

Hemorrhoids and Varicose Veins: A Review of Treatment Options

Douglas MacKay, ND Candidate 2001

Abstract

Hemorrhoids and varicose veins are common conditions seen by general practitioners. Both conditions have several treatment modalities for the physician to choose from. Varicose veins are treated with mechanical compression stockings. There are several over-the-counter topical agents available for hemorrhoids. Conservative therapies for both conditions include diet, lifestyle changes, and hydrotherapy which require a high degree of patient compliance to be effective. When conservative hemorrhoid therapy is ineffective, many physicians may choose other non-surgical modalities: injection sclerotherapy, cryotherapy, manual dilation of the anus, infrared photocoagulation, bipolar diathermy, direct current electrocoagulation, or rubber band ligation. Injection sclerotherapy is the non-surgical treatment for primary varicose veins. Non-surgical modalities require physicians to be specially trained, own specialized equipment, and assume associated risks. If a non-surgical approach fails, the patient is often referred to a surgeon. The costly and uncomfortable nature of treatment options often leads a patient to postpone evaluation until aggressive intervention is necessary. Oral dietary supplementation is an attractive addition to the traditional treatment of hemorrhoids and varicose veins. The loss of vascular integrity is associated with the pathogenesis of both hemorrhoids and varicose veins. Several botanical extracts have been shown to improve microcirculation, capillary flow, and vascular tone, and to strengthen the connective tissue of the perivascular amorphous substrate. Oral supplementation with *Aesculus hippocastanum*, *Ruscus aculeatus*, *Centella asiatica*, *Hamamelis virginiana*, and bioflavonoids may prevent time-consuming, painful, and expensive complications of varicose veins and hemorrhoids.

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Introduction

Every general practitioner sees a large number of patients who suffer from problems associated with venous insufficiency. Two of the most common manifestations of venous insufficiency are varicose veins and hemorrhoids. The prevalence of these two conditions is astonishing. In population studies the prevalence of varicose veins has been reported to be 10-15 percent for men and 20-25 percent for women.¹ In a recent cross-sectional study, the age-adjusted prevalence of varicose veins was 58 percent for men and 48 percent for women.² Over three-quarters of individuals in the United States have hemorrhoids at some point in their lives, and about half of the population over age 50 requires treatment.³

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The Merck Manual defines hemorrhoids as “Varicosities of the veins of the hemorrhoidal plexus, often complicated by inflammation, thrombosis, and bleeding.”⁴ It has been suggested this is an oversimplification of the nature of hemorrhoids. A more recent definition is, “Vascular cushions, consisting of thick submucosa containing both venous and arterial blood vessels, smooth muscle, and elastic connective tissue.”⁵ While everyone has this tissue, it is the enlargement, bleeding and protrusion that create pathology. The crossroads to the development of varicose veins and hemorrhoids is the loss of vascular integrity. Considering the combined prevalence of varicose veins and hemorrhoids, venous insufficiency and its manifestations are an extremely common medical problem that every physician should be prepared to treat.

Hemorrhoids

Historical Perspective on Hemorrhoids

Hemorrhoids are mentioned in ancient medical writings of every culture, including Babylonian, Hindu, Greek, Egyptian, and Hebrew. The word “hemorrhoid” 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 anus.⁶ Prior to the 1800s hemorrhoids were treated simply by poultice, bed rest, or, in difficult cases, by the application of a red hot poker. A simpler method was prayer to the patron saint of hemorrhoid sufferers, St. Fiacre, an Irish priest who lived in the seventh century.⁷ Injection therapy was begun in 1869 by Morgan of Dublin using iron persulfate, and was a relief to many who had endured the medical treatment of the time.⁸ As late as 1888 the only other recommended treatment (apart from the above mentioned) was abstinence from alcohol, sitting in cane chairs, and half a pint of cold spring water injected into the rectum after a morning fast.⁹ The

founding of St. Mark’s Hospital in 1935 by Fredrick Salmon, who is given credit for the first ligation of hemorrhoids, marked a turning point in the treatment of hemorrhoids.¹⁰

Hemorrhoid Histology

As mentioned, there are variant definitions of the histology of the hemorrhoid tissue, but they are universally classified according to anatomical origin. Internal hemorrhoids consist of redundant mucus membrane of the anal canal with the origin above the dentate (ano-rectal) line. External hemorrhoids have an epithelial component and originate below the dentate line.⁷ Internal hemorrhoids are further graded based on the extent to which the tissue descends into the anal canal (Table 1).

Differential Diagnosis

When a patient presents 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 indicated, including a rectal examination, a proctoscopic exam, and in some cases a sigmoidoscopy. There are several conditions producing symptoms similar to hemorrhoids that must be considered. To rule out grave causes of ano-rectal bleeding, such as anal or rectal carcinoma, one gastroenterologist suggests, “All patients over forty years old, even with typical hemorrhoidal bleeding, must undergo flexible sigmoidoscopy (or colonoscopy).”⁷

Other types of ano-rectal pathology that must be ruled out include anal fissures, which can cause pain with defecation and be associated with rectal bleeding. The pain will be described as burning or tearing, as opposed to the achiness or feeling of fullness after defecation described by patients with hemorrhoids. Perirectal abscesses are less common in the general population but should be considered in patients with diabetes or other immunocompromising conditions.¹¹ Anal

Table 1: Grading of Hemorrhoids

First degree

"The mucosa barely prolapses, 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. Clinically speaking there is no obvious external abnormality."

Second degree

"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

"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

"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."

From Dennison AR, Whiston RJ, Rooney S, et al. The management of hemorrhoids. *Am J Gastroenterol* 1989;84:475-481.

fistulas can cause drainage, soiling of underwear, and discomfort. Mucosal diseases such as ulcerative proctitis, colitis, or Crohn's disease can present with rectal bleeding and should be ruled out. Perianal condylomas cause pruritis, local irritation, pain and bleeding. Skin tags can be remnants of past external hemorrhoids and commonly co-exist with fissures. A rectocele can cause fullness in the rectum, giving the patient a similar sensation to an internal hemorrhoid.

It is common for patients to associate pruritis ani with hemorrhoids. In some cases swelling of external hemorrhoids and skin tags can prevent proper anal hygiene, which can cause marked itching. Hemorrhoids themselves do not produce significant itching.³ When a patient presents with pruritis ani, many

assume it is the sequela of hemorrhoidal disease. However, a mindful physician will consider causes such as allergic reactions, perianal dermatitis, microorganisms, parasites, oral antibiotics, hygiene, systemic disease (e.g., diabetes mellitus, liver disease), heat, and hyperhidrosis.⁴

Etiological Factors

The exact cause of enlarged and symptomatic hemorrhoids is debated, and numerous etiologies have been suggested. Some of the earliest proposed etiologies included temperament, body habits, customs, passions, sedentary life, tight-laced clothes, climate, and seasons.¹² Recent studies implicate gravity, intrinsic weakness of the blood vessel wall, heredity, increased intra-abdominal pressure

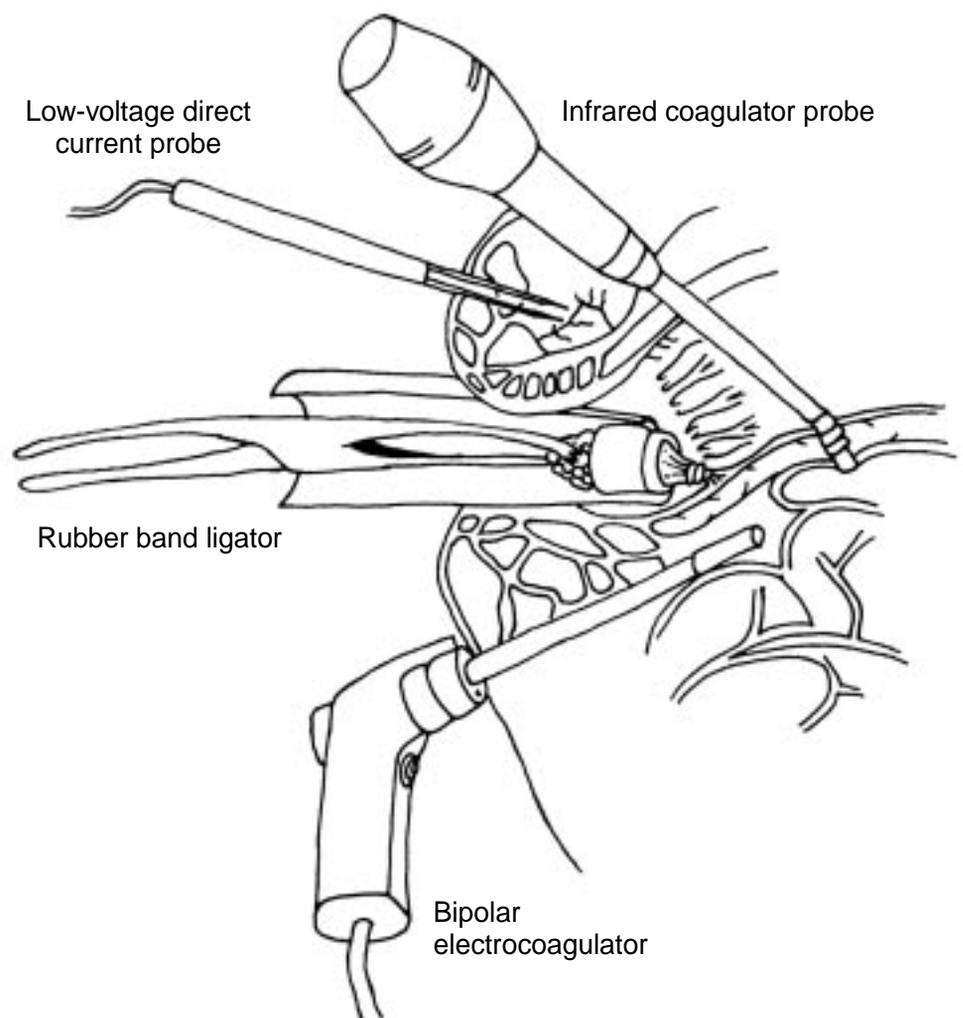
from many causes, including prolonged forceful valsalva during defecation or resistance training, obstruction of venous outflow secondary to pregnancy or pelvic masses, and constipated stool in the rectal ampulla.^{11,13} As a patient ages and has continual presence of one or more of the factors mentioned, the integrity of the hemorrhoid “cushions” deteriorates, and the hemorrhoids begin to bulge and descend into the anal canal. When the cushion bulges into the canal, it is exposed to potential trauma and irritation from the passage of stool.

Conventional Approaches

Despite thousands of years and millions of patients with pain, discomfort, and perceived embarrassment of hemorrhoids, the exact nature and cause of the condition is not clear, and the standard treatments are, at best, imperfect. Dietary manipulation, vascular tonifying agents, injection sclerotherapy, cryotherapy, manual dilation of the anus, infrared photocoagulation, bipolar diathermy, direct current electrocoagulation, rubber band ligation, and hemorrhoidectomy are all standard considerations for the treatment of hemorrhoids.

The treatments can be grouped into conservative (diet and vascular tonification); non-excisional (sclerotherapy, cryotherapy, manual dilation, photocoagulation, diathermy, and electrocoagulation); and surgical methods (ligation and hemorrhoidectomy). “Conservative methods with or without nonexcisional treatments are preferred to surgical methods.”¹²

Figure 1: Surgical and Non-surgical Approaches to Hemorrhoid Treatment



Key to Figure 1:

Rubber Band Ligation:

A device is used to place one or two small rubber bands securely around the base of the hemorrhoid. The rubber bands are left in place to close off the blood supply to the hemorrhoid. The hemorrhoid and the rubber bands fall off after seven to ten days, leaving a small sore that will heal over time.

Direct Current Electrocoagulation:

A small probe is inserted into the hemorrhoid, and very low levels of electrical current are applied for six to ten minutes. The electrical current closes off the blood supply to the hemorrhoid. One group of hemorrhoids is treated at a time, so patients must return for additional treatments.

Infrared Coagulation:

The device is used to deliver four to five 1.5-second applications of infrared light to close off the blood supply to the hemorrhoid. One area is treated per office visit. Additional visits may be necessary, usually one month apart. Patients may experience a little bleeding between the fourth and tenth days after the procedure.

Bipolar Electrocoagulation:

The probe is used to deliver electrical current for two seconds to the hemorrhoid. This will close off the blood supply to the hemorrhoid. This procedure is similar to infrared coagulation and direct current electrocoagulation.

Adapted from: Pfenninger JL, Surrell J. Nonsurgical treatment options for internal hemorrhoids. *Am Fam Physician* 1995;52:821-834.

Figure 1 illustrates surgical and non-surgical approaches to hemorrhoid treatment.

Some of the conventional approaches are not without potential complications. Injection sclerotherapy has resulted in cases of anaphylactic shock.¹⁴ Cryotherapy is cumbersome to perform and is associated with severe rectal pain and discharge.¹⁵ Manual dilation often requires general anesthetic and admission to the hospital. If dilation is not performed carefully the results may be disastrous.¹⁶ Septic complications, including death, have resulted from rubber band ligation.¹⁷ Hemorrhoidectomy, although indicated in extreme

cases unresponsive to conservative treatment, is extremely painful and requires a four to six week recovery.

Nonexcisional Techniques in Hemorrhoid Treatment

The potential disadvantages of sclerotherapy, banding, manual dilation, and surgery have led to the development of a new generation of nonexcisional techniques for the treatment of hemorrhoidal disease. Infrared photocoagulation, bipolar diathermy, and electrocoagulation are the most recent additions to

the plethora of modalities to consider. These modalities aim to affect sclerosis of the vascular root and to fix the mucosa to the underlying submucosa and muscle.¹⁸ There have been several studies showing the efficacy of these treatments as comparable to the semi-invasive therapeutic modalities. A study of 758 patients with symptomatic hemorrhoidal disease concluded that all three techniques, performed on an outpatient basis with little or no sedation, are effective modalities for first- and second-degree hemorrhoids. Moreover, direct current electrocoagulation was associated with less discomfort and fewer complications and can be effective in third- and fourth-degree hemorrhoids.¹⁹

Although direct current electrocoagulation was utilized in 1867, and explained by Wilbur E. Keeseey, MD in 1934, doctors today oddly consider it one of the new generation of modalities.²⁰ A study of 120 patients using direct current electrocoagulation treating a total of 590 hemorrhoid segments reported all patients were successfully treated and remained symptom free at a mean duration of follow-up of 23 months. The researchers concluded that direct current electrotherapy is an effective, painless, and safe outpatient treatment approach to all grades of internal and mixed hemorrhoid disease.²¹ Direct current electrotherapy has also been shown to be effective, safe, and cost effective in the treatment of chronic anal fissures associated with internal hemorrhoids.²² One author suggests patients postpone evaluation of suspected hemorrhoids due to fear of the treatment modality, hospitalization, cost, and time of disability, leading to progression of the hemorrhoid or late diagnosis of serious gastrointestinal disease.²¹ Patients must be made aware of less invasive, relatively inexpensive, outpatient treatment options.

Varicose Veins

Epidemiological Factors in Varicose Veins

Chronic venous disease of the lower limbs is one of the most common medical conditions seen in clinical practice.²³ There is some disagreement over the actual prevalence of chronic venous insufficiency due to the lack of a standardized definition. There have been several large epidemiological studies with varied criteria for venous disease. Definitions range from “any prominent superficial vein in the lower extremity” to “a vein which has permanently lost its valvular efficiency and, as a result of continuous dilation under pressure, in the course of time becomes elongated, tortuous, pouched and thickened.” Callam, reviewing an analysis of published data on the epidemiology of varicose veins, assessed all of the studies with regard to age range and distribution of study population; criteria used to diagnose varicose veins; geographical site of the study population; and methods used to assess venous disease. He reported half of the adult population manifesting minor venous disease, and less than half (women 20-25%; men 10-15%) having visible varicose veins.²⁴

Diagnostic Factors

Patients will often self-diagnose varicose veins and present to the physician with elongated, dilated, tortuous superficial veins (usually in the legs) whose valves have become incompetent. Patients may experience aching, fatigue, or heat that is relieved by elevation or wearing compressive hosiery. Symptoms are not always related to the degree or size of the varicose veins.²⁵ Patients who present with asymptomatic varicosities often seek treatment for cosmetic reasons. Primary varicose veins are not associated with deep venous disease, and treatment is indicated to relieve symptoms and improve appearance. Treatment is rarely required to prevent further complications. Varicosities that occur

secondary to obstruction and valvular incompetence of the deep venous system are much more serious because of the associated risk of pulmonary thromboembolism.¹

Physicians evaluating a patient for presumed varicose veins must rule out other possible causes for the presenting symptoms: lumbar nerve root irritation can cause an aching sensation in the leg; peripheral neuritis causes a burning sensation in the leg; and arterial insufficiency may present with intermittent claudication. A deep vein thromboembolism can present with calf pain, and patients on estrogen have an increased risk. Osteoarthritis of the hip and knee are also considerations in the differential diagnosis of varicose veins. The pain associated with varicose veins is uniquely relieved with leg elevation.

Pathogenesis and Etiological Factors

The pathogenesis of varicose veins is thought to include increased venous and capillary pressures, increased capillary permeability, chronic edema, repeated inflammation, and stasis.¹ Some of the risk factors associated with developing varicose veins are obesity, high systolic blood pressure, cigarette smoking, low levels of physical activity, pregnancy, abdominal or pelvic masses, ascites, and occupations that require prolonged standing.^{1,25,26}

Conventional Treatment of Varicose Veins

Standard treatment for varicose veins is mechanical compression, sclerotherapy, or surgery. Compression therapy is achieved with lightweight hosiery for small, mildly symptomatic varicose veins. Advanced cases require a heavier elastic support stocking. Mechanical compression is inconvenient, uncomfortable, and subject to poor compliance.²⁷ Additionally patients can apply the elastic bandage too tightly, producing a tourniquet effect. Even when applied correctly, bandages can rapidly

loosen and become ineffective.²⁵ Injection sclerotherapy is used to treat all degrees of primary varicose veins. The aim of sclerotherapy is to destroy the vein by fibrosis. Sodium tetradecyl sulfate 1% solution is injected, while the vein is emptied of blood, causing damage to the intima of the vein and permanent fibrosis. Sclerotherapy does not require hospitalization, and the patient resumes normal activity after the procedure. Painful varicose veins with recurrent phlebitis or skin changes are considered indications for surgery.²⁵ General practitioners must refer to a vascular surgeon for surgery and should consider this only if indicated.

Dietary and Hydrotherapy Approaches to Hemorrhoids and Varicose Veins

Dietary Recommendations

Diet therapy is a widely accepted modality in the management of hemorrhoids and varicose veins. Many physicians consider the first line of therapy to be a high fiber diet with commercial fiber supplements and enough oral fluids to produce soft, but well formed and regular bowel movements.²⁸ A low fiber diet can result in small hard stools that can cause patients to strain during bowel movements. This strain increases intra-abdominal pressure, subsequently increasing pressure on the veins of the lower legs and the hemorrhoidal cushions. Over time this can deteriorate vascular integrity. A high fiber diet is an important component to the prevention and treatment of both hemorrhoids and varicose veins.²⁸ This in addition to hydrotherapy, proper anal hygiene, and avoiding activities that require the patient to strain are the foundation of the approach of many family practitioners to these conditions.

Hydrotherapy

The warm sitz bath is the hydrotherapy indicated for conditions associated with increased pelvic congestion.^{25,29,30} The warm sitz

bath is an effective non-invasive therapy for uncomplicated hemorrhoids and varicose veins, but requires a high degree of patient compliance.

Specific Nutrients and Botanicals for the Prevention and Treatment of Varicose Veins and Hemorrhoids

A major component of a safe and effective therapy for both varicose veins and hemorrhoids, that is often overlooked, is the use of botanical and nutritional therapies. Several botanical extracts have been shown to improve microcirculation, capillary flow, and vascular tone, and strengthen connective tissue of the perivascular amorphous substrate. The goals of botanical and nutritional support are consistent with the philosophy of treating the cause of a disease. Conversely, the bulk of standard treatments for varicose veins and hemorrhoids are geared toward removing the problem or palliating the disease. Additionally, the low compliance associated with treatments such as hydrotherapy, mechanical compression therapy, and diet and lifestyle changes renders oral dietary supplementation an attractive option. The use of nutritional and botanical agents for the treatment of hemorrhoids and varicose veins is possibly the missing link to an effective conservative approach to these diseases. Early intervention with conservative therapies may prevent time-consuming and expensive complications of varicose veins and hemorrhoids.

Centella Asiatica (Gotu Kola)

Centella asiatica is a tropical medicinal plant with a long history of therapeutic use. An important active constituent of *Centella asiatica*, asiaticoside, was isolated and purified in 1940 and the first systematic clinical studies were carried out in 1945.³¹ Pharmaceutical *Centella* preparations are titrated for the pentacyclic triterpene derivatives asiatic acid, madecassic acid, and

asiaticoside.³² Most clinical studies of *Centella asiatica* used either undefined alcohol or aqueous extracts or one of the following extracts: TECA, TTFCA, or TTF. The extracts TECA (titrated extract of *Centella asiatica*) and TTFCA (total triterpenoid fraction of *Centella asiatica*) are combinations comprised of asiatic acid (30%), madecassic acid (30%), and asiaticoside (40%). The *Centella* extract TTF (total triterpenic fraction) is comprised of asiatic acid and madecassic acid (60%) in a ratio not clearly defined, in combination with asiaticoside (40%).³²

Rigorous clinical investigation of *Centella asiatica* has been conducted on chronic venous insufficiency and varicose veins. *Centella* has the potential to enhance connective tissue integrity, elevate antioxidant levels in wound healing, and improve capillary permeability.³³⁻³⁵ A randomized, multicenter, placebo-controlled, double-blind study investigated *Centella* extract in the treatment of venous insufficiency. Ninety-four patients received either TECA in two different doses (120 mg/day; 60 mg/day) or placebo over a two-month period. Results were evaluated subjectively by the patients' symptoms and objectively by plethysmography. The TECA groups resulted in significant improvements ($p < 0.05$) in symptoms of heaviness in the lower limbs, edema, and overall evaluation by the patient. Venous distensibility, measured by a mercury strain gauge plethysmograph at three occlusion pressures, was improved for the TECA groups but aggravated for the placebo group.³⁶ The differences in the effect of the different TECA doses were not significant, but did reveal a dose-effect relationship.

Mucopolysaccharides are one of the main components of the amorphous cellular matrix (ground substance) that maintains vascular integrity. The biochemical action of *Centella* extract was shown to reduce serum levels of lysosomal enzymes involved in the degradation of mucopolysaccharides. The

TTFCA extract was administered (30 mg three times daily) to 20 patients with severe varicose veins in the leg over an observation period of three months. Prior to the treatment, elevated baseline serum lysosomal enzymes were established (beta-glucuronidase 1.8 +/- 0.4 microM/min/L, beta-N-acetylglucosaminidase 23.1 +/- 0.4 microM/min/L, and arylsulfatase 0.078 +/- 0.003 microM/min/L) indicating an increased mucopolysaccharide turnover in subjects with varicose veins. During the treatment period these levels fell progressively. At the end of the three-month trial there was a significant reduction in the serum levels of the lysosomal enzymes (beta-glucuronidase 1.2 +/- 0.05 microM/min/L, beta-N-acetylglucosaminidase 17.7 +/- 0.7 microM/min/L, arylsulfatase 0.042 +/- 0.003 microM/min/L). These reductions were interpreted as evidence of a positive effect of the TTFCA extract on the pathogenesis of varicose veins.³⁷

In a double-blind, placebo-controlled study the effects of Centella extract on capillary filtration rate was investigated. *Centella asiatica* (TTFCA) extract was administered to 62 patients at two different doses (90mg/day; 180mg/day). Capillary filtration rate was evaluated in comparison to placebo. At the end of the four-week treatment period there was a dose-dependent reduction in capillary filtration rate measured by plethysmography. In comparison with the placebo group, the dose-dependent improvements seen in the TTFCA group were significant. The reduced capillary filtration rate was associated with improvement in microcirculation and in clinical symptoms.^{35,38} In addition, local application of TTFCA extract has been shown to improve vascular tone. In a double-blind study involving 80 patients, Centella extract was applied locally three times daily to patients with various venous disorders (including hemorrhoids and varicose veins). Patients, physicians, and ultrasonic examination noted subjective and objective improvements in symptoms.³⁹

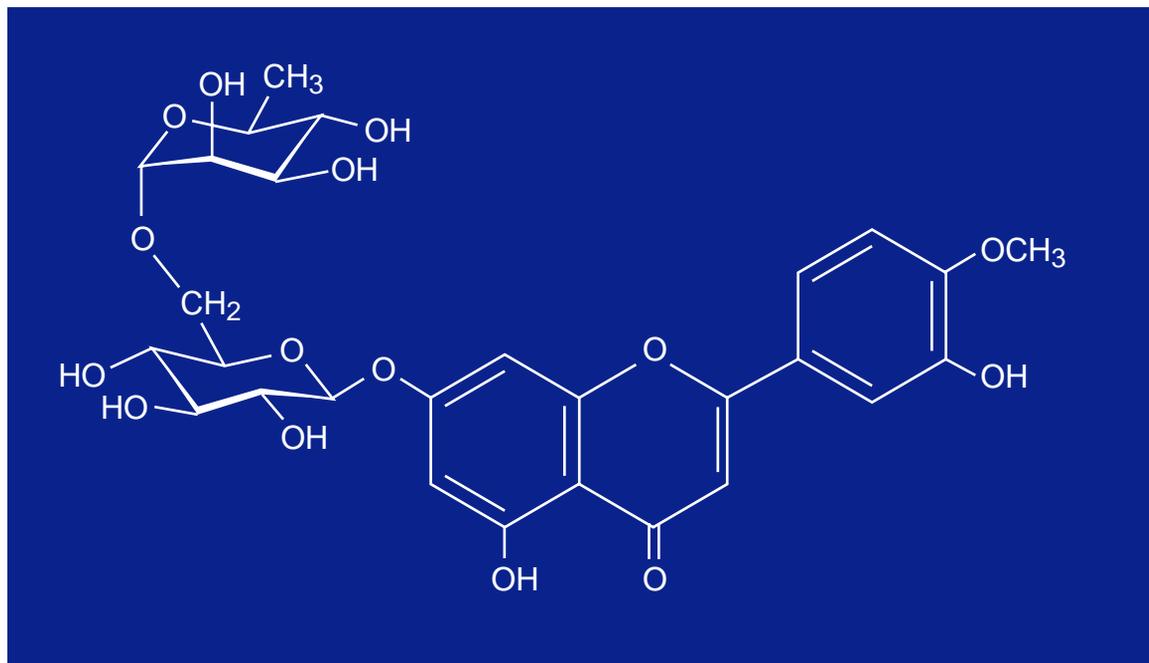
Bioflavonoids: Diosmin, OPCs, and Hesperidin

Bioflavonoids, particularly diosmin (Figure 2), oligomeric proanthocyanidin complexes (OPCs), and hesperidin, have demonstrated efficacy in the treatment of hemorrhoids and varicose veins. These bioflavonoids exhibit phlebotonic activity, vasculoprotective effects, and antagonism of the biochemical mediators of inflammation.⁴⁰ OPCs, diosmin, and hesperidin have been the subject of numerous clinical trials on efficacy and safety in the treatment of varicose veins and hemorrhoids.

There has been extensive research on the flavonoid mixture containing 90-percent diosmin and 10-percent hesperidin (Daflon 500, Les Laboratoires, Servier, France). Several randomized controlled studies have established its efficacy in the treatment of varicose veins and hemorrhoids. The safety of these flavonoids has been established through animal studies, and confirmed clinically in long-term trials. Data collected on more than 2,850 patients treated with 450 mg diosmin and 50 mg hesperidin twice daily for up to one year confirms it is well tolerated and has no contraindications to its use.^{41,42} Side effects are rare and mild with an incidence and nature similar to that found with placebo in double-blind, controlled trials.⁴¹

A double-blind, placebo-controlled trial of 120 patients reported the efficacy of Daflon in the treatment of acute and chronic symptoms of hemorrhoids.⁴³ The group was divided in half and matched at entry for general characteristics, clinical features, length of history, and acute episodes. Patients received the flavonoid mixture at a dose of two 500 mg tablets daily or placebo for two months. Subjects were evaluated on pain, pruritis, discharge, bleeding, edema, erythema, and bleeding on examination. Mean parameter scores and overall symptom scores fell significantly in the treated group. A similar

Figure 2: Diosmin



double-blind, placebo-controlled study examined 100 patients suffering an acute hemorrhoid attack. These patients received Daflon in a loading dose of three 500 mg tablets twice daily for the first four days and two tablets twice daily the following three days. The clinical severity of proctorrhagia, anal discomfort, pain, and anal discharge diminished to a greater extent in the treatment group.⁴⁰

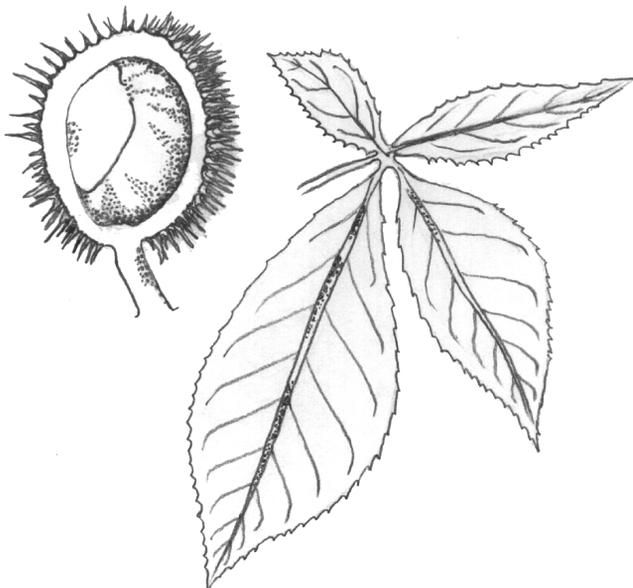
During pregnancy many of the treatment options for hemorrhoids, such as injection, rubber band ligation, and surgery are contraindicated.⁴⁴ A study of pregnant women suffering from acute hemorrhoids who were treated with Daflon showed remarkable results. Fifty women were treated for eight weeks before delivery and four weeks after delivery using a seven-day loading dose of six tablets for four days, and four tablets for three days, followed by a maintenance dose of two tablets per day. Over half of the women reported relief from symptoms by the fourth day of treatment and fewer relapses occurred during the antenatal period. Treatment did not affect

pregnancy, fetal development, birth weight, infant growth, or feeding.⁴²

Animal studies have shown flavonoids reduce neutrophil activation, mediate inflammation, and decrease soluble endothelial adhesion molecules.⁴⁵ Human trials have shown the ability of flavonoids to improve venous tone and vein elasticity assessed by plethysmography and to decrease plasma markers of endothelial activation.^{46,47} Additionally, clinical trials conducted in Germany using Daflon (two 500 mg tablets daily) showed highly statistically significant improvements in chronic venous insufficiency, venous leg ulcers, and hemorrhoids.⁴⁸

Professor Jacques Masquelier of the University of Bordeaux in France patented a method of extracting OPCs from pine bark in 1951 and from grape seeds in 1970.⁴⁹ Since that time OPCs have become known primarily for their antioxidant and free radical scavenging properties, but have also been shown to inhibit the enzymes hyaluronidase, elastase, and collagenase.^{50,51} These enzymes can degrade connective tissue structures, leading to

Figure 3: Aesculus Hippocastanum



***Aesculus Hippocastanum* (Horse Chestnut)**

Horse chestnut seed extracts (HCSE) (Figure 3) are used clinically to relieve the subjective symptoms and reduce the objective signs of chronic venous insufficiency.⁵⁶ The active component of the extract is thought to be the triterpenic saponin, aescin.⁵⁷ HCSE has been shown to exhibit venotonic, vascular protective, anti-inflammatory, and free-radical scavenging properties.⁵⁸ *In vitro* studies have shown HCSE inhibited the activity of the enzymes elastase and hyaluronidase. These enzymes are involved in enzymatic proteoglycan degradation, which compromises part of the capillary endothelium and the extravascular matrix.⁵⁷ These properties make HCSE ideal for the treatment of both varicose veins and hemorrhoids.

HCSE appears to reduce abnormally increased capillary permeability and associated edema.⁵⁹ A randomized, partially-blinded, placebo-controlled study of 240 patients showed a gradual decrease in edema, reaching a maximum at the end of the 12-week trial. This study used 50 mg aescin twice daily for 12 weeks, which resulted in a 25-percent reduction of mean edema volume.⁵⁹ The authors proposed that further edema reduction is possible because a steady state was not achieved in the 12-week trial period. An HCSE study using rats showed 200 mg/kg body weight of aescin effectively reduced increased vascular permeability, induced by both acetic acid and histamine, and inhibited hind paw edema induced by carrageenin.⁶⁰

A criteria-based, systematic review of double-blind, placebo-controlled trials of oral HCSE for patients with chronic venous insufficiency was published in the *Archives of Dermatology* in 1998. This review identified 13 studies with 1,083 total patients that met the strict inclusion criteria. The author concluded that HCSE is safe and effective in the symp-

increased vascular permeability. OPCs have demonstrated preferential binding to areas characterized by a high content of glycosaminoglycans such as the capillary walls.⁵² This feature makes them effective in decreasing vascular permeability and enhancing capillary strength, vascular function, and peripheral circulation.

In a double-blind study, 71 patients with peripheral venous insufficiency received 300 mg OPCs from grape seed per day. A significant reduction in functional symptomatology was observed in 75 percent of the treated patients compared to 41 percent of the patients given placebo.⁵³ In another study, measurements confirmed that a single administration of 150 mg OPCs increased venous tone in patients with widespread varicose veins.⁵⁴

In a double-blind clinical trial, a group of geriatric patients with low capillary resistance were treated with 100-150 mg OPCs or placebo. Over half of the patients in the treatment group demonstrated noticeable improvement in capillary resistance after approximately two weeks. All patients in this group reached the maximum attainable results after three weeks.⁵⁵

omatic short-term treatment of chronic venous insufficiency.⁶¹ Additional rigorous randomized, controlled trials are essential to verify HCSE's usefulness in chronic venous insufficiency and to explore the safety of long-term use.

Ruscus Aculeatus **(Butcher's Broom)**

Extract of *Ruscus aculeatus* is effective in increasing venous tone because of its anti-inflammatory and astringent properties.⁶² The active biochemical constituent is proposed to be the saponin glycoside ruscogenin.⁵⁷ Herbalists of various cultures have historically used *Ruscus aculeatus* for the treatment of varicose veins and hemorrhoids.⁶³ There is an increasing body of scientific literature to support these traditional folk medicine uses.

Increased macromolecule permeability through gaps between endothelial cells of post-capillary venules is associated with inflammatory reactions and edema. A group of French researchers used the hamster cheek pouch experimentally as an *in vivo* model of macromolecule permeability. Their early experiments showed intravenous Ruscus extract significantly inhibited the macromolecular permeability-increasing effect of bradykinin, leukotriene B₄, and histamine.⁶⁴ Later studies showed Ruscus extract applied topically dose-dependently inhibited the macromolecular permeability-increasing effect of histamine.⁶² The efficacy of topical Ruscus extract indicates the response is a result of the extract and not a product of its metabolism. Ruscus extract has also shown *in vivo* inhibition of elastase, part of the enzyme system involved in degrading perivascular structural components.⁵⁷

Human trials have shown patients with chronic venous insufficiency given oral Ruscus extract maintained venous tone and improved venous emptying in comparison to placebo-treated patients.⁶⁵ In another study patients with chronic venous insufficiency given oral Ruscus extract had a decrease in

capillary filtration rate, measured by plethysmography within two hours of administration.⁶⁶ Additionally, healthy volunteers exhibited a decrease of ten percent in venous capacity two hours after ingestion of oral Ruscus extract.⁶⁷

Hamamelis Virginiana **(Witch Hazel)**

Witch hazel extract, high in tannins and volatile oils, is a well-known medicinal tree from the deciduous forest of Atlantic North America. Witch hazel has a long therapeutic tradition and is used primarily for its astringent, anti-inflammatory, and local hemostatic effects.⁶⁸ In folk medicine it has been used for venous conditions, including hemorrhoids and varicose veins. Witch hazel decoctions are easily found on the shelf of most pharmacies, yet the literature available regarding its efficacy and mechanisms of action is limited. Witch hazel bark is used topically in minor injuries of the skin, local inflammation of the skin and mucous membranes, hemorrhoids, and varicose veins.⁶⁹

Studies have investigated the mechanism of action responsible for the astringent and antiphlogistic properties of Witch hazel. Witch hazel extract has been shown *in vivo* to inhibit alpha-glucosidase as well as human leukocyte elastase, enzymes which contribute to the degradation of connective tissue. Vascular integrity is compromised by the increase in activity of these enzymes. Witch hazel also exhibited a strong antiphlogistic effect in the croton oil ear edema test in the mouse.⁷⁰ The authors of these clinical trials proposed the antiphlogistic activity of Witch hazel extract is likely due to the presence of proanthocyanidins consisting of flavan units such as (+) – catechin, and (-) – epicatechin. Considering the widespread availability of Witch hazel extracts, it is essential for more scientific literature to be published regarding its efficacy in the treatment of hemorrhoids and varicose veins.

Conclusion

General practitioners encounter a large number of patients suffering from the manifestations of decreased vascular integrity, two of the most common being varicose veins and hemorrhoids. Conservative therapies such as diet, hydrotherapy, mechanical compression for varicose veins, topical agents for hemorrhoids, and lifestyle factors are the standard non-invasive approaches to these conditions. The next line of therapy involves the use of semi-invasive non-surgical modalities including electrocoagulation, sclerotherapy, cryotherapy, photocoagulation, and diathermy. These modalities require specific training, specialized equipment, and are associated with some risk.

As with all disease, the primary treatment for varicose veins and hemorrhoids is prevention. Patients with risk factors for developing these conditions should be identified through history and physical exam before aggressive intervention is necessary. The use of diet, lifestyle, and hydrotherapy in addition to botanical agents such as *Aesculus hippocastanum*, *Ruscus aculeatus*, *Centella asiatica*, *Hamamelis virginiana*, and bioflavonoids can intervene in the pathogenesis of decreased vascular integrity. Early intervention with these non-invasive therapies may prevent time-consuming and expensive complications of both varicose veins and hemorrhoids.

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