude that fall on the land in anticipation of winter. After the main range of the Rocky Mountains was covered with snow, we spent long evenings reading. During that part of the day not given over to writing and research, we ventured forth on cross-country skis.

We returned to Nashville in December to spend Christmas with our children, grandchildren, and extended families. On the drive back, I experienced an urgency to urinate that would not be denied. Fortunately, a deserted cornfield just off the freeway provided me with sufficient cover and blessed relief. Reassured by previously normal PSA tests, I was certain the possibility of infection was high and made an appointment with a urologist.

Infection was not detected, but my PSA level had risen significantly. My urologist strongly suggested an ultrasound biopsy. The results: a fast-growing, probably very aggressive cancer. I spent much of January anxiously reviewing options, spending as much time as possible in the medical school library at Vanderbilt. Alternatives were murky. I gradually became more deeply aware that significant risks and uncertain benefits accompanied each therapy and that alternate paths were contested.

After reviewing research, further consultation with my physicians, long conversations with my wife, and listening to my own body, we decided that surgery was the best option for me at that time. So in early 1994 I entered Vanderbilt Medical Center and underwent surgery for the removal of my prostate. The cancer had spread to my lymph nodes but, thankfully, had not metastasized to my bones.

Hormone therapy was the recommended course of treatment, so I began monthly injections of Lupron. Every month upon entering the Vanderbilt clinic, a flood of memories swept over me as I relived aspects of the operation and despaired of what had happened to me. Finally, after a year of treatment, I decided to give up my testicles.

After the orchiectomy I was still physically able to do almost all that I wanted. But I was impotent, and despite considering all the possibilities, from penile implants to pumps, I remained in a state of despair. As a consequence of trying to sort out this complex emotional tangle, I gradually became aware of how deep my gender socialization had been. Not only had I a sense of having been mutilated, I had also lost the very capacities that were symbolically associated with manhood in American society. I no longer had a prostate, I was incapable of an erection, and I had no testicles. More fundamentally, I had lost the capacity to experience desire.

The sudden loss of libido produced forms of suffering I had not anticipated. The initial forms were stimulated by my context: I taught at a university each day; on campus and elsewhere, I encountered young people caught in the throes of raging hormones. Because I had lost the capacity to experience desire did not mean that I was not tormented by memories of desire. Surrounded by the presence of youthful Eros, expressed in forms of touching or longing looks, I began to feel a crushing weight of loss. Why was this happening? After all, mine was a mature sexuality fully integrated, I thought, into my personality.

But such experiences continued and they produced increased suffering. The sight of young males walking across the campus tormented me. I began to envy their capacities and, most fundamentally, their possession of what I had lost. I hated these feelings; and sometimes I
hated myself for having them. But they were difficult to suppress, and they continued to break into ugly blooms in my experience. As I endured the suffering produced by unwanted fantasies, I finally began to see what was producing them. Like a range of mountains that appears in the distance, those structures of meaning that had formed the capacities for my erotic responses came gradually into focus.

When these meanings became clearer, I confronted an idea that I had read about in literature by feminist scholars: male sexuality was excessively genital in its focus. Confronting this idea at a deep emotional level was shattering; and allowing it to have an affective impact on my experience began to deconstruct my previously taken-for-granted expressions of erotic pleasure. As a consequence of my male socialization, how restricted these “pleasures” now appeared, and, more painfully, I began to sense how much I had missed.

All of this was not new to my wife. She had been saying many of these things for years, but I was not listening. The loss of capacities, body parts, and what I thought of as my essential maleness was less important to her than the intimacy that accompanied other forms of reciprocal communication: touching, holding, sharing feelings, and being deeply present to one another. As a consequence of these insights, a surprising disgust arose in me, and now I began to hate my previous sexual responses: how insensitive, narrow, and compulsive they had been. And, in a phrase that seemed to summarize all that I was feeling, how goatish!

What I had not yet realized was the deeper significance of testosterone deprivation. It was clear that this manipulation of my body had probably postponed my death, and for that I was grateful. While I did not fully grasp what it would mean to live in a male body without potency, I had not begun to contemplate the meaning of continuing to live without the experience of desire. Desires are always directed toward a subject or an object, and erotic desires are no different. But when desire is radically extinguished, then the way it had been shaped as well as the objects and subjects of its focus still remained as memories. Without the urgency of desire, these memories stood out in ways that were both painful and instructive.

Male socialization had taught me to imagine the female body in a certain manner, to focus my erotic attention on particular body parts, to objectify and depersonalize these body parts, and to understand sexual pleasure as focused almost entirely on orgasm. These structures of the embodied imagination had shaped my experience of desire. The practices, language, and example of other males in my environment powerfully enforced them. I had been so deeply formed by that world that there was virtually no transcendence of it in my experience. Again, I was plunged into despair and, finally, into hatred of the structure of desire that was still alive in my memory and projected in my imagination.

I still struggle with these issues, but at least some feelings of acceptance and consent to my condition are beginning to be stronger than the more negative and destructive responses. At the same time, I am increasingly aware of several things that I consider invaluable. I have learned, first, that women are embodied in much more complicated ways than I had ever imagined. Second, relationships between men and women are complicated—inevitably so—by Eros. But for me, there is a sense of transcendence and peace in being able to experience persons as the complex beings they are without being so completely captured by the undercurrent of desire. Third, there is richness and creative playfulness in human relationships that is distorted by patterns of male socialization. Fourth, the terrain of manhood is much richer and fuller of possibilities than I had ever imagined.

I have survived and, in many ways, flourished for almost 10 years. Six of these years have been characterized by excellent quality of life on many levels. But there have been other losses and some deepened suffering connected with aggressive treatment. In the fall of 2000, for example, when I was again on leave in Montana, I experienced kidney failure as a consequence of lymph node swelling that blocked my ureters. I now have two nephrostomy tubes that require care but that are partially internal so that I urinate “normally.” It became clear, however, that if my quality of life were to be sustained I would have to undergo further treatment.

After consultation with my oncologist, I endured 6 months of chemotherapy with Taxol, which gave me about 4 additional months of satisfactory quality of life. Then in the spring of 2002, I was diagnosed with cancer progression in my right femur and some involvement in my left hip. I underwent surgery and a pin was placed from the top of my femur to my knee. My left hip was radiated at the same time. My recovery was successful, and I went from a wheelchair to a walker to a cane and then to full mobility.

With the blessings of my surgeon and my oncologist, my wife and I left in July 2002 for another research trip to Montana. But after less than 2 weeks I lost bladder control
as well as my ability to walk. An MRI revealed serious spinal cord compression, and we were immediately flown back to Nashville where I endured another surgery to decompress the spinal cord. This surgery was apparently successful and I am now proceeding from the wheelchair to the walker; my hope is for full mobility.

These surgeries were defined as “palliative,” but the last one had real authority. The pain was significant, and recovery has been slower than I would like. My condition is different now, and the sense of loss has a different quality and weight. I clearly anticipate the loss of my world. But I am not simply contemplating this possibility; it is a powerful sensibility that arises within me daily. Nurtured by a supportive network of friends, family, and groups like Gilda’s Club and Alive Hospice in Nashville, I feel a strange peace descend on me. My life seems to have come full circle as meaning folds back upon itself and deepens in a manner that makes more and more sense.

Certainly my experience will not characterize all who read this description. In part, the quality of my experience is dependent on having had sufficient time to assimilate the meaning of what has happened to me. First I lost desire. Now I am gradually losing my body, and I will soon lose my life, my wife, my family, my friends, and the whole beautiful world. I hope that other readers in my situation will have sufficient time to integrate their experiences as I have, and I hope these reflections are helpful for their respective journeys.

Colors

Leonard F


More than the chill in the air, more than the shortening days, more than the echoing calls of migrating geese, there was one sure sign that winter was imminent-ski racks. Well before the first snows ever touched the Rocky Mountains, some primal force compelled the residents of Denver, Colorado, to mount ski racks on their cars, just as it compelled the Canada geese to fly south.

But there was no ski rack on my car. I was beyond noticing the changes around or in me. Besides, I just didn’t have time. I had become preoccupied and absorbed by the demands of a rotating internship. Chronically sleep deprived, perennially behind, and feeling more than a little overworked, neither I nor my circadian rhythms seemed to be able to adjust to the unremitting routine of every second and every third night call. Now, 5 months into this 12-month ordeal, I had completed my obstetric and surgical rotations and had started ward medicine-a tedious and joyless service that was viewed by all but the most zealous among us as penance for any stimulation or fulfillment that we might otherwise salvage from the rest of the internship year.

Outside the medicine wards, the November days had continued to shorten. As daylight became little more than a dim memory, I found myself living in a colorless rod-vision-gray world, illuminated only by the stark fluorescent fixtures of the hospital and the cold mercury-vapor street lamps that cut through the darkness of my morning and evening commutes. I no longer even saw the sun rise or set. But, as a fellow intern pointed out, it hardly mattered. After all, there was nothing beautiful about a sunrise if you were too bleary-eyed to focus on it.

Populating my colorless, gray world were the gray-haired ward medicine patients. We interns all knew that somewhere outside the confines of the hospital lurked the Supreme Nursing Home Triage Officer. It was his duty to ensure that every night on call we each received at least one demented, aphasic patient with a chief complaint of “won’t eat,” “less responsive,” or “no bowel movement for 2 weeks.” Then for the ensuing days, weeks, and months of our ward medicine rotations (and we feared it could become years), we visited these poor souls twice daily on ward rounds—a monotonous ritual that seemed to reflect the dearth of vitality and spontaneity that so characterized us, our mentors, and our surroundings.

So it was with no sense of joy or adventure that particular night on call that I trudged toward the emergency department for my third admission of the evening. As I wandered down the fluorescent-lit corridors, I tried to calculate how many hours of sleep debt I had accrued to that point in my internship. My calculations were still
incomplete when the ED nurse pointed me toward the curtained cubicle containing my new patient. There, with an IV in her left arm and leaning over a stainless steel emesis basin, was Carol. She appeared pale, fatigued, and acutely ill, but in-between her retching and rapid respirations she managed to acknowledge my presence with a weak smile. Carol was being admitted with a diagnosis of diabetic ketoacidosis.

Having learned at least something from 5 months as an intern, I rapidly assessed the situation. Here was a patient who was about my age, could talk, had an acute clinical problem, and had not come from a nursing home. Maybe there had been a mistake. Maybe I had gone into the wrong cubicle. Maybe the Supreme Nursing Home Triage Officer was temporarily indisposed. It didn’t matter. She was my patient now. Before anyone could correct the obvious error, I pushed gurney, IV, emesis basin, and Carol out of the ED and up to the wards.

By morning, both Carol and I were still tired but feeling better-she because her metabolic derangements were coming under control, and I because I now had a patient whom I looked forward to seeing on rounds. Not only was she my first patient with diabetic ketoacidosis, she was my first ward medicine patient with whom I could carry on a “normal” conversation.

Over the next few days, I spent as much time as I could talking with Carol. She had what we then called juvenile-onset diabetes. The term fit well, for diabetes had taken control of her life when she was just 12 years old. Now, 19 years later, it had also taken her eyesight, robbed her of sensation in her feet, and was well on its way to claiming her kidneys. Yet she was cheerful, upbeat, and thankful for what she had been allowed to do in her life. When she began to lose her vision 2 years before, she had learned to read Braille, and she planned to help others do the same. She knew she would soon be on dialysis, yet she accepted its inevitability and was hopeful that she would be a candidate for a kidney transplant. She had only one small regret. That fall she had been in the Rockies, and though she could feel their grandeur and beauty, she could no longer see their striking yellow aspens or rugged green landscape and azure sky. She truly longed to see the colors of a Rocky Mountain fall just one more time.

I did not tell Carol I had missed the aspens that fall. Being too busy, too immersed, too overwhelmed hardly seemed an adequate excuse. How could I tell her I had not seen those brilliant fall colors simply because I had not made an effort to open my eyes? After a mere 5 months of internship, I had become jaded and unseeing, with neither the time nor the inclination to experience the overwhelming beauty of life. Diabetes had taken Carol’s eyesight. Internship had apparently taken mine.

Carol went home after 4 days in the hospital, and she was not readmitted during my internship year. As with most of my patients from that year, I never saw her again. Yet her effect on me and my internship did not end with her discharge. Though the call schedules, the demands, and the dehumanizing routines did not change, my perspectives slowly did. Both inside and outside the hospital, I began to notice the ever-present life, light, and colors. I even found that I could talk with my gray-haired patients, and they had much to teach me if I just made the effort to listen. And I have never since missed seeing the colors of fall. Nor has a fall passed that I have not thought of Carol, the person who helped me see them.
Laughter, the Best Medicine

A mother and her child were at a wedding.
The little boy looks at his mom and asks, “Mommy, why does the girl wear white?”
His mom replies, “The bride is in white because she’s happy and this is the happiest day of her life.”
The little boy thinks about this, and then says, “Well then, why is the boy wearing black?”

A man was walking down the street one day when he noticed a small boy trying to press a doorbell on a house across the street. However, the doorbell was too high for him to reach. After watching the boy’s efforts for some time, the man moved closer to the boy’s position.
He stepped smartly across the street, walked up behind the little fellow and, placing his hand kindly on the child’s shoulder, gave the doorbell a solid ring.
Crouching down to the child’s level, the man smiled benevolently and asked, “And now what, my little man?”
The boy replies, “Now we run!”

Some of the actual signs displayed in non-English speaking countries...
In the lobby of a Moscow hotel:
“You are welcome to visit the cemetery where famous Russian and Soviet composers, artists, and writers are buried daily except Thursday.”
In a hotel in Athens:
“ Visitors are expected to complain at the office between the hours of 9 and 11 a.m. daily.”
In a Tokyo hotel:
“Is forbidden to steal hotel towels please. If you are not person to do such thing is please not to read notis.”

Think Wise

The only way of finding the limits of the possible is by going beyond them into the impossible.

— Arthur C Clarke

Write to Us

We would like to hear from you. Write to us at publication@himalayahealthcare.com
Derma care REDEFINED... naturally!

Himalaya HERBAL HEALTHCARE

presents a range of effective, safe, and clinically proven products in derma care & hair care

**Clarina®**
- **ANTI-ACNE FACE WASH GEL**
  - Cleanses skin.
  - Controls acne

**Clarina®**
- **ANTI-ACNE FACE MASK**
  - Controls oil.
  - Cleanses pores.
  - Clears acne

**Clarina®**
- **ANTI-ACNE CREAM**
  - Clears acne effectively and safely

**Clearvital™**
- **ANTI-WRINKLE GEL**
  - Clears wrinkles, vitalizes skin

**Bleminor™**
- **CREAM**
  - For blemish-free skin

**Hairzone®**
- **SOLUTION**
  - Prevents hair fall, promotes hair growth
Launching shortly...

Liv.52® HB
(CAPSULE)

For the management of hepatitis B infection