Down Memory Lane

Founder Chairman Mr M Manal felicitates Dr Rustom Jal Vakil on his path-breaking work on hypertension published in the *British Heart Journal*. The product used by Dr Vakil was Serpina (Himalaya).

The first Head of R&D of The Himalaya Drug Company, Dr Roshan M Captain (second from left) with Dr Rustom Jal Vakil (third from left), founder Chairman Mr M Manal (third from right) and other distinguished guests at the felicitation function.
Message from the Chairman

The Himalaya Drug Company was founded by my father in 1930, long before I was born, with a clear vision to bring Ayurveda to society in a contemporary form. New formulations were created by referring to ancient Ayurvedic texts, selecting widely available Indian herbs and subjecting dozens of these herbs and combinations to modern pharmacological, toxicological, and safety tests to create new drugs and therapies. The most promising formulations then underwent clinical trials by doctors and institutions of modern medicine. The breakthrough came in 1949 (after I was born!) when the *British Heart Journal* published the work of India’s pioneer in cardiology, Dr Rustom Jal Vakil. He researched *Rauwolfia serpentina*, the world’s first successful blood pressure lowering agent. The product Dr Vakil used for his work was Serpina (Himalaya)!

As an offshoot of this vision, in the year 1961, The Himalaya Drug Company started publication of the journal “Probe—Exploring ancient and modern medical learning” with the objective to provide latest research updates to the medical community. It was the belief of its publishers that, through high standards of medical journalism and usefulness, Probe would be accepted by doctors all over the nation.

Over the years, the readership of Probe increased in volumes and the publication spread its wings overseas. Today, Probe is read in more than 35 countries.

With great humility, I present to you the 50th anniversary issue of Probe. On this occasion, I thank you, our readers, for your kind support through the years, for your trust and prescriptions of Himalaya products and for being a part of this milestone moment.

Warm personal regards,

Meraj Manal
Chairman
Himalaya Global Holdings Ltd.
(Parent of The Himalaya Drug Company Worldwide)
meraj.manal@himalayaglobalholdings.com

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Dr Pralhad S Patki, MD
Editor in chief

Probe—Exploring ancient and modern medical learning, initiated as an offshoot of The Himalaya Drug Company’s (HDC) vision of bringing Ayurveda to society in a contemporary form, has been publishing latest research works that fascinates all classes of readers in the medical fraternity. Since its inception, a major effort has been made to keep up the high standards of this journal to which everyone is accustomed to. On the occasion of the completion of 50 years of this journal, we assure you that we shall continue featuring such similar contents that help in your clinical practice.

In this second issue of 50th anniversary volume of Probe, we have featured a unique and varied series of articles that include the journey of this journal, growth of HDC over the past half century, research and development at HDC, corporate social responsibility of HDC, and your feedbacks on various pharmaceutical products. This issue also features interesting sections such as herb profiles, herb reviews, upcoming events, and much more.

Do write to us with your valuable feedbacks, comments, and suggestions on this special issue of Probe at publications@himalayahealthcare.com.
Rauwolfia serpentina (Apocynaceae)
a.k.a. Sarpgandha (Sanskrit), Rauwolfia (English).

The pharmacological properties of Rauwolfia serpentina were first discovered by the founder of The Himalaya Drug Company. This led to the introduction of Serpina®, the world’s first antihypertensive drug in 1934.
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Clinical Insight

Clinical Performance of Tentex Royal in Patients with Erectile Dysfunction

Kah TK, et al.


**ABSTRACT**

**Aim:** The aim of this study was to assess the efficacy, safety, and tolerability of Tentex Royal capsules administered once daily in subjects with erectile dysfunction.

**Methods:** Thirty-four consecutive patients with erectile dysfunction fulfilling inclusion criteria were included in this study. Prior to treatment, all study participants underwent a detailed medical examination and evaluation with International Index of Erectile Function, Andropause score, and prior treatments for erectile dysfunction. All patients received Tentex Royal capsules in dose of 2 capsules once daily for the period of 6 weeks.

**Results:** Thirty-four men with a mean age of 48.91 ± 10.47 years completed the study. In this study, increase in level of testosterone was observed but was insignificant. International Index of Erectile Function score increased significantly after Tentex Royal treatment. Changes in blood pressure levels, serum prostate specific antigen (PSA) level, prolactin level, serum lipids, liver profile, hemoglobin, and packed cell volume (PCV) were not significant after the treatment.

**Conclusion:** Tentex Royal is clinically effective and safe in the management of erectile dysfunction.

**Key Words**

Erectile dysfunction, Tentex Royal, International Index of Erectile Function score, Andropause score

**Introduction**

The use of oral therapy has long been preferred over invasive procedures such as injection therapy for erectile dysfunction (ED). The primary concern with oral therapy for erectile dysfunction has centered on cardiovascular-related events.1 Because phosphor-diesterase-5-inhibitors (PDE-5) promote vasodilation, they inherently have the potential to cause hypotension. The concern has been greatest in elderly patients with pre-existing cardiovascular disease. Among patients seeking treatment for erectile dysfunction, there are those who do not use the usual treatments available today.2 For these men alternative treatment such as Tentex Royal can be an acceptable option, if it meets patient’s expectations on efficacy, safety, and tolerability.

Tentex Royal, manufactured by The Himalaya Drug Company, Bangalore, India is a polyherbal combination, which is recommended for the management of the ED. It contains powders of *Tribulus terrestris*, *Curculigo orchioides*, *Piper betle*, *Asteracantha longifolia*, *Prunus amygdalus*, *Blepharis edulis*, and *Crocus sativus*; and extracts of *Tribulus terrestris*. Previous study on Tentex Royal concluded its efficacy and safety in patients of ED.3
Methodology

Aim
The primary aim of this study was to assess the efficacy, safety, and tolerability of Tentex Royal capsules administered once a daily in subjects with ED.

Study design
This study was an open study conducted to evaluate the safety and efficacy of Tentex Royal capsules.

Primary outcome measures
The primary end point was change from baseline in the erectile function (EF) domain of the International Index of Erectile Function (IIEF) and Andropause score.

Secondary outcome measures
Safety profile evaluation of Tentex Royal capsules.

Inclusion criteria
- Male patients 21 to 65 years of age.
- ED of a continual duration of 6 months.
- Mild-to-moderate ED documented at screening.
- Agree not to use any other treatment for ED, including herbal and over-the-counter medications during the study.

Exclusion criteria
- Current treatment with antihypertensive medication.
- Clinically significant cardiovascular disease.
- Subjects who have significant heart disease.
- Subjects with history of significant central nervous system injuries (including stroke or spinal cord injury) within the last 6 months.
- Subjects who have received any investigational drug within 30 days of their first visit.
- Use of any treatment for erectile dysfunction within 7 days of first visit or during the study.
- Thirty-four consecutive patients with erectile dysfunction fulfilling inclusion criteria were included in this study. Written informed consent was obtained from each patient before entering the study. Prior to treatment, all study participants underwent a detailed medical exam that included information about the severity of the ED and prior treatments for ED. Patients also received a routine physical examination.
- All patients received Tentex Royal capsules in dose of 2 capsules once daily for the period of 6 weeks. Response to treatment was assessed on entry, at week 3 and at the end of the treatment.

Assessment
Efficacy was assessed using the IIEF, a 15-item, self-administered questionnaire (Annexure No. 1). Patients completed the IIEF at the start of the study (baseline visit) and again at the follow-up visit.
- Andropause Questionnaire was developed to find out Andropause score (Annexure No. 2). All subjects completed Andropause Questionnaire on entry and at the follow-up visit.
- Hemoglobin (Hb%), packed cell volume (PCV), prostate-specific antigen (PSA), prolactin level, testosterone level, fasting blood sugar (FBS), lipid profile, liver profile was done before and after treatment. Also weight, body mass index (BMI), and blood pressure (BP) was determined before initiating and after treatment.

Adverse events
All the adverse events, either reported by the patients or observed by investigators, were recorded in case record forms, with the information about severity, date of onset, duration, and action taken regarding the study drug. The relation of adverse events to the study product was predefined as “unrelated,” “probable,” and “possible.”
- Patients were allowed to voluntarily withdraw from the study, if they experienced serious discomfort during the study or sustained clinical events requiring specific treatment.

Data analysis
Statistical analysis was carried out using parametric and nonparametric Student’s “t” test to find out the level of significance. The severity score was expressed as mean ± SD. The minimum level of significance was fixed at \( P < 0.05 \). Statistical analysis was carried out using GraphPad Prism Software, Version 4.01.

Results
Thirty-four men completed the study. Mean height and BMI was 166.25 ± 25 and 25.42 ± 3.38, respectively (Table 1). Mean Andropause score reduced from 25.35 to 17.39, which was statistically significant. There was increase in the level of testosterone, but it was not significant. IIEF score increased from 12.18 to 14.77 and was statistically significant (Table 2).
- Significant reduction in fasting blood sugar level was observed at the end of treatment.
- Changes in BP levels, serum PSA level, prolactin level, serum lipids, liver profile, Hb%, and PCV were not significant after the treatment (Table 3). No adverse effects were reported throughout the study duration.

Discussion
Available treatment options for ED include oral therapies, surgical treatment, injections, and mechanical
Clinical Insight

Table 1. Evaluation of Effect of Tentex Royal

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Pretreatment (mean ± SD)</th>
<th>Posttreatment (mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>73.07 ± 9.99</td>
<td>73.00 ± 9.68</td>
</tr>
<tr>
<td>BMI score (mean ± SD)</td>
<td>25.42 ± 3.38</td>
<td>25.32 ± 3.35</td>
</tr>
<tr>
<td>Waist (cm) (mean ± SD)</td>
<td>92.14 ± 10.06</td>
<td>91.50 ± 10.39</td>
</tr>
</tbody>
</table>

Figures are mentioned in mean ± SD.

Table 2. Evaluation of Effect of Tentex Royal in Erectile Dysfunction

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Pretreatment (mean ± SD)</th>
<th>Posttreatment (mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Andropause score</td>
<td>25.35 ± 15.25</td>
<td>17.39 ± 16.66*</td>
</tr>
<tr>
<td>IIEF score</td>
<td>12.18 ± 4.55</td>
<td>14.77 ± 6.02**</td>
</tr>
<tr>
<td>Testosterone (ng/dL)</td>
<td>570.4 ± 181.8</td>
<td>628.4 ± 175.1</td>
</tr>
</tbody>
</table>

*P<0.005 as compared to pretreatment values; **P<0.001 as compared to pretreatment values. Figures are mentioned in mean ± SD.

Table 3. Evaluation of Effect of Tentex Royal in Erectile Dysfunction

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Pretreatment</th>
<th>Posttreatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>BP-systolic (mmHg)</td>
<td>87.14 ± 4.69</td>
<td>86.00 ± 7.40</td>
</tr>
<tr>
<td>BP-diastolic (mm Hg: Fig)</td>
<td>146.1 ± 13.61</td>
<td>136.9 ± 13.80</td>
</tr>
<tr>
<td>PSA (ng/mL)</td>
<td>1.21 ± 0.78</td>
<td>1.19 ± 0.80</td>
</tr>
<tr>
<td>Prolactin (ng/dL)</td>
<td>7.26 ± 2.77</td>
<td>6.46 ± 2.84</td>
</tr>
<tr>
<td>Total cholesterol (TC) (mg/dL)</td>
<td>194.6 ± 41.06</td>
<td>197.2 ± 37.44</td>
</tr>
<tr>
<td>HDL-c (mg/dL)</td>
<td>50.35 ± 10.64</td>
<td>51.30 ± 11.71</td>
</tr>
<tr>
<td>TC: HDL-c ratio</td>
<td>3.98 ± 1.06</td>
<td>4.04 ± 1.29</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>154.4 ± 88.49</td>
<td>128.2 ± 76.62</td>
</tr>
<tr>
<td>LDL-c (mg/dL)</td>
<td>113.4 ± 28.22</td>
<td>120.2 ± 28.56</td>
</tr>
<tr>
<td>SGPT (U/L)</td>
<td>32.55 ± 16.80</td>
<td>33.00 ± 20.02</td>
</tr>
<tr>
<td>SGOT (U/L)</td>
<td>30.20 ± 9.50</td>
<td>31.60 ± 13.56</td>
</tr>
<tr>
<td>GGT (U/L)</td>
<td>48.55 ± 45.08</td>
<td>47.00 ± 40.43</td>
</tr>
<tr>
<td>Hb (%)</td>
<td>14.78 ± 1.22</td>
<td>14.67 ± 1.45</td>
</tr>
<tr>
<td>PCV (%)</td>
<td>45.57 ± 3.40</td>
<td>44.06 ± 7.77</td>
</tr>
<tr>
<td>FBS (mg/dL)</td>
<td>112.6 ± 28.61</td>
<td>95.85 ± 11.60</td>
</tr>
</tbody>
</table>

Figures are mentioned in mean ± SD.

Clearly oral treatments are generally the first choice. The most effective oral treatments are the PDE5 inhibitors. The three currently available PDE-5 inhibitors are Sildenafil, tadalafl, and vardenafil. In clinical trials, the most common adverse effects of PDE-5 inhibitors use included headache, flushing, dyspepsia, nasal congestion, and impaired vision, including photophobia and blurred vision. PDE-5 inhibitors are contraindicated with drugs containing nitrates. The US Food and Drug Administration (FDA) advises any person taking a PDE-5 inhibitor who experience a sudden hearing loss should discontinue the intake of the medicine and consult a doctor immediately.

The 1999 American College of Cardiology/American Heart Association (ACC/AHA) Expert Consensus Document noted that PDE-5 inhibitors may be dangerous for people who have coronary artery disease, heart failure, and low blood pressure and for those who are taking many different drugs for high blood pressure.

It is well documented that PDE-5 inhibitors can produce transient visual symptoms, such as a change in color hue perception, where the patient may perceive a blue tinge to the visual world (cyanopsia), and increased sensitivity to light.

Studies on Tentex Royal showed that it did not produce any type of adverse effects.

This study observed significant improvement in IIEF score, and there was a reduction in Andropause score. Also, there were no clinically significant changes in the hematological and biochemical parameters. No significant adverse reactions were noted.

Tentex Royal contains a number of pharmacologically active agents. Recently, a chemical compound isolated from *Tribulus terrestris* L. called protodioscin has been identified.

Protodioscin is proved to increase the serum dehydroepiandrosterone (DHEA) level of infertile men, DHEA is an endogenous hormone serves as precursor to male and female sex hormones. Speculations have been made that its mechanism of action involves the conversion of protodioscin to DHEA.

In turn, DHEA may increase cell membrane integrity and functions, thereby resulting in better sexual performance and the general feeling of well being.

*T terrestris* increases the intracavernous pressure in the penis and enhanced sexual behavior. This is possibly due to the ability of the herb to increase...
androgen (testosterone) levels and the subsequent release of nitric oxide (NO) from the nerve endings innervating the corpus cavernosum, resulting in improved blood flow to the penis and in turn improvement in the functioning of the musculature in the penile region.28

Published scientific studies have found that T terrestris possess aphrodisiac properties, and this has been attributed to its androgen increasing effects.29 Also, studies have shown that T terrestris possess pro-erectile properties making it a useful adjunct in the treatment of ED.30

Asteracantha longifolia helps in the release of NO from the endothelium and nitrergic nerve endings. Also, it contains active principles having pro-erectile activity.21 P antygdalus, an aphrodisiac, significantly increases sperm motility and sperm contents without producing any spermatotoxic effect.22 B edulis and C sativus have reported aphrodisiac properties.23,24 Psychological distress such as anxiety and depression also contribute to erectile dysfunction.25 C sativus has potent antidepressant action.26 P antygdalus is a nerve tonic and improves psychotropic function.27

Erectile dysfunction demonstrates decreased intracavernous blood flow, loss of smooth muscle relaxation, decreased endothelial nitric oxide synthases (NOS) and neuronal NOS, increased inducible NOS expression, diffused cavernous fibrosis, and increased cavernous levels of the oxidative product 8-epi-prostaglandin F2-alpha, an F2-isoprostane. Long-term use of antioxidants increases intracavernous blood flow, improves erectile response, and smooth muscle relaxation in ED.28

The herbal formulation evaluated in this study, has proved desirable pharmacological activity in terms of improvement in penile erection without an associated adverse effect. It appears to be a safe alternative to PDE-5 inhibitors and can be utilized as a medication to improve sex on demand.

**Conclusion**

This study observed that the use of Tentex Royal capsules has significant increase in IIEF score and reduction in Andropause score. There were no clinically significant changes in the hematological and biochemical parameters, and there were no clinically significant adverse reactions found, which is reflected in the excellent patient compliance. Tentex Royal capsules are clinically effective and safe option in the management of ED.

**References**

Testosterone and Cardiovascular Risk in Patients with Erectile Dysfunction

Corona G, et al.


Aim

To evaluate the association between testosterone (T) levels and cardiovascular (CV) risk in subjects with erectile dysfunction (ED) and to verify whether their body mass index (BMI) might represent a possible confounder in testosterone-related CV stratification.

Material and Methods

A consecutive series of 2269 male patients attending the outpatient clinic for ED was studied. The assessment of CV risk was evaluated using the engine derived from the Progetto Cuore study.

Results

After adjustment and for BMI and associated morbidities, sex hormone binding globulin bound (SHBG) and unbound T levels decreased as a function of CV risk assessed thorough Progetto Cuore risk engine. In addition, a higher prevalence of hypogonadism-related symptoms and signs was associated with a higher CV risk. Among factors included in the Progetto Cuore risk engine age, total and HDL cholesterol and diabetes were all significantly associated with CV risk-dependent modification of total and calculated free-T levels. When the relationship between SHBG bound and unbound testosterone and CV risk was evaluated as a function of obesity (BMI >30 kg/m²), all the aforementioned associations were confirmed only in nonobese patients.

Conclusions

Hypogonadism could be associated either with an increased or reduced CV risk, depending on the characteristics of subjects. Low T observed in obese patients might represent the result of higher CV risk rather than a direct pathogenetic mechanism.
A Review on the Pathophysiology of Erectile Dysfunction


**ABSTRACT**

Erectile dysfunction (ED) affects up to 50% of men between the ages of 40 and 70 years. Treatment with PDE-5 inhibitors is effective in the majority of men with ED. Brief information about the characterization of ED and related disease conditions are discussed in this article.

**Key Words**

Erectile dysfunction, nitric oxide, diabetes, cardiovascular disease

**Introduction**

The process of achieving penile erection involves the integration of psychological, neurological, and vascular processes, which combine to initiate a physiologic response within the penile vasculature. Endothelial mediated dilation of arteriolar smooth muscle results in increased blood flow into the sinusoids of the corpora cavernosum and subsequent filling while simultaneously relaxing to increase compliance. This filling obstructs venous outflow from the penis by compression of the veins against the tunica albuginea, resulting in penile erection. Erectile dysfunction (ED) is defined as a difficulty in initiating or maintaining penile erection adequate for sexual relations. One of the largest current studies of ED, the Massachusetts Male Aging Study, found that ED may be present in up to half of the male population between 40 and 70 years old. This condition has been estimated to affect 150 million individuals worldwide and data from the ENIGMA study in 2004 suggested that the condition is prevalent in approximately 17% of all European men. ED may present with comorbidities of hypertension, diabetes mellitus, obesity, and atherosclerosis. Alcoholism, illicit drug use, and pharmacologic agents such as β-blockers, diuretics, and antidepressants have also been suggested to play a role in the etiology of ED.
Characterization of ED

ED can be classified as developing from psychological, neurological, hormonal, and vascular pathologies, or combinations of these factors.

Psychological

Psychological factors such as stress, depression, schizophrenia, and a lack of sexual arousability lead to difficulty in achieving an erection. ED may be caused by diseases that interfere with libido, and therefore the brain's perception of arousal, such as Alzheimer disease, stroke, Parkinson disease, or brain trauma. Injury to the spinal cord may interrupt neural pathways to the sacral region, preventing or inhibiting the process of achieving an erection.

Hormonal

Hormones such as adrenocorticotropic hormone, oxytocin, prolactin, and androgens, especially testosterone, have been implicated in the modulation of erectile function. Hypogonadism plays a significant role in ED as it is believed that a threshold level of testosterone is necessary for erection to occur, and as men start aging, there is a natural decrease in testosterone production further contributing to ED.

Vascular

Peripheral arterial disease and endothelial dysfunction seen in diabetes mellitus, atherosclerosis, coronary disease, and hypertension also contribute to the development of ED. It has also been hypothesized that ED is an early harbinger of cardiovascular disease. Along with these causes, failure to occlude venous outflow from the sinusoids of the corpora can be a contributing factor for ED. This may develop from degeneration of the tunica albuginea, loss of myogenic venous responses, trauma, or endothelial/smooth muscle dysfunction in the corpora.

Nitric oxide and ED

Nitric oxide (NO) is thought to be the main vasoactive neurotransmitter involved in the erectile response and is released from nonadrenergic, noncholinergic (NANC) neurons as well as from the endothelium. An erection is dependent primarily upon a neurovascular, NANC mechanism peripherally, and on the central nervous system. Nitric oxide synthase (NOS) is the enzyme responsible for the conversion of L-arginine to NO and L-citrulline. NOS has been identified within neuronal tissue (nNOS), endothelium (eNOS), and epithelial tissue within pelvic and urogenital structures of males. In addition to NO released from NANC nerves, shear forces also stimulate NO production by eNOS in the endothelium. NO diffuses across smooth muscle cell membrane and activates soluble guanylate cyclase, which in turn catalyzes production of cyclic guanosine monophosphate (cGMP) from intracellular guanosine triphosphate (GTP). A cGMP-dependent protein kinase is activated, membrane hyperpolarization occurs through potassium channels in the smooth muscle cell membrane and there is an increase in uptake of Ca2+ into stores (endoplasmic reticulum). This hyperpolarization leads to blockade of membrane Ca2+ channels, decreasing calcium influx and causing smooth muscle cell relaxation. This relaxation produces dilation of arteries/arterioles resulting in increased blood flow into corporal sinuses in both systolic and diastolic phases. The cavernosal sinuses expand while trapping arterial inflow. Compression of the subtunical venous plexuses between the tunica albuginea and the peripheral sinusoids reduces venous outflow from the penis. In addition, the tunica stretches to capacity and further occludes emissary veins between the inner circular and longitudinal layers further decreasing venous outflow. The partial pressure of oxygen increases from 35 mmHg to 90 mmHg and the intracavernosal pressure reaches approximately 100 mmHg, which raises the penis from a flaccid nonerecile state to a fully erect state (full-erection phase). Additional pressure increase results from contraction of the ischiocavernosus muscles (rigid erection phase). When the smooth muscle is then contracted, arterial inflow is reduced to a minimum and the penis assumes a flaccid state. A cGMP-specific phosphodiesterase (type 5) breaks down the cGMP to GTP and terminates membrane hyperpolarization, attenuating the relaxation of vascular smooth muscle cells.

NO is intimately involved in many of the known etiologies and comorbidities of ED. Endothelial dysfunction is caused by a decrease in formation or increase in oxidation of NO. Due to this dysfunction, the penis is not perfused sufficiently to fill the cavernosal sinusoids and cause an erection. This lack of endothelial-dependent vasodilation links ED with diabetes, cardiovascular disease (CVD), and hypertension—emphasizing the vital role that loss of endothelial/NO-dependent vasodilation plays in ED. Reactive oxygen species (ROS) have also been implicated in type 1 diabetic ED and studies demonstrating that blockade of ROS prevent impairment of NO-mediated vasodilation. Another major process linking NO and ED is impairment of NANC nerves or nNOS mediated NO release. Studies have found that type 1 diabetic animals have dysfunctional relaxation of the corpora cavernosa in response to electrical stimulation, which indicates an NANC nerve impairment. Type 2 diabetic animal models have also been found to be deficient in penile nNOS.
Related Disease States

Despite the successful use of PDE-5 inhibitors, there is still a significant population of patients that remain refractory to this therapy. ED in individuals with chronic disease states such as diabetes mellitus (DM) and CVD often remains refractory because of the reliance of these drugs on functional NO release. Therefore, the examination of these disease states may provide useful insight into the etiologies of ED.

Diabetes

The Massachusetts Male Aging Study found that diabetic men are 3 times more likely to develop ED compared to their nondiabetic counterpart. In diabetic men, peripheral vasculopathy and neuropathy are intimately involved in the development of ED. Chronic hyperglycemia may lead to micro- and macrovasculopathy, including endothelial dysfunction. Autonomic and peripheral neuropathies also develop commonly in these individuals with poor glycemic control. The risk factors for diabetic ED include glycemic control, advanced age, duration of diabetes, and diabetic complications such as retinopathy. Hyperlipidemia, hypertension, and obesity are also all independent risk factors for diabetic men.

Cardiovascular disease

Cardiovascular diseases and ED are closely related because both disease states involve impaired vascular endothelial function and decrease bioavailability of NO. Therefore, a high coprevalence between ED and CVD exists. Risk factors such as hypertension, hypercholesterolemia, smoking, and DM are also common between the two disease states. It is logical that microvascular disease associated with ED should precede macrovasculopathies and studies have found that ED is significantly associated with CVD as well as CVD mortality. However, ED does not improve prediction of CVD beyond the traditional risk factors included in the Framingham risk score. Standard therapy of PDE-5 inhibitors is strongly contraindicated in patients who are taking nitrates, as this may lead to severe hypotension and even death, thus further excluding these patients from current therapies. In men with hypertension, rather than high-blood pressure arterial stenosis is associated with the development of ED. It has been shown in spontaneously hypertensive rats that vascular relaxation, dependent on cavernosal endothelium and NO donors, is inhibited before systemic vascular changes occur. This suggests that changes to the eNOS associated with ED may precede systemic endothelial dysfunction in hypertensive patients. Oxidative damage from superoxide anion may also be important in the association between ED and hypertension. In human subjects, hypertension has been correlated with a decrease in endothelial-mediated smooth muscle relaxation and it has been proposed that NO may be unable to overcome the sympathetic neural activity and other procontractile mediators that are involved in establishing/maintaining the penis in a flaccid state (eg, ET-1, neuropeptide Y, prostanoids, norepinephrine, and angiotensin II, etc). In vivo studies in rodents to model ischemia/hypertension have been performed using an iliac artery ligation to reduce perfusion. This procedure results in a decrease in both myelinated and nonmyelinated fiber diameter of nerves innervating the penis, corporal smooth muscle depletion of myofilaments, and fewer endothelial cells surrounding the vasculature. As endothelial dysfunction has been associated with a variety of detrimental vascular diseases such as atherosclerosis, hypertension, and hypercholesterolemia, it was determined at the Second Princeton Consensus Conference of 2006 that ED is a telltale warning sign of silent vascular disease and that a man with ED without cardiac symptoms should be considered as an “at risk” cardiovascular patient until proven otherwise.

Drug-induced ED

It has been reported that the side effects of certain pharmacological agents may play a role in up to 25% of newly presenting ED cases. Antihypertensive drugs can produce ED as a side effect. Thiazide diuretics have been reported to produce more ED than other antihypertensive agents. A clear mechanism has not yet been elucidated, though it has been suggested that diuretics interfere with smooth muscle relaxation. Calcium channel antagonists and ACE inhibitors have fewer detrimental effects on sexual function than diuretics, centrally acting-agents and beta-blocking therapies. The aldosterone antagonist, spironolactone, is commonly prescribed for heart failure and can be used for hypertension. It can lead to ED by what is thought to be an antiandrogenic mechanism where hydrotestosterone is completely inhibited from binding androgenic receptors due to the structural similarity of spironolactone to androgens. Atenolol and propranolol are two b-blocking agents that have been associated with ED due to their antiadrenergic effects as well as mild psychological depression resulting in reduced libido. Centrally acting antihypertensives such as clonidine
can act to inhibit erectile function by depressing adrenergic output. Methyldopa has a similar side effect profile in respect to ED with greater prevalence when compared to clonidine. Many antidepressant pharmacotherapies report ED as a common side effect. Increased prolactin levels associated with the use of the H2-antagonist cimetidine and the phenothiazine antipsychotics, chlorpromazine, and thioridazine, have also been associated with ED.

Priapism

Priapism is defined as an erection that lasts more than 4 hours beyond sexual stimulation or that is not related to sexual stimulation. The prolonged duration of erection associated with ischemic and intermittent priapism can result in destruction of sinusoidal endothelium and necrosis of cavernosal smooth muscle cells. Priapism is prevalent in patients with sickle cell disease (SCD). In SCD, free hemoglobin is reported to act as a scavenging molecule oxidizing NO and forming methemoglobin. The outcome of these processes is hemolytic endothelial dysfunction in which there is abnormal activity of important vasoactive signaling molecules and mechanisms such as NO, PDE-5, adenosine, and Rhokinase. The destruction of corporal and smooth muscle that occurs with ischemic priapism often results in ED. Priapism may also result from the use of erectile function promoting agents that have a long duration of action.

Subclinical Renal Dysfunction is Independently Associated with Cardiovascular Events in Rheumatoid Arthritis: The CARRE Study

Van Sijl AM, et al.


**Background**

Patients with rheumatoid arthritis (RA) have double the risk of cardiovascular (CV) disease, largely independently of traditional CV risk factors. Renal dysfunction is associated with CV morbidity and mortality in the general population, but data on this association in RA are lacking.

**Objective**

To investigate the association between renal function and CV events in RA.

**Methods**

The CARRÉ Study is an ongoing prospective cohort study of Dutch patients with RA, which records CV events. Glomerular filtration rate (GFR) was estimated with the abbreviated Modification of Diet in Renal Disease formula. Logistic regression determined the association between estimated GFR and the occurrence of CV events.

**Results**

Three hundred fifty-three patients were followed up for 3 years, and 23 (7%) had a CV event. Patients who had an event had a significantly lower baseline GFR than those who did not (59 vs 79 mL/min, *P* = .001). This association remained significant after adjustment for traditional risk factors. In this analysis, a decrease in GFR of 5 mL/min was associated with a 30% (95% CI, 7%–59%) increase in the occurrence of CV events. During follow-up, an unfavorable change in GFR was noted in patients who later had a CV event compared with those who did not.

**Conclusion**

These data confirm that, in RA, renal dysfunction is associated with a higher risk of CV disease independently of traditional CV risk factors.
Evaluation of Clinical Efficacy and Safety of Rumalaya Liniment in Orthopedic Patients

Das SK, et al.

**Abstract**

This study was planned to evaluate the efficacy and safety of Herbal liniment (Rumalaya liniment) in orthopedic disorders. One hundred patients of either sex in the age group of 10 to 63 years were enrolled in the study after they fulfilled the inclusion and exclusion criteria. Patients applied Herbal liniment over the affected area, twice daily with gentle rubbing for a period of 1 month. Statistical analysis of changes in various parameters from baseline values was evaluated by Wilcoxon Signed Rank test. This study indicated that there was a significant reduction in pain, joint tenderness, joint swelling, mobility restriction, and early morning joint stiffness. In patients with periarthritis shoulder joint, osteoarthritis knee joints, and nonspecific arthritis, there was moderate reduction of pain. There were no adverse events reported or observed during the entire period.

**Key words**

Orthopedic, sprain, arthritis, herbal liniment

**Introduction**

With high speed transportations, mechanization, industrialization, and sports activities, the incidence of trauma, including trivial injury and certain orthopedic joint problems, are constantly increasing in the society. Simple movements, walking, bending, and turning, require using hip and knee joints. Normally, all parts of these joints work together and the joint moves easily without pain. But when the joint becomes diseased or injured, the resulting pain can severely limit one’s ability to move and work. The International Association for the Study of Pain has defined pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.” According to the World Health Organization, pain is the most common reason for which patients visit their physician. Pain can be divided into two basic categories, acute and chronic. A common definition of acute pain is “the normal, predicted physiological response to an adverse chemical, thermal, or mechanical stimulus associated with surgery, trauma, and acute illness.” Even brief intervals of acute pain can induce long-term neuronal remodeling and sensitization (plasticity), chronic pain, and lasting psychological distress.
Chronic pain refers to pain that persists after an injury, pain related to a persistent or degenerative disease, and long-term pain from an unidentifiable cause. Chronic pain may be caused by the body’s response to acute pain. One of the frustrating aspects of chronic pain is that the stimulus may be unknown. For example, the stimulus cannot be identified in as many as 85% of individuals suffering lower back pain.

The common causes of joint pain are osteoarthritis (OA), rheumatoid arthritis, post-traumatic arthritis, and avascular necrosis. Joint pain can also be caused by deformity or direct injury to the joint. In some cases, joint pain is made worse by the fact that a person will avoid using a painful joint, weakening the muscles, and making the joint even more difficult to move. To meet with these problems, various methods of treatment including conservative and surgical are in practice. Conservatively, analgesics, muscle relaxant gel, and pain relieving liniments are some of the simplest external application methods for relieving pain. One of the most commonly prescribed types of drugs are the nonsteroidal anti-inflammatory agents (NSAIDs), which has to be taken for long term to reduce both pain and swelling caused by arthritis. NSAIDs are among the most widely used medications, but the side effects of these drugs frequently include gastrointestinal ulceration, indigestion, burning, and bleeding.

A relatively new class of anti-inflammatory drugs called COX-2 inhibitors may provide significant benefits in the treatment of OA. COX-2 inhibitors were claimed to be devoid of ulcer-promoting effects; however, this promise has been unfulfilled, and there are concerns about the cardiovascular safety of COX-2 inhibitors. In rare cases, serious stomach problems, such as bleeding, can occur without warning. NSAIDs and COX-2 inhibitors should not be taken by people who are allergic to aspirin. Another type of medication prescribed to reduce severe pain and swelling are corticosteroids. Corticosteroid injections offer quick, effective pain relief. However, they can be used only a few times a year because they weaken bone and cartilage. Also, as corticosteroids can cause other potentially serious side effects, their use must be monitored by a physician.

The term “complementary medicine” describes a range of preparations, including herbal medicines, homoeopathic remedies, essential oils, and dietary supplements, which mainly sit outside conventional medicine. The use of complementary medicine is a popular health care approach in the United Kingdom, and there are signs that the use of such products is continuing to increase. Patients and the public use complementary medicines for health maintenance, for the treatment or prevention of minor ailments, and also for serious, chronic illnesses.

Many complementary medicines, particularly herbal medicines, have a long history of traditional use. The use of herbs to treat illness has its roots in an ancient holistic healing tradition that originated in Asia more than 3000 years ago. Largely discounted by 19th and 20th century practitioners of western medicine, healing practices incorporating herbal remedies, such as Traditional Chinese Medicine, Japanese Kampo, and Indian Ayurveda are rapidly gaining acceptance in the west as we enter the 21st century. Herbal medicines are complex mixtures of minimally processed medicinal plants (eg, plant parts that are boiled to make a tea). In conjunction with other components of traditional healing, philosophies such as acupuncture or massage and herbal medicines are used to treat a large range of symptoms and ailments. Herbal drug treatment has been known for centuries as a part of traditional medicine. Nowadays, it is still considered a useful and natural way to treat several medical conditions, including mental disturbances. The most frequently treated mental conditions include mood disorders (mainly depression), anxiety disorders, somatoform disorders, age-related cognitive decline, and sometimes psychotic disorders.

Herbal liniment (Rumalaya liniment) is a polyherbal formulation and it contains extracts of proven herbs like 
Poriaea corylifolia, Piper nigrum, Pinus longifolia, Gaultheria fragrantissima, Sesamum indicum, Cinnamomum camphora, Mentha arvensis, and Carum cuminum. This study was planned to evaluate the efficacy and safety of Herbal liniment in orthopedic disorders.

Application of Herbal liniment as a treatment modality has been evaluated in 100 patients attending the outpatient clinic of Department of Orthopedics, Olatpur Hospital at Bairoi, Cuttack, Orissa.

**Methodology**

**Aim of the study**

The present study was aimed to evaluate the clinical efficacy and long-term safety of Herbal liniment (Rumalaya liniment) in orthopedic problems.

**Study design**

This study was an open clinical trial conducted in the Department of Orthopedics, Olatpur Hospital at Bairoi, Cuttack, Orissa during April 2007 to July 2007.
Inclusion criteria

One hundred patients of either sex in the age group of 10 to 63 years were enrolled in the study. A written informed consent was obtained from all these patients. All included patients had clinical symptoms of either of the following:

Sprain of knee, ankle, elbow, wrist, and metacarpophalangeal and interphalangeal joints of fingers. Muscle strain periarthritis shoulder joint (frozen shoulder), OA knee joints (injury to joints without fracture), and nonspecific arthritis (tennis elbow).

Exclusion criteria

Patients with established hypertension; renal, hepatic, or cardiac failure; on long-term steroid treatment; and patients suffering from autoimmune disorder, spastic condition, or genetic disorders were excluded from the study.

Study procedures

The trial was conducted in 100 patients with a mean age of 41.1 ± 13.1 years with 56 male and 44 female patients. Duration of illness ranged between 2 days to 7 years. Out of 54 male patients, 16 were smokers and 7 were alcoholics. The nature of orthopedic injury was due to various factors like fall or accident, traumatic, osteoarthritis, sprain, periarthritis, frozen shoulder, jerk, tennis elbow, etc. The diagnosis of the concerned disease was confirmed by clinical examination. The study duration was 1 month. The evaluation parameters included symptomatic relief in pain intensity, swelling, tenderness, and movement. Score for pain intensity, swelling, and tenderness was done using 0 to 3 scale where 0: no pain, 1: mild, 2: moderate, and 3: severe. With regard to movement, the scoring was 0: no restriction, 1: mild restriction, 2: moderate restriction, and 3: severe restriction. All patients were advised to apply Herbal liniment over the affected area, twice daily for a period of 1 month.

Follow-up and assessment

The patients were followed up at fortnightly interval during which evaluation of the clinical parameters was recorded. A complete clinical and orthopedic evaluation was carried out at the end of the study.

Primary and secondary outcome measures

The predefined primary outcome measures for efficacy were relief of pain, swelling, and tenderness. Secondary outcome measures were short- and long-term and patient compliance to therapy.

Statistical analysis

Statistical analysis was carried out using Wilcoxon Signed Rank test. The scores for symptomatic relief of 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 4.01.

Results

A total of 100 patients who were enrolled completed the study. They were in the age group ranging between 10 and 63 years.

The results and the statistical significance for various parameters are shown in Tables 1 and 2.

Incidence (%) of Symptom Score Before and After the Treatment

The patients with sprain, muscle strain, injury to joints, and tennis elbow experienced substantial relief from pain. Swelling and tenderness also reduced considerably. Patients with osteoarthritis, nonspecific arthritis, and periarthritis shoulder joint had temporary relief from pain and required additional therapy.

Those patients who had received additional sample of liniment had considerable relief from pain; in fact, many of them were comfortable after using two bottles of liniment indicating the long-term safety and efficacy of Herbal liniment.

There was good compliance to the treatment and no adverse events were reported or observed in the study patients during the entire study period. None of the patients withdrew from the study.

| Table 1. Effect of Herbal Liniment on Clinical Parameters |
|----------------|-----------|----------------|----------------|
| Symptomatic relief | Mean score | Before | After | P value |
| Pain intensity | 2.35 ± 0.54 | 1.05 ± 0.58 | <.0001 |
| Swelling | 2.15 ± 0.65 | 1.38 ± 0.64 | <.0001 |
| Tenderness | 2.34 ± 0.56 | 1.63 ± 0.66 | <.0001 |
| Movement | 2.45 ± 0.69 | 1.51 ± 0.73 | <.0001 |

| Table 2. Effect of Herbal Liniment on Incidence (%) of Symptom Score Before and After Treatment |
|----------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| Symptomatic relief | Before treatment (% incidence) | | | | | |
| | None | Mild | Moderate | Severe | None | Mild | Moderate | Severe |
| Pain intensity | 0 | 3.3 | 58.7 | 38.0 | 14.13 | 66.3 | 19.6 | 0 |
| Swelling | 3.3 | 4.4 | 66.3 | 26.1 | 8.7 | 44.6 | 46.7 | 0 |
| Tenderness | 0 | 4.4 | 57.6 | 38.0 | 9.8 | 17.4 | 72.8 | 0 |
| Movement | 2.2 | 4.4 | 40.2 | 53.3 | 14.1 | 20.7 | 65.2 | 0 |
Adverse events

Most patients under trial were satisfied with the use of Herbal liniment. Two patients had more pain and swelling after massaging the liniment, which was corrected within 2 to 3 days of continued application of the liniment.

Discussion

Pain is an unpleasant feeling that is conveyed to the brain by sensory neurons. The discomfort signals actual or potential injury to the body. However, pain is more than a sensation or the physical awareness of pain; it also includes perception, the subjective interpretation of the discomfort. Perception gives information on the location of the pain, intensity, and something about its nature. The various conscious and unconscious responses to both sensation and perception, including the emotional response, add further definition to the overall concept of pain. A survey conducted in approximately 26,000 patients has indicated that one adult in five suffers from chronic pain, and out of these 21.5% have experienced pain lasting for longer than 6 months. Pain is the third leading reason for absence from work in the United States, where the problem of chronic pain translates into an annual expenditure of at least $50 billion.1

In general, musculoskeletal pain—often in the form of arthritis, nonarticular rheumatism, peripheral neuro pathies, and low back disorders—represents the most common cause of CNMP (chronic nonmalignant pain). Exposure to low social support, low social anchorage, or low social participation significantly increases the odds of a high level of pain. Most patients do not attribute chronic musculoskeletal pain to injury, but those who do report significantly higher levels of emotional distress.1

For the last few decades, orthopedic treatment modalities like analgesics and external application of muscle relaxant ointments, gels, and liniments have been used to relieve pain of minor injury and certain orthopedic problems. Use of analgesic, either oral or parenteral, has many associated complications like gastritis, abdominal distension, constipation, and loose motions. Moreover, analgesics cannot be used for prolonged period considering the risk of above complications. Therefore, the ideal method for relieving pain in minor trivial injury to muscles and ligaments is a simple method of external application of gel or liniment. There is no time limitation regarding the duration of treatment by external applications. This can be used for prolonged period. In this study, it was observed that at the end of the study there was much relief of pain from muscle spain, injury to joints, and tennis elbow. Swelling and tenderness also reduced considerably. These findings suggest the synergistic action of the ingredients of Herbal liniment. M arvensis provides potent analgesic action, and thus, is used externally in rheumatism, neuralgia, headaches, etc.24,25 G fragrantissima contains 98% methyl salicylate, a known analgesic. It is applied externally in rheumatism, sciatica, and neuralgia due to its analgesic properties.27 P nigrum,21 S indicum,22 and C copticum29 are well known for their analgesic activity. M arvensis26 and P longifolia18–20 have potent anti-inflammatory action that penetrates superficial inflamed tissues, increases blood flow to the affected area, and inhibits the release of pro-inflammatory chemomediators. As a result, it reduces swelling associated with muscle spain and ligament injury. Therefore, there is no time limitation regarding duration of treatment by the external application. This can be used for prolonged period in minor injury and certain orthopedic disorders. Preclinical studies on RL were required prior to skin application. The aim of the study was to evaluate the possible cytotoxic effects of RL and a commercial sample (CS) on mouse embryo fibroblasts and human keratinocytes using neutral red uptake, (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) and resazurin assay. The CTC50 values obtained for RL was significantly higher than that of CS, which revealed that RL is less toxic to CS. RL was less toxic (<17%) on both cell lines at 400 µg/mL and was nontoxic at further lower concentrations, whereas the toxicity of CS was above 59% even at 400 µg/mL.

It was observed from the present study that by using 3 different assay methods and 2 different cell lines, the toxicity of RL was significantly lower than that observed with CS. From this study, it could be concluded that RL could be safer to skin due to their low cytotoxicity as compared with CS.
with inflammatory conditions, shortens recovery time, and increases mobility of the joints. *M. arvensis*,27 *P. longifolia*,19 and *C. camphora*23 are used as rubefacients for external application. They produce redness of the skin by causing dilation of the capillaries and increasing blood circulation, thus distracting from the deep-seated pain and providing relief in various rheumatic conditions such as lumbago, arthritis, and neuralgia. *P. corylifolia*16 and *M. arvensis*28 are potent antioxidants, and act synergistically with the anti-inflammatory property of Herbal liniment.

**Conclusion**

A total of 100 patients with various types of muscle injury and some orthopedic problems, such as having pain, swelling, and muscle spasms were treated by Herbal liniment (Rumalaya liniment). The experience after using Herbal liniment has confirmed that the main clinical benefits were relief from pain and reduction in swelling and muscle spasms. However, the symptoms of chronic diseases like OA and frozen shoulder were not relieved completely. The liniment was found most effective in ligament or muscle injury like sprain, strain, muscle spasm, tennis elbow, and injury to joint. The liniment was found less effective in OA of joints, periarthritis of shoulder, etc. Oral or parenteral analgesic should be given for effective treatment and for synergetic action to relieve pain. No adverse reactions were reported by any of the patients.

**References**

2010 Update of the ASAS/EULAR Recommendations for the Management of Ankylosing Spondylitis


ABSTRACT

This first update of the Assessment of Spondyloarthritis International Society/The European League against Rheumatism (ASAS/EULAR) recommendations on the management of ankylosing spondylitis (AS) is based on the original paper, a systematic review of existing recommendations and the literature since 2005 and the discussion and agreement among 21 international experts, 2 patients, and 2 physiotherapists in a meeting in February 2010. Each original bullet point was discussed in detail and reworded if necessary. Decisions on new recommendations were made—if necessary after voting. The strength of the recommendations (SOR) was scored on an 11-point numerical rating scale after the meeting by email. These recommendations apply to patients of all ages that fulfill the modified NY criteria for AS, independent of extra-articular manifestations, and they take into account all drug and nondrug interventions related to AS. With a mean score of 9.1 (range 8–10) the SOR was generally very good.

First Update of the Assessment of Spondyloarthritis International Society/The European League Against Rheumatism (ASAS/EULAR) Recommendations for the Management of Ankylosing Spondylitis (AS)

The overarching principles of the management of patients with AS are:

- AS is a potentially severe disease with diverse manifestations, usually requiring multidisciplinary treatment coordinated by the rheumatologist.
- The primary goal of treating the patient with AS is to maximize long-term health-related quality of life through control of symptoms and inflammation, prevention of progressive structural damage, preservation/normalization of function, and social participation.
- Treatment of AS should aim at optimal care and must be based on a shared decision between the patient and the rheumatologist.
• The optimal management of patients with AS requires a combination of nonpharmacological and pharmacological treatment modalities.

Comment
Patients with AS present with different disease manifestations and a high proportion may run a severe course of disease. The main health problems of patients with AS have recently been listed as part of an International Classification of Functioning, Disability, and Health consensus process. It is important to stress that the rheumatologist is the expert who should take the lead in the management of patients with AS. The major aim for the treatment of rheumatic diseases is the preservation and gain of short- and long-term health-related quality of life. The general view is that this is best achieved through control of symptoms and inflammation—with the aim to prevent deformity and disability due to structural damage caused by new bone formation and the decline of function and social participation.

SOR: 9.5 ± 0.1.

Thereafter, the bullet points were discussed point by point in considerable detail, and agreement was achieved on 11 points.

The updated recommendations are:

General Treatment
The treatment of patients with AS should be individualized according to:
• The current manifestations of the disease (axial, peripheral, enthesal, extra-articular symptoms and signs).
• The level of current symptoms, clinical findings, and prognostic indicators.
• The general clinical status (age, gender, comorbidities, concomitant medications, psychosocial factors).

Comment
This general bullet point was not changed. It stresses that there may be considerable variation in how AS patients may present to the rheumatologist. The aim of management and appropriate interventions may thus also differ substantially. This implies that these aims must be tailored to the unique features of the particular AS patient.

SOR: 9.5 ± 0.1.

Disease Monitoring
The disease monitoring of patients with AS should include:
• Patient history (eg, questionnaires)
• Clinical parameters
• Laboratory tests
• Imaging
All according to the clinical presentation as well as the ASAS core set.

The frequency of monitoring should be decided on an individual basis depending on:
• Course of symptoms
• Severity
• Treatment

Comment
This bullet point was not changed.

Nonpharmacological Treatment
The cornerstone of nonpharmacological treatment of patients with AS is patient education and regular exercise.

Home exercises are effective. Physical therapy with supervised exercises, land or water based, individually or in a group, should be preferred as these are more effective than home exercises.

Patient associations and self-help groups may be useful.

For comparison, the old recommendation was nonpharmacological treatment of AS should include patient education and regular exercise. Individual and group physical therapy should be considered. Patient associations and self-help groups may be useful.

Comment
This bullet point was changed according to the systematic literature review (SLR) and the recent Cochrane review on the subject, and was supported by the view of an experienced physiotherapist (HD) and the participating patients.

SOR: 8.8 ± 0.4.

Extra-articular Manifestations and Comorbidities
The frequently observed extra-articular manifestations, eg, psoriasis, uveitis, and chronic inflammatory
bowl disease (IBD) should be managed in collaboration with the respective specialists.

Rheumatologists should be aware of an increased risk of cardiovascular disease and osteoporosis.

**Comment**

This is a new bullet point, with agreement being achieved after considerable discussion. The main argument was that extra-articular manifestations are rather frequent in AS and the entire spectrum of spondyloarthritis, and that they constitute a frequent challenge in management that clearly requires cooperation between specialties.

On the other hand, there are frequent comorbidities that require the attention of the managing rheumatologist. These include low bone mineral density, osteoporotic fractures, and cardiovascular diseases, which have been reported to occur in AS and spondyloarthritis at an increased rate compared with the general population.

The rheumatologist is encouraged to identify patients at risk and the potential additional risk factors. At this time, it is difficult to make a clear-cut recommendation on the management of osteopaenia and osteoporosis for patients with AS in the absence of any studies on the subject.

Regarding the management of cardiovascular risk, there are recent EULAR recommendations that propose an annual risk assessment related to national guidelines. Although this is mainly intended for patients with rheumatoid arthritis (RA), these same guidelines should also be considered for patients with AS and psoriatic arthritis. Rheumatologists are referred to local guidelines for the management of cardiovascular risk and, if no local guidelines are available, the management should be carried out according to the systematic coronary risk evaluation (SCORE) function. In addition to appropriate cardiovascular risk management, aggressive suppression of the inflammatory process is recommended to lower the cardiovascular risk further.

**SOR:** 9.0 ± 0.3.

**Changes in the Disease Course**

If a significant change in the course of the disease occurs, other than inflammation, such as a spinal fracture, should be considered and appropriate evaluation, including imaging, should be performed.

**Comment**

This is a new recommendation. The major point is that changes in the course of the disease should be carefully evaluated and magnetic resonance imaging (MRI) performed—especially in situations in which the nature of back pain changes. An experienced spinal surgeon may need to be consulted. It seems important to stress that not all AS patients with spinal fractures have neurological symptoms (and not all need to be operated on).

There are other important differential diagnoses such as spinal infections.

**SOR:** 9.0 ± 0.3.

**Discussion**

The ASAS/EULAR recommendations were successfully updated.

A patient version of the recommendations will be developed. We encourage translation of these recommendations into various languages in collaboration between rheumatologists and patients. After presentation at the EULAR 2010 meeting in Rome and publication in the EULAR journal, individual countries can now take on dissemination.

The collaboration between ASAS and EULAR has again been very successful and should be continued for the next update that may be renamed according to the new classification criteria for axial spondyloarthritis. There will be a need for further discussion as to whether the new criteria for peripheral spondyloarthritis should give rise to separate recommendations for these patients.

Even though it was decided that these recommendations concentrate on AS, the authors are aware of the fact that treating patients with nonradiographic axial spondyloarthritis is also very important. There are now data of clinical trials available that address this question in a controlled manner.

The original publication has already set a standard for the management of patients with AS. As we feel that this update has even improved the original set, we are confident that these recommendations will be useful for patients and health care workers, including rheumatologists and other physicians treating patients with AS, as well as physiotherapists.
Evaluation of the Efficacy and Safety of Diaper Rash Cream in the Management of Infantile Irritant Diaper Dermatitis

Sukanta Chatterjee, et al.


**ABSTRACT**

Infantile irritant diaper dermatitis (IIDD) is an inflammation of the infantile skin covering the groin, lower stomach, upper thighs, and buttocks. IIDD may become difficult to treat, if the area becomes infected or the infant develops allergy to medications applied to the area. This study was conducted to evaluate the efficacy and safety of diaper rash cream in the management of IIDD.

The study was a prospective, phase III clinical trial, conducted as per the good clinical practice guidelines. A total of 15 infants suffering from IIDD and whose parents were willing to give informed written consent were included in the study. Before beginning the study, the “diaper rash cream” was applied in a test dose and observed for the development of any immediate hypersensitivity manifestations for a period of 30 minutes. If there were no immediate hypersensitivity manifestations, the parents were advised to apply the “diaper rash cream” once daily, after bath for a period of 2 weeks, on the skin covering the groin, lower stomach, upper thighs, and buttocks. All the infants were followed up on the 7th and 14th day of application, and at each follow-up visit, a detailed clinical examination was carried out.

There was a significant improvement in the clinical manifestations of IIDD in all the included infants within 3 days, and there was complete recovery from the clinical manifestations of IIDD, after a week’s application, in all the included infants. The positive benefits observed in this study might be due to the synergistic action of the active ingredients of the formulation namely, anti-inflammatory activities (*Aloe vera*, *Vitex negundo*, and *Rubia cordifolia*), antibacterial activities (Zinc calx, *A vera*, *V negundo*, and *R cordifolia*), wound-healing activities (*A vera*), and antioxidant activities (*V negundo*, *Prunus amygdalus*, and *R cordifolia*). Therefore, it can be concluded that “diaper rash cream” is effective and safe in the management of IIDD.

**Key Words**

Infantile irritant diaper dermatitis, diaper rash, allergy

**Introduction**

Diapers are used for the care of infants, young children, and incontinent or paralyzed individuals to prevent fecal soiling and for social convenience. However, the use of diaper poses a risk of developing “irritant diaper dermatitis,” which is commonly known as “diaper rash.” Recent innovations in diaper technology have led to development of super absorbent disposable diapers, emollient delivering diapers, and breathable diapers, and these new types of diapers reduce the incidence of diaper dermatitis. The nonbiodegradable material used in super absorbent diapers is, however, a matter of serious concern because of its toxic effects and environmental pollution.1

Infantile irritant diaper dermatitis (IIDD) is an inflammation of the infantile skin covering the groin, lower stomach, upper thighs, and buttocks. IIDD may become difficult to treat, if the area becomes infected or the infant develops allergy to medications applied to the area.

The “diaper rash cream” is a polyherbal formulation recommended for the prevention and treatment of irritant diaper dermatitis, and contains the powders of Zinc calx, extract of *Aloe vera* and the oils of *Prunus amygdalus*, *Vitex negundo*, and *Rubia cordifolia*. This study was
conducted to evaluate the efficacy and safety of “diaper rash cream” in the management of IIDD.

**Aim of the study**

This study was planned to evaluate the clinical efficacy and safety (short- and long-term) of “diaper rash cream” in the management of IIDD.

**Study design**

The study was a prospective, phase III clinical trial, conducted at the Well Baby Clinic, at the Department of Pediatrics, Medical College and Hospital, Kolkata, from September to December 2004, as per the good clinical practice guidelines.

**Methods and Materials**

**Inclusion and exclusion criteria**

A total of 15 infants suffering from IIDD born at term with a birth weight of more than 2500 g (having appropriate gain in weight, length, and head circumference, and a normal psychomotor development on pediatric physical examination), and whose parents were willing to give informed written consent were included in the study. Infants who were under some medication for systemic or topical disease and those infants whose parents were unwilling to give written informed consent before entering the study were excluded from the study.

**Study procedure**

The parents who brought their infants for routine check up at the Well Baby Clinic were informed about the study product, its effects, duration of study period, their responsibilities, the importance of compliance, ethical aspects, and overall plan of the study. Informed consent was obtained in writing from the parents of all the included infants.

At the initial visit, a detailed medical history was obtained by interviewing the parents regarding any dermatological problem, or any adverse effect following the use of any baby product previously in the infant. Then, a detailed physical examination of the infant was carried out including the dermatological system.

Before beginning the study, the “diaper rash cream” (Batch No.: 40601-RD) was applied in a test dose and observed for the development of any immediate hypersensitivity manifestations for about 30 minutes. If there were no immediate hypersensitivity manifestations, the parents were advised to apply the “diaper rash cream” once daily, after bath for a period of 2 weeks, on the skin covering the groin, lower stomach, upper thighs, and buttocks.

All the infants were followed up on the 7th and 14th day of application, and at each follow-up visit, a detailed clinical examination was carried out. The parents were advised to discontinue the product, if they noticed any adverse effect.

**Adverse events**

All the adverse events, either reported or observed by the parents were recorded along with information about the onset, severity, duration, and site of the adverse reaction. The signs and symptoms of immediate skin irritation and delayed hypersensitivity reactions were evaluated as per the standard reference guidelines. The scoring scales for various adverse effects were as follows:

- Scoring scale for evaluating erythema: no erythema – 0, very slight erythema – 1, well-defined erythema – 2, moderate-to-severe erythema – 3, and very severe erythema – 4.
- Scoring scale for evaluating edema: no edema – 0, very slight edema – 1, slight edema – 2, moderate edema – 3, and severe edema – 4.
- Scoring scale for evaluating pruritus and urticaria: nil pruritus and urticaria – 0, very slight pruritus and urticaria – 1, well-defined pruritus and urticaria – 2, moderate-to-severe pruritus and urticaria – 3, and severe pruritus and urticaria – 4.

The relation of adverse events to the study product was predefined as “Unrelated” (a reaction that does not follow a reasonable temporal sequence from the time of application of the product and not localized to the whole site of application), “Probable” (follows a known responsible pattern to the suspected product, but could have been produced by the baby’s clinical state and localized at the site of application), “Possible” (follows a known responsible pattern to the suspected product that could not be reasonably explained by the known characteristics of the baby’s clinical state and localized at the site of application).

**Results**

There was a significant improvement in the clinical manifestations of IIDD in all the included infants within 3 days and there was a complete recovery from all the clinical manifestations of IIDD after a week’s application in all the included infants.

There was a significant reduction in itching among 10 infants, from the 3rd day onward, and all the infants were relieved of itching from the 5th day. There was also a significant reduction in itching among 7 infants, with regard to erythematos scaly diaper area, which often involves papulovesicular or bullous lesions, fissures, and erosions from the 3rd day onward, and all the infants were relieved of papulovesicular or bullous lesions, fissures, and erosions by the 6th day. Also, there were no clinically significant adverse reactions with excellent compliance.
There were no clinically significant adverse reactions (either reported by the parents or observed by the investigators) during the entire study period. There were no dropouts, and the overall compliance to the use of the product was excellent.

Discussion

Infantile irritant diaper dermatitis, a frequent condition, is a form of contact dermatitis, occurs due to the interaction of multiple factors (increased wetness, elevated local skin pH, fecal enzymes, and microorganisms), and manifests as an erythematous rash. Increased wetness in the diaper area makes the skin more susceptible to damage by physical, chemical, and enzymatic mechanisms. Wet skin increases the penetration of irritant substances. The urease enzyme found in the stratum corneum liberates ammonia from cutaneous bacteria, which has an irritant effect on nonintact skin. Lipases and proteases in feces mix with urine on nonintact skin and cause an alkaline surface pH, adding to the irritation. (Feces in breastfed infants have a lower pH, and breastfed infants are less susceptible to diaper dermatitis.) The bile salts in the stools enhance the activity of fecal enzymes, adding to the effect.2,3

_Candida albicans_ has been identified as a contributing factor to diaper dermatitis, and the infection often occurs after 48 to 72 hours of active eruption. _C. albicans_ has been isolated from the perineal area in as many as 92% of children with diaper dermatitis. Other microbial agents have been isolated less frequently, perhaps more as a result of secondary infections. In a clinical study, Ferrazzini et al. investigated the relevance of Candida sp. and _Staphylococcus aureus_ colonization in IIDD and determined the correlation between the extent of colonization and the severity of disease. The results showed a significant, positive correlation between severity of disease and extent of _Candida_ spp. colonization at all swab locations (the colonization by _S. aureus_ was nonsignificant).4 In a study by Dorko et al the occurrence of _Candida_ spp. was determined in infants, with diaper dermatitis, and the most frequently isolated species was _C. albicans_, followed by _C. parapsilosis, C. tropicalis, C. pulcherrima, C. guilliermondii_, and _C. zeylanoides_. Other organisms present in the mixed culture from the diaper area were _S. aureus, Escherichia coli_, and few strains of streptococci (groups B and D), and _Proteus mirabilis_. Infants diapered exclusively in disposable diapers showed less rash than those diapered exclusively or sometimes in cloth diapers.5

The principle treatment of diaper dermatitis is to keep the skin in the nappy area as dry as possible with frequent nappy change, and using absorbent disposable diapers known to reduce the incidence of diaper dermatitis. Absorbent disposable diapers do not allow urine to come into contact with the skin, and can hold large amounts of urine. For all practical purposes, these diapers need to be changed only when they become soiled with feces or they get so heavy that they are down near the child’s ankles.6

This study observed complete recovery from IIDD in all the included infants after 8 weeks’ application. Also, there were no clinically significant adverse reactions, and the overall compliance to the use of the product was excellent. The positive benefits observed in this study might be due to the synergistic action of the active ingredients of the formulation.

Zinc has been widely used in the treatment of diaper dermatitis and various studies have demonstrated the antibacterial efficacy of zinc oxide. Collipp et al. observed significant reduction in the incidence of diaper rash with oral zinc supplementation.7 In another study, Collipp et al noted that IIDD was associated with reduced hair zinc, and infants with the least hair had lower zinc levels than infants with the most hair.8 Baldwin et al conducted a study to determine the clinical benefits of a novel disposable diaper designed to deliver a zinc oxide and petrolatum-based formulation continuously to the skin during use. They evaluated the prevention of skin irritation and barrier damage from a standard skin irritant in an adult arm model. The results revealed that, exposure to the formulations directly on adult skin prior to an irritant challenge was associated with significant reduction in skin barrier damage and skin erythema, and greatest reductions were seen for the zinc containing formulations. Wearing of the formulation-treated diaper was also associated with a significant reduction in skin erythema and diaper rash compared to the control product.9

The principle constituents of _Aloe barbadensis_ are anthraquinones (aloemodin and aloin A (barbalin)),10 cinnamoyl, p-coumaroyl, feruloyl, caffeoyl aloesin, aloemannan,11 acemannan, verectin,12 elgonica dimer A, and bisbenzopyran.13 _A. vera_ has anti-inflammatory, antifungal, immunosuppressive, and wound-healing properties. The active ingredients of _A. vera_ have been found to exhibit immunosuppressive, anti-inflammatory activities, bradykinin degrading, and cell proliferation-stimulating activities.13 Ali et al found that anthraquinones from _A. vera_ are responsible for the antifungal activity.13 The constituents of
A barbadensis have wound-healing properties. Davis et al evaluated the extracts of A vera for topical anti-inflammatory activity, and the results showed that small amounts of A vera given topically inhibit inflammation induced by a moderate amount of irritant. Another study by the same author demonstrated the antioxidant and anti-inflammatory effects of aloesin derivative (isorabachromone) in A vera. As A vera has long been used to promote wound healing, the inhibitory effects of aloesin derivatives for cyclooxygenase (Cox)-2 and thromboxane (TXA 2) synthase were examined and the participation of p-coumaroyl and feruloyl ester groups in the aloesin skeleton was demonstrated, which explain, the wound-healing effects of A vera. Bautista-Perez et al demonstrated the antioxidant and anti-inflammatory activities of Bautista-Perez et al demonstrated the free radical scavenging activity of V negundo. Dharmasiri et al confirmed the anti-inflammatory, analgesic, and antihistamine properties of V negundo. Perumal et al reported the potent antibacterial activity of V negundo against E coli, Klebsiella aerogenes, Proteus vulgaris, and Pseudomonas aerogenes. The principal constituents of R cordifolia are purpurin, munjistin, purpuroxanthin, pseudopurpurin, and rubiadin. anthraquinones (cordifoliol and cordifodiol) and a naphthoic ester (rubialactone). R cordifolia has antioxidant antibacterial and anti-inflammatory activities. Tripathi et al demonstrated the antioxidant activity of R cordifolia, which inhibited lipid peroxidation in a dose-independent manner. Cai et al demonstrated the antioxidant activity of hydroxyanthraquinones from R cordifolia. Qiao et al demonstrated the antibacterial activity of the constituents in R cordifolia. Jain et al demonstrated the anti-inflammatory activity of the constituents of R cordifolia.

Conclusion

IIDD is an inflammation of the infantile skin covering the groin, lower stomach, upper thighs, and buttocks. IIDD may become difficult to treat, if the area becomes infected or the infant develops allergy to medications applied to the area. This study was conducted to evaluate the efficacy and safety of “diaper rash cream” in the management of IIDD.

There was a significant improvement in the clinical manifestations of IIDD in all the included infants within 3 days; and there was complete recovery from the clinical manifestations of IIDD, after a week’s application, in all the included infants.

There was a significant reduction in itching among 10 infants from the 3rd day onward and all the infants were relieved of itching from the 5th day. There was also a significant reduction in 7 infants, with regard to erythematous scaly diaper area, which often involves papulovesicular or bullous lesions, fissures, and erosions from the 3rd day onward, and all the infants were relieved of papulovesicular or bullous lesions, fissures, and erosions by the 6th day. Also, there were no clinically significant adverse reactions, and the overall compliance to the use of the product was excellent.

The positive benefits observed in this study might be due to the synergistic action of the active ingredients of the formulation namely, anti-inflammatory activities (A vera, V negundo, and R cordifolia), antibacterial activities (Zinc calx, A vera, V negundo, and R cordifolia), wound-healing activities (A vera), and antioxidant activities (V negundo, P amygdalus, and R cordifolia). Therefore, it can be concluded that “diaper rash cream” is effective and safe in the management of IIDD.

References

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A Review on Diaper Dermatitis

Diaper dermatitis or diaper rash, most commonly observed in infants 9 to 12 months old, affects all infants at least once in their first 3 years of life. It is characterized by redness and mild swelling of the skin in the diaper area comprising the perineum, buttocks, proximal thighs, and lower abdomen. Diaper dermatitis does not usually involve the intertriginous areas. Skin redness can range from mild to appearing burned or raw. In severe cases, the skin may blister or peel leaving raw areas that may bleed or ooze fluid. Baby with a diaper rash is often uncomfortable and fusses or cries when the diaper area is washed or touched. Diaper dermatitis can also be seen in children who are incontinent or paralyzed.

Rarely, specific dermatitis in the diaper area can be seen in children with psoriasis, atopic dermatitis (eczema), and seborrhea. Seborrheic diaper dermatitis is characterized by salmoncolored greasy lesions with a yellowish scale that involves the intertriginous areas. Here other parts of the body are also affected.

Psoriatic diaper dermatitis is suspected when the dermatitis fails to respond to empirical therapy for weeks. The typical silvery scale is usually not seen as the area tends to be moist. Skin biopsy confirms the diagnosis.

Candidial diaper dermatitis appears as a bright red rash with sharp borders and satellite papules and pustules. Candidial diaper dermatitis also involves the intertriginous areas. It is occasionally associated with oral thrush. It may follow a course of oral or parental antibiotics. Examination of pustule contents by KOH preparation shows the typical budding yeasts and pseudohyphae of Candida.

Etiology

- Feces and urine
- When the bacteria in the stool react with urine, ammonia is formed. This can cause a rash to develop. When babies have diarrhea, the stools may be acidic and cause skin irritation.
- Friction
- Friction of sensitive baby skin against a wet diaper can cause a reddish shiny area on the exposed skin.
- Chemicals
- Sometimes the fragrance within a disposable diaper (nowadays most of the diapers available in the market are odourless), or detergent used to wash a cloth diaper can cause skin irritation and lead to rash. Allergy to wipes can also cause rashes.
- Newer foods
- Introduction of new foods including semisolids can cause a change in the stool composition and render the skin susceptible to rash. It is also possible that the baby’s skin is sensitive to something in the breastfeeding mother’s diet.
- Infection
- The warmth and moisture within a heavy diaper form a milieu conducive to growth of bacteria, but more commonly yeast like Candida. Babies on antibiotics for long, or whose nursing mothers are on antibiotics for long can have Candida dermatitis in the diaper area. Newborns with oral thrush can sometimes develop Candida infection in the perianal area too. Some babies can develop bacterial infection over the rash, with purulent discharge, resembling impetigo.

Predisposing Factors

Diaper dermatitis is commonly seen in the following situations.

- When solid foods are added to the baby’s diet
- When the baby receives antibiotics
- Continuously wet or infrequently changed diapers
- Diarrhea
- Use of plastic pants to cover diapers
Diaper rash is thought to occur due to:

- Rubbing of sensitive skin against the wet diaper
- Acid in the urine and feces
- Cleaning agents such as diaper wipes
- Reaction to laundry detergent, soap, lotion, or the elastic of plastic pants

Complications of Diaper Rash

Secondary staphylococcal bacterial infection of the affected area may occur, which requires treatment with oral and topical antibiotics. This is suspected when:

- Pustules on an erythematous base are seen in the area.
- Infant develops fever.
- Affected area develops yellow-colored crusts suggesting impetigo.

Management

The best treatment for diaper rash is to keep the baby’s skin as clean and dry as possible. Most diaper rashes last a few days and can be treated at home. The following advice can be given to parents:

- Change diapers as soon as urine or stool has been passed.
- Clean soiled area with warm clean water and pat dry. Avoid using chemical wipes or soap. Do not rub the area.
- Use barrier creams over the area before placing another diaper. Disposable diapers are superabsorbent and keep the area dry. It may be a good idea to change the brand and see the response in case the baby’s skin is allergic to one brand.
- Keep the diaper area open to air for a few hours every day.
- Avoid using plastic covers or tight diapers. It may help to use over-sized diapers to increase air circulation in the affected area.
- Use talcum powder to protect the skin against moisture. However, it is no longer recommended due to the risk of inhalation into the lungs. Prescribe a short course of topical steroid creams only in resistant or severe cases.

Treatment includes local application of barrier creams and zinc oxide. If there is Candida dermatitis, an antifungal topical application like nystatin, miconazole, clotrimazole or ketoconazole would be useful. If there is bacterial infection like impetigo, topical and sometimes systemic antibiotics would be required. Rarely, when the rash is severe enough to cause skin excoriation or bullous eruptions, a mild steroid application might be required for the anti-inflammatory effect. Ointments that contain vitamin A have been suggested as possible treatment for diaper rash, but the results of a systematic review published in 2009 shows that there is not enough evidence to say whether vitamin A is effective for treating or preventing diaper rash; more research is required in that regard.
Diaper dermatitis, an acute inflammatory reaction of skin in the perineal area, is an extremely common pediatric condition and causes considerable parental anxiety. The presence of irritants from feces and urine with the concurrent mechanical friction and occlusion creates an environment in the diapered area that renders the skin prone to diaper dermatitis. Besides being a source of discomfort to the infant, these skin irritations pose a risk of secondary infections.

A number of factors play a role in development of diaper dermatitis, including prolonged exposure to excreta, alterations in skin pH or increased hydration, changes in skin microbial flora, and increase in local temperature and humidity. As a consequence, the skin becomes susceptible to friction from movement under the diaper. Occlusion, maceration, and possibly Candida and bacteria may all play a role. Oils, soaps, and powders can be irritants and aggravate the eruption.

To better understand the frequency of diaper dermatitis, treatment practices, and the importance of previously identified etiologic factors, a questionnaire survey of parents who had children wearing diapers (n = 532) attending a large United Kingdom district general hospital was undertaken. At the time of survey, only 16% of the study population had diaper dermatitis. Forty-eight percent of the study population had never had an episode of diaper dermatitis. In a multivariate analysis, current diaper dermatitis was independently associated with four factors: presence of oral thrush, number of previous episodes, frequency of diaper changes, and diarrhea.

Recurrent episodes of diaper dermatitis were associated with increasing age, lack of barrier cream use, current diaper rash, and frequency of diaper changes. It most commonly presents as an acute irritant contact dermatitis but a great number of dermatoses can manifest with lesions in the diaper area and have to be considered in differential diagnosis.

Impaired skin barrier function
Skin irritation in diaper dermatitis is thought to begin with the impairment of the skin barrier caused by the conditions of the diapered skin, including occlusion, moisture, friction, and alkaline skin pH that favors proteolytic enzyme activity.

A study was conducted to build on the current understanding of diaper dermatitis and to define noninvasive measurable parameters that relate to the pathophysiology of this skin condition. This study included 16 infants with mild or moderate diaper dermatitis and 19 infants without any clinical skin symptoms as controls (all infants were 3–25 months of age). Three skin sites were examined with noninvasive bioinstrumentation:

(a) control nonirritated site outside of the diaper (upper thigh),
(b) control nonirritated site on the buttock (inside the diaper), and
(c) diaper dermatitis involved site (for the dermatitis group only).

The parameters assessed included skin water barrier by transepidermal water loss (TEWL), skin moisture level by skin conductance, skin pH, and skin erythema by diffuse reflectance spectroscopy.

Results of this study showed that the apparent concentration of oxyhemoglobin was significantly higher on the dermatitis site compared with the two controls. TEWL and skin conductance values were also higher on the involved site compared with the controlled sites, indicating impaired barrier function. Lastly, skin surface pH was significantly more alkaline for both diapered areas (rash and control) compared with the air-exposed thigh site. These findings are consistent with the current understanding of pathologic skin changes in diaper dermatitis. In this study, the authors demonstrated for the first time that noninvasive methods can document parameters relevant to diaper dermatitis in vivo.

Recent decades have seen great improvements in our understanding of diaper dermatitis and our ability to develop new and better products to protect baby skin. Better diaper designs and the development of pH-buffered baby wipes have improved the care of skin in the diaper area. Continuing research offers the promise of new products with additional benefits for caregivers and infants. At the same time, evidence supports frequent diaper changes, use of super absorbent diapers, and protection of perineal skin with a product containing petrolatum and/or zinc oxide as effective ways of managing diaper dermatitis.

References
Turmeric Extract Comparable to Ibuprofen in Treating Knee Osteoarthritis Symptoms


Osteoarthritis (OA), a degenerative joint disorder, is a common cause of disability for both men and women. Nonsteroidal anti-inflammatory drugs (NSAIDs) are the most common form of treatment for relieving pain associated with OA, but they can cause serious adverse side effects that impact gastrointestinal, renal, and cardiac health. Curcumin present in turmeric (Curcuma longa, syn. C domestica, Zingiberaceae) extracts has been reported to have anti-inflammatory and antioxidant properties. Researchers from Mahidol University in Bangkok, Thailand conducted a study to determine the efficacy and safety of a turmeric extract in reducing pain and improving function in patients with knee OA.

The study included adult subjects who had primary knee OA according to the American Rheumatism Association criteria. To be included in the study, patients had to have knee pain and radiographic osteophytes, as well as at least 1 of the following characteristics: being older than 50 years of age, suffering from morning joint stiffness lasting less than 30 minutes, and/or experiencing crepitus on motion. Patients reporting a pain score of ≥5 of 10 in a numerical rating scale were recruited. All patients were randomly allocated to receive either ibuprofen (400 mg twice daily) or turmeric extract (500 mg curcuminoids 4 times daily) for 6 weeks.

The patients were assessed every 2 weeks. The main outcomes were pain on level walking and pain on stair climbing, measured by a numerical rating scale, as well as knee functions assessed by the time spent on a 100-m walk and going up and down 10 steps. All patients had blood tests assessing complete blood count, liver function, and renal function at week 0 and week 6.

Of 190 patients screened, 107 were selected for the study; 52 were randomly assigned to the curcuminoid group and 55 to the ibuprofen group. Of those, 45 patients in the curcuminoid group and 46 patients in the ibuprofen group completed the study. Most of the patients were overweight (average BMI>25) elderly women. The duration of symptoms before entering the trial was approximately 20 months. Half of the patients had bilateral knee OA. At baseline, the mean pain scores on level walking and on the stairs, as well as the time spent on the 100-m walk and on the flight of stairs were similar between the 2 groups.

The authors report that the mean scores of all outcomes in both groups at week 6 were significantly improved when compared with the baseline values. For example, from week 0 to week 6, the scores for pain on level walking dropped from 5.3 ± 2.3 to 2.7 ± 2.5 for the curcumin group and from 5.0 ± 1.9 to 3.1 ± 2.3 in the ibuprofen group. There was no significant difference in those parameters between the 2 groups, except that pain on stair climbing was less for those taking curcuminoids (P = .016). Also, the curcuminoid group seemed to spend less time on the 100-m walk and going up and down a flight of stairs. Many patients in the curcuminoid extract group who experienced bloating symptoms and passing gas described these symptoms as beneficial gastrointestinal effects, whereas those in the ibuprofen group reported gastrointestinal irritation symptoms.

Regarding satisfaction, most patients rated themselves as having moderate-to-high satisfaction (91.1% in the curcuminoid group, 80.4% in the ibuprofen group). The patients in the ibuprofen group had better compliance to the treatment regimen than those in the curcuminoid extract group (90.1% vs 82.8%, P = .001). This finding was attributed by the researchers to the fact that ibuprofen was given twice a day, whereas curcuminoid extract had to be taken 4 times a day.

These results suggest that curcuminoid extracts of turmeric might be as effective as ibuprofen in alleviating knee pain and improving knee functions, with a trend toward a greater effect in patients receiving curcumin extracts. The authors recommend more studies with an adequate sample, a higher dose of ibuprofen in the comparison group, and a double-blind technique to demonstrate the efficacy of turmeric extracts in alleviating knee pain and improving knee function.
Should Patients with Erectile Dysfunction be Evaluated for Cardiovascular Disease?

Ewane KA, et al.

The landmark Massachusetts Male Ageing Study shed new light on the prevalence of erectile dysfunction (ED) and drew attention to ED as a disease of ageing. Over the years, ED has been linked to the development of cardiovascular disease (CVD) in some patients. There is clear evidence that ED and CVD share a similar risk factor profile. CVD is one of the most recognizable causes of mortality and early detection coupled with prevention of mortality from CVD has been the prime interest of many researchers. Consequently, there has been a multidisciplinary curiosity regarding the proposal to use ED as a marker for future CVD. In fact, there have been several proposals to use ED as a screening tool for future CVD. A comprehensive search of two main databases—PubMed and Cochrane Library using a combination of keywords such as acute myocardial infarction, coronary artery disease (CAD), and ED was performed. Journal articles from January 2000 to June 2011 were reviewed. All articles discussing the relationship between ED and CVD in the English language were included. All the relevant randomized controlled trials, cohort and retrospective studies, and review articles were included in the overall analysis in an attempt to answer the question whether all patients with ED should be clinically evaluated for CVD. The results showed a link between ED and the development of future CVD in some patients, but ED was not shown to be an independent risk predictor that is any better than the traditional Framingham risk factors. Screening for CVD may, however, be rewarding in younger patients with severe ED and in patients with concurrent CVD risk factors.

Vascular Function and Morphology in Rheumatoid Arthritis: A Systematic Review

Sandoo A, et al.

Objectives: Rheumatoid arthritis (RA) associates with significantly increased morbidity and mortality from cardiovascular disease (CVD). This may be due to complex interactions between traditional CVD risk factors, systemic rheumatoid inflammation, and the vasculature. The current literature was reviewed to answer: (i) whether there is sufficient evidence that patients with RA have altered vascular function and morphology compared with normal controls; (ii) whether there is sufficient evidence to determine if such changes relate predominantly to systemic inflammation; and (iii) whether any changes of vascular function and morphology in RA can be modified with therapy.

Methods: The MEDLINE database was searched to identify publications from 1974 to 1 November 2010 pertaining to vascular function and morphology in RA. The total number of articles included in the present review was 93. This included 57 cross-sectional studies, 27 longitudinal studies without randomization and 9 longitudinal studies with randomization.

Results: Vascular function and morphology was impaired in RA relative to healthy controls. The majority of studies reported no associations between systemic inflammation and vascular function. Treatment with anti-inflammatory medication resulted in both transient and long-term improvements in the vasculature, but only a few studies reported associations between change in inflammation and change in vascular function and morphology.

Conclusion: The link between systemic inflammation and vascular function and morphology is not wholly supported by the available literature. Long-term studies examining specific predictors (including CVD risk factors) on the vasculature in RA are needed.
**Dermatology**

**Beginning at the Bottom: Evidence-based Care of Diaper Dermatitis**

Heimall L M, et al.


Diaper dermatitis (DD), an acute inflammatory reaction of skin in the perineal area, is an extremely common pediatric condition. Nurses’ practice of preventing and treating DD is inconsistent and often not evidence-based. In addition, a 2008 Skin Injury Prevalence Study at our hospital revealed that 24% of inpatients had DD. The authors developed a project to determine a consistent and evidence-based approach to DD prevention and treatment including the availability of products. A complete literature review was conducted in addition to benchmarking with other pediatric hospitals, consultation with topic experts, and evaluation of current nursing practice prior to revising the existing perineal skin care nursing standard. The evidence supports frequent diaper changes, use of super absorbent diapers, and protection of perineal skin with a product containing petrolatum and/or zinc oxide. As supported by the literature, we revised the standard to include improvements in practice as well as product updates for prevention and treatment. Hospital-wide implementation of the revised standard included training “Skin Care Champions” to educate staff and support practice improvements. Ongoing education and monitoring by the Skin Care Champions is necessary to further improve the prevention and treatment of DD for our patients.

**Documentation of Impaired Epidermal Barrier in Mild and Moderate Diaper Dermatitis In Vivo Using Noninvasive Methods**

Stamatas GN, et al.


The presence of irritants from feces and urine with the concurrent mechanical friction and occlusion creates an environment in the diapered area that renders the skin prone to diaper dermatitis. Besides being a source of discomfort to the infant, these skin irritations pose a risk of secondary infections. In this study, we used noninvasive in vivo techniques to define measurable parameters that correlate with diaper dermatitis pathophysiology. In 35 infants (16 with mild or moderate and 19 without diaper dermatitis) we compared skin of diapered areas afflicted with diaper dermatitis to lesion-free diapered sites and to skin outside the diapered area (thigh). Our findings show significantly elevated cutaneous erythema, pH, and hydration, with significantly compromised water barrier function in involved areas compared to nonlesional sites both within and outside the diapered area. Furthermore, skin pH in nonlesional diapered skin for the diaper dermatitis cohort was significantly higher compared to the nondiapered sites. These observations are consistent with the current understanding of pathological skin changes in diaper dermatitis. In this study, we demonstrate that noninvasive methods can document relevant parameters to diaper dermatitis in vivo.
Gastroenterology

Prevalence and Risk Factors of Gastrointestinal Disorders in Patients with Rheumatoid Arthritis: Results from a Population-based Survey in Olmsted County, Minnesota.

Myasoedova E, et al.

Objectives: To compare the prevalence of gastrointestinal (GI) disorders in rheumatoid arthritis (RA) versus non-RA subjects and to describe determinants of GI disorders in RA.

Methods: The bowel disease questionnaire was completed by RA and non-RA subjects. RA patients also completed the health assessment questionnaire (HAQ).

Results: The study responders included 284 RA and 233 non-RA subjects. Abdominal pain/discomfort, postprandial fullness, nausea, and stool leakage were significantly more common in RA versus non-RA (odds ratios [OR] = 1.8; 1.9; 4.0; 8.2). The use of laxatives, proton pump inhibitors, NSAIDs, acetaminophen, and narcotics was more commonly reported in RA versus non-RA (OR = 2.0; 1.7; 3.0; 2.0; 1.9). Age <60 and HAQ ≥1 were associated with dyspepsia, irritable bowel syndrome, gastroesophageal reflux disease, and GI symptom complex overlap in RA.

Conclusion: Several upper and lower GI disorders were significantly more prevalent in RA versus non-RA subjects. Age <60 and physical function impairment (HAQ ≥1) were associated with GI disorders in RA.

Overlap of Dyspepsia and Gastroesophageal Reflux in the General Population: One Disease or Distinct Entities?

Choung RS, et al.
Neurogastroenterol Motil. 2011.

Background: The overlap of dyspepsia and gastroesophageal reflux (GER) is known to be frequent, but whether the overlap group is a distinct entity or not remains unclear. The aims of the study was to evaluate whether the overlap of dyspepsia and GER (dyspepsia-GER overlap) occurs more than expected due to chance alone, and evaluate the risk factors for dyspepsia-GER overlap.

Methods: In 2008 and 2009, a validated Bowel Disease Questionnaire was mailed to a total of 8006 community sample from Olmsted County, MN. Overall, 3831 of the 8006 subjects returned surveys (response rate 48%). Dyspepsia was defined by symptom criteria of Rome III; GER was defined by weekly or more frequent heartburn and/or acid regurgitation.

Results: Dyspepsia and GER occurred together more commonly than expected by chance. The somatic symptom checklist score was significantly associated with dyspepsia-GER overlap versus GER alone or dyspepsia alone [OR = 1.9 (1.4, 2.5), and 1.6 (1.2, 2.1), respectively]. Insomnia was also significantly associated with dyspepsia-GER overlap versus GER alone or dyspepsia alone [OR = 1.4 (1.1, 1.7), OR = 1.3 (1.1, 1.6), respectively]. Moreover, proton pump inhibitor use was significantly associated with dyspepsia-GER overlap versus dyspepsia alone [OR = 2.4 (1.5, 3.8)]. Conclusions and Inferences Dyspepsia-GER overlap is common in the population and is greater than expected by chance.
Influence of Reproductive Factors in the Clinical and Laboratory Parameters of Rheumatoid Arthritis

Skare TL, Mendes LR.


Purpose: To study if rheumatoid arthritis (RA) is influenced by age at menarche, number of pregnancies, and reproductive life span.

Methods: This was a cross-sectional and retrospective study of medical records of 247 RA patients. Data were collected on menarche, menopause, number of pregnancies, autoantibodies, serositis, rheumatoid nodules, and functional index of Steinbrocker. Association studies were done using the Student’s t and Mann-Whitney tests and correlation was determined by the Pearson and Spearman tests. The level of significance adopted was 5%.

Results: The mean age at diagnosis of RA was 43.2 ± 14.1 years, the median age at menarche was 13 years, and the median number of pregnancies was 3. Rheumatoid factor was present in 63.9% of the patients, 20% had antinuclear factor, 8.8% rheumatoid nodules, 2.8% had pleural effusion, and 2.4% had pericarditis. The Steinbrocker functional index showed that 45.6% had a score of 1, 40.8% a score of 2, 3 score of 9.1, and 4.3% a score of 4. An inverse correlation between the number of pregnancies and age at onset of RA was found.

Conclusion: A precocious menarche and brief reproductive life indicate a poor prognosis regarding pleurisy. A larger number of pregnancies and late menopause show a protective effect, delaying the onset of the disease.

The Relationship Between Oral Contraceptive Use and Functional Outcome in Women with Recent-onset Inflammatory Polyarthritis

Camacho EM, et al.


The purpose of this study was to examine functional outcome and oral contraceptives (OC) use in women with inflammatory polyarthritis (IP).

Patient-reported history of OC use in 663 women who were born after 1945 and who had not used OCs during follow-up were studied. OC use during follow-up was additionally investigated in 265 women who were <50 years old and had not undergone menopause or hysterectomy during follow-up. Functional ability was assessed using the Health Assessment Questionnaire (HAQ), with adjustment for age at symptom onset.

In the investigation analyzing OC use before symptom onset, patients who had used OCs before symptom onset had lower HAQ scores throughout follow-up than patients who had not taken OCs before symptom onset. Patients who were taking OCs at baseline had lower HAQ scores over time than women who were not taking OCs at baseline, but had previously done so. In the investigation analyzing OC use during follow-up, OC use during follow-up was associated with lower HAQ scores over time than no OC use during follow-up; however, this was only significant for women with moderate or severe functional disability at the previous assessment.

Conclusion: OC use is generally associated with a beneficial functional outcome in IP, and use before and at symptom onset appeared to have the most consistent benefit.
Hepatology

Liver Fibrosis in Patients with Psoriasis and Psoriatic Arthritis on Long-term, High Cumulative Dose Methotrexate Therapy

Lindsay K, et al.


**Objectives:** Dermatologists and rheumatologists have differed in their use of serial liver biopsy and liver function tests (LFT) to monitor the risk of hepatic fibrosis in long-term methotrexate (MTX) therapy. It is judged safe to monitor LFT only in rheumatoid arthritis (RA). Whilst there are few studies in psoriatic arthritis (PsA) to justify this approach, it is widely used in rheumatology practice. The study aimed to assess prevalence of hepatic fibrosis in both psoriasis and PsA patients on long-term MTX therapy.

**Methods:** A prospective study of 54 patients with psoriatic disease had a liver biopsy according to dermatology guidelines on long-term MTX treatment with full assessment of risk factors. Previously, monitoring these patients was in accordance with ACR guidelines with 3-monthly LFT.

**Results:** MTX treatment duration was a mean of 6.9 years, with a mean cumulative dose of 4396 mg. There were no cases of advanced fibrosis or of cirrhosis and mild early fibrosis in 11 (22%) patients. The presence of early mild changes was related to the number of risk factors that the patient had for hepatic fibrosis [also the risk factors for nonalcoholic steatohepatitis (NASH)]. Pro-collagen 3 N-terminal peptide (PIIINP) was unhelpful in PsA and frequently elevated despite normal liver biopsy.

**Conclusions:** Despite other risk factors for NASH, monitoring for hepatic fibrosis using serial liver function and ACR guidelines tests alone as in RA appears safe in psoriasis and PsA. Liver biopsy ought to be considered to assess the liver if LFT are persistently elevated. PIIINP is misleading in active PsA.

Sexual Functioning in Patients with End-stage Liver Disease Before and After Transplantation

Sorrell JH, Brown JR.


The effects of end-stage liver disease (ESLD) on sexual functioning are complex and often overlooked in the context of chronic illness and the transplantation evaluation. The aim of the present study is to report on the prevalence of sexual dysfunction in patients with ESLD presenting for liver transplantation evaluation, as well as to examine a cohort after transplantation. Participants included 173 consecutive adult outpatients with ESLD who presented for orthotopic liver transplantation evaluation. All transplant candidates underwent a psychiatric evaluation, and a sexual history was taken by the transplant psychiatrist. Patients who received a liver transplant were contacted by telephone for follow-up (n = 39). The following domains were explored: sexual frequency, satisfaction, ability to orgasm, sexual interest, and, for men, erectile dysfunction. Before transplantation, high levels of sexual dysfunction were found, with women showing higher levels of dysfunction than men. Increased age and more severe liver disease were related to lower sexual frequency and satisfaction. Contrary to previous work, the cause of disease (alcoholic liver disease) was not related to sexual functioning before transplantation. Those with erectile dysfunction before transplantation showed continued dysfunction after transplantation. An additional finding was an age and gender bias against taking a sexual history from older women. Overall, for both men and women, the findings point to continued and persistent sexual dysfunction after transplantation. Findings may help transplant teams routinely inquire into the sensitive domain of sexual functioning early on, and thereby provide an opportunity for treatment.
Infections

The Effect of Bedside Ultrasound on Diagnosis and Management of Soft Tissue Infections in a Pediatric Emergency Department

Iverson K, et al.


Background: Presentation of skin and soft tissue infections (SSTIs) to the pediatric emergency department (PED) has increased. Physical examination alone can be inadequate in differentiating cellulitis from an abscess. The purposes of this study were to determine the effect of bedside ultrasound (US) in improving diagnostic accuracy for SSTIs in the PED and to evaluate its effect on the management of patients with SSTIs.

Methods: We conducted a prospective study of a convenience sample of children who presented to an inner-city PED with signs and symptoms of SSTI. The treating physician’s pretest opinions regarding the need for incision and drainage and procedural sedation were collected. A bedside US was performed by trained PED physicians to evaluate for cellulitis versus abscess. The treating physician was made aware of the US findings, and the effect on management was recorded.

Results: Sixty-five patients were enrolled, of whom 47 had US-proven abscess and 18 had cellulitis. The sensitivity of US for detection of abscess was 97.5% (95% CI, 90.1%–99.5%), and the specificity was 69.2% (95% CI, 57.8–72.4%). In comparison, the sensitivity for physical examination alone for detection of abscess was 78.7% (95% CI, 71.4%–84.4%), and the specificity was 66.7% (95% CI, 47.6%–81.6%). Ultrasound disagreed with clinical examination and changed management in 9 (13.8%) of 65 patients.

Conclusions: Emergency department bedside US improves accuracy in diagnosis of SSTIs. Bedside US changes management in a small but significant number of patients with SSTIs.

Impact of Helicobacter pylori Infection and Microscopic Duodenal Histopathological Changes on Clinical Symptoms of Patients with Functional Dyspepsia

Mirbagheri SA, et al.


Aim: To evaluate the microscopic histopathological changes in duodenal tissue and its relationship to the severity of symptoms in patients with functional dyspepsia while taking the effect of Helicobacter pylori infection into account.

Methods: Several gastric and duodenal biopsy specimens were obtained in 217 patients with functional dyspepsia and were evaluated for Helicobacter pylori infection and histopathological changes. Severity of symptoms was assessed by Leeds Dyspepsia Questionnaire (LDQ) and its relationship to histopathological changes and Helicobacter pylori infection status was assessed.

Results: Helicobacter pylori infection was associated with presence and severity of microscopic duodenitis (P<.001). In Helicobacter pylori-infected patients, the presence of microscopic duodenitis was independent of microscopic gastritis (P = .74). Severity of dyspepsia symptoms was not higher in Helicobacter pylori-infected patients than noninfected patients (P = .15), but in the presence of Helicobacter pylori infection and microscopic gastritis, microscopic duodenitis significantly worsened the LDQ symptom severity score (P<.001). In multivariate analysis, the odds of experiencing severe symptoms in patients with severe microscopic duodenitis was 2.22 times greater than in individuals with very mild, mild, or moderate duodenitis.

Conclusions: Microscopic duodenitis in Helicobacter pylori-infected patients may play a major role in producing and aggravating symptoms in FD patients and may be a determinant factor to consider in whether to treat Helicobacter pylori infection in functional dyspepsia.
Neurology

Erectile Function, Sexual Desire, and Psychological Well-being in Men with Epilepsy

Duncan S, et al.


**Objective:** The aim of this study was to explore the effects of anxiety, depression, and self-reported quality of life (QOL) on sexual function of men with epilepsy (MWE).

**Methods:** Sixty-nine MWE taking one antiepileptic drug and 50 controls were recruited. All completed sexual function questionnaires, the Hospital Anxiety and Depression Scale (HADS), and the World Health Organization Brief Quality of Life Questionnaire (WHOQOL-BREF). Blood was taken to analyze testosterone and dihydroepiandrosterone sulfate levels.

**Results:** Compared with controls, MWE reported higher levels of anxiety, depression, and psychological distress; lower overall quality of life and health; and lower levels of sexual desire and erectile function. Seizure frequency did not affect any of these variables, and testosterone levels did not correlate with sexual desire or erectile function. Simple linear regression showed a significant negative correlation between sexual desire and indices of anxiety, depression, and psychological distress. Multiple linear regression using overall QOL as dependent variable showed that anxiety, depression, psychological distress, and the Psychological Well-Being subscale of the WHOQOL-BREF predicted 48% of its variability. Interestingly, sexual function and seizure status did not.

**Conclusion:** MWE reported lower levels of sexual desire and were more likely to report erectile dysfunction than controls. But the most important determinant of QOL was psychological status, not seizure frequency or sexual function.

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Loss of Libido in Parkinson’s Disease

Kummer A, et al.


The frequency of loss of libido in Parkinson’s disease (PD) and its relation to neurological symptoms, depression, anxiety, fatigue, and cognitive performance are assessed.

The response of 90 PD patients of both genders to item “loss of libido” from the Beck Depression Inventory (BDI) was analyzed. A structured psychiatric interview (MINI-Plus) evaluated the presence of major depression and generalized anxiety disorder. Clinical assessment also comprised neurological examination, which included all sections of the Unified Parkinson’s Disease Rating Scale (UPDRS), Hoehn-Yahr and Schwab-England Scale (SES). The Frontal Assessment Battery (FAB), the Mini Mental State Examination (MMSE), and the PD Fatigue Scale (PDFS) were also performed.

The frequency of loss of libido was 65.6%, and 42.6% of men also complained of erectile dysfunction. Higher BDI scores (P<.001) correlated with a greater loss of libido. Neurological features associated with higher loss of libido were predominance of motor symptoms on the left side of the body (P = .026), autonomic dysfunction (P = .012), higher UPDRS scores (P = .006), and lower scores on SES (P = .003). Patients with lower performance on FAB (P<.001) and MMSE (P = .002), and with higher scores on PDFS (P<.001) had less interest in sex. Loss of libido is frequent in PD and depression may be its main predictor. However, decreased interest in sex was not associated with antidepressant therapy.
Ocular Involvement and Its Manifestations in Rheumatoid Arthritis Patients

Markowitz E, et al.

Harefuah. 2011;150(9):713-718, 751.

To study the type, occurrence and nature of ocular involvement amongst patients with rheumatoid arthritis (RA), and to identify demographic, clinical and/or laboratory variables associated with eye involvement in RA. The research was conducted among 61 patients diagnosed with RA. Comprehensive rheumatologic tests were administered and general health was examined with a prepared questionnaire. Additionally, the subjects’ personal files were examined with data collected from general serum rheumatologic tests and details regarding medications administered. The patients were given a comprehensive eye examination. The subjects were also questioned regarding their dry eye syndrome and a specular microscopy test was performed.

The majority of the research subjects (90.2%) were women. Their average age was 51.9 ± 13.21 years; 31.1% of the subjects complained of eye dryness and, during the eye examination, 85% were found to be suffering from dry eye. The study found a correlation between the objective indicators of keratitis sicca and the following parameters: laboratory values for SGOT ($P < 0.03$), ESR ($P < 0.05$), Cr ($P < 0.05$), TG ($P < 0.03$), LDL ($P < 0.01$), Hb ($P < 0.01$), ALP ($P < 0.01$), in addition to prednisone medication ($P < 0.03$, df = 2, $x^2 = 7.02$) and methotrexate ($P < 0.03$, df = 2, $x^2 = 8.88$). No correlation was found with the following parameters: age, disease duration, smoking, disease severity, other background diseases, and additional laboratory findings including RF and ANA measurements, and consuming other anti-RA medications. The average results of the specular microscopy test were $2116.15 \pm 416.59$ for the right eye and $2125.67 \pm 446.14$ for the left eye.

The significance of the specular microscopy test results is that corneal damage found in RA patients occurs only to the external layer and does not affect the endothelial layer.

The study indicates that keratitis sicca is prevalent among RA patients and must be taken into account regardless of the degree that the disease has progressed, because the severity of the dryness is not dependent on disease progression.

Tuberculous Scleritis in a Patient with Rheumatoid Arthritis

Biswas J, et al.


Objective

Scleritis is an ocular inflammatory disorder commonly associated with systemic autoimmune diseases. Researchers report a case of nodular scleritis with an etiological diagnosis of tuberculosis wherein diagnosis was possible only after histopathological examination of the enucleated eye.

Method of Study

A 52-year-old female patient was referred as a case of nodular scleritis not responding to topical and oral anti-inflammatory agents. She was being treated with immunosuppressives for rheumatoid arthritis by her rheumatologist. Scleritis improved initially but worsened in few months with development of complications. Eye was enucleated and histopathological examination revealed tuberculous bacilli in retinal pigment epithelial cells.

Conclusion

Infective scleritis should be suspected in cases of scleritis, which progress despite treatment. Reactivation of latent Mycobacterium tuberculosis may occur especially in patients on long-term systemic immunosuppressive treatment. Early detection and aggressive treatment is necessary for preventing morbidity or mortality due to these infections.
**Orthopedics**

**Sexual Dysfunction in Rheumatoid Arthritis Patients: Arthritis and Beyond**

El Miedany Y, et al.

*Clin Rheumatol.* 2011.

Rheumatoid arthritis (RA) treatment has been shown to improve quality of life. There is little data regarding the impact of the disease and treatments on sexual function. The aim of this study was to describe the results of an assessment of sexual activity/sexual satisfaction of RA patients, identify the sexual dysfunction features, and assess their association with disease activity/disease activity parameters and other systemic risk factors/comorbidities. Consecutive RA patients attending the outpatient rheumatology clinic completed the multidimensional patient-reported outcome measures questionnaire. There are three questions screening for sexual dysfunction: patients who ticked any of the boxes were further assessed. Men completed the Sexual Health Inventory for Men; whereas women completed the Female Sexual Function Index. All patients underwent clinical assessment of disease activity parameters and cardiovascular risk. Among 231 RA patients included in this study, 49/91 (53.8%) men and 64/140 (45.7%) women reported sexual dysfunction. Among men, erectile dysfunction significantly correlated \( (P < .01) \) with pain score, cardiovascular disease, age, disease activity, fatigue score, intramuscular steroid injection, and tender joint count. Among women, sexual dysfunction was significantly correlated \( (P < .01) \) with occurrence of secondary Sjogren’s syndrome, pain score, cardiovascular disease, hip joint involvement, disease activity, and tender joint count. Sexual dysfunction is common among RA patients. Erectile dysfunction in men, and problems with orgasm, arousal, and satisfaction in women were the most prevalent manifestations. The significant correlation of sexual dysfunction with CVD may help to identify patients at high risk of cardiovascular disorders.

**Insufficiency Fractures of the Feet and Lower Limbs in Rheumatoid Arthritis**

Pauser J, et al.


**Background:** Insufficiency fractures are generally a rare event, especially of the hindfoot. These are often overlooked in the initial stage; however, they must be regarded as a differential diagnosis in the range of possible causes in patients with rheumatoid arthritis and unclear complaints.

**Material and Methods:** Outpatients in an arthritis care unit from 2009 to 2011 were analyzed for fractures of the hindfoot and distal tibia.

**Results:** A total of six patients with seven fractures without adequate trauma were found in the cohort. All patients had received disease modifying therapy and corticosteroids. All fractures could be successfully treated without surgery.

**Conclusion:** Insufficiency fractures in patients with rheumatoid arthritis are a typical finding after several years of the disease. They are directly related to the disease and medication and can usually be successfully treated conservatively.
The Incidence of Spondylolysis and Spondylolisthesis in Children with Osteogenesis Imperfecta

Hatz D, et al.


**Background:** Spondylolysis and spondylolisthesis are common abnormalities of the lumbar spine. The incidence of these diagnoses is recognized in the healthy population. However, their incidence in osteogenesis imperfecta (OI) patients is less well defined.

**Methods:** Lateral radiographs were reviewed on all available patients to assess the incidence of spondylolysis and spondylolisthesis in this patient population. The morphology of the pedicle and pars interarticularis was also evaluated to identify any abnormalities or dysplasia of these structures.

**Results:** One hundred ten of the 139 patients treated in the OI clinic met the inclusion criteria for this study. Of these patients, 79% (87 of 110) were ambulatory. The overall incidence of spondylolysis in this pediatric OI population was found to be 8.2% (9 of 110) at an average age of 7.5 years. The incidence of spondylolisthesis was 10.9% (12 of 110) at an average age of 6.5 years with 75% (3 of 12) being isthmic type and 25% (3 of 12) dysplastic.

**Conclusions:** This study found that the incidence of spondylolysis in a group of children with OI was much higher than in the normal pediatric population, which has been reported to be 2.6% to 4.0%. This incidence was also found to be higher than previously reported incidence of spondylolysis in OI patients (5.3%). The incidence of spondylolisthesis was also found to be much higher than that of the normal pediatric population (4.2%).

Early Predictors of Juvenile Sacroiliitis in Enthesitis-related Arthritis

Pagnini I, et al.


**Objective:** To identify early predictors of sacroiliac (SI) involvement in a cohort of patients with enthesitis-related arthritis (ERA).

**Methods:** During a 7-year follow-up period, all consecutive patients fulfilling the ILAR classification criteria for ERA were enrolled. Data collected included demographic, clinical, and laboratory variables at disease onset, at the onset of inflammatory back pain, and at the last available follow-up visit. Pelvis radiographs and dynamic magnetic resonance imaging (MRI) scans for SI joints were obtained simultaneously in all patients who developed inflammatory back pain.

**Results:** Fifty-nine children with ERA were studied; 40 male, 19 female; median age at disease onset 9 years 4 months (range 6 years 6 months to 13 years 3 months). At a median interval after disease onset of 1 year 3 months, 21 children reported symptoms of inflammatory back pain. In all cases, radiographs of SI joints were negative, while dynamic MRI revealed acute sacroiliitis in 17 cases. Multivariate analysis showed that the early predictors of SI were the number of active joints ($P<.03$) and the number of active entheses ($P<.001$) at onset.

**Conclusion:** In our cohort, roughly 30% of children with ERA/juvenile idiopathic arthritis develop clinical and MRI evidence of sacroiliitis, detectable with dynamic MRI as early as 1 year after disease onset. Additional data from larger case series are needed to assess the specificity and sensitivity of this technique in the early phase of the disease and to confirm the rate of SI involvement reported in this cohort.
Clinical Practice Pearls

Male Sexual Dysfunction

Erectile dysfunction (ED) and premature ejaculation (PE) are the two most prevalent male sexual dysfunctions. The most recent summary of the European Association of Urology (EAU) guidelines on ED was published in 2006. The EAU’s Guidelines Office decided to expand these guidelines to include PE. Therefore, the new guidelines include an update of the ED guidelines and a completely new section on PE based on a review of available scientific information, current research, and clinical practice in the field.

ED is highly prevalent and shares common risk factors with cardiovascular disease. Diagnosis of ED is based on medical and sexual history, including validated questionnaires. Physical examination and laboratory testing must be tailored to the patient’s complaints and risk factors.

PE has prevalence rates of 20% to 30% and may be classified as lifelong (primary) or acquired (secondary). Diagnosis of PE is based on medical and sexual history assessing intravaginal ejaculatory latency time, perceived control, distress, and interpersonal difficulty related to the ejaculatory dysfunction. Physical examination and laboratory testing may be needed in selected patients only.

Erectile Dysfunction

Definition
ED is the persistent inability to attain and maintain an erection sufficient to permit satisfactory sexual performance. ED affects physical and psychosocial health and has a significant impact on the quality of life (QoL) of sufferers and their partners and families.

Epidemiology
Epidemiologic studies of ED suggest that approximately 5% to 20% of men have moderate-to-severe ED. The difference in reported incidences is probably due to differences in the methodology and in the age and socioeconomic status of the study populations.

Risk factors
- Lack of exercise
- Obesity
- Smoking
- Hypercholesterolemia
- Metabolic syndrome
- Radical prostatectomy (RP)

Diagnosis
The minimal diagnostic evaluation must be performed in every patient with ED. Because of the potential cardiac risks associated with sexual activity, the Second Princeton Consensus Conference stratified patients with ED wanting to initiate or resume sexual activity into three risk categories.

The low-risk group included asymptomatic patients with fewer than three risk factors for coronary artery disease (excluding male gender), mild or stable angina (evaluated and/or being treated), uncomplicated past myocardial infarction, left ventricular dysfunction or congestive heart failure (New York Heart Association class I), postsuccesful coronary revascularisation, controlled hypertension, and mild valvular disease. All other patients were included in intermediate- or high-risk categories and required a cardiology consultation prior to engaging in sexual activity (sexual activity for high-risk patients is not recommended).

Although most patients with ED can be managed within the primary care setting, some circumstances require specific diagnostic testing.

- Nocturnal penile tumescence and rigidity testing using Rigiscan should take place for at least two nights. A functional erectile mechanism is indicated by an erectile event of $\geq 60\%$ rigidity recorded on the tip of the penis lasting for $\geq 10$ min.
- The intracavernous injection test provides limited information about vascular status.
- Duplex ultrasound provides a
simple (albeit intrusive) way of assessing vascular status.

- If duplex ultrasound is normal, vascular investigation is unnecessary as indicated by a peak systolic blood flow >30 cm/s and a resistance index >0.8.
- If the ultrasound is abnormal, however, arteriography and dynamic infusion cavernosometry and cavernosography should be performed only in patients who are potential candidates for vascular reconstructive surgery.

Treatment

Only certain types of ED have the potential to be cured with specific treatments.

- For psychogenic ED, psychosexual therapy may be given either alone or with another therapeutic approach, but this therapy takes time and has had variable results.
- For posttraumatic arteriogenic ED in young patients, surgical penile revascularisation has a 60% to 70% long-term success rate.
- For hormonal causes of ED, testosterone replacement therapy is effective but should be used only after other endocrinologic causes for testicular failure have been excluded. Although some data suggest that testosterone administration does not cause prostate cancer, it is currently contraindicated in men with a history of prostate carcinoma or with symptoms of prostatism.
- Close follow-up is necessary, including digital rectal examination, serum prostate specific antigen testing, and hematocrit assessment as well as monitoring of the development of hepatic or prostatic disease.
- Although there is some debate, the use of pro-erectile drugs following RP seems important in achieving erectile function following surgery. Several trials have shown higher rates of recovery of post-RP erectile function in patients receiving any phosphodiesterase type 5 inhibitor (PDE5-I) or intracavernosal injections (therapeutic or prophylactic). Rehabilitation should start as soon as possible following RP. Most men with ED will be treated with options that are not cause specific. This approach requires a structured treatment strategy that depends on efficacy, safety, invasiveness, and cost as well as patient and partner satisfaction. The choice of treatment options must consider the effects on patient and partner satisfaction and other QoL factors as well as efficacy and safety.

Premature Ejaculation

Definition

The Second International Consultation on Sexual and Erectile Dysfunction has defined PE as “ejaculation with minimal stimulation and earlier than desired, before or soon after penetration, which causes bother or distress, and over which the sufferer has little or no voluntary control.” The International Society for Sexual Medicine has adopted a completely new definition, and the first evidence-based definition, for lifelong PE: “Premature ejaculation is a male sexual dysfunction characterized by ejaculation which always or nearly always occurs prior to or within about one minute of vaginal penetration; and inability to delay ejaculation on all or nearly all vaginal penetrations; and negative personal consequences, such as distress, bother, frustration and/or the avoidance of sexual intimacy.” All definitions have taken into account the time to ejaculation, the inability to control or delay ejaculation, and the negative consequences (bother/distress) from PE.

PE may be classified as lifelong (primary) or acquired (secondary). Lifelong PE is characterized by onset from the first sexual experience and remains a problem throughout life. Ejaculation occurs too quickly, either before vaginal penetration or <1 to 2 min afterward. Acquired PE is characterized by a gradual or sudden onset, with ejaculation being normal before onset of the problem. Time to ejaculation is short but not usually as fast as in lifelong PE. PE is a common male sexual dysfunction, with prevalence rates of 20% to 30%. Limited data suggest that the prevalence of lifelong PE, defined as intravaginal ejaculatory latency time (IELT) <1 to 2 min, is about 2% to 5%.

The etiology of PE is unknown, with little data to support suggested biological and psychological hypotheses, including anxiety, penile hypersensitivity, and serotonin receptor dysfunction. In contrast to ED, the prevalence of PE is not affected by age.

Risk factors

Risk factors for PE are generally unknown. PE has a detrimental effect on self-confidence and on relationship with the partner. It may cause mental distress, anxiety, embarrassment, and depression; however, most men with PE do not seek help.

Diagnosis

Diagnosis of PE is based on the patient’s medical and sexual history. The history should classify PE as lifelong or acquired and determine whether PE is situational (under specific circumstances or with a
specific partner) or consistent. Special attention should be given to the length of time of ejaculation, degree of sexual stimulus, impact on sexual activity and QoL, and drug use or abuse. It is also important to distinguish PE from ED. The use of IELT alone is not sufficient to define PE because there is significant overlap between men with and without PE. In everyday clinical practice, self-estimated IELT is sufficient. Diagnosis should be multidimensional and should assess IELT, perceived control, distress, and interpersonal difficulty due to ejaculatory dysfunction.

The need to assess PE objectively has produced several questionnaires, such as

- Premature ejaculation diagnostic tool (PEDT)
- Premature ejaculation profile (PEP)
- Index of premature ejaculation (IPE)
- Male sexual health questionnaire ejaculatory dysfunction (MSHQ-EjD).

Physical examination includes a brief examination of the vascular, endocrine, and neurologic systems to identify underlying medical conditions associated with PE or other sexual dysfunctions, such as chronic illness, endocrinopathy, autonomic neuropathy, Peyronie’s disease, urethritis, or prostatitis. Laboratory or physiologic testing should be directed by specific findings from history or physical examination and is not routinely recommended.

**Treatment**

As PE causes few (if any) problems, treatment should be limited to psychosexual counseling. Before beginning treatment, it is essential to discuss patient expectations thoroughly. ED or other sexual dysfunction or genitourinary infection (e.g., prostatitis) should be treated first or at the same time as PE. Various behavioral techniques have demonstrated benefit in treating PE. In lifelong PE, behavioral techniques are not recommended for first-line treatment. They are time intensive, require the support of a partner, and can be difficult to do.

**Erectile dysfunction**

- Poor health in general is likely to concur with a low level of sexual desire/interest and ED.
- Increased physical activity is associated with a lower risk of ED.
- ED may be more prevalent in Hispanic men after controlling for other factors.
- Prevalence for ED increases with aging even when controlling for other diseases.
- Increase in prevalence rates for ED is seen in men who smoke as a stand-alone risk.
- Recent literature dealing with obesity and the metabolic syndrome shows clear association with components of the syndrome—diabetes mellitus, hypertension and hypogonadism.
- Hormonal and endocrine disorders are clearly associated with ED and other sexual disorders in men.
- Prolactin-secreting tumors are highly associated with decreased libido in men. Diabetes mellitus is highly associated with ED and decreased sexual desire.
- Cardiovascular disease and hypertension are major risk factors associated with ED.
- Other urological diseases including lower urinary tract symptoms have been associated with ED.
- Surgery in the pelvic region and trauma serve as risk factors for ED and/or ejaculatory disorders as they may damage vital neurological and vascular pathways necessary for erection.

**References**


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Topiramate-related Reversible Erectile Dysfunction in Temporal Lobe Epilepsy

Hung LC, et al.

Topiramate (TPM) is a newer antiepileptic drug with high efficacy in treating various neurological disorders, especially epilepsy and migraine. The adverse effects of TPM therapy are mainly central nervous system-related somnolence and dizziness. There are rare reports about the role of TPM on sexual effects, but with inconsistent results. In this report, we describe a 31-year-old man who developed erectile dysfunction after several months of using TPM. Complete urological and sexual psychiatric evaluations were carried out. There was lack of an identifiable organic basis and psychiatric pathology in this patient. The erectile dysfunction improved only after the termination of TPM, documenting the temporal relationship. We reviewed and discussed the clinical aspect of using TPM in erectile dysfunction. This case and the rare cases of erectile dysfunction in using TPM reported in the literature show that TPM is worth paying attention to whenever it is prescribed in a wide range of neurological disorders.

A Case of Pulmonary Tuberculosis and Tuberculous Pleuritis During Treatment with Etanercept for Rheumatoid Arthritis

Taniguchi H, et al.

A 64-year-old woman, afflicted with rheumatoid arthritis, consulted our hospital because of her clinical deterioration. Her doctor started treating her with etanercept and prednisolone 10 mg/d, but without preventive chemotherapy for tuberculosis, because her chest CT showed only mild interstitial pneumonia, and her tuberculin test showed a slightly positive reaction. Her symptoms improved, but her chest x-ray showed infiltration after two and a half months of treatment, and right pleural effusion after four and a half months of treatment. A diagnosis of pulmonary tuberculosis and tuberculous pleuritis was made because of an increase of adenosine deaminase in pleural effusion. She was treated with isoniazid, rifampicin, and ethambutol, resulting in a successful clinical course. Her sputum culture was positive, and a nucleic acid amplification of mycobacterium tuberculosis complex was positive. When prescribing etanercept, close attention to the possibility of developing tuberculosis in the patient is advised.
Intradermal Indocyanine Green for In Vivo Fluorescence Laser Scanning Microscopy of Human Skin: A Pilot Study

Jonak C, et al.

The increased need for noninvasive diagnosis is currently satisfied by reflectance laser scanning microscopy. To date, the superior method of fluorescence laser scanning microscopy is not generally applied in dermatology and predominantly restricted to fluorescein as fluorescent tracer, which has a number of limitations. Therefore, the researchers searched for an alternative fluorophore matching a novel skin imaging device to advance this promising diagnostic approach.

Using a Vivascope®-1500 Multilaser microscope, it was found that the fluorophore Indocyanine-Green (ICG) is well suited as a fluorescent marker for skin imaging in vivo after intradermal injection. Its fluorescence properties are compatible with the application of a near-infrared laser, which penetrates deeper into the tissue than the standard 488 nm laser for fluorescein. ICG-fluorescence turned out to be much more stable than fluorescein in vivo, persisting for more than 48 hours without significant photobleaching whereas fluorescein fades within 2 hours. The well-defined intercellular staining pattern of ICG allows automated cell-recognition algorithms, which was accomplished with the free software CellProfiler, providing the possibility of quantitative high-content imaging. Furthermore, the superiority of ICG-based fluorescence microscopy for selected skin pathologies, including dermal nevi, irritant contact dermatitis, and necrotic skin was demonstrated.

The results introduce a novel in vivo skin imaging technique using ICG, which delivers a stable intercellular fluorescence signal ideal for morphological assessment down to sub-cellular detail. The application of ICG in combination with the near infrared laser opens new ways for minimal-invasive diagnosis and monitoring of skin disorders.

The Use of Muscle Near-infrared Spectroscopy in Sport, Health, and Medical Sciences: Recent Developments

Hamaoka T, et al.

Near-infrared spectroscopy (NIRS) has been shown to be one of the tools that can measure oxygenation in muscle and other tissues in vivo. This review paper highlights the progress, specifically in this decade that has been made for evaluating skeletal muscle oxygenation and oxidative energy metabolism in sport, health, and clinical sciences.

Development of NIRS technologies has focused on improving quantification of the signal using multiple wavelengths to solve for absorption and scattering coefficients, multiple pathlengths to correct for the influence of superficial skin and fat, and time-resolved and phase-modulated light sources to determine optical pathlengths. In addition, advances in optical imaging with multiple source and detector pairs as well as portability using small wireless detectors have expanded the usefulness of the devices. NIRS measurements have provided information on oxidative metabolism in various athletes during localized exercise and whole-body exercise, as well as training-induced adaptations. Furthermore, NIRS technology has been used in the study of a number of chronic health conditions. Future developments of NIRS technology will include enhancing signal quantification. In addition, advances in NIRS imaging and portability promise to transform how measurements of oxygen utilization are obtained in the future.
Acitretin-associated Erectile Dysfunction: A Case Report

Rossi M, Pellegrino M.


Abstract

Introduction

Two cases of impotence following a treatment with etretinate have been reported in the literature. Acitretin is the principal active metabolite of etretinate. We report a case of erectile dysfunction associated with the use of acitretin.

Case presentation

A 39-year-old Caucasian man referred his incapacity to reach and maintain a penile erection during a course of acitretin for the treatment of a severe form of psoriasis. Physical examination, laboratory findings, and psychological analysis did not reveal any abnormalities. Two weeks after the withdrawal of acitretin, the patient reported a normalization of his sexual activity.

Conclusion

Retinoids have been associated with male reproductive system dysfunctions in human and animal studies. Clinicians should be aware of the possibility of acitretin-induced erectile dysfunction.

Introduction

Acitretin is a synthetic aromatic retinoid used to treat dermatologic diseases, especially psoriasis and related skin disorders. The major adverse effects observed with retinoids treatment have been essentially embryotoxicity, teratogenicity, mucocutaneous reactions, pruritus, hypertriglyceridemia, hypercholesterolemia, increases in liver transaminase concentrations, and bone abnormalities. Acitretin is the principal active metabolite of etretinate, formerly approved for psoriasis, but withdrawn from the market because of its undesirable pharmacokinetic profile. We report a case of erectile dysfunction following a treatment with acitretin.

Case presentation

A 39-year-old Caucasian man affected by psoriasis from approximately 2 years presented to our outpatient department with a worsening of his psoriatic lesions previously controlled by topical steroids and ultra-violet therapy.

The patient had no history of tobacco or alcohol use and he had not undergone any major surgery. He was not taking drugs and his routine blood tests, hepatitis markers, coagulation parameters, thyroid function, and chest radiography were all found to be normal.

After histological examinations, he started a treatment with acitretin 25 mg/die. His psoriatic plaques resolved after 2 months and the dose was reduced to 20 mg/die.

In a follow-up visit the patient reported his incapacity to reach and maintain a penile erection sufficient to perform a sexual act from approximately 45 days. The patient also referred the absence of morning erections. Physical examination of the external genital organs revealed neither fibromatous plaques, nor signs of vascular, endocrine, or neurological diseases. Laboratory findings did not show any alterations and clinical symptoms of depression were not present.

We hypothesized a role of acitretin in the genesis of the erectile dysfunction, thus we decided to withdraw the drug with the consent of the patient. After 2 weeks, he reported a normalization of his sexual activity and decided not to start a new course of acitretin despite worsening of his psoriatic lesions.

Discussion

A literature search using PubMed did not reveal any case reports on the association between acitretin use and erectile dysfunction. However, we retrieved two cases of impotence related to etretinate therapy. Etretinate has been detected in the plasma of
patients receiving acitretin, because it is readily esterified in vivo to produce etretinate, especially in the presence of ethanol.\(^1\)

In the first case, the authors associated the erectile dysfunction with the use of etretinate in a 37-year-old patient with symptoms of depression on the basis of a positive dechallenge.\(^2\)

The second case, described in a 40-year-old patient without symptoms of depression, was confirmed by a positive rechallenge.\(^3\)

Acitretin has been associated to erectile dysfunction during spontaneous surveillance. We retrieved 2 cases in the database of the Netherlands Pharmacovigilance Centre LAREB\(^4\) and 6 cases in the database of the Medical and Healthcare products Regulatory Agency of United Kingdom.\(^5\)

Other retinoids were involved in cases of erectile dysfunction. During a prospective study designed to evaluate the efficacy and safety of isotretinoin in the treatment of acne, six male patients referred difficulties in maintaining penile erection in association with clinical symptoms of depression.\(^6\) One case of ejaculatory disorder related to the use of isotretinoin has been reported.\(^7\) Retinoids activity on male reproductive system was observed in animal studies. Single neonatal treatment with retinol dramatically reduced the sexual activity of adult male rats.\(^8\) In animals treated with retinoids, testicular atrophy with spermatogenetic arrest was described.\(^9\)

Our diagnosis is based only on the anamnesis and a positive dechallenge, as the patient preferred not to contact an urologist for his dysfunction and he did not agree to resume the treatment with acitretin, therefore a rechallenge was not possible.

On the basis of the literature review, we hypothesize a class effect of retinoids on erectile function. According to the animal studies,\(^8,9\) erectile dysfunction associated with retinoids therapy could be caused by a direct action on the male reproductive system, although a role of depression cannot be excluded.\(^10\)

Patients are reluctant to report sexual dysfunctions during their contacts with practitioners, therefore it is likely that the incidence of similar effects may result underestimated.

**Conclusion**

To our knowledge, no case of acitretin-associated impotence has been published to date. The case described has been reported to the Italian Pharmacovigilance System and to the manufacturer of the drug. Prescribers of the drug, particularly dermatologists, should be aware of the possibility of such adverse reactions during a treatment with acitretin.

**References**

Upcoming Events

Event: Radiation Research Methods as a diagnostic and therapeutic support in oncology
Date: May 5 to 6, 2012
Venue: Kiev, Ukraine

Event: Global Healthcare and Medical Tourism Conference
Date: May 6 to 8, 2012
Venue: Las Vegas, Nevada, United States
For more details, log on to http://meditourexpo.net

Event: Gastroenterology: A clinical and scientific update
Date: May 11, 2012
Venue: London, United Kingdom
For more details, log on to http://www.rsm.ac.uk/academ/cvc08.php

Event: The newest technology in modern Cardiology
Date: May 12 to 13, 2012
Venue: Odessa, Ukraine
For more details, log on to http://www.nbscience.com/14.html

Event: Women’s Health
Date: May 13 to 20, 2012
Venue: New York, United States
For more details, log on to http://www.continuingeducation.net/coursedetails.php?program_number=999

Event: Pain Management/Neurology/Compliance
Date: May 12 to 21, 2012
Venue: Oslo, Norway
For more details, log on to http://www.continuingeducation.net/coursedetails.php?program_number=1043

Event: Issues of Obstetrics, Gynecology and Perinatology
Date: May 17 to 18, 2012
Venue: Yalta, Ukraine
For more details, log on to http://www.nbscience.com/16.html

Event: Medical Ethics & Legal Medicine
Date: May 28, 2012 to June 7, 2012
Venue: Civitavecchia, Italy
For more details, log on to http://www.continuingeducation.net

Event: Alternative Medicine: Health and Longevity
Date: June 2 to 3, 2012
Venue: Kiev, Ukraine
For more details, log on to http://www.nbscience.com/18.html

Event: World Conference on Interventional Oncology 2012
Date: June 14 to 17, 2012
Venue: Chicago, Illinois, United States
For more details, log on to http://www.wcio2012.org/p/cm/ld/fid=1

Event: Family Medicine: Dermatology Review
Date: June 16 to 23, 2012
Venue: Seattle, Washington, United States
For more details, log on to http://www.continuingeducation.net/coursedetails.php?program_number=1009
Tentex® forte (TABLET)
Effective non-hormonal sex stimulant for men

Introduction
Tentex forte, a phytopharmaceutical formulation, is recommended for the treatment of low libido and male sexual weakness. Tentex forte improves libido and maintains penile erection by acting through the neuronal centers in the brain, alleviates performance-related anxiety, and ensures satisfactory coitus. Tentex forte is safe for long-term use.

Composition
Each Tentex forte tablet contains:

Ext.
- Latakasthuri (Hibiscus abelmoschus) 10 mg

Pdrs.
- Ashvagandha (Withania somnifera) 65 mg
- Vriddadaru (Argyreia speciosa) 32 mg
- Kapikachchu (Mucuna pruriens) 32 mg
- Trivanga 32 mg
- Shilajeet (Purified) 32 mg
- Kumkuma (Crocus sativus) 25 mg
- Shuddha kupilu (Strychnos nux vomica) (detoxified) 16 mg
- Makardhwaj 16 mg
- Salabmisri (Orchis mascula) 16 mg
- Akarakarabha (Anacyclus pyrethrum) 16 mg
- Bala (Sida cordifolia) 16 mg
- Shalmali (Bombax malabaricum) 16 mg
- Maricha (Piper nigrum) 5 mg

Processed in Bala (Sida cordifolia), Shatavari (Asparagus racemosus), Vidari (Ipomoea digitata), Nagavalli (Piper betle), Ashvagandha (Withania somnifera), Gokshura (Tribulus terrestris), Guduchi (Tinospora cordifolia), Vriddadaru (Argyreia speciosa), Khadira (Acacia arabica) fruit, and Dashamoola.

Clinical Pharmacology
Tentex forte boosts libido and helps maintain penile erection by its androgenic, aphrodisiac, antioxidant, and adaptogenic actions.

Tentex forte acts on the neuronal centers in the brain, i.e., the hypothalamus and limbic system, to improve libido. Tentex forte improves and helps maintain penile erection. The antistress and adaptogenic actions of Tentex forte help alleviate anxiety associated with sexual performance.

Indications
- Low libido
- Male sexual weakness

Dosage
2 tablets twice daily for 4 to 6 weeks. Repeat the course every 6 months, if necessary.

Adverse Effects
No adverse effects have been reported.

Contraindications
Tentex forte is contraindicated in patients with chronic renal disease and cardiac failure.

Special Precautions
None. Tolerated well and found safe.

Presentation
Box of 10 blister-pack strips of 10 tablets each.

Pharmacological Actions of Principal Ingredients
1. Androgenic action:
Inadequate circulating testosterone levels result in male sexual dysfunction.

*Mucuna pruriens* increases testosterone level in blood, and thus, has a beneficial action in male sexual disorders.

Protodioscin, a precursor of testosterone from *Tribulus terrestris*, gets converted to...
dehydroepiandrosterone (DHEA), and thus improves flow-mediated vasodilation of the penile arteries. Vasodilation is a function dependent on the endothelium-derived nitric oxide (NO), as NO is the principal mediator of vascular smooth muscle relaxation in erectile tissue and penile arteries.

Argyreia speciosa has androgen-like activities, useful in male sexual disorders.

2. Aphrodisiac property:

Hibiscus abelmoschus, Mucuna pruriens, Withania somnifera, and Tribulus terrestris possess aphrodisiac properties that enhance sexual desire, sexual drive, and performance.

Orchis mascula and Argyreia speciosa have aphrodisiac and tonic properties.

3. Antioxidant action:

Oxidative stress mediated through superoxide radicals and other reactive oxygen species (ROS) is central to impaired cavernosal function in male sexual dysfunction. Also, endothelial dysfunction due to other comorbid conditions like diabetes and cardiovascular diseases are associated with male sexual dysfunction.

Withania somnifera, Mucuna pruriens, Crocus sativus, Sida cordifolia, Piper nigrum, Ipomoea digitata, Tinospora cordifolia, and Asparagus racemosus have potent antioxidant activity, and help alleviate male sexual dysfunction.

Piper betle has potent antioxidant and vasorelaxant activity mediated by inhibition of NO synthase inhibitor.

4. Adaptogenic action:

Emotional stress directly disturbs the physiological functioning of the hypothalamic-pituitary hormonal pathways, thus contributing to male sexual dysfunction.

Adaptogens are the drugs of choice for the management of stress-related disorders, which increase resistance against multiple (physical, chemical, or biological) stressors, and have renormalizing influence without disturbing the normal physiological functions.

Withania somnifera, Asparagus racemosus, and Tinospora cordifolia are potent adaptogens.

Makardhwaj and Shilajeet (Purified) are adaptogens, which provide stimulating action for preventing and managing stress, thus bringing rejuvenation.

5. Other beneficial actions:

Mucilage from Hibiscus abelmoschus possesses demulcent and tonic properties.

Sida cordifolia is used in nervous disorders, general debility, and sexual inadequacy.
Tentex Royal® (CAPSULE)
Enhances desire and improves performance

Introduction
Tentex Royal, a phytopharmaceutical formulation, is recommended for erectile dysfunction (ED) of varied etiology (diabetes, cardiovascular diseases (CVDs), and endothelial dysfunction). Tentex Royal improves desire, increases blood flow to the penile tissues, and thus improves erection. With Tentex Royal, there is no risk of priapism, blindness, distorted color vision, or fibrosis. Tentex Royal is safe for long-term use.

Composition
Each Tentex Royal capsule contains:
Pdrs.
Kokilaksha
(Asteracantha longifolia) 145 mg
Vatada (Prunus amygdalus) 126 mg
Sunishannaka
(Blepharis edulis) 115 mg
Kumkuma (Crocus sativus) 14 mg
Ext.
Gokshura (Tribulus terrestris) 100 mg
Processed in Musali (Curculigo orchioides) and Nagavalli (Piper betle).

Clinical Pharmacology
Tentex Royal has androgenic, aphrodisiac, antidepressant, anxiolytic, and antioxidant actions.

Pharmacological Actions of Principal Ingredients
1. Androgenic action:
Protodioscin from Tribulus terrestris improves sexual desire and enhances erection. It gets converted to dehydroepiandrosterone (DHEA) and improves flow-mediated dilation of penile arteries. This results in vascular smooth muscle relaxation in erectile tissue, and thus, enhanced erection.

Indication
Erectile dysfunction (ED) of varied etiology (diabetes, CVDs, and endothelial dysfunction).

Dosage
2 capsules once daily, 1 hour before sexual intercourse, for 6 to 12 weeks. It is necessary to continue the treatment for a minimum of 6 weeks without interruption for satisfactory correction of erectile dysfunction.

Adverse Effects
No adverse effects, including weight gain, were reported in phase I and III clinical trials.

Contraindications
No absolute contraindications.

Special Precautions
Patients on antihypertensive or antianginal drugs.

Presentation
Box of 10 blister-pack strips of 10 capsules each.
Crocus sativus, used as an aphrodisiac, and in premature ejaculation, has results in satisfactory sexual performance.

3. Antidepressant and anxiolytic actions:
ED is associated with diabetes and hypertension. It is more prevalent in aging men. Psychological distress such as anxiety and depression also contribute to higher levels of premature ejaculation and ED rates. Crocus sativus has potent antidepressant action.

Prunus amygdalus is a nervine tonic and improves psychotropic function.

4. Antioxidant action:
ED demonstrates decreased intracavernous blood flow, loss of smooth muscle relaxation, decreased endothelial NOS and neuronal NOS, increased inducible NOS expression, diffused cavernous fibrosis, and increased cavernous levels of the oxidative product 8-epi-prostaglandin F2 alpha, an F2-isoprostane. Long-term use of antioxidants increases intracavernous blood flow, improves erectile response and smooth muscle relaxation in ED. Crocus sativus and Prunus amygdalus are potent antioxidant agents, which reduce lipid peroxidation with a concomitant increase in enzymatic activity of superoxide dismutase, catalase, and glutathione peroxidase.

Asteracantha longifolia, Curculigo orchioides, and Piper betle have potent antioxidant activity.

5. Other beneficial actions:
Adrenergic, cholinergic, and vasoactive intestinal polypeptidergic (VIPergic) nerves in the penis are affected in diabetes mellitus, and thus, may contribute to the development of ED in diabetic patients. Tribulus terrestris has acetylcholinesterase-inhibitory activity, and thus supports in managing ED in diabetic patients.

The antihypertensive action of Tribulus terrestris helps in managing ED in patients with a history of hypertension.
Speman® (TABLET)
Gives hope to childless couples

Introduction
Speman, a phytopharmaceutical formulation, is recommended for the treatment of male infertility due to oligospermia. Speman significantly improves sperm count, sperm quality, sperm morphology and motility, and thus helps increase conception rate in men. Speman is safe, with no adverse effects.

Composition
Each Speman tablet contains:
Pdrs.
Salabmisri (Orchis mascula) 130 mg
Kokilaksha (Asteracantha longifolia) 64 mg
Vanya kahu (Lactuca scariola) 32 mg
Kapikachchu (Mucuna pruriens) 32 mg
Suvarnavang 32 mg
Exts.
Vriddadaru (Argyreia speciosa) 64 mg
Gokshura (Tribulus terrestris) 64 mg
Jeevanti (Leptadenia reticulata) 64 mg
Shaileyam (Parmelia perlata) 32 mg

Clinical Pharmacology
Speman has potent androgenic and antioxidant actions, which increase testosterone levels, spermatogenesis, and sexual desire. Speman promotes spermatogenesis by improving the testicular, seminal vesicle and epididymal functions, and improves sperm count and the quality of semen by increasing the LH-FSH producing basophil cells in the pituitary.

Indication
Oligospermia.

Dosage
Initially, 2 tablets twice daily, followed by 1 tablet twice daily. Duration of treatment may vary from 4 to 6 months.

Adverse Effects
No adverse effects have been reported.

Contraindications
No absolute contraindications.

Special Precautions
Speman is found to be safe and well-tolerated.

If testicular functions do not improve in spite of long-term treatment with Speman, as a monotherapy or an adjuvant to other spermatogenic drugs, additional investigations may be required.

Presentation
Sealed packs of 60 tablets.

Pharmacological Actions of Principal ingredients
1. Androgenic action:
Speman, due to its specific composition, promotes spermatogenesis by improving testosterone levels in men with testicular spermatogenic failure, which is enabled by specialized herbs.

Protodioscin from Tribulus terrestris converts to DHEA (Dehydroepiandrosterone), a precursor of testosterone, which improves sexual desire and sustains penile erection.

Mucuna pruriens has aphrodisiac activity.

Leptadenia reticulata is used as a restorative, and stimulant, and is useful as an adjuvant in aphrodisiac medications.

Parmelia perlata, an aphrodisiac, is helpful in seminal weakness.

Asteracantha longifolia is helpful in impotence, spermatorrhea, and seminal debilities.

Suvarnavang, an invigorator, aphrodisiac and rejuvenator, induces health, vigor, and generates semen of high quality.

Argyreia speciosa, an aphrodisiac, is used in common sexual disorders in the male.
2. Antioxidant action:

*Mucuna pruriens* is a potent antioxidant, and reduces oxidative damage to sperm by preventing disruption in the membrane integrity of spermatozoa.

The actives isolated from *Lactuca scariola*—quercetin-3-O-beta-D-glucopyranoside, luteolin-7-O-beta-D-glucopyranoside, luteolin, quercetin, kaempferol, and 1beta, 13-dihydractin—have potent antioxidant activity.

3. Other beneficial actions:

*Orchis mascula* is a well-known nutrient and restorative in loss of sexual power.

*Lactuca scariola* possesses sedative and nutritive properties, and is a rejuvenator.

*Tribulus terrestris*, a tonic, is used to treat spermatorrhea and diseases of the genitourinary tract.

*Asteracantha longifolia* is used in disorders of the genitourinary system.

Suvarnavang is useful in gonorrhea and spermatorrhea.

*Argyreia speciosa* is effective in gonorrheal infection, which affects fertility.
Confido® (TABLET)
Restores his confidence

Introduction
Confido is a phytopharmaceutical formulation recommended for the management of ejaculation disorders such as premature ejaculation, spermatorrhea, and nocturnal emission. Confido regulates the process of ejaculation. Confido also helps raise the threshold of sexual stimuli, and reduces performance anxiety.

Composition
Each Confido tablet contains:

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pdrs. Salabmisri (Orchis mascula)</td>
<td>78 mg</td>
</tr>
<tr>
<td>Kokilaksha (Asteracantha longifolia)</td>
<td>38 mg</td>
</tr>
<tr>
<td>Vanya kahu (Lactuca scariola)</td>
<td>20 mg</td>
</tr>
<tr>
<td>Kapikachchu (Mucuna pruriens)</td>
<td>20 mg</td>
</tr>
<tr>
<td>Suvarnavang</td>
<td>20 mg</td>
</tr>
<tr>
<td>Exts. Vriddadaru (Argyreia speciosa)</td>
<td>38 mg</td>
</tr>
<tr>
<td>Gokshura (Tribulus terrestris)</td>
<td>38 mg</td>
</tr>
<tr>
<td>Jeevanti (Leptadenia reticulata)</td>
<td>38 mg</td>
</tr>
<tr>
<td>Shaileyam (Parmelia perlata)</td>
<td>20 mg</td>
</tr>
<tr>
<td>Sarpagandha (Rauwolfa serpentina) standardized to contain 1.5 mg of the total alkaloids.</td>
<td></td>
</tr>
</tbody>
</table>

Clinical Pharmacology
Confido renormalizes ejaculation disorders by its androgenic, aphrodisiac, fertility-enhancing, anxiolytic, and antioxidant actions.

Confido is a nonhormonal therapy, acting on the neuronal centers in the brain and locally on the sex organs, directly or indirectly. Confido reduces anxiety. By acting through the neuroendocrine pathway, Confido regulates the process of ejaculation.

Indications
- Premature ejaculation
- Spermatorrhea
- Nocturnal emission

Dosage
Premature ejaculation: 1 tablet twice daily for 2 to 4 weeks, or till symptoms are rectified.

Spermatorrhea and nocturnal emission: 1 tablet twice daily for 4 to 6 weeks, or till symptoms are rectified.

Adverse Effects
No adverse effects have been reported.

Contraindications
No absolute contraindications.

Special Precautions
None. Tolerated well and found safe.

Drug Interactions
No clinically significant drug interactions have been reported.

Presentation
Sealed packs of 60 tablets.

Pharmacological Actions of Principal Ingredients

1. Androgenic action:
Inadequate circulating testosterone levels result in male sexual dysfunction.

Protodioscin, a phytochemical agent in Tribulus terrestris and a precursor of testosterone, converts to dehydroepiandrosterone (DHEA) and improves flow-mediated vasodilation of the penile arteries along with spermatogenesis. The vasodilation is dependent on the endothelium-derived nitric oxide (NO), as NO is the principal mediator of vascular smooth muscle relaxation in erectile tissue and penile arteries.

Mucuna pruriens increases sperm count and testosterone levels, and thus, has a beneficial action in male sexual disorders.

Leptadenia reticulata treats sexual disorders like improper erection, night emission, premature ejaculation, spermatorrhea, and functional impotence.

2. Aphrodisiac action:
Orchis mascula, Suvarnavang, Argyreia speciosa, Lactuca scariola, Parmelia perlata,

Mucuna pruriens, and Tribulus terrestris are aphrodisiacs that improve sexual desire and drive,
which subsequently improves sexual performance.

3. Fertility-enhancing action:

*Asteracantha longifolia*, Suvarnavang, *Argyreia speciosa*, *Tribulus terrestris* are helpful in impotence, spermatorrhea, and seminal debilities.

4. Anxiolytic action:

*Rauwolfia serpentina* has remarkable anxiolytic action, which controls the anxiety associated with sexual performance. Its anxiolytic activity is due to raubasine, which has benzodiazepine-agonist type activity. *Lactuca scariola* has anxiolytic property, which is supported by its sedative and demulcent activities.

5. Antioxidant action:

*Asteracantha longifolia*, *Lactuca scariola*, and *Mucuna pruriens* are antioxidants.
Himcolin® (GEL)
Strengthens erectile power & improves sexual potency

Introduction
Himcolin, a phytopharmaceutical formulation, is recommended for topical treatment of erectile dysfunction (ED). An ideal choice in patients intolerant to systemic therapy, the topical application of Himcolin exerts local vasodilatory action, has soothing and moisturizing effects, and initiates and maintains the coitus reflex.

Composition
Each gram of Himcolin gel contains:

- Oils
  - Jyotishmati (Celastrus paniculatus) 200 mg
  - Latakasthuri (Hibiscus abelmoschus) 150 mg
  - Vatada (Prunus amygdalus) 100 mg
  - Nirgundi (Vitex negundo) 100 mg
  - Karpasa (Gossypium herbaceum) 50 mg
  - Mukulaka (Pistacia vera) 50 mg
  - Jatiphalam (Myristica fragrans) 30 mg
  - Jatipatri (Myristica fragrans - Mace) 30 mg
  - Lavanga (Syzygium aromaticum) 30 mg
  - Taja (Cinnamomum cassia) 30 mg
  - Base q.s. ad 1 g

Processed in Ashvagandha (Withania somnifera), Gunja (Abras precatorius), Ashwatha (Ficus religiosa), Akarakaarabha (Anacyclus pyrethrum), and Shatavari (Asparagus racemosus).

Clinical Pharmacology
Himcolin enhances nitric oxide (NO) synthesis in penile tissue, and has smooth muscle relaxant, antioxidant, and aphrodisiac actions. Himcolin causes vasodilation of the penile tissue and corrects ED, and, has soothing and moisturizing properties.

Indications
Erectile dysfunction (ED)

Directions for Use
Adequate quantity of Himcolin gel to be applied on the penis and pubic region, with a gentle massage, before sexual intercourse. Application on glans penis to be avoided.

Adverse Effects
No adverse affects have been reported.

Contraindications
No absolute contraindications.

Special Precautions
None. Accepted well by most patients and found safe.

Presentation
Transparent lamitubes of 30 g.

Pharmacological Actions of Principal Ingredients
1. NO synthesis-enhancing action:
Himcolin causes vascular engorgement of the penis, and thus strengthens and sustains erection.

Withania somnifera has NO synthesis-enhancing activity, which relaxes corporal smooth muscle, promotes endothelium-derived penile vasodilation and erection.

Vitex negundo has analgesic and anti-inflammatory activities, helpful in reducing pain and swelling in orchitis (inflammation of the testes). It causes vasodilation and has a soothing effect on the area applied.

2. Smooth muscle relaxant action:
Himcolin causes vascular engorgement of the penis and strengthens and sustains erection due to its additional smooth muscle relaxant action.

Cinnamomum cassia acts as a vascular and nerve stimulant, accelerating smooth muscle relaxation.

Celastrus paniculatus relaxes penile vascular smooth muscles, which causes vasodilation and results in penile erection. It acts as a rubefacient, which stimulates sensitive nerves of the penis.

Prunus amygdalus has demulcent and nerve tonic properties, which
enhance the smooth muscle relaxant action.

3. Antioxidant action:
*Celastrus paniculatus* and *Prunus amygdalus* have potent antioxidant activity. *Vitex negundo*, *Myristica fragrans*, *Syzygium aromaticum*, *Cinnamomum cassia*, *Withania somnifera*, and *Asparagus racemosus* have potent antioxidant actions, which control and prevent local oxidative damage, and correct the impaired cavernosal function in ED.

5. Aphrodisiac activity:
*Myristica fragrans*, *Syzygium aromaticum*, and *Hibiscus abelmoschus* have aphrodisiac activity.
What is sexual dysfunction?
Sexual dysfunction, or sexual problem, refers to a problem during any phase of the sexual response cycle that prevents the individual or couple from experiencing satisfaction from sexual activity.

What causes sexual problems?
Sexual dysfunction can be a result of either physical or psychological problem.

- Physical causes – Many physical and/or medical conditions can cause problems with sexual function. These conditions include diabetes, heart and vascular (blood vessel) disease, neurological disorders, hormonal imbalances, chronic diseases such as kidney or liver failure, and alcoholism, and drug abuse. In addition, the side effects of certain medications, including antidepressant drugs, can affect sexual desire and function.

- Psychological causes – These include work-related stress and anxiety, concern about sexual performance, marital or relationship problems, depression, feeling of guilt, and effects of past sexual trauma.

What are the common male sexual problems?
The most common sexual problems in men are ejaculation disorders, erectile dysfunction, and low sexual desire.

What are ejaculation disorders?
Ejaculation is where semen is squirted out of the penis during an orgasm. It is a reflex action controlled by the central nervous system. It is triggered when the sexual act reaches a critical level of excitement.

Ejaculation problems are quite common, with an estimated 20–30% of men experiencing at least one episode during their lifetime, which includes delayed, painful, or too early ejaculation.

There are different types of ejaculation disorders, including:
- Premature ejaculation – This refers to ejaculation that occurs before or soon after penetration without the achievement of orgasm by the partner.
- Inhibited or retarded ejaculation – This is when the ejaculation is delayed.
- Retrograde ejaculation – This occurs when at orgasm, the ejaculate is forced back into the bladder rather than through the urethra and out to the end of the penis.

What is erectile dysfunction?
Erectile dysfunction is defined as the inability to attain and/or maintain an erection suitable for intercourse. Causes of erectile dysfunction include diseases affecting blood flow, such as atherosclerosis (hardening of the arteries); nerve disorders; psychological factors, such as stress, depression, and performance anxiety (nervousness over his ability to sexually perform); and injury to the penis. Chronic illness and certain medications can also cause erectile dysfunction.

What is low sexual desire?
Low sexual desire, or loss of libido, refers to a decrease in desire for, or interest in sexual activity. Reduced libido can result from physical or psychological factors. It is generally associated with low levels of the hormone, testosterone. It may also be caused due to psychological problems, such as anxiety and depression; medical illnesses, such as diabetes and high blood pressure;
certain medications, including some anti-depressants; and problems in relationship.

How are male sexual problems diagnosed?

The doctor will begin the diagnosis after a thorough study of symptoms. Then, the doctor may recommend various tests to rule out any medical problems that may be contributing to the sexual dysfunction, or may refer to specialists like urologist, endocrinologist, neurologist, sex therapist, veneroellogist, and counselors.

What are the tests used to evaluate sexual problems?

Several tests can be used to evaluate the causes and extent of sexual problems. They include:

- **Blood tests** – These tests are done to evaluate hormone levels.
- **Vascular assessment** – This involves an evaluation of the blood flow to the penis. A blockage in a blood vessel supplying blood to the penis may be contributing to erectile dysfunction.
- **Sensory testing** – Particularly useful in evaluating the effects of diabetic neuropathy (nerve damage), sensory testing measures the strength of nerve impulses in a particular area of the body.
- **Nocturnal penile tumescence (NPT) and rigidity testing** – This test is used to monitor the erections that occur naturally during sleep. This test can help determine if a man’s erectile problems are due to physical or psychological causes.

Can sexual problems be treated?

The success of treatment for sexual dysfunction depends on the underlying cause of the problem. The outlook is good for dysfunction that is related to a treatable or reversible physical condition. Mild dysfunction that is related to stress, fear, or anxiety often can be successfully treated with counseling, education, and improved communication between partners.

What are the treatment options that are available for treating male sexual dysfunction?

Many cases of sexual dysfunction can be corrected by treating the underlying physical or psychological problems. Treatment strategies may include the following:

- **Medical treatment** – This involves treatment of any disease/condition that may be contributing to a man’s sexual dysfunction.
- **Medications** – Medications, such as anxiolytics, stress relievers, medications that may help improve sexual function in men by increasing blood flow to the penis, multivitamins, and general tonics.
- **Hormones** – Men with low levels of testosterone may benefit from hormone supplementation (testosterone replacement therapy).
- **Psychological therapy** – Therapy with a trained counselor can help a person address the feelings of anxiety, fear or guilt that may have an impact on sexual function.
- **Mechanical aids** – Aids such as vacuum devices and penile implants may help men with erectile dysfunction.
- **Education and communication** – Education about sex and sexual behaviors and responses may help a man overcome his anxieties about sexual performance. Open dialogue with the partner about the needs and concerns also helps to overcome many barriers to a healthy sexual life.

Can sexual problems be prevented?

While sexual problems cannot be prevented, dealing with the underlying causes for sexual dysfunction can help the patient understand, and cope-up with the problem better. Certain instructions can be followed in order to maintain good sexual health:

- Follow the doctor’s treatment plan for any medical/health conditions.
- Limit alcohol intake.
- Quit smoking.
- Deal with any emotional or psychological issues such as stress,
depression, and anxiety. Get treatment as needed.

- Increase communication with your partner.

**When to consult the doctor?**

In course of time, many men experience the problem of sexual dysfunction. However, when the problems are persistent, they can cause disinterestedness in man and his partner resulting in negative impact on their relationship. When the sexual dysfunctional problems are more frequent, the patient should consult the doctor for further evaluation and treatment.

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**Dear Doctor,**

We hope you found this article useful for your patients. You can order for FREE reprints of this article by using the tear-out card enclosed in this issue, and use them as patient information leaflets in your clinic.

– Editor
World over, there is a growing awareness and concern for health and a strong shift from curative advised health care to preventive health care. To tune in to the trend early on, The Himalaya Drug Company, in March 2002, launched Pure Herbs, a range of individual herb extracts like Tulasi, Neem, and Brahmi.

The Himalaya Pure Herbs brand is a range of specially selected individual herbs that can be used individually to treat/manage specific ailments and maintain wellness of the body. Himalaya Pure Herbs has the pure and concentrated goodness of herbs in the right measure that are scientifically tested and guaranteed for the highest quality and potency.

Benefits of Herbs

Herbs have been used, both as food and medicine, for centuries to eliminate excesses and minimize deficiencies in body. The value of using herbs lies particularly in their mildness to the body. While herbs may provide nutrition to the body, their primary function is to stimulate or improve body functions. Recent research has helped prove and define the pharmacological activities of individual herbs.

Why Pure Herbs?

The herbs that feature in the Pure Herbs range have remarkable benefits and are proven for their authenticity, quality, and efficacy. Everyone can benefit from the goodness of these herbs, irrespective of sex, body type, or state of health and metabolic functions. Pure Herbs, the pure and concentrated strength of a single herb in the right measure, stimulate and improve body functions.

Each Pure Herb is a potent extract and a treasure of active constituents that work by synergistic activity to produce the desired effect. The range gives physicians the choice of prescribing the herbs individually or in combinations to treat various ailments. The readily consumable form (capsules) ensures patient compliance.

Although primarily indicated for lifestyle disorders, Pure Herbs can be used for general maintenance of health and also in chronic disease management. In other words, it provides both preventive as well as curative benefits.

Salient Features of Pure Herbs

The Pure Herbs range is a unique range of potent herb extracts and is perhaps the biggest range of single herbs in the pharmaceutical market. More than half of the herbs in this range are for preventive use and can address problems of modern lifestyle such as stress, oxidative damage, and low immunity. These herbs are cost effective and can be safely consumed for longer durations. The herbs are packed in smart, user-friendly and portable containers. Each pack is contains 60 capsules and, keeping consumer economics and convenience in mind, is designed for one full month of supply.

The Pure Herbs Range

The Pure Herbs range includes amalaki as an antioxidant, arjuna for blood circulation, ashvagandha for anti-stress, bael for intestinal comfort, brahmi for alertness, gokshura for improving vitality, guduchi for immunomodulation, haridra for allergy care, kapikachhu for men's health, karela to regulate metabolism, lasuna for cholesterol protection, manjishtha for skin health, meshashringi for carbohydrate metabolism, neem for skincare, punarnava for urinary support, shallaki for joint pain, shatavari for women's health, shigru for joint care, shuddha guggulu for cholesterol regulation, sunthi for anti-nausea, tagara as relaxant, trikatu for gastric support, triphala as prokinetic cleanser, tulasi for cough and cold, vasaka for respiratory care, vrikshamla for weight control, and yasthimadhu for gastric care.
Salient features of Himalaya Pure Herbs

- Pure and concentrated herb in capsules with all its attendant benefits
- Well-defined pharmacological actions
- Identification, determination, and validation of active compounds in Pure Herbs using high-performance thin layer chromatography (HPTLC)
- Identification of total marker profile in Pure Herbs with accuracy and specificity using liquid chromatography-mass spectrometry (LC-MS)
- Scientifically tested to avoid batch to batch variation
- Guaranteed for the highest quality and potency

The Pure Herbs range

- Stimulate organic functions
- Possess therapeutic and nutritive values
- Improve and maintain healthy state of the body and mind
Clinical Insight

Withania somnifera is classified in Ayurveda, the ancient Hindu system of medicine, as a rasayana, a group of plant-derived drugs reputed to promote physical and mental health, augment resistance of the body against disease and diverse adverse environmental factors, revitalize the body in debilitated conditions, and increase longevity. These attributes are remarkably similar to the properties ascribed to adaptogens like Panax ginseng in contemporary medicine. As such, the adaptogenic activity of a standardized extract of W somnifera roots was investigated against a rat model of chronic stress (CS). The stress procedure was mild, unpredictable footshock, administered once daily for 21 days to adult male Wistar rats. CS induced significant hyperglycemia, glucose intolerance, increase in plasma corticosterone levels, gastric ulcerations, male sexual dysfunction, cognitive deficits, immunosuppression, and mental depression. These CS-induced perturbations were attenuated by W somnifera (25 and 50 mg/kg po) and by P ginseng (100 mg/kg po), administered 1 hour before footshock for 21 days. The results indicate that W somnifera, like P ginseng, has significant antistress adaptogenic activity, confirming the clinical use of the plant in Ayurveda.

Herbal Notes

**Withania somnifera**

*Sanskrit/Indian name:* Ashvagandha  
*English name:* Winter cherry  

**Adaptogenic Activity of Withania somnifera**  
Bhattacharya SK, Muruganandam AV.  

**Bacopa monnieri**

*Sanskrit/Indian name:* Brahmi  
*English name:* Thyme-leaved Gratiola  

**Neuroprotective Effect of Bacopa monnieri**  
Limpeanchob N, et al.  
*J Ethnopharmacol.* 2008;120(1):112-117.

**Withania somnifera** Dunal is classified in Ayurveda, the ancient Hindu system of medicine, as a rasayana, a group of plant-derived drugs reputed to promote physical and mental health, augment resistance of the body against disease and diverse adverse environmental factors, revitalize the body in debilitated conditions, and increase longevity. These attributes are remarkably similar to the properties ascribed to adaptogens like Panax ginseng in contemporary medicine. As such, the adaptogenic activity of a standardized extract of W somnifera roots was investigated against a rat model of chronic stress (CS). The stress procedure was mild, unpredictable footshock, administered once daily for 21 days to adult male Wistar rats. CS induced significant hyperglycemia, glucose intolerance, increase in plasma corticosterone levels, gastric ulcerations, male sexual dysfunction, cognitive deficits, immunosuppression, and mental depression. These CS-induced perturbations were attenuated by W somnifera (25 and 50 mg/kg po) and by P ginseng (100 mg/kg po), administered 1 hour before footshock for 21 days. The results indicate that W somnifera, like P ginseng, has significant antistress adaptogenic activity, confirming the clinical use of the plant in Ayurveda.

**Bacopa monnieri** is extensively used in traditional Indian medicine as a nerve tonic and thought to improve memory. To examine the neuroprotective effects of Brahmi extract, its protection against the beta-amyloid protein (25-35) and glutamate-induced neurotoxicity in primary cortical cultured neurons was tested. Neuroprotective effects were determined by measuring neuronal cell viability following beta-amyloid and glutamate treatment with and without Brahmi extract. Mechanisms of neuroprotection were evaluated by monitoring cellular oxidative stress and acetylcholinesterase activity. Results demonstrated that Brahmi extract protected neurons from beta-amyloid-induced cell death, but not glutamate-induced excitotoxicity. This neuroprotection was possibly due to its ability to suppress cellular acetylcholinesterase activity but not the inhibition of glutamate-mediated toxicity. In addition, culture medium containing Brahmi extract appeared to promote cell survival compared to neuronal cells growing in regular culture medium. Further study showed that Brahmi-treated neurons expressed lower level of reactive oxygen species suggesting that Brahmi restrained intracellular oxidative stress which in turn prolonged the lifespan of the culture neurons.

From this study, the mode of action of neuroprotective effects of Brahmi appeared to be the results of its antioxidant to suppress neuronal oxidative stress and the acetylcholinesterase inhibitory activities.
**Aloe vera**

**Sanskrit/Indian name:** kumara  
**English name:** Barbados Aloe  

Evaluation of the Antipsoriatic Activity of Aloe vera Leaf Extract Using a Mouse Tail Model of Psoriasis  

Dhanabal SP, et al.  
*Phytother Res.* 2011.

*Aloe vera* gel is used traditionally for the treatment of skin diseases, including psoriasis. An ethanolic extract of the gel was assessed for antipsoriatic activity using a mouse tail model of psoriasis. The extract produced a significant differentiation in the epidermis, as seen from its degree of orthokeratosis (85.07% ± 3.36%) when compared with the negative control (17.30% ± 4.09%). This was equivalent to the effect of the standard positive control, tazarotene (0.1%) gel, which showed a 90.03% ± 2.00% degree of orthokeratosis. The ethanolic extract of *A. vera* leaf gel also produced a significant increase in relative epidermal thickness when compared with the control group, whereas the standard tazarotene showed no change. Taken together, the extract showed an overall antipsoriatic activity of 81.95%, compared with 87.94% for tazarotene, in the mouse tail model for psoriasis.

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**Asteracantha longifolia**

**Sanskrit/Indian name:** Kokilaksha  
**English name:** Hygrophila  

Effect of Asteracantha longifolia Seeds on the Sexual Behavior of Male Rats  

Chauhan NS, et al.  

The aim of the present study was to study the effect of seeds of *Asteracantha longifolia* on the sexual behavior of male albino rats. The ethanolic extract of seeds of *A. longifolia* was administered to groups of rats in 100, 150, and 200 mg/kg doses for a period of 28 days, and the action compared with control rats. The changes in body and organ weight, sexual behavior, histo-architecture, and fructose levels of seminal vesicles were observed. The sexual behavior was assessed by determining parameters such as mount frequency (MF), intromission latency, mount latency (ML), and post-ejaculatory latency. The ethanolic extract exhibited pronounced anabolic effects in treated animals, as evidenced by gains in the body and reproductive organ weights. Increased spermatogenesis due to treatment with extracts was also witnessed in transverse section. The treatment further markedly affected sexual behavior of the animals, as reflected by the reduction of ML, increase in MF, and enhanced attractability toward females. A significant increase in the sperm count as well as fructose levels of seminal vesicles was noted.

Source: www.weatheredwind.org
Himalaya Baby Care Products

Himalaya’s inception can be traced back to the year 1930 when Mr. M. Manal, founder of The Himalaya Drug Company, decided to present Ayurveda to the world in a contemporary form and unravel the mystery behind the 5000-year-old system of medicine. As a result, products of Himalaya are rooted in Ayurveda and backed by years of research—a true synergy of thousands of years of herbal wisdom and modern scientific research. Eight decades later, we have our presence in 67 countries with a range of over 200 products spanning pharmaceutical, personal care, baby care, and animal health. It covers the entire wellness spectrum, offering head-to-toe herbal health care catering to all kinds of people and their different needs.

Liv.52, a liver protective, and Bonnisan, a health tonic for infants and children, are classic examples of innovative research of Himalaya. These products have become a vital part of the family’s health regimen. Bonnisan, for instance, is widely trusted by doctors, pediatricians and mothers, for its safety and efficacy.

With a legacy of research expertise in herbal medicine, including therapeutic products for child health, the next step for Himalaya was “naturally” a range of herbal baby care products.

A comprehensive portfolio that suits every need of your baby, the Himalaya baby care range includes clinically proven pharmaceutical-grade herbal products based on Ayurvedic formulations. Therapeutic herbs such as khus-khus, Indian madder, licorice, and olive have been used in these products to provide gentle care to your baby. Each product, clinically tested by pediatricians in leading hospitals, has 100% herbal actives specially blended to make it safe, effective, mild, and soothing.

The uniqueness of the range lies in understanding the needs of babies and combining it with Ayurveda’s philosophy of child care. Known as “Kaumarabhritiya” or complete care for the child, the philosophy encompasses nursing, nourishing, and supporting the needs of the child to grow into a happy and healthy adult.
A Preliminary Study on the Safety and Efficacy of HD-03/ES* Therapy in Patients with Chronic Hepatitis B: A Prospective Clinical Study

Bhattacharya AK, Patki PS.

ABSTRACT

In vitro studies indicated that HD-03 has surface antigen suppression and Hepatitis B virus (HBV) elimination activities. Acute and sub-acute toxicity studies indicated that HD-03/ES is devoid of significant toxicity following acute and repeated administration in rats. This study was undertaken to evaluate the safety and efficacy of the formulation HD-03/ES capsules in the management of patients with chronic hepatitis-B (CHB) infection. An open clinical study was carried out in one hundred and six patients with CHB infection and was treated with HD-03/ES capsules twice daily in the morning and evening for a period of 6 months. Clinical, biochemical, and HBV markers were monitored before and after initiation of therapy. Statistically significant improvements were observed in clinical, biochemical, and HBV markers after administration of HD-03/ES capsules. Adverse effects were mild and never warranted withdrawal of the drug. The results of this preliminary study indicate that HD-03/ES might be a safe and effective treatment for the treatment of CHB.

Key Words
HD-03/ES, chronic hepatitis B, clinical trial, HBsAg, ALT normalization, HBV DNA

*HD-03/ES is marketed as Liv.52 HB

Introduction

Ever since the identification of Australian Antigen in 1967, which is now known as hepatitis B surface antigen (HBsAg), hepatitis B infection has emerged as one of the top ten leading causes of death in the world. Hepatitis B virus (HBV) is a serious public health problem worldwide and major cause of chronic hepatitis, cirrhosis, and hepatocellular carcinoma (HCC). It was estimated that approximately 2 billion people have serological evidence of past or present HBV infection and more than 350 million people are chronic carriers of HBV.4 Approximately 75% of chronic carriers live in Asia and the Western Pacific.2 It has been reported that 15% to 40% of HBV infected patients would develop cirrhosis, liver failure, or HCC3 and 500,000 to 12,000,000 people die of HBV infection annually.4,5 Because of the high HBV-related morbidity and mortality, the global disease burden of HBV is substantial. At the moment, ongoing therapies of hepatitis B: interferon (IFN), lamivudine, and most recently adefovir dipivoxil have limited long-term efficacy. Improvement in treatment options will reduce morbidity and mortality for some individuals who are chronically infected.6
HD-03/ES capsules—is a herbal formulation consisting of 125 mg each of hydroalcoholic extracts of the herbs *Cyperus rotundus* and *Cyperus scariosus*. Acute and sub-acute toxicity studies conducted in rats indicated that HD-03/ES is devoid of significant toxicity following acute and repeated administration in rats (data on file). Therefore, the objective of the present clinical study was to determine whether HD-03/ES administration is safe and effective for human administration in the management of chronic hepatitis B (CHB).

**Materials and Methods**

An open prospective controlled clinical trial was carried out in the Department of Medicine, Surat Medical College, Surat, Gujarat, India between the years 2003 and 2007 to evaluate the safety and efficacy of the herbal formulation HD-03/ES capsules alone in the management of hepatitis B. They were selected from those attending the outpatient Department of Medicine, Surat Medical College Surat. Informed written consent was obtained from all study participants and the protocol of the study was approved by the ethical committee of the institute. The study in general was conducted in accordance with Declaration of Helsinki and GCP Guidelines.

Patients with a history of hepatitis B or who were HBsAg carriers for at least 6 months, who still had symptoms and signs of hepatitis as well as abnormal liver function, and positive HBsAg, were diagnosed as having CHB infection in the present study.

**Inclusion criteria**

Patients aged 18–60 years with their “serum alanine aminotransferase” (ALT) level being 41–240 µL and who had positive serum HBsAg were enrolled.

**Exclusion criteria**

Patients above 60 years or those aged less than 18 years, patients in pregnancy or in breastfeeding period; patients who had hepatitis C or other hepatic viral infection, autoimmune hepatitis, and drug-induced hepatitis or alcoholic hepatitis; patients with severe complications of the cardiovascular, renal, or hematopoietic system and patients with mental diseases were excluded. Patients were excluded, if they had decompensated liver disease (defined by serum albumin ≤36 g/dL, bilirubin ≥15 g/dL, prothrombin time ≥2 s prolonged, or a history of ascites, variceal hemorrhage, or hepatic encephalopathy), pancytopenia (defined as hemoglobin <11 g/dL, white cell count <4000/mm³ or platelets <105/mm³). Patients with a history of using IFN or anti-viral agents or corticosteroids or immunosuppressive drugs were excluded.

**Treatment**

Each patient was asked to take two capsules of HD-03/ES one capsule in the morning after breakfast and one capsule at bedtime for a period of 24 weeks.

**Recording and observation of symptoms and signs**

At the time of entry into the study, the signs and symptoms of hepatitis such as loss of appetite, nausea/vomiting, fatigue, weight loss, sense of well-being, jaundice, and hepatomegaly were assessed as present or absent, and if present the severity was noted as mild, moderate, or severe.

**Liver function**

The patients had liver function examination every month during the treatment, including contents of serum proteins, total bilirubin (TB), and activities of ALT and AST (aspartate aminotransferase).

**Etiological markers of hepatitis B**

Serum samples collected from patients were stored at −20°C until analysis. Serum was assayed for HBsAg, at baseline, 16 and 24 weeks after therapy using commercially available enzyme-linked immunosorbent assay kits of Roche. HBV DNA was detected by polymerase chain reaction.

**Safety analysis**

Safety analysis included data for all treated patients during dosing. The primary safety end point was discontinuation of study medication because of adverse events. Other safety evaluations included incidence of adverse effects.

**End points**

The primary end point was HBsAg clearance. Secondary end points included HBV DNA levels and ALT normalization to 40 IU/L at the end of treatment as well as clinical signs and symptoms.

**Statistical analysis**

The intention-to-treat analysis included all randomized patients who were HBsAg positive at baseline and received at least one dose of the study medication. Data were expressed as mean ± SD. One-way ANOVA with Bonferroni’s Multiple Comparison Test or Dunnett’s Multiple Comparison Test was performed wherever appropriate using GraphPad version 4.00 for Windows, GraphPad Software, San Diego, California, USA, www.graphpad.com A P-value of <.05 was taken as statistically significant.
Results

One hundred and twelve patients (82 males and 30 females) aged between 18 and 45 years with a mean age of 33.8 years participated in this open study. One hundred and six patients completed the 6-month study as planned and the rest were lost to follow-up (one after the 1st month, three after the 3rd month, and two after the 5th month). The mode of transmission of HBV was unknown in most (61.7%) with blood transfusion history being present in 11.7% and history of hemodialysis in 13.3%.

Clinical response

The effect of HD-03/ES therapy on clinical signs and symptoms of hepatitis—weight loss and jaundice is shown in Table 1. Although there is progressive weight gain in the subjects treated with HD-03/ES capsules, the levels did not reach statistical significance. Clinical manifestations of hepatitis improved significantly in HD-03/ES-treated patients and jaundice has virtually disappeared in all but one of the subjects after 24 weeks of therapy.

Liver function tests and ALT normalization

Elevated ALT was present in all the patients (Table 2). The median ALT level was 672 U/L. As shown in the table, there was a progressive and statistically significant reduction in the level of ALT and this got normalized in many patients (Table 3). Only thirty-one patients, who completed therapy did not achieve the set goal, but their elevations ranged between 41 and 75 IU/L (41–45=10; 46–50=15; 51–55=2; 56–60=2; 65–70=1; and 71–75=1).

Virological response

Before the treatment, HBsAg was detected in all the patients (Table 3). In 45% of patients, HBsAg became negative and this occurred within 3 to 6 months after initiation of HD-03/ES therapy.

Table 2. Effect of HD-03/ES Therapy on Liver Function Tests in Patients of CHB (n=106)

<table>
<thead>
<tr>
<th>No.</th>
<th>Time (weeks)</th>
<th>Alanine Aminotransferase—ALT (U/L)</th>
<th>Aspartate Aminotransferase—AST (U/L)</th>
<th>Protein total (g/dL)</th>
<th>Protein Fraction globulin (g/dL)</th>
<th>Bilirubin (total) (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0</td>
<td>1498.1 ± 682</td>
<td>479.8 ± 404.9</td>
<td>6.7 ± 0.6</td>
<td>2.9 ± 0.6</td>
<td>6.7 ± 0.9</td>
</tr>
<tr>
<td>2</td>
<td>16</td>
<td>63.2 ± 50.1*</td>
<td>65.1 ± 53.0**</td>
<td>6.6 ± 0.8</td>
<td>3.0 ± 0.6</td>
<td>1.5 ± 0.8**</td>
</tr>
<tr>
<td>3</td>
<td>24</td>
<td>34.8 ± 13.9*</td>
<td>29.7 ± 15.7**</td>
<td>6.7 ± 0.8</td>
<td>3.1 ± 0.6</td>
<td>1.1 ± 0.4**</td>
</tr>
</tbody>
</table>

*p<.05, **p<.01.

Safety

No serious or life-threatening side effects were observed. Tiredness was the only adverse effect reported by 16 patients during various periods of therapy and was not severe enough to warrant withdrawal of therapy. Renal function tests showed normal level of BUN and blood creatinine during HD-03/ES treatment.

Discussion

Surface antigen suppression and HBV virus elimination activities of herbal extract containing *C. rotundus* and *C. scariosus* were examined using two HBsAg expressing human hepato-cellular carcinoma cell lines, PLC/PRF/5, and HepG2.2.215. The efficacy of the plant extract to eliminate the DHBV was assessed in experimentally infected Pekin ducks in a duck model.
study. Our investigations indicated that the extracts could reversibly inhibit cell growth and suppress HBsAg expression in both human hepatocellular carcinoma cell line models (data on file). The present study had shown that twice daily administration of HD-03/ES capsules for a period of 6 months is highly effective in curtailing the signs and symptoms associated with CHB. ALT levels returned to near normal by the end of the study period confirming the results of the in vitro studies.

The goal of treatment for CHB is to prevent cirrhosis, hepatic failure, and hepatocellular carcinoma. This goal is best achieved by eradicating HBV before irreversible liver damage occurs.7 Hence, the ultimate end point of antiviral therapy for CHB infection is loss of HBsAg, which is accompanied by disease remission in terms of ALT normalization.8 In this study, HBsAg cleared in 49% of patients and ALT normalization was obtained in 65% of patients. This coupled with its excellent safety profile may make HD-03/ES an alternative to conventional therapies like α-IFN and lamivudine, which are costly at present and whose use are associated with dose limiting side-effects9-11 in the management of CHB.

In view of the good efficacy and excellent safety profile, HD-03/ES has the potential to become an alternative to conventional therapy for CHB. To conclude the potential benefit of HD-03/ES in the management of CHB, it should be investigated in a large cohort of patients with long periods of follow-up.

References


Non-contraceptive Benefits of Hormonal Contraceptives

Schindler AE.


Besides the contraceptive effect of the various hormonal contraceptives, it is intended to demonstrate the noncontraceptive health benefits for treatment and prevention of bleeding problems, menstruation-related pain and other disorders, such as premenstrual syndrome and signs of androgenization. The effectiveness can be improved by choosing the proper progestogen with antiandrogenic action. Treatment but also prevention can be achieved with hormonal contraceptives in benign proliferative diseases of women, such as ovarian cysts, endometriosis, adenomyosis, endometrial hyperplasia, myoma, and benign breast disease. Furthermore, hormonal contraceptives such as estrogen/progestogen combinations reduce pelvic inflammatory disease, rheumatoid arthritis, asthma symptoms, and preserve bone density. In addition, a major impact in oncological prevention seems to be possible for ovarian, endometrial, and colon cancer, and these positive preventive effects seem to persist also after discontinuation of hormonal contraceptives. In addition, practical concepts for hormonal contraceptive selection will be outlined.
Meta-analysis Demonstrates that Cinnamon Lowers Fasting Blood Glucose

Cinnamon (Cinnamomum spp.) bark has been used around the world as a spice and also in traditional Chinese medicine. Cinnamon bark contains a high amount of the broadly bioactive and antioxidant compounds known as procyanidins. Cinnamon preparations have been well-studied for their ability to lower fasting blood glucose (FBG) concentrations and for its impacts on insulin concentrations and signaling, both important metabolic parameters in the assessment of type 2 diabetes mellitus (T2DM). Previous meta-analyses conducted on this research have concluded that such research is inconclusive or reported no significant effects; however, since these meta-analyses were published, 3 new clinical studies with large populations and/or long treatment periods have been completed. As a result, this paper consists of a meta-analysis of the effect of cinnamon on FBG including the new papers.

To obtain studies, the search terms used were “cinnamon” and “glucose” in addition to related words. Databases searched included Biosis, PubMed, and 2010 abstracts for the American Diabetes Association and the Federation of American Societies for Experimental Biology. The authors included randomized, placebo-controlled studies that reported results of long-term use of cinnamon bark powder or cinnamon bark extract on FBG.

The search yielded 8 clinical studies that met the inclusion criteria. Seven used Cinnamomum aromaticum syn. C cassia, and one did not report the species used. Four studies tested cinnamon or cinnamon extract on T2DM patients, 2 studies included patients with impaired FBG, 1 study involved patients with metabolic syndrome and prediabetes, and 1 study tested healthy subjects. Of the 5 studies that used cinnamon extract, 3 mentioned using an aqueous extract, while 1 used CinSulin® (an aqueous extract manufactured by Tang-An Medical in Beijing, China). The cinnamon extract used in other 2 studies is not defined. The duration of treatments ranged from 5.5 to 16 weeks, and the dosages of cinnamon or cinnamon extract varied widely from 500 mg to 9 g daily. The number of patients or subjects in each clinical study was between 20 and 136 people with 5 studies having 20 to 25 subjects.

The results of the meta-analysis show that cinnamon and cinnamon extract supplementation significantly lowered FBG (-0.49 ± 0.2 mmol/L [8.77 ± 3.52 mg/dL], \( P = .025, n = 8 \)). Cinnamon extract alone also significantly lowered FBG (-0.48 ± 0.17 mmol/L [8.7 ± 3.10 mg/dL], \( P = .008, n = 5 \)). Funnel plot analysis revealed only limited publication bias.

The authors conclude that, “The results of [this] meta-analysis show that the intake of cinnamon/cinnamon extract by type 2 diabetics or prediabetics does lower their blood glucose significantly, albeit modestly.” Although the hypoglycemic activity of cinnamon is comparable with metformin, the conventional pharmaceutical drug frequently prescribed for patients with T2DM, more mechanistic work is needed to definitively use cinnamon alongside this drug for diabetes therapy. Furthermore, no distinction was made concerning the type of extracts used in the studies. Water extracts may be preferable since they exclude nonpolar compounds with known toxicity (the newly included studies used a water extract of cinnamon).

Excerpted from Herbal Gram. 2011;91:34.
I prescribe your oral product, HiOra-GA, to my patients. One of the patients conveyed that on using HiOra-GA for 7 days, her bleeding gums and halitosis problems were well controlled and that she was very happy with the results. Thanks for introducing this product range for dentistry.

Dr SK Agarwal, BDS, Oro-dental Surgeon
Sirka, Rajasthan

Oral products of The Himalaya Drug Company give promising and encouraging results. One of my patients was suffering from oral ulcer on the lateral side of his tongue and despite receiving treatment since January 2010, he was not responding to any drugs. Cytological investigations revealed squamous cell mild nuclear atypical (degenerative) changes. The patient then switched over to Ayurvedic medicine. Along with classical Ayurvedic medicine, I prescribed him HiOra SG ointment for local application. HiOra SG gave encouraging results and at the end of 4 months of its use, the oral ulcer was completely cured and all clinical signs and symptoms associated with the condition were alleviated.

Dr AV Daharwal, Raipur, Chhattisgarh

It gives me immense pleasure to inform you that I have been prescribing Bresol tablets for one of my patients suffering from chronic asthma and that he is totally symptom-free in a course of around 3 months. In the past, the patient was compelled to use rotahaler for more than six times during nights. However, presently he has stopped using it, but still feels absolutely fine. Bresol tablets were used as an adjuvant therapy along with my in-house medicines formulated as per “Panchabhautik Chikitsa” aspect of treatment. The patient is under my observation and will continue to be so for a period of 6 months. I am sure he will not experience any relapse and so is the patient assured.

Dr Sameer D Bagwan, Kolhapur, Maharashtra

I started prescribing Bresol syrup (5 mL BID) for an 8-year-old child with bronchial asthma. After taking Bresol for 8 weeks, the patient felt much better and discontinued the use of inhaler.

Dr A Shyam Mohan, Civil Surgeon Specialist (Pediatrics)
Hyderabad, Andhra Pradesh

I was suffering from allergic rhinitis since last 40 years. I was using antiallergics along with nasal drops for about four to five times a day. After using Bresol tablets at a dosage of 2 tablets BID for 2 weeks followed by 1 tablet BID for past 45 days, I stopped using any antiallergics and nasal drops. I would like to thank The Himalaya Drug Company for developing such a medication for the treatment of allergic rhinitis.

Dr Rastogi RK, Dehradun

A young female aged 25 years was suffering from allergic rhinitis from a long period. She had recurrent attacks of running nose and cough. I advised her to take Bresol syrup and Septilin tablets for 3 to 4 months, regularly. She was symptom-free. Her son aged 2 years was also suffering from recurrent attack of rhinitis and cough. I advised Septilin and Bresol syrups for 6 months. He was also symptom-free for a long period.

Dr Vikas M Patney, Kolhapur, Maharashtra

A 50-year-old female presented with chronic urinary tract infection and pus cells in urine for several years. The patient reported of using several types of antibiotics for these conditions. All antibiotics were stopped and she was advised to take 1 Septilin tablet TDS and 2 Cystone tablets TDS. It was found that pus cells disappeared within 2 months. A 35-year-old female was suffering from dry and irritating cough since 2 months. There was no history of fever, weight loss, and hemoptysis. Cough increased during early mornings and late nights. Investigations such as blood test and x-ray of chest showed normal results. T3, IgA, and IgM were negative. The patient was diagnosed of allergic bronchitis. The advised treatment was 2 teaspoonfuls of Bresol syrup TDS and 1 Septilin tablet TDS. Dramatic results were observed after this treatment. Dry cough was remarkably reduced within 2 to 3 days. The patient was advised to continue the same treatment for another 2 to 3 months.

Dr Rajesh Gupta, Moga, Punjab

It gives me immense pleasure to inform you that I am prescribing HiOra-K toothpaste and HiOra-Shine toothpaste, regularly. HiOra-K toothpaste is quite effective in reducing tooth sensitivity without any adverse effects (as reported by a large number of my patients). HiOra-Shine toothpaste is effective in removing stains on tooth surfaces, based on my personal experience and as observed by my patients. I wish good success for both the HiOra products.

Dr Sarmah M, Dental and Oral Surgeon
Sivasagar, Assam

I am pleased with the oral care products of The Himalaya Drug Company, especially HiOra-K, HiOra-GA, and HiOra-SG. The responses patients show are very encouraging and this has helped me to dispense more than 150 units per month. Keep up the good work. Thank you.

Dr Agnelo Chang, Sakinaka, Mumbai

I have prescribed Confido to a large number of my patients with premature ejaculation and have got remarkable success in majority of them.

Pradip Kumar Sahana, Consultant Dermatologist, Venereologist, and Leprologist
Gurudasi Para (west), Burdwan

I am prescribing Septilin syrup and tablet in my clinical practice since past 7 years. It is especially beneficial in long-term use and works as a good immunomodulator.

Dr AB Gunnal, Consulting Child Disease Specialist
Ambajogai, Maharashtra

I have started prescribing Bresol to my patients with asthma, chronic obstructive pulmonary disease, and eosinophilia. Most of them have responded very well after 4 weeks of using this drug.

Dr Ganeesh Mahadevan, Senior Consultant Physician and Diabetologist
Secunderabad, Andhra Pradesh

I am immensely happy to give HiOra K MouthWash, HiOra Shine, and HiOra GA to my patients, they reported satisfactory results as well as quality product in Herbal range. The MouthWash is also highly effective in periconitis. I wish all the success.

Dr Rajendra Chauhan, Dental Surgeon
Ahmedabad
I have been using Himalaya herbal products from past 1 year. It has given excellent results to my patients, especially in dentinal hypersensitivity and halitosis problems.

Dr Basant Sharma, Dental Surgeon
Pilani

My personal experience with Liv.52 group is excellent. It is the only drug with 0% side effects and 100% main effects. A challenging case of hepatocellular failure due to ethanol abuse was successfully treated by me. The patient recovered completely with Liv.52 DS. My overall experience with The Himalaya Drug Company is very good. They have a very good rapport with Doctors. They have very low-priced products.

Dr B Ramana Rao, Bangalore, Karnataka

I am prescribing The Himalaya Drug Company’s, Lukol, since 10 years (approximately). This is good for women’s health and improves general well-being. It is very good for excessive and abnormal vaginal discharges.

Dr Veena Sinha, Obstetrics and Gynecology Specialist, Bhagalpur, Bihar

Lukol is effective in nonspecific discharge (per vagina) and chronic cervicitis. It should be used for at least 6 to 8 months.

Dr Meenakshi Gupta, Obstetrics and Gynecology Specialist, Gorakhpur, Uttar Pradesh

It gives me great pleasure to write a feedback on The Himalaya Drug Company’s product, Gasex. In my opinion, it is a wonderful drug and I have been prescribing it from the past 18 years of my practice. I found good results for conditions such as bowel regulation, acid peptic disease, and other gastrobiliary disorders. I would like to thank the company for launching such a wonderful drug.

Dr Ajay Kumar Shukla, Nishatganj, Lucknow

I have been prescribing Septilin from past 20 years. In my clinical experience, Septilin is the best scientifically proven drug from The Himalaya Drug Company. As an immunomodulator and anti-infective, Septilin has shown promising results post-bacterial and post-viral infections, and above all in patients with tuberculosis.

In pediatric population, Septilin is a useful adjuvant in upper respiratory tract infection, lower respiratory tract infection, and Kochs adenopathy. The product brings about good clinical improvement, shortens hospitalization, and avoids postdisease complications.

Dr Aref Hussain, Consulting Physician Partur, Maharashtra

I, Dr SS Raman, have been prescribing Pilex tablets and ointment from past 20 years. I found the drug very useful in my clinical experience.

Dr SS Raman, Kollam, Kerala

First I would like to congratulate on very successful all over India launching of your dental products. I would like to express very surprising results of your products that I have never seen over my career. I think this is because of the herbal origin and quality research and development of the products. Ultimately, I would like to expect that in further we will be receiving this kind of great products for the benefits of patients.

Dr Vishnu Kumar Didwania, Jawahar Nagar, Jaipur
Review

Book

Exercise Therapy in the Management of Musculoskeletal Disorders
Fiona Wilson-O’Toole, et al.

Publisher: Wiley-Blackwell, 2011
ISBN: 9781405169387
Price: US$ 54.99
Length: 280 pages

"Exercise Therapy in the Management of Musculoskeletal Disorders” covers the fundamentals of using exercise as a treatment modality. It evaluates the evidence, and offers practical ideas for the use of exercise therapy in the management of musculoskeletal disease in different areas of the body and for differing pathologies, with emphasis on all patient groups. “Exercise Therapy in the Management of Musculoskeletal Disorders” will be invaluable to undergraduate and qualified physiotherapists who are designing rehabilitation programs for patients with musculoskeletal disorders, and to students and practitioners of sports science.

Contemporary Treatment of Erectile Dysfunction: A Clinical Guide
Kevin T McVary

Publisher: Springer, 2010
ISBN: 9781603275354
Price: 159,95 € (Hardcover), € 49,95 (Soft cover)
Length: 287 pages

Erectile dysfunction can affect all age groups. Numerous physical and emotional risk factors may contribute to the problem. These risk factors can range from chronic diseases and medications to psychological factors. In the US alone, it has been estimated that 18 to 30 million men suffer from erectile dysfunction. This number has increased significantly as awareness of the disorder has heightened. Researchers and health care professionals now have a better understanding of what causes erectile dysfunction and the effective medications and nonmedication treatments used to treat the condition. Comprehensive and state-of-the-art, "Contemporary Treatment of Erectile Dysfunction: A Clinical Guide” synthesizes the literature and covers all aspects of treating erectile dysfunction and other related male sexual dysfunctions. This invaluable title offers all physicians, residents, and fellows—and even medical students and other health professionals such as nurse practitioners and physician assistants—an essential reference for enhancing diagnosis and treatment of this debilitating disorder.
The National Arthritis Foundation (NAF) was registered as a charitable body in 1984 and is the largest public organization in Singapore. Their vision and mission are embodied in the acronym CARE, namely, Care for patients; Advocate against arthritis; Research to fight arthritis; Educate patients and the public on arthritis.

NAF is devoted to the three-fold aims of helping people with arthritis, educating patients and the public on arthritis, and supporting arthritis research.

- **Patient Welfare**—Financial subsidies for needy patients for medical and surgical treatments through the Patient Subsidy Care Programme.
- **Public and Patient Education**—Initiatives include the dissemination of patient education pamphlets and conducting of regular public forums.
- **Encouraging research on arthritis**

The British Skin Foundation

The British Skin Foundation (BSF) is the only UK charity dedicated to skin disease research. Their aim is to raise money for research projects that will hopefully result in cures or at the very least, a better understanding of the numerous skin conditions that affect millions of lives in the UK. To date BSF has funded over 260 projects totalling seven million pounds looking into a variety of skin diseases, such as skin cancer, eczema, hidradenitis suppurativa, and psoriasis to name but a few. Aside from providing financial support to research projects, the other goal of BSF is to focus on awareness and education. They work through their fundraising events, media work, and campaigns to dispel the myth that skin disease is not a serious issue.
Quiz corner

Crossword

Theme: Product names of The Himalaya Drug Company

Across
3. It is effective in reducing hair fall and improving hair growth and tensile strength of hair. (8)
4. This product is prescribed for enhancing neurological functions in patients with neurodegenerative disorders, and improving memory and cognitive functions. (6)
5. A phytopharmaceutical formulation recommended for the clinical management of benign prostatic hyperplasia. (9)
8. This product is extremely useful in the management of chronic constipation, and constipation during postoperative and nonambulatory periods. (8)
9. A phytopharmaceutical formulation recommended for the management of acne. (7)
10. A phytopharmaceutical formulation, safe and effective in relieving burning micturition and soothing inflamed urinary mucosa. (7)

Down
1. This drug is recommended for the prevention and treatment of common gastrointestinal disorders in infants and children. (8)
2. This product is a natural blood detoxifier, prescribed for the management of acute and chronic dermatitis, urticaria, hyperpigmentation in chronic dermatitis, and cutaneous manifestations of worm infections. (5)
6. This polyherbal drug is effective in the treatment of male infertility due to oligospermia. (6)
7. A polyherbal formulation indicated for the management of cough of varied etiology. (6)

Answers to Medical Crossword 6 (Vol. L No. 4 Jul-Sep 2011)
Across: 1) Menorrhagia 8) Dysmenorrhea 9) E. coli 10) Colposcope
Down: 2) Amenorrhea 3) Menorrhagia 4) Pressey 5) Chronic 6) Endometriosis 7) Positive
Hermann Senator: A Clinical All-rounder with a Special Interest in Rheumatology

Kaiser H.


Differentiation of the so-called rheumatic diseases according to scientific principles started in France and England in the 17th century, reaching a high-point in the 19th century. In Germany, it was the pathological anatomists and surgeons who first gave their attention to diseases of the musculoskeletal system. In 1875, Hermann Senator was the first German specialist in internal medicine to describe this field in the Handbook of Special Pathology and Therapy. Later, he repeatedly gave his attention to rheumatic diseases, in particular their therapy. In principle, he was one of the last all-rounders insofar as he wrote monographs, handbook contributions, as well as many individual works on all areas of internal medicine, including neurology and pediatrics. Although he was head of various departments and clinics at the Charité in Berlin and a widely renowned physician with a reputation as one of the best professors, he was never awarded the title of full professor. The reason for this? He was Jewish!

Dr Paul Gerson Unna: Meticulous Researcher in the field of Dermatology

Ney Romiti.


Dr Paul Gerson Unna is well known almost only for the revolutionary Unna boot, which has a minor significance when compared to his extensive and outstanding contribution to the formation and pioneering spirit in Dermatology, both in terms of his research and educational performance. The originality of this meticulous researcher was delineated when he detailed the structure of the skin, characterizing its differentiation into four layers and indicating the basal layer as responsible for regeneration of the epidermis. It was in 1894, that he published “Histopathology of the Skin Diseases.” This work was the result of exhaustive research on the anatomicopathological findings consecrated at that time, and also original concepts that were opposed to many of the pre-established doctrines. That book became the basis for all those who were attracted to Dermatology. Even today, the chapter on “Nevi” is a classic. Pathological complementation, enhanced with clinical details and therapeutic orientations, deserve special mention. At this time, he developed the original staining methods to reveal and differentiate the structures and composition of the skin. In this manner, he identified the plasmatic, nevus cells, the composition of collagen and elastin, spongiosis, the balloon and reticular degeneration of the spinous layer in chickenpox, zoster, and other bullae. His bibliographical production was extensive, which included over 500 publications, notably the Atlas of Histology and Pathology of the Skin that merited several editions between 1896 and 1910.
A Man of His Words

Seidel HM.


It never occurred to me that the man who came to see me when I was sick was anything other than my family’s physician. Being sick gave me the honored comfortable spot on the sofa in what we called our living room. There, I waited expectantly for his house call. My mother always drew the shades to dim the room and there was quiet until he came.

The pattern was repeated often over the years. He did not elicit much in the way of a history, usually just the “chief complaint”: “He’s hot” or “His head hurts” or “His neck is swollen.” The only pause before he sat beside me on the edge of the sofa was to wet a tongue blade because he knew I gagged very easily and he said it would help. (It never seemed to me that it did.)

Then there would come the inevitable moment, after poking me a bit and looking into my ears and throat, he would pull a leather case from his bag. It was—in my child’s mind’s eye—huge. When opened, it presented a double row of small bottles filled with variegated pills. This was in the 1920s and early 1930s. I cannot now imagine what they might have been other than sugar and aspirin. No matter, the colors attracted me and his choice excited me. He made the selection and, disappointingly, never gave me the option. Still, I felt badly about it only once. My mother had to bribe me to swallow the “wrong” color by giving me The Count of Monte Cristo, still my favorite book. The book’s final words are “Wait and hope.” I did wait eagerly for his visit and I certainly hoped for the right color.

There was never much chitchat at the end of his visits because English was not yet my mother’s or father’s forte, but what the doctor instructed was understood and carried out. I am still impressed with the deference my parents always showed him. Compliance was never an issue. Neither was payment. The final phase of the visit was invariably introduced with a single question: “What do I owe you, Doctor?” Happily, we always had the required two or three dollars. Ours was a common story for our doctor. He took care of many immigrant families like ours in Rutherford, New Jersey, where he both lived and maintained his office, and in Passaic and Paterson and many others of the towns sited one upon the other in Passaic and Bergen counties. We were one of them. I was born in St Mary’s Hospital in Passaic not very long after my parents passed through Ellis Island. Our doctor did most of his hospital work at Passaic General, but he saw me at St Mary’s and he was a constant visitor to our home as my brother and I grew up.

There was one dramatic moment when my brother needed to have what I now know was a myringotomy. The procedure was accomplished on our kitchen table (after I had been banished to the back yard). For the most, though, aside from my appendicitis some months later, the visits were for unthreatening complaints and, as we grew older, we made the trip across the river to Rutherford. The office was not imposing. The doctor and his family lived in the house but there was a separate entrance for the office. The space even then seemed small to me. I remember lots of magazines—medical journals?—somewhat helter-skelter. And there was not a lot of talk. A visit to Ridge Road a few years ago did not suggest that too much had changed, at least on the outside. There was still a shingle up, I believe belonging to our doctor’s son.

My father, always well groomed, always crisp, was then my template for how grown men might look. Our doctor was not. Rumpled is what comes to mind now, a suit that was likely always gray, and hair that was
likely always a bit awry, a man not heavy, not very tall, not particularly imposing. He did not seem physically to command our space. It was his “doctorhood” that did the commanding.

I had appendicitis when I was 6 years old. The doctor examined me in my bed in the room I shared with my brother. No sofa then. Afterward, voices beyond the door were muted. It was the habit of the time to keep the child essentially uninformed. My mother told me years later when I was in medical school that she was terrified, but she was a bit placated because our doctor assured her that the surgeon had been trained at Johns Hopkins School of Medicine. Maybe so. There was such a man in Passaic, but I had my operation at a hospital in Paterson. My later reflections on that episode confirmed the nascent impressions I had of the power of the physician.

I cannot recall exactly when I found out that our doctor was something other than a physician. It was probably some time during my college years. I certainly did not know it when I asked him for a letter of recommendation when I applied to college. That letter—it came back into my hands about the time I was an associate dean at Johns Hopkins—claimed that I was “a boy of intelligence, industry and excellent character” who would “carry out whatever tasks entrusted to him with distinction” and that I was “a young man well above the average in all the qualities that make up a good student.” These fine words did not help me get into Cornell or Columbia, but I was claimed by Johns Hopkins. The letter was signed “W. C. Williams, M.D., U. of Pa. Med. 1906.”

There were a few times when Dr Williams talked with me about medicine. It is easy to repeat what he told me: “If you have heard one half the stories I have heard and if you have listened to them, you will have had a satisfying career.” I have! And I persist in the conceit that one day, after a house call to see me, he paused in his automobile to write on his prescription pad:

Complaint

They call me and I go.
It is a frozen road
past midnight, a dust
of snow caught
in the rigid wheeltracks.

The door opens.
I smile, enter and
shake off the cold.
Here is a great woman
on her side in the bed.
She is sick,
perhaps vomiting,
perhaps laboring
to give birth to
a tenth child. Joy! Joy!

Night is a room
darkened for lovers,
through the jalousies the sun
has sent one golden needle!
I pick the hair from her eyes
and watch her misery
with compassion.

—William Carlos Williams

Liv.52 HB: World’s First Herbal Drug for the Management of Hepatitis B

Launched in 1955, Liv.52, a phytopharmaceutical formulation of The Himalaya Drug Company (HDC) that ensures optimum liver function, is the top selling herbal drug in India. Liv.52 is prescribed as the first line of treatment or as an adjuvant in the management of viral hepatitis, alcoholic liver disease, anorexia/loss of appetite, and other liver disorders.

In recent times, the evidence of hepatitis B virus (HBV) infection is increasing rapidly and emerging as a global health concern. According to the World Health Organization, about 40 million people are currently infected with HBV in India. HBV carriers are at the risk of complications such as chronic hepatitis, cirrhosis, and hepatocellular carcinoma.

An effective treatment for hepatitis B had been under research at the Research and Development center of HDC for more than a decade. The scientists at HDC screened over 100 plants to identify herbs/composition of herbs that possess therapeutic properties required for the treatment of HBV infection. Extensive research showed that two herbs—Nut Grass (Latin name: *Cyperus rotundus*; Sanskrit name: Mustaka) and Cypriol (Latin name: *Cyperus scariosus*; Nagaramustaka)—have potent antiviral properties. Thus, a new formulation containing these two key herbal ingredients was developed by our scientists.

The herbal formulation, known as Liv.52 HB, was first tested on in vitro models or hepatic cell lines. Results showed that the drug suppresses the replication of viral DNA involved in hepatitis B, and eliminates the virus by reverse transcriptase inhibition. It suppresses the virus by binding itself to hepatitis B surface antigen (HBsAg). Liv.52 HB was subjected to clinical trials in leading hospitals and institutes across India such as Sion Hospital (Mumbai), Osmania Medical College Hospital (Hyderabad), and Maulana Azad Medical College (Delhi).

Reports from clinical trials on Liv.52 HB have been published in international journals like *Antiviral Research* and *World Journal of Gastroenterology*. A US patent has been filed for Liv.52 HB, a breakthrough herbal formulation for hepatitis B.
Corporate Social Responsibility

Prison Rehabilitation Project

Community development has been the core focus of The Himalaya Drug Company’s (HDC) corporate social responsibility. The company through its contract farming initiatives has engaged local farmers for herb cultivation. The programs ensure that farmers are fairly paid and freed from exploitation of middle agents.

Recently, HDC decided to step up its efforts and commence a one-of-a-kind initiative that rehabilitates prisoners. In 2011, HDC signed a memorandum of understanding (MoU) with the Department of Prison Rehabilitation, Government of Karnataka for the cultivation of medicinal herbs at an open air prison, in the outskirts of Bangalore.

Under this program, prisoners are trained on Good Agricultural and Collection Practices, provided with seeds, and given technical assistance by HDC’s agro-technology team. This could help prisoners earn a regular income for their efforts.

In phase I of the program, inmates cultivated herbs on four acres of land. Alfalfa is the first herb to be grown in the prison, which is a key ingredient in Liv.52 Vet. The herb was chosen because it takes only 60 days to be harvested. The quick harvest time, will help inmates see the benefits of their efforts more quickly. The harvested herb will be procured by the HDC.

The program will be later expanded to cover 10 acres and cultivation of herbs such as Ashvagandha (Withania somnifera), Kalmegh (Andrographis paniculata) and Tulasi (Ocimum sanctum) are being considered.

Currently, HDC is in the process of expanding this initiative that will see the company tying up with other open air prisons in different parts of the country. The company is already in advanced talks with prison authorities in Andhra Pradesh.
Laughter, the Best Medicine

A soldier serving in Hong Kong was annoyed and upset when his girl wrote breaking off their engagement and asking for her photograph back. He went out and collected from his friends all the unwanted photographs of women that he could find, bundled them all together and sent them back with a note saying, “I regret to inform you that I cannot remember which one is you – please keep your photo and return the others.”

During the Persian Gulf War, I was assigned to go to Saudi Arabia. As I was saying good-bye to my family, my 3-year-old son, Christopher, was holding on to my leg and pleading with me not to leave.

“No, Daddy, please don’t go!” he kept repeating.

We were beginning to make a scene when my wife, desperate to calm him, said, “Let Daddy go and I’ll take you to get a pizza.”

Immediately, Christopher loosened his death grip, stepped back, and in a calm voice said, “Bye, Daddy.”

An accountant and his neighbor went to the Natural History museum one day.

While standing near the dinosaur he said to his neighbor: “This dinosaur is 2 billion years and 10 months old.”

“Where did you get this exact information?”

“I was here 10 months ago, and the guide told me that the dinosaur is 2 billion years old.”

A husband and wife came for counseling after 20 years of marriage. When asked what the problem was, the wife went into a passionate, painful tirade listing every problem they had ever had in the 20 years they had been married.

She went on and on and on: neglect, lack of intimacy, emptiness, loneliness, feeling unloved and unlovable, an entire laundry list of unmet needs she had endured over the course of their marriage.

Finally, after allowing this to go on for a sufficient length of time, the therapist got up, walked around the desk and, after asking the wife to stand, embraced and kissed her passionately as her husband watched with a raised eyebrow. The woman shut up and quietly sat down as though in a daze.

The therapist turned to the husband and said, “This is what your wife needs at least three times a week. Can you do this?”

The husband thought for a moment and replied, “Well, I can drop her off here on Mondays and Wednesdays, but on Fridays, I fish.”

Think Wise

You are today where your thoughts have brought you; you will be tomorrow where your thoughts take you.

- James Allen

Your Feedback Matters to Us!

We would like to hear from you on this special issue of Probe.

Please write to us with your views at publications@himalayahealthcare.com
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from
The Himalaya Drug Company

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Help your patients beat the BLUES of ED with RED...

**Tentex Royal** (CAPSULE)
Enhances desire and improves performance

For low libido...

**Tentex forte** (TABLET)
Effective non-hormonal sex stimulant for men

In erectile dysfunction...

**Himcolin** (GEL)
Strengthens erectile power & improves sexual potency

In various ejaculatory disorders...

**Confido** (TABLET)
Restores his confidence

In oligospermia...

**Speman** (TABLET)
 Gives hope to childless couples