

HEMORRHOIDS – A COMMON AILMENT AMONG ADULTS, CAUSES & TREATMENT: A REVIEW**BHARAT GAMI**

Pharmaceutical Biotechnology lab, Ipcowala Santram Institute of Biotechnology & Emerging Sciences, Dharmaj 388430, Gujarat India.

Email: bharat11_gami@yahoo.com

Received: 12 Feb 2011, Revised and Accepted: 18 May 2011

ABSTRACT

Hemorrhoid is one of the most common gastrointestinal disorders seen by the general practitioners. Hemorrhoids have several treatment modalities and diagnosis. In initial stages conservative treatments can be applied, but over a period when the hemorrhoids get worst, the disease should be treated by several non-operative treatments like Sclerotherapy, rubber bend ligation, infrared photocoagulation, cryotherapy, bipolar diathermy, and direct-current electrotherapy. When hemorrhoids cannot be addressed by non-surgical treatment, normal or alternative method like surgical methods is applied. There are several over the counter herbal medicine (oral & ointment base creams), available as botanicals for hemorrhoids. It has been proved by scientific studies that botanicals improve microcirculation, capillary flow, vascular tone, and to strength the connective tissue of the perivascular amorphous substrate.

Keywords: Hemorrhoids, Botanicals, Gastrointestinal disorder, Photocoagulation

INTRODUCTION

Hemorrhoids or piles are a common ailment among adults. More than half of men and women aged 50 years and older will develop hemorrhoid symptoms during their lifetime¹. Hemorrhoids are rare in children but now days several reports state the occurrence of hemorrhoids in children², and in elderly people³. In United States three-quarter of individuals have hemorrhoids at some point in their lives, and about half of them over age 50 required treatment⁴, and much smaller percentage approximately 4% seek medical treatment for the condition. Hospital based proctoscopy studies show prevalence rates of hemorrhoids with a symptomatic state in 86% of patient⁵. According to The Merck Manual definition hemorrhoids is "Varicosities of the veins of the hemorrhoidal plexus, often complicated by inflammation, thrombosis, and bleeding"⁶. But a recent definition of hemorrhoids is "Vascular cushions, consisting of thick submucosa containing both venous and arterial blood vessels"⁷.

Chronological inspection of Hemorrhoids

It has been estimated that hemorrhoids can affect both men and women⁸. Hemorrhoids are mentioned in ancient medical writings of every culture⁹. The word "hemorrhoids" is derived from the Greek "haema"= blood, and "rhoos"= flowing, and was originally used by Hippocrates to describe the flow of blood from the veins of the anus¹⁰. Commonly in society it is known as piles, the word pile is derived from Latin, meaning a ball or a mass, as this condition may not always be accompanied by bleeding, the word piles is better used for this condition¹¹. John Andrene remarks that common people call them piles and the aristocracy calls them hemorrhoids, the French call them figs, means to clot¹².

Histology of hemorrhoids

Hemorrhoidal tissue, cushions of tissue within the anal canal that contain blood vessels and supporting tissue made up of muscle and elastic tissue, are present in all individuals⁴. Universally hemorrhoids are classified according to anatomical origin as shown in fig 1. Internal hemorrhoids are consisting of redundant mucus membrane of the anal canal with the origin above the dentate (ano-rectal) line, and external hemorrhoids have an epithelial component and originate below the dental line¹³. Internal hemorrhoids or true hemorrhoids are further graded based on the extent to which the tissue descends in to the anal canal. First degree Hemorrhoids "The mucosa barely prolapse, but with severe straining may be trapped by the closing of the anal sphincter. Subsequently, venous congestion occurs occasionally, resulting in discomfort and/or

bleeding". Second degree Hemorrhoids "With further protrusion of the mucosa, the patient complains of an obvious lump, but this disappears spontaneously and rapidly after defecation unless thrombosis occurs" Third degree Hemorrhoids "In chronic hemorrhoidal disease, the persistent prolapsing produces dilatation of the anal sphincter, and the hemorrhoids protrude with minimal provocation and usually require manual replacement". Fourth degree Hemorrhoids "These are usually described as external hemorrhoids and are protruding all the time unless the patient replaces them, lies down, or elevates the foot of the bed. In these fourth degree hemorrhoids, the dentate line also distends, and there is a variable external component consisting of redundant, permanent perianal skin"¹³. On basis of lithotomy position there are usually three major hemorrhoidal cushions originated to the right posterior, right anterior, and left lateral position known as 3,7, and 11 o'clock position of the anal^{14,15}.

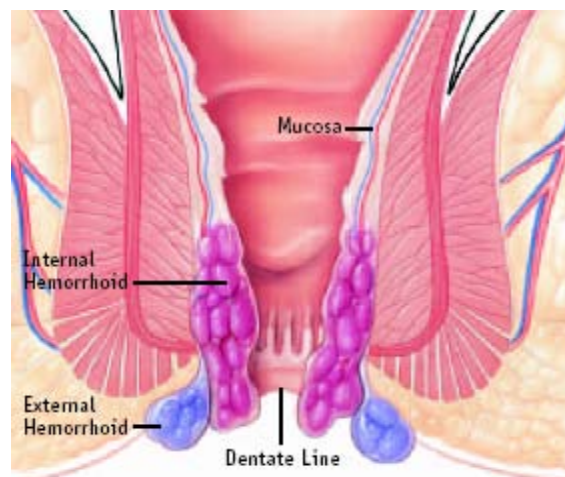


Fig. 1: Schematic presentation of types of Hemorrhoids

Diagnosis of hemorrhoids

Patient with rectal discomfort, swelling, pain, discharge, and bleeding at the time of defecation, it is prudent not to assume it is a result of hemorrhoids, a full evaluation is necessary, including a rectal examination, a proctoscopic examination, and in some cases a sigmoidoscopy or colonoscopy^{13,16}. The doctor will examine the anus and rectum to look for swollen blood vessels that indicate hemorrhoids and will also perform a close rectal exam with gloved,

lubricated finger to feel for abnormalities, with an anoscope a hollow lighted tube useful for view of internal hemorrhoids¹⁷.

Pain is absent unless complications supervene, for this reason, any patient complaining of 'painful hemorrhoids' must be suspected of having another condition, and examine accordingly¹⁵. Several other diseases like rectal or anal carcinoma, colon cancer, and other digestive problem produce same symptoms like hemorrhoids, so it is advisable to see a doctor if patient have any rectal bleeding^{18,19}.

Causes of hemorrhoids

The actual cause of hemorrhoids is not known⁵. Few of the earliest proposed cause include temperament, body habits, customs, passions, sedentary life, tight-laced clothes, climate, and seasons¹³. Hemorrhoids are common in patients with spinal-cord injuries, constipation, chronic diarrhea, poor bathroom habits, postponing bowel movements, and a poor-fiber diet are also considered to be contributing causes²⁰. By recent studies implicate gravity intrinsic weakness of the blood vessel wall, heredity, genetic predisposition, increased intra-abdominal pressure from many causes, including prolonged forceful valsalva defecation, obstruction of venous outflow secondary to pregnancy, and constipated stool in the rectal ampulla^{21,22}. Alcoholic cirrhosis or other causes of portal obstruction can cause severe hemorrhoids. More rarely but much more importantly, haemorrhoids may reflect collateral anastomotic channels that develop as a result of portal hypertension²³.

Treatment of hemorrhoids

The natural evolution of hemorrhoids is benign but hemorrhoids tend to get worse over time, and it should be treated as soon as it occurs²⁴. The best treatment is always prevention²⁵. Despite thousands of years and millions of patients with pain, discomfort and perceived embarrassment of hemorrhoids, exact natural cause of hemorrhoids is yet not clear so slandered treatment are, at best, imperfect⁹, but several surgical and non-surgical techniques are used to treat hemorrhoids.

Non-operative Treatment

Numbers of methods that do not involve surgical excision are available to treat patients with hemorrhoids. These procedures are usually performed in the office setting and do not require anesthesia.

Sclerotherapy

Morgan in Dublin first described it in 1869, and it is reserved for first and second-degree hemorrhoids. A submucosal injection of 5 ml of 5 % phenol in oil, 5 % quinine and urea, or hyper tonic (23.4 %) salt solution at the base of the hemorrhoidal complex causes thrombosis of vessels, sclerosis of connective tissue, and shrinkage and fixation of overlying mucosa. It takes only minutes to perform though an anoscope²⁶. Khoury et.al., performed trial and found 89.9 % of the patient's quared, who had initially been treated with medical therapy²⁷. Sclerotherapy is minimally invasive it cause some complications, like pain variably reported in 12 % - 70 % of patients^{26,28,29}, Impotence³⁰, urinary retention & abscess³¹, anaphylactic shock³².

Cryotherapy

Cryotherapy used for internal hemorrhoids, and in which enlarged internal hemorrhoids destroyed, initial report related efficacy of techniques were enthusiastic³³. It is a time consuming techniques as compare the techniques and subsequent reports have shown disappointing results³⁴. Complications with cryotherapy are prolonged pain, foul-smelling discharge, and greater need for addition therapy³⁵. It is cumbersome to perform and is associated with severe rectal pain and discharge³⁶. So now days cryotherapy is rarely used for treatment of hemorrhoids patients³⁷.

Rubber Band Ligation (RBL)

Rubber Band Ligation is most commonly used for first-second or third degree hemorrhoids. Some authorities also recommended RBL for fourth degree hemorrhoids after operative reduction of the incarcerated prolapse³⁸. RBL relies on tight encirclement of redundant mucosa connective tissue and blood vessels in the hemorrhoidal complex. Internal hemorrhoids ligation can be performed in the office setting with one of several commercially available advance instruments so procedure becomes a one-person effort³⁹. Endoscopic variceal ligators have also been shown to be effective tools for hemorrhoid ligation⁴⁰. In one session RBL can be performed up to 3 hemorrhoids⁴¹⁻⁴³. About 80 % of success rate was found by Wroblewski et al with five years of follow-up after treatment⁴⁴⁻⁴⁷.

The most common complication of RBL is pain, reported in 5 %-60% of treated patients^{26,43,48,49}. Other complication with RBL is abscess, urinary retention, band slippage, prolapse and thrombosis of adjacent hemorrhoids, and bleeding from ulcer occur in < 5 % of patients, Necrotizing pelvic sepsis (rare complication)^{50,51}, prolapse and bleeding were the most frequent reoccurrent symptoms⁴⁶.

Bipolar Diathermy

Bipolar diathermy is applied one-second pulse of 20 W until the underlying tissue coagulates. Several complications like pain, bleeding, fissure or spasm of the internal spincter was observed in about 12% of the patients^{52,53}. For second and third degree hemorrhoids multiple application of bipolar diathermy to the same site are required⁵⁴. Successes rate in bipolar diathermy was ranging from 88% to 100%^{36,52-55}. Prolapsing tissue dose not eliminate by bipolar diathermy and up to 20 % patients will required excisional hemorrhoidectomy^{54,55}.

Direct-Current electrotherapy

Direct current electro coagulation was utilized in 1876, and explained by Wilbur E. Keeseey, MD in 1934, but doctors today oddly considered it as one of the new generation of modalities⁵⁶. Direct-current electrotherapy required the prolonged up to 14 minutes application of 110-V direct current to the base of hemorrhoidal complex well above the transition zone^{36,53,42,55,57-59}. Multiple treatments to same site are required in up to 30 % of patients⁵⁷, and time of electric treatment depends upon the degree of hemorrhoids. A direct-current electrotherapy technique has not been widely accepted because of the lengthy treatment time and the limited control of prolapse in higher-grade hemorrhoids⁵⁹. Complication observed after direct-current therapy was pain (33%), ulcer formation (4%), and bleeding (10 %) ^{36,58}.

Infrared photocoagulation (IRC)

IRC was introduced in late seventies by Nath⁶⁰. In IRC coagulation of the tissue is done by focuses of infrared radiation from a tungsten-halogen lamp via a polymer probe tip^{13,21}. During the IRC treatment mechanical presser and radiation energy are applied simultaneously in a manner that can eliminate the disadvantage occur in electro coagulation like grounding the patients & charring of the tissue⁶¹. At one time 2-6 hemorrhoids can be treated by IRC treatments²⁶.

As such IRC is free from any hazards and has proved to be an effective and safe method for treatment of early grade bleeding internal hemorrhoids⁶², while in electro coagulation an obvious risk of electric current passing through the body, which may cause pain full muscular spasms⁶³. By the randomized studies with IRC, 67%-96% of success rets of patients with first or second degree bleeding hemorrhoids has been reported^{13,26}.

Surgical or operative Treatment

In normal cases hemorrhoidal diseases can be treated by the dietary modifications tropical medications. But in certain cases surgical procedure are necessary to provide satisfactory long-term relief in cases involving a greater degree prolepses, a variety of operative techniques are employed to address the problem⁶⁴. Hemorrhoidal surgery is known as hemorrhoidectomy, in hemorrhoidectomy

techniques include excising internal & external components in 1-3 quadrants around the anal canal⁶⁵. ⁶⁶ banding of internal hemorrhoids and excising the external component ³⁸ or performing a circular excision of the internal hemorrhoids and Prolapsing rectal mucosa proximal to the dentate line⁶⁷⁻⁶⁹. Reoccurrence following a properly performed hemorrhoidectomy is uncommon⁷⁰.

Surgical hemorrhoidectomy can be performed with either open or closed techniques. Open hemorrhoidectomy known as Milligan-Morgan hemorrhoidectomy in which the internal & external components of each hemorrhoid are excised and the skin is left open in a 3-leaf clover pattern that heals secondarily for 4-8 weeks⁶⁵. Techniques developed in 1937 at UK and widely performed there. Closed hemorrhoidectomy developed in US in 1952, and it is known as Ferguson hemorrhoidectomy, in which each hemorrhoid component is excised and the wounds are closed primarily⁶⁶.

The complication with varied frequency occurred in hemorrhoidectomy such as urinary retention 2%-36%^{31,71}, Bleeding 0.03% - 6%^{31,71-75}, anal stenosis 0%-6%^{67,68}, infection 0.5%-5.5%³¹, and in continence 2%-12%^{67,68}. Sphincter defect also noted up to 12% of patients⁷⁶.

Alternative approach to conventional hemorrhoidectomy is stapled hemorrhoidectomy (SH), was introduced in 1993 and first described by Longo in 1998, by modifying the circular stapling device commonly used for low rectal anastomoses⁷⁷. This techniques also known as other name like stapled anoplasty, stapled circumferential mucosectomy, longo's hemorrhoidectomy, stapled anopexy, stapled prolapsectomy, and stapled hemorrhoidopexy, PPH techniques⁷⁸.

Due to the several complications like severe pain and bleeding⁷⁹, operation cost because of postpartum hemorrhages (PPH) device⁸⁰,

length of stay⁸¹, rectal perforation ⁸², retroperitoneal sepsis⁸³, pelvic sepsis⁸⁴ Smooth muscle fiber detected in stapled that some from internal anal sphincter⁸⁵ procedure has not been adopted widely in United states and Canada, only some reports coming from the North America⁸⁶.

Several randomized trials were done to compare PPH with open hemorrhoidectomy, and found PPH is to be as effective's conventional surgery^{81, 86}. For grade three and grade four hemorrhoids PPH is the effective with the potential to involve less pain and a shorter recovery time than conventional hemorrhoidectomy⁸⁷.

Treatment of hemorrhoids with Botanicals

Medicinal plants are grouped for many commercial purposes in the broader category 'medicinal and aromatic plants' (MAPs), covering not only plants used medicinally, but also for neighboring and overlapping purposes, for instance as foods, condiments and cosmetics⁸⁸. The term 'botanicals' is becoming commonly used for a wide range of plant-based products. It is estimated that 70-80% of people worldwide rely chiefly on traditional, largely herbal medicine to meet their primary healthcare needs⁸⁹. The global demand for herbal medicine is not only large, but also growing⁹⁰. The world market for herbal remedies in 1999 was calculated to be worth US\$ 19.4 billion, with Europe in the lead (US\$ 6.7 billion), followed by Asia (US\$ 5.1 billion), North America (US\$ 4.0 billion), Japan (US\$ 2.2 billion), and then the rest of the world (US\$ 1.4 billion)⁹¹. Based on human studies ayurvedic medicinal plant uses were, classified as following according to the treatment categories (Fig.2), and for different gastrointestinal disease, 12 % of plants are used^{92, 92}.

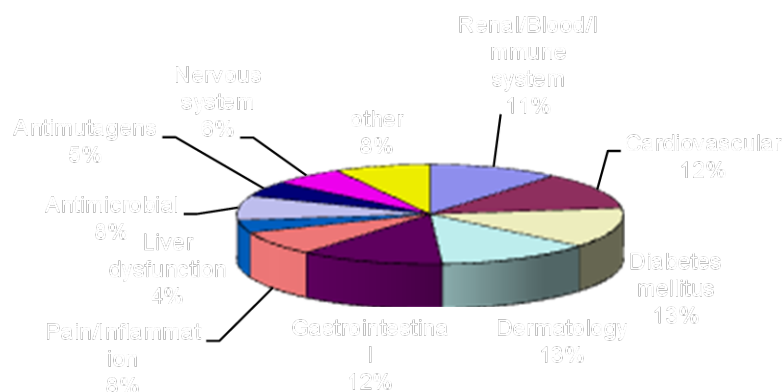


Fig. 2: Utilization of botanicals for treatment of diseases of different discipline

Prevention is the best treatment for hemorrhoids²⁵, but treatments with certain botanicals is also useful in the hemorrhoid discomfort. Botanicals used internally or topically, can treat early stages of hemorrhoids effectively and can be used as adjuncts in higher stages of hemorrhoids, where surgical treatment is necessary.

Botanical treatments and nutritional therapy are safe & effective therapy for hemorrhoids and also varicose veins⁹, although botanical treatments for hemorrhoids have been poorly researched. Several botanical extracts have been shown to improve microcirculation, capillary flow, vascular tone, and strengthen connective tissue of the perivascular amorphous substrate⁹. One recent finding showed effects of botanical taken orally for treatment of hemorrhoids, is due to the contribution of

free radical scavenging properties, to the pathogenesis of hemorrhoids and varicose veins ⁹³.

Plants have several properties which is make them effective for the treatment of hemorrhoids, like antioxidant, anti-inflammatory, anti-oedema and hepatoprotective. Several polyherbal products are available in the markets for the treatments of hemorrhoids; here we discuss some of the plants, which were scientifically studied for their antihemorrhoidal properties.

Ruscus aculeatus (Butcher's Broom)

Plant has long history of clinical use as a treatment of hemorrhoids and it is approved by German Commission E⁹⁴. Butcher's broom is typically administered in capsule form and frequently paired with trimethyl hesperidin chalcone a flavonoid complex and ascorbic acids,

alcoholic extracts, and in the form of tea. The active biochemical constituents is proposed to be the saponin glycoside ruscogenin⁹⁵.

Plants is well known for its pharmacological properties like anti-inflammatory and astringent, which is responsible for increasing venous tone, a positive step for hemorrhoid treatments^{96, 97}. Bennani et al carried out open-label multicenter study with 124 patients and 69 % of efficacy of plant as antihemorrhoidal was found⁹⁸. Patients treated with butcher's broom were show statistically significant improvement in a variety of symptoms like pain, local signs, and overall severity, after seven days⁹⁴. Plant well studied in chronic vascular insufficiency (CVI), and scientific research and clinical evidence in favor to support that this traditional folk medicines uses⁹⁹. Plant extract reported for its in vivo inhibition of elastase- a part of the enzyme system involved in degrading perivascular structural component⁹⁶. In one study plant extract given orally was reduced capillary filtration rate and decrease ten percent venous capacity, within two hours of administration¹⁰⁰.

Hemorrhoids is common among pregnant women and surgery treatment is very difficult, in such condition butcher's broom showed an improvement in maternal symptoms without any negative effects on the fetus, and with high degree of safety¹⁰¹.

***Aesculus hippocastanum* (Horse Chestnut)**

Plant is the most widely prescribed oral remedy for venous edema in Germany, some twenty clinical trials studies for the CVI and found positive effects, and so German Commission E has approved the use of plant extract for CVI treatment¹⁰², other reports support the use of plants for the treatment of CVI¹⁰³. The active component of the horse chestnut seed extracts (HCSE), is thought to complex mixture of saponin, collective referred as aescins^{96, 102, 103}, it also contain flavonoids and tannins^{104- 106}. Recent studies showed pharmacodynamic actions like anti-oedematous, anti-inflammatory, venotonic and free-radical scavenging properties of horse chestnut is attributed to the aescins^{8, 96}. In vitro studies showed HCSE inhibit activity of elastase & hyaluronidase enzymes, responsible for degradation of proteoglycan degradation of the capillary endothelium and extra vascular matrix⁹⁶.

A randomized partially blinded placebo-controlled study showed HCSE reduce abnormally increased capillary permeability and associated edema¹⁰⁶. An HCSE study using rats showed 200mg/kg body weight of aescin effectively reduced increased vascular permeability, induced by both acetic acid and histamine, and inhibited hind paw edema induced by carrageenin¹⁰⁷. In-depth systematic review of double blind, placebo-controlled trials of oral HCSE on 1,083 patients with CVI were done and conclude HCSE is safe and effective in the symptomatic short-term treatment of CVI. In one double blinded placebo-controlled study, with acute

symptomatic hemorrhoids patients, showed that 40 mg aescin administered three times per day for up to two months reduced symptoms, reduction in bleeding, and swelling^{108, 109}.

***Collinsonia canadensis* (Stone root)**

The eclectic physicians found stone root is useful in-patient with sings of congestion¹¹⁰. Kathyl A & Eric Y found stone root will often rapidly resolve hemorrhoids symptoms and they favor its use in these types of individuals. Phytochemical research on stone root showing that it contains flavonoids and saponin¹¹¹, and isolated flavonoids have been shown to be of benefit for hemorrhoids patients⁹.

***Centella asiatica* (Gotu kolu)**

Centella asiatica topical medicinal plant with active constituent asiaticoside, first isolated and purified in 1940, and first systematic clinical studies were carried out in 1945¹¹², other active metabolites used in pharmaceutical preparations are titrated for the pentacyclic tri terpenes derivatives like asiatic acid, madecassic acid, and asiaticoside^{113, 114}. Rigorous clinical investigation of *Centella asiatica* has been conducted on CIV and varicose veins¹¹⁵. Centella has the potential to enhance connective tissue integrity, elevated antioxidant level in wound healing, and improve capillary permeability^{116, 117}. A randomized multicenter, placebo-controlled double-blind study with Centella extract in the treatment of venous insufficiency, resulted in significant improvement in symptoms of heaviness in the lower limbs, venous distensibility¹¹⁸.

The Centella extract was shown to reduce serum level of lysosomal enzyme involved in the degradation of mucopolysaccharides – one of the main component of the amorphous cell matrix that maintain vascular integrity, which is a positive effect of Centella extract on pathogenesis of varicose veins¹¹⁹. In one double-blind, placebo – controlled study the effect of TTFCA (total triterpenoid fraction of *Centella asiatica*) extract was administered orally and after for week significant results were found, reduced capillary filtration rate, and improvement in microcirculation and other clinical symptoms¹¹⁷, and locally applied TTFCA extract three times daily can help to patients with varicose venous disorder including hemorrhoids and varicose vein¹²⁰.

***Hamamelis virginiana* (Witch Hazel)**

Plant is native to North America, and plant has a long history for treatment of hemorrhoids. Witch hazel extract contain volatile oil, flavonoids and tannins¹⁰⁴. Witch hazel has a long therapeutic tradition used primarily for its astringent, anti-inflammatory and local haemostatic effects¹²¹. Bark of plants topically used in hemorrhoids and varicose vein, minor injuries of the skin, and local inflammation of the skin¹²².

Table 1: Plants reported for antihemorrhoidal properties.

SNo	Plant name	Chemical constitute	Family	Part use	Reference
1	<i>Centella asiatica</i>	Triterpen, saponin	Apiaceae	Whole plant	113- 121
2	<i>Aesculus Hippocastanum</i> L.	triterpen saponin,	Hippocastanaceae	Seeds	102
3	<i>Ruscus Aculeatus</i>	Saponin glycoside ruscogenin.	Liliaceae	Rhizomes	96 - 99
4	<i>Hamamelis Virginiana</i>	Tannins and volatile oils	Hamamelidaceae	Bark	123
5	<i>Gingko biloba</i>	Bioflavonoid, Hesperidin	Ginkgoaceae.	Leaves	124
6	<i>Rosa canina</i>	Vitamin C	Rosaceae	Fruits	125
7	<i>Silybum marianum</i>	Flavonolignans silydisnin, silychristine, and Silymarin	Asteraceae	Fruits , Seeds	126
8	<i>Commiphora mukul</i>	Diterpenoids	Burseraceae	Gum-resin	127
9	<i>Azadirachta indica</i>	Sulphur containing bitter principle	Meliaceae	Seeds	128
10	<i>Embllica officinalis</i>	Vitamin C Tannin	Euphorbiaceae	Fruits	128
11	<i>Terminalia chebula</i>	Tannin	Combretaceae	Fruits	129
12	<i>Cassia fistula</i>	Tannin	Caesalpinaceae	pod	130
13	<i>Calendula officinalis</i> L.	Salicyclic acid	Asteraceae	Essential oil	131
14	<i>Mimosa pudica</i> L.	--	Fabaceae	Whole plant	132
15	<i>Vitex negundo</i>	Tannin	Verbenaceae	Whole plant	133

16	<i>Eclipta alba</i>	Alkaloids	Asteraceae	Whole plant	134
17	<i>Plantago ovate</i>	Mucilage	Plantaginaceae	Seeds	16
18	<i>Collinsonia canadensis</i> L.	Flavonoids Saponins.	Lamiaceae	--	112
19	<i>Matricaria recutita</i> L.		Astereaceae	Dried flower	135
20	<i>Lupinus albus</i>	Vitamin C, vitamin E	Fabaceae	--	136, 137
21	<i>Vateria indica</i>	Bitter resin	Dipterocarpaceae	--	136, 137
22	<i>Mentha piperita</i>	Pungent oil	Labiatae	Leaves	136, 137
23	<i>Aloe vera</i>	Anthraquinone glycoside	Liliaceae	Dried juice of leaves	136, 137
24	<i>Cupressus sempervirens</i>	--	Cupressaceae	Needles and twigs of young branches	138
25	<i>Pelargonium graveolens</i>	--	Geraniaceae	Leaves and stem	138
26	<i>Juniperus communis</i> L.	--	Cupressaceae	Essential oil	139, 140

In European countries and America herbalists typically use witch hazel both as internal and topical remedy for hemorrhoids, and thus both the European Scientific Cooperative on phytotherapy and France have approved the herb's combined used for treatments of hemorrhoids¹⁰⁴.

In vitro study of witch hazel extract show plant extract inhibit α -glucosidase and human leukocyte elastase enzyme which contribute to the degradation of connective tissue, extract also exhibited a strong antiphlogistic effect in the croton oil ear edema test in the mouse¹²².

Apart from these plants several other plants are used in various forms for the treatment of hemorrhoids, and they are components of polyherbal formulations. In table -1 plants are described with their scientific name, useful part, family, and reference, which are reported antihemorrhoidal properties alone or in combination with other herbs.

Topical treatments

In tropical treatment of hemorrhoids to assist locally in claming inflammation and for stopping bleeding and swelling are highly useful. The late Rudolf Fritz Weiss a German physiotherapist, favored the best treatment of acute hemorrhoids with wet compress, he also recommended arnica compresses using 1-2 teaspoons of arnica tincture per half-liter of water for compress. Alternatively he suggested the use of an oak decoction or a chamomile infusion for acute hemorrhoids¹³⁷.

Hamamelis Virginiana alone will often suffice to soothe minor symptoms of acute inflammation; effect of these plants is attributed to presence of tannin in the plant¹³⁷. Several cream based ointments, essential oils are available in markets over the counter drugs for the topical treatment of hemorrhoids, like Neo Healer's Piles Treatment Cream[®] 138, Hemorrhoids No More[®] 137, and Pilex ointment[®] 141.

Flavonoids and Tocotrienols for hemorrhoids treatment

A number of flavonoids have been reported to have anti-inflammatory effects and to strengthen blood vessels, so many preparations made for treatment of hemorrhoids, from purified or crude extracts of flavonoids. Several scientific studies favored treatment of hemorrhoids with flavonoids¹⁴². But scientific study showed that all flavonoids couldn't provide the effective treatment for acute hemorrhoids¹⁴³. Recent study regarding the flavonoids and symptomatic hemorrhoids was carried out by Alonso et al and they reported, reduction in the risk of bleeding, persistent pain, itching, and reoccurrence, but yet more in-depth study with effective methodological quality needed for the apparent beneficial effects of flavonoids for the treatments of hemorrhoids¹⁴⁴.

Flavonoids particularly diosmin, oligomeric proanthocyaniding complexes (OPCs) and hesperidin, have demonstrated efficacy in the treatment of hemorrhoids and varicose veins. These flavonoids exhibit phlebotonic activity, vasculoprotective effects and antagonism of the biochemical mediators of inflammation¹⁴⁵.

Animal studies have shown flavonoids reduce neutrophil activation, mediate inflammation, and decrease soluble endothelial adhesion molecules¹⁴⁶. Human trials have shown the ability of flavonoids to

improve venous tone and vein elasticity assessed by plethysmography, and significant improvement in CVI, venous leg ulcers, and hemorrhoids¹⁴⁷. Hemorrhoids treatment during the pregnancy is bit difficult by injection, RBL, and surgery and these techniques are contradicted, and flavonoid treatment is the best option, clinical trials shows treatment did not affect pregnancy, fetal development, birth weight, infant growth and feeding¹⁴⁸.

Prof. Jacques Nasquelir, France have first received patent for the method of isolation of OPSc from pine bark, in 1951, and from grape seeds in 1970¹⁴⁹. In vitro studies shows OPSc to inhibit the enzymes hyaluronidase, elastase, and collagenase, also reported for their antioxidant and free radical scavenging properties¹⁵⁰, and OPSc have demonstrated preferential binding to areas characterized by a high content of glycosaminoglycans such as the capillary walls, these properties make them effective in decreasing vascular function, and peripheral circulation, which is beneficial for the treatment of hemorrhoids¹⁵¹.

Tocotrienols are collectively known as vitamin E, and are identical in structure to tocopherols except for the degree of saturation in their side chain, having properties of antioxidant¹⁵². Tocotrienols are found in high concentration in palm oil and rice bran oil, and are well investigated for their nutritional, antioxidant activity, cholesterol lowering, anti-cancer effects and protection against atherosclerosis¹⁵³. In double-blind placebo-controlled clinical trials tocotrienols found to be improvement in overall symptoms of hemorrhoids⁸.

Hydrotherapy and Dietary approaches to Hemorrhoids

Dietary habit is the key link for the number of diseases, and diet therapy for hemorrhoids is a widely accepted modality. High fiber diet with commercial fiber supplements and enough oral fluids to produce soft, well-formed and regular bowel movements, high fiber diet is an important component to the prevention and treatment of both hemorrhoids and varicose veins.

One old myth regarding the diet and hemorrhoids is that "spicy food, including red hot chili powder, produces hemorrhoid symptoms". Recently one randomized controlled double-blinded trial reported no evidence to support this myth¹⁵⁴.

The warm sitz bath is the hydrotherapy recommended for the conditions associated with increased pelvic congestion, it is non-invasive therapy for uncomplicated hemorrhoids and varicose veins, but requires a high degree of patient's compliance^{6, 155}.

Medical/Drug Treatment

Effective medical/drug therapy is useful to control the acute phase (bleeding) so that definitive therapy like banding, injection sclerotherapy, IRC, cryotherapy, and surgery can be scheduled at a convenient time. Several modern and traditional drugs (oral/local) are being increasingly used in all grades of symptomatic hemorrhoids. Drugs like psyllium husk, corticosteroid creams³⁷ Nitroglycerin ointment¹⁵⁶, calcium dobesilate, nifedipine¹⁵⁷. Other polyherbal drugs also well studied for the treatment of the hemorrhoids such as Daflon 500[®] from Les, Laboratories, France¹⁵⁸, Preparation H[®] Hemorrhoidal Cooling Gel from Wyeth, Madison, New Jersey¹⁵⁶, Soft gel Capsules[®] from Gelfipharma International,

Lodi, Italy⁸, and Pilex[®] tablet and ointment from the Himalaya Drug Company Bangalore, India¹⁵⁹.

CONCLUSION

A haemorrhoid is a common discomfort, that is getting worse by prolonging immediate treatment, in the adult, which directly affect the economy. Apart from the prominent symptoms of bleeding and pain; colonoscopy and proctoscopy give the correct state of condition. Non-operative treatment methods are used for the patients with the first second and third degree hemorrhoids; very few patients with fourth degree haemorrhoids need surgery call treatment. As in case of every disease prevention is the best common treatment, haemorrhoids can also be reduced by changes in life style, diet habit, and intake of appropriate dose of respective botanicals, which can also intervene in the pathogenesis to decrease vascular integrity.

REFERENCE

- Bailey HR: Innovations for age-old problem: hemorrhoids in the female patient. *Female Patient*. 2004; 29:17-23.
- Heaton ND, Davenport M, Howard ER: Symptomatic hemorrhoids and anorectal varices in children with portal hypertension. *J Pediatr Surg*. 1992; 27(7): 833-835.
- Navarra L, Pietroletti R, Maggi G, Leardi S, Simi M: Diagnosis and treatment of haemorrhoids in the elderly: results from 291 patients. *Techniques in Coloproctology*. 2000; 3(3): 127-130.
- Liebach JR, Cerda JJ: Hemorrhoids: modern treatment methods. *Hosp Med*. 1991; 53: 68.
- Madoff RD, Fleshman JW: American Gastroenterological Association technical review on the diagnosis and treatment of hemorrhoids. *Gastroenterol*. 2004; 126:1463-1473.
- Berkow R (ed). *The Merck Manual of Diagnosis and Therapy*. 16th ed. Rahway, NJ: Merck; 1992: 855-856.
- Thomson WH: The nature of haemorrhoids. *Br J Surg*. 1975; 62:542-552.
- Silvia V, Elena B, Micaela T, Sinona A, Gianfranco A, Stefano Manfredini: Antioxidant herbal supplements for hemorrhoids developing a new formula. *Nutafoods*. 2004; 3(3): 19-26.
- Douglas Mackay Hemorrhoids and Varicose Veins: a review of treatment options. *Alternative Medicine Review*. 2001; 6(2): 126-140.
- Leff E: Hemorrhoids. *Postgrad Med*. 1987; 82:95-101.
- Gheewala M N, Miss Punekar SV, Mahendrakar M N: Therapy of piles with Pilex tablets and ointment. *The Antiseptic*. 1971; 68: 342-347.
- Rangnekar G V, Arora O P: Treatment of piles with indigenous drug pilex tablets and ointment along with styplon. *Indian Medical Journal*. 1974; 68: 240-243.
- Dennison AR, Whiston RJ, Rooney S, Morris DL: The management of hemorrhoids. *Am J Gastroenterol*. 1989; 84:475-481.
- Chaurasia's Human Anatomy 3rd edition, Vol. 2, CBS -New Delhi, 338.
- Charles VM, Russell RCG: Revised ed. *Bailey & Love's short practice of surgery* 21th edition, Chapman & Hall, London 1991.
- Loder PB, Kamm MA, Nicholls RJ, Phillips RK: Haemorrhoids: pathology, pathophysiology and aetiology. *Br J Surg*. 1994; 81: 946-954.
- www.Hemorrhoids.net, information retrieved on 20th July 2009.
- www.fascg.org, information retrieved on 19th Aug 2009.
- www.digestive.niddk.nih.gov/index.htm, information retrieved on 2nd Sept 2009.
- 20.Yarnell E: *Naturopathic Gastroenterology*, Wenatchee WA, HealingMountain Publishing 2000.
- Pfenninger JL, Surrell J: Nonsurgical treatment options for internal hemorrhoids. *Am Fam Phys* 1995; 52:821-834.
- Parks AG: Surgical treatment of haemorrhoids. *Br J Surg*. 1956; 43:337-338.
- Ramzi S. Cotran, Tucker Collins, Vinay Kumar: *Robbin's pathologic basis of diseases*. 6th edition, 1999, W.B.Saunders company
- Orlay G: Haemorrhoid- a review *Aust Fam Physician*. 2003; 32: 523-526.
- Brisinda G How to treat haemorrhoids, Prevention is best; haemorrhoidectomy needs skilled operators, *BMJ*. 2000, 321: 582-583.
- Walker AJ, Leicester RJ, Nicholls RJ, Mann CV: A prospective study of infrared coagulation, injection and rubber band ligation in the treatment of haemorrhoids. *Int J Colorectal Dis* 1990; 5: 113-116.
- Khoury GA, Lake SP, Lewis MC, Lewis AA: A randomized trial to compare single with multiple phenol injection treatment for haemorrhoids. *Br J Surg*. 1985; 72:741-742.
- Sim AJ, Murie JA, Mackenzie I: Three year follow-up study on the treatment of first and second-degree hemorrhoids by sclerosant injection or rubber band ligation. *Surg Gynecol Obstet*. 1983; 157:534-536.
- Sim AJ, Murie JA, Mackenzie I. Comparison of rubber band ligation and sclerosant injection for first and second degree haemorrhoids—a prospective clinical trial. *Acta Chir Scand*. 1981; 147: 717-720.
- Bullock N: Impotence after sclerotherapy of haemorrhoids: case reports. *Br Med J*. 1997; 314:419.
- Bleday R, Pena JP, Rothenberger DA, Goldberg SM, Buls JG: Symptomatic hemorrhoids: current incidence and complications of operative therapy. *Dis Colon Rectum*. 1992; 35:477-481.
- Wiener Medizinische Wochenschrift Conservative treatment of haemorrhoids 2004, 154(3-4):50-55.
- O'Callaghan JD, Matheson TS, Hall R: Inpatient treatment of prolapsing piles: cryosurgery versus Milligan-Morgan haemorrhoidectomy. *Br J Surg*. 1982; 69:157-159.
- Goligher JC: Cryosurgery for hemorrhoids. *Dis Colon Rectum*. 1976; 19:213-218.
- Smith LE, Goodreau JJ, Fouty WJ: Operative hemorrhoidectomy versus cryodestruction. *Dis Colon Rectum*. 1979; 22:10-16.
- Yang R, Migikovskiy B, Peicher J: Laine Randomized, prospective trial of direct current versus bipolar electrocoagulation for bleeding internal hemorrhoids. *Gastrointest Endosc*. 1993; 39:766-769.
- Robert DM, James WF: American Gastroenterological Association Technical Review on the Diagnosis and Treatment of Hemorrhoids. *Gastroenterology*. 2004; 126: 1463-1473.
- Rasmussen OO, Larsen KG, Naver L, Christiansen J: Emergency haemorrhoidectomy compared with incision and banding for the treatment of acute strangulated haemorrhoids. A prospective randomised study. *Eur J Surg*. 1991; 157: 613-614.
- Budding J: Solo operated haemorrhoid ligator rectoscope. A report on 200 consecutive bandings. *Int J Colorectal Dis*. 1997; 12: 42-44.
- Trowers EA, Ganga U, Rizk R, Ojo E, Hodges D: Endoscopic hemorrhoidal ligation: preliminary clinical experience. *Gastrointest Endosc*. 1998; 48:49-52.
- Lee HH, Spencer RJ, Beart RW J: Multiple hemorrhoidal bandings in a single session. *Dis Colon Rectum*. 1994; 37:37-41.
- Lau WY, Chow HP, Poon GP, Wong SH: Rubber band ligation of three primary hemorrhoids in a single session. A safe and effective procedure. *Dis Colon Rectum*. 1982; 25:336-339.
- Khubchandani IT: A randomized comparison of single and multiple rubber band ligations. *Dis Colon Rectum*. 1983; 26:705-708.
- Wroblewski DE, Corman ML, Veidenheimer MC, Coller JA: Longterm evaluation of rubber ring ligation in hemorrhoidal disease. *Dis Colon Rectum*. 1980; 23:478-482.
- Steinberg DM, Liegois H, Alexander-Williams J: Long term review of the results of rubber band ligation of haemorrhoids. *Br J Surg*. 1975; 62:144-146.
- Kanellos I, Goulimaris I, Vakalis I, Dadoukis I: Long-term results of rubber-band ligation for second degree haemorrhoids, a prospective study. *Techniques in Coloproctology*. 2000; 4(2): 99-101.

47. Buchmann P, Seefeld U: Rubber band ligation for piles can be disastrous in HIV-positive patients. *Int. J of Colo Dise.* 1989; 4(1): 57-58.
48. Ambrose NS, Hares MM, Alexander-Williams J, Keighley MR: Prospective randomised comparison of photocoagulation and rubber band ligation in treatment of haemorrhoids. *Br Med J (Clin Res Ed)*, 1983; 286:1389-1391.
49. Templeton JL, Spence RA, Kennedy TL, Parks TG, Mackenzie G, Hanna WA: Comparison of infrared coagulation and rubber band ligation for first and second degree haemorrhoids: a randomized prospective clinical trial. *Br Med J (Clin Res Ed)*, 1983; 286: 1387-1389.
50. O'Hara VS: Fatal clostridial infection following hemorrhoidal banding. *Dis Colon Rectum.* 1980; 23:570-571.
51. Russell TR, Donohue JH: Hemorrhoidal banding. A warning. *Dis Colon Rectum.* 1985; 28:291-293.
52. Jensen DM, Jutabha R, Machicado GA, Jensen ME, Cheng S, Gornbein J, Hirabayashi K, Ohning G, Randall G: Prospective randomized comparative study of bipolar electrocoagulation versus heater probe for treatment of chronically bleeding internal hemorrhoids. *Gastrointest Endosc.* 1997; 46: 435-443.
53. Randall GM, Jensen DM, Machicado GA, Hirabayashi K, Jensen ME, You S, Pelayo E: Prospective randomized comparative study of bipolar versus direct current electrocoagulation for treatment of bleeding internal hemorrhoids. *Gastrointest Endosc.* 1994; 40: 403-410.
54. Dennison A, Whiston RJ, Rooney S, Chadderton RD, Wherry DC, Morris DL: A randomized comparison of infrared photocoagulation with bipolar diathermy for the outpatient treatment of hemorrhoids. *Dis Colon Rectum.* 1990; 33:32-34.
55. Hinton CP, Morris DL: A randomized trial comparing direct current therapy and bipolar diathermy in the outpatient treatment of third-degree hemorrhoids. *Dis Colon Rectum.* 1990; 33: 931-932.
56. Keesey WE: Obliteration of hemorrhoids with negative galvanism. *Arch Phys Ther X-ray Radium.* 1934; 1:533-546.
57. Norman DA, Newton R, Nicholas GV: Direct current electrotherapy of internal hemorrhoids: an effective, safe, and painless outpatient approach. *Am J Gastroenterol.* 1989; 84:482-487.
58. Zinberg SS, Stern DH, Furman DS, Wittles JM: A personal experience in comparing three nonoperative techniques for treating internal hemorrhoids. *Am J Gastroenterol.* 1989; 84:488-492.
59. Varma JS, Chung SC, Li AK: Prospective randomised comparison of current coagulation and injection sclerotherapy for the outpatient treatment of haemorrhoids. *Int J Colorectal Dis.* 1991; 6:42-45.
60. Nath G, Kreitmaier A, Kiefhaber P: Neue Infrarot koagulation smethode. *Verhandl ungsband des 3 Kongresses der Deutscher Gesellschaft fur Gastroenterologie.* Munchen 1976, S. 17. Erlangen: Permed Verlag.
61. Pravin J Gupta: Infrared coagulation: A preferred option in treating early hemorrhoids. *Acta Cirurgica Brasileria.* 2004; 19(1):74-78.
62. O'Holleran TP: Infra red photocoagulation of hemorrhoids. *Nebr Med J.* 1990; 75(11): 307-8.
63. Leicester RJ, Nicholls RJ, Mann CV: Infrared coagulation: a new treatment for hemorrhoids. *Dis Colon Rectum.* 1981; 24(8):602-5.
64. MacRae HM, Temple LK, McLeod RS: A meta-analysis of hemorrhoidal treatments. *Semin C R Surg.* 2002; 13:77-83.
65. Milligan ET, Morgan CN, Jones LE: Surgical anatomy of the anal canal and the operative treatment of haemorrhoids. *Lancet.* 1937; 2:1119-1124.
66. Ferguson JA, Mazier WP, Ganchrow MI, Friend WG: The closed technique of hemorrhoidectomy. *Surgery.* 1971; 70:480-484.
67. Devien CV, Pujol JP: Total circular hemorrhoidectomy. *Int Surg.* 1989; 74:154-157.
68. Boccasanta P, Venturi M, Orio A, Salamina G, Reitano M, Cioffi U, Floridi A, Strinna M, Peracchia A: Circular hemorrhoidectomy in advanced hemorrhoidal disease. *Hepatogastroenterology.* 1998; 45:969-972.
69. Wolff BG, Culp CE: The Whitehead hemorrhoidectomy. An unjustly maligned procedure. *Dis Colon Rectum.* 1988; 31:587-590.
70. Granet E: Hemorrhoidectomy failures: causes, prevention and management. *Dis Colon Rectum.* 1968; 11:45-48.
71. Reis Neto JA, Quilici FA, Cordeiro F, Reis JA J: Open versus semi-open hemorrhoidectomy: a random trial. *Int Surg.* 1992; 77:84-90.
72. Devien CV, Pujol JP: Total circular hemorrhoidectomy. *Int Surg.* 1989; 74:154-157.
73. Hiltunen KM, Matikainen M: Anal dilatation, lateral subcutaneous sphincterotomy and haemorrhoidectomy for the treatment of second and third degree haemorrhoids. A prospective randomized study. *Int Surg.* 1992; 77:261-263.
74. Ho YH, Tan M: Ambulatory anorectal manometric findings in patients before and after haemorrhoidectomy. *Int J Colorectal Dis.* 1997; 12:296-297.
75. Ho YH, Seow-Choen F, Goh HS: Haemorrhoidectomy and disordered rectal and anal physiology in patients with prolapsed haemorrhoids. *Br J Surg.* 1995; 82:596-598.
76. Felt-Bersma RJ, van Baren R, Koorevaar M, Strijers RL, Cuesta MA: Unsuspected sphincter defects shown by anal endosonography after anorectal surgery. A prospective study. *Dis Colon Rectum.* 1995; 38:249-253.
77. Abbasakoor F, Nelson M, Beynon J, Patel B, Carr ND: Anal endosonography in patients with anorectal symptoms after haemorrhoidectomy. *Br J Surg.* 1998; 85:1522-1524.
78. Longo A: Treatment of hemorrhoidal disease by reduction of mucosa and hemorrhoidal prolapse with a circular stapling device: a new procedure. *Proceedings of the 6th World Congress of Endoscopic Surgery.* June 3, 1998. Mundozzi Editore, 1998.
79. Pernice LM: The author replies. *Dis Col Rect.* 2002; 45:572.
80. Ravo B, Amato A, Bianco V: Complications after stapled hemorrhoidectomy: can they be prevented? *Tech Coloproctol.* 2002; 6:83-88.
81. Khalil KH, O'Bichere A, Sellu D: Randomized clinical trial of sutured versus stapled closed haemorrhoidectomy. *Br J Surg.* 2000; 87:1352-1355.
82. Ganio E, Altomare DF, Gabrielli F: Prospective randomized multicentre trial comparing stapled with open haemorrhoidectomy. *Br J Surg.* 2001; 88:669-74.
83. Ripetti V, Caricato M, Arullani A: Rectal perforation, retroperitoneum, and pneumomediastinum after stapling procedure for prolapsed hemorrhoids: report of a case and subsequent considerations. *Dis Colon Rectum.* 2002; 45:268-270.
84. Maw A, Eu KW, Seow-Choen F: Retroperitoneal sepsis complicating stapled hemorrhoidectomy: report of a case and review of the literature. *Dis Colon Rectum.* 2002; 45:826-828.
85. George BD, Shetty D, Lindsey I, Mortensen NJ, Warren BF: Histopathology of stapled haemorrhoidectomy specimens: a cautionary note. *Colorectal Dis.* 2002; 4:473-476.
86. Singer MA, Cintron JR, Fleshman JW: Early experience with stapled hemorrhoidectomy in the United States. *Dis Col Rect.* 2002; 45:367-9.
87. Racialbitto A., Aliotta I, Corsaro G: Hemorrhoidal stapler prolapsectomy vs. Milligan hemorrhoidectomy: a long-term randomized trial. *Int J Colorectal Dis.* 2004; 19:239-244.
88. Glenn SP: A new treatment option for grads III and IV hemorrhoids. *J Family Prac.* 2004; 799-804.
89. Schippmann, U., Leaman, D. J. & Cunningham, A. B. (2002). *Impact of cultivation and gathering of medicinal plants on biodiversity: global trends and issues.* Inter- Department Working Group on Biology Diversity for Food and Agriculture, Food and Agricultural Organisation of the United Nations, Rome, Italy.

90. Pei Shengji: Ethnobotanical approaches of traditional medicine studies: some experiences from Asia. *Pharmaceutical Botany*. 2001; 39: 74-79.
91. Srivastava, R: Studying the information needs of medicinal plant stakeholders in Europe. *TRAFFIC Dispatches*. 2000; 15: 5.
92. Laird, SA, Pierce, AR: Promoting sustainable and ethical botanicals: strategies to improve commercial raw material sourcing. 2002. Rainforest Alliance, New York, USA.
93. Sarah Khan and Michael J. Black: Therapeutic Plants of Ayurveda: A Review of Selected Clinical and Other Studies for 166 Species. *The J Alternative and Complementary Medicine*. 2001; 7(5): 405-515.
94. Wail MA, Suleiman SA, Kadoumi OF, Nasr MA, Superoxide radical concentration and superoxide dismutase (SOD) enzyme activity in varicose vein. *Ann Thorac Cardiovasc Surg*. 2002; 8: 286-290.
95. Abascal K, Yarnell E: Butcher's broom: Herb's potential too often swept under the rug. *Alt Comp Ther*. 2002; 8:177-186.
96. DeCombarieu E, Fuzzati N, Gattesco F, Giori A., Lovati M., Pace R, Identification of *Ruscus* saponins by HPLC-MS analysis. *Fitoterapia*. 2002; 73: 583-596.
97. Bouskela E, Cyrino FZ, Marcelon G: Possible mechanisms for the inhibitory effect of *Ruscus* extract on increased microvascular permeability induced by histamine in hamster cheek pouch. *J Cardiovasc Pharmacol*. 1994; 24:281- 285.
98. Lozes A, Boccalon H: Double blind study of *Ruscus* extract: venous plethysmographic results in man. *Inter Angiol*. 1984; 3:95-98.
99. Bennani A, Biadillah MC, Cherkaoui A: Acute attack of hemorrhoids: Efficacy of Cyclo 3 Forte® based on results in 124 cases reported by specialists. *Phlebologie*. 1999; 52: 89-93.
100. Werbach M, Murray M: Botanical Influence on Illness. Tarzana, CA: Third Line Press; 1994:579.
101. Rudofsky G: Plethysmographic studies of the venous capacity and venous outflow and venotropic therapy. *Inter Angiol*. 1984; 3: 99-102.
102. Leutenegger S, Martinaggi P: Cyclo 3 Fort® and pregnancy. *Gazette Medicale*. 1988; 95:33-36.
103. Blumenthal M: The ABC Clinical Guide to Herbs. Austin, TX: American Botanical Council, 2003.
104. Pitter MH, Ernst E: Horse chestnut seed extract for chronic venous insufficiency 2004. *Cochrane Database Syst Rev*. 2:CD003230.
105. Blumenthal M: The ABC Clinical Guide to Herbs. Austin, TX: American Botanical Council, 2004. Bastyr University, Kenmore, Washington.
106. Blumenthal M, Goldberg A, Brinckmann J: Herbal Medicine: The Expanded Commission E Monographs. Newton MA: Integrative Medicine Communications, 2000.
107. Guillaume M, Padioleau F: Veinotonic effect, vascular protection, antiinflammatory and free radical scavenging properties of horse chestnut extract. *Arzneimittelforschung*. 1994; 44:25-35.
108. Matsuda H, Li Y, Murakami T: Effects of escins Ia, Ib, IIa, and IIb from horse chestnut, the seeds of *Aesculus hippocastanum* L., on acute inflammation in animals. *Biol Pharm Bull*. 1997; 20:1092-1095.
109. Pittler MH, Ernst E: Horse-chestnut seed extract for chronic venous insufficiency. A criteria-based systematic review. *Arch Dermatol*. 1998; 134:1356-1360.
110. Sirtori CR. Aescin: Pharmacology, pharmacokinetics and therapeutic profile. *Pharmacol Res*. 2001; 44:183-193.
111. Felter HW: The Eclectic Materia Medica. Sandy, OR: Eclectic Medical Publications, 1994.
112. Joshi BS, Moore KM, Pelletier SW: Saponins from *Collinsonia canadensis*. *J Nat Prod*. 1992; 55:1468-1476.
113. Kartnig T: Clinical Applications of *Centella Asiatica*: Herbs, Spices and Medicinal Plants. Recent Advances in Botany, Horticulture and Pharmacology. Phoenix, AZ: Oryx Press; 1988.
114. Brinkhaus B, Lindner M, Schuppan D, Hahn EG: Chemical, pharmacological and clinical profile of the East Asian medical plant *Centella asiatica*. *Phytomedicine*. 2000; 7:427- 448.
115. Matsuda H, Morikawa T, Ueda H, Yoshikawa M: 2001. Medical foodstuffs. XXVII. Saponin constituents of gotukola(2):structures of new ursane-and oleanane-type triterpene oligoglycosidase, centellasaponin B, C, D, from *Centella asiatica* cultivated in Sri Lanka. *Chem Pharm Bull (Tokyo)* 49: 1368-1371.
116. Cesarone MR, Laurora G, De Sanctis MT: Microcirculatory activity of *Centella asiatica* in venous insufficiency: A double-blind study. *Minerva Cardioangiol*. 1994; 42:299-304.
117. Tenni R, Zanaboni G, De Agostini MP: Effect of the triterpenoid fraction of *Centella asiatica* on macromolecules of the connective matrix in human skin fibroblast cultures. *Ital J Biochem*. 1988; 37:69-77.
118. Belcaro GV, Grimaldi R, Guidi G: Improvement of capillary permeability in patients with venous hypertension after treatment with TTFCA. *Angiology*. 1990; 41:533-540.
119. Pointel JP, Boccalon H, Cloarec M: Titrated extract of *Centella asiatica* (TECA) in the treatment of venous insufficiency of the lower limbs. *Angiology*. 1987; 38:46-50.
120. Arpaia MR, Ferrone R, Amitrano M: Effects of *Centella asiatica* extract on mucopolysaccharide metabolism in subjects with varicose veins. *Int J Clin Pharmacol Res*. 1990; 4:229-233.
121. Allegra C, Pollari G, Criscuolo A: *Centella asiatica* extract in venous disorders of the lower limbs. Comparative clinico-instrumental studies with a placebo. *Clin Ter*. 1981; 99:507-513.
122. Bremness L. The Complete Book of Herbs. New York: Penguin Books; 1994:273.
123. Fleming T: PDR for Herbal Medicines. Montavel, NJ: Medical Economics Company; 1998:885-887.
124. Sumboonnanonda K, Lertsithichai P: Clinical study of the Ginkgo biloba- Troxerutin-Hepataminol hce in the treatment of acute hemorrhoidal attacks *J Med Ass Thai*. 2004; 87 137-142.
125. Daels-Rakotoarison DA, Gressier B, Trotin F, Brunet C, Luyckx M, Cazin JC: Effect of Rosa canina fruit extract on neutrophil respiratory burst *Phytother Res*. 2002; 16:157-161.
126. Boerth J, Strong KM: The clinical utility of Milk Thistle(*Silybum marianum*) in Cirrhosis of the Liver. *J Herb Pharmacother*. 2002; 2(2):11-17.
127. Nandkarni K M: Indian Materia Medica. Vol.1, 167, 1996.
128. Wealth of India: CSIR New Delhi India. Vo. 1(A) 504, 1985.
129. Nadkarni K M: Indian Materia Medica. Vol. 1 pp 480, 1996.
130. ICMR: Medicinal Plants of India. Vol 1 377, 1976.
131. Kirtikar and Basu: Indian Medicinal Plants. Vol. 3 pp 2220, 1985.
132. Indian Medicinal Plants. Orient Longman Ltd., Madras, India Vol. 5 p 263, 1994.
133. Pandey G S: Bhavaprakasa Nighantu 9th Ed. pp 28, 1993.
134. Nadkarni K M: Indian Materia Medica. Vol. 1 pp 234, 1992.
135. Joy J L, Kuttan R: Amla Res Bulletin. Vol 15 pp 68, 1995.
136. Moesgaard F, Nielsen ML, Hansen JB, Knudsen JT: High fiber diet reduces bleeding and pain in patients with hemorrhoids: a doubleblind trial of Vi-Siblin. *Dis Colon Rectum* 1982; 25:454-456
137. Weiss RF. Weiss's Herbal Medicine, classic ed. Stuttgart: Thieme, 2001.
138. <http://www.hemorrhoids-help.com/hemorrhoids-help-order.html>, information retrieved on 20th April 2009.
139. <http://www.essentialhealth.com.au>, information retrieved on 21st December 2009.
140. www.fonils.com/hemnomor.html, information retrieved on 18th Feb 2010.
141. Bisarya, RK, Sachdev, NK, Karim, SI: Treatment of Piles by Pilex Tablets and Ointment. *Indian Medical Gazette*. 1976; 4: 147.
142. Sinnatamby CS: The treatment of hemorrhoids. Role of hydroxyethylrutosides, troxerutin (Paroven; Varmoid; Venoruton). *Clin Trials J*. 1973; 2:45-50.
143. Thorp RH, Hughes ESR. A clinical trial of trihydroxyethylrutoside ("Varemoid") in the treatment of hemorrhoids. *Med J Aust*. 1970; 2:1076-8.
144. Alonso-Coello, Zhou Q, Martinez-Zapata MJ, Mills E., Heels-Ansdell D, Johanson JF, Guyatt G: Meta-analysis of flavonoids for the treatment of hemorrhoids. *Br J Surg*. 2006; 93(8); 909-920.

145. Cospite M: Double-blind, placebo-controlled evaluation of clinical activity and safety of Daflon 500 mg in the treatment of acute hemorrhoids. *Angiology*. 1994; 45:566-573.
146. Smith PD: Neutrophil activation and mediators of inflammation in chronic venous insufficiency. *J Vasc Res*. 1999; 36:24-36.
147. Struckmann JR: Clinical efficacy of micronized purified flavonoid fraction: an overview. *J Vasc Res*. 1999; 36:37-41.
148. Buckshee K, Takkar D, Aggarwal N: Micronized flavonoid therapy in internal hemorrhoids of pregnancy. *Int J Gynaecol Obstet*. 1997; 57:145-151.
149. Murray M, Pizzorno J: *The Textbook of Natural Medicine* 2nd ed. London: Churchill Livingstone; 1999: 899-902.
150. Tixier JM, Godeau G, Robert AM, Hornebeck W: Evidence by *in vivo* and *in vitro* studies that binding of pycnogenols to elastin affects its rate of degradation by elastases. *Biochem Pharmacol*. 1984; 33: 3933-3939.
151. Harmand MF, Blanquet P: The fate of total flavonolic oligomers (OGFT) extracted from "*Vitis vinefera* L." in the rat. *Eur J Drug Metab Pharmacokin*. 1978; 1:15-30.
152. Packer L: Interactions among antioxidants in health and diseases: vitamin E and its redox cycle. *Proc Soc Exp Bio Med*. 1992; 200:271-276.
153. Qureshi AA, Sami SA, Salser WA, Khan FA: Dose-dependent suppression of serum cholesterol by tocotrienol-rich fraction (TRF25) of rice bran in hypercholesterolemic humans. *Atherosclerosis*. 2002; 161:199-207.
154. Altomare DF., Rinaldi M., LaTorre F: Red chilli pepper and hemorrhoids: The explosion of a myth. Results of a prospective, randomized, placebo-control trial. *Dis. Colon Rectum*. 2006; 49:1018-1023.
155. Boyle W, Saine A: *Lectures in Naturopathic Hydrotherapy*. Sandy, OR: Eclectic Medical Publications. 1988: 89-90.
156. Gorfine SR: Treatment of benign anal disease with topical nitroglycerin. *Dis Colon Rectum*. 1995; 38:453-456.
157. Miscra MC: Imlitemsu Drug treatment of hemorrhoids. *Drugs*. 2005; 65(11):1481-1491.
158. Godeber P: Daflon 500 mg in the treatment of hemorrhoidal disease: a demonstrated efficacy in comparison with placebo. *Angiology*. 1994; 45:574-578.
159. Agrawal RC, Kapadia LA: Treatment of piles with indigenous drug pilex tablets and ointment along with styplon. *Prob*. 1982; 30(3): 201-204.