

Edited By:  
Thomas G. Guillems Ph.D.

# VENOUS DISORDERS: More than a cosmetic concern.

**F**or many years, veins have been thought to function only as passageways for blood to flow back into the heart. This has given way in recent years to an understanding that the venous system performs many functions that are vital to the whole circulatory network; such as their capability of constricting and dilating, storing large volumes of blood for use in other areas of the circulation, and even to regulate cardiac output. The alteration of venous blood flow can result in a number of conditions including: Chronic venous insufficiency (CVI), varicose veins, venous thrombosis, pulmonary embolism (a complication of deep vein thrombosis (DVT)), hemorrhoids, lower limb edema, and venous ulcers. These conditions are considered by many to be 'incurable'. We hope to show here that various natural ingredients have a profound effect on these conditions and their related symptoms.

Venous insufficiency has a complex pathology, having a dramatic impact on the quality of life of the patient (1). In fact chronic venous disease of the lower limbs is one of the most common conditions affecting humankind (2), with as many as 8 million Americans suffering from these conditions (3). A recent article reviewed the increasing incidence of deep vein thrombosis and found that between 1966 and 1990 the incidence of DVT was about 1 per 1000 annually, which was "virtually equivalent to the incidence of stroke" (4). While some might think that such problems are simply cosmetic, the underlying pathology can lead to a number of serious consequences.

The primary cause of venous disease is increase distention of the vessel walls, which seems to have a genetic component. Other factors would include hormone imbalance (especially pregnancy), certain oral contraceptives (5), prolonged hydrostatic load (extended periods of standing), or abdominal pressure on veins. Symptoms would include the pigmentation of the skin in the affected area, dermatitis, hemorrhages or thrombophlebitis. Tissue hypoxia and local edema can then lead to inflammation and infection, which will favor the likelihood of leg ulcers (between 400,000 and 500,000 patients in the U.S. (6)). Such is the spiral of untreated venous conditions of the lower limbs.

## Standard Treatment

The goal of most treatments for venous disease is the elimination or reduction of edema, varicosities, ulcers (if present), pain, skin discoloration, 'spider veins' and/or the change in venous flow as measured by ultrasonography or similar methods.

### Mechanical:

Patients with CVI are often told to simply elevate the effected leg above heart level for 30 minutes several times daily. This will help reduce the edema and improve the circulation in the small vessels nearest the skin. In more advanced cases, various forms of compression are required to improve leg circulation. Compression stockings are very common in the treatment of CVI and varicose veins, and have been shown to increase blood flow in the deep veins, diminish venous reflux, as well as improve ulcer healing. Unfortunately, compression stockings have low compliance. This is due in part to the uncomfortable nature of wearing them, cosmetic considerations, as well as the difficulty in putting them on correctly. Patients with massive edema can use intermittent pneumatic compression pumps, which compress the leg to a preset pressure, periodically throughout the day. Again compliance is a key issue.

### Drug Therapy:

The use of drug therapy is limited in the treatment of CVI and varicose veins. Infected leg ulcers are usually treated as other open skin infection, topically or orally. The use of topical and/or oral enzyme treatment to improve healing may be warranted. The use of diuretics is not uncommon for advanced cases of edema, although usually restricted to a short period of time. Most other drugs are secondary to improving wound healing or cosmetically related.

Injection therapy designed to sclerose the vein can be used to treat most varices. This is done by injecting sclerosant (something like sodium tetradecyl sulfate) into an 'empty vein' to promote scarring, and disuse of that particular vein. This procedure does not normally require hospitalization, and may need to be repeated several times until fully accomplished. Tissue scarring and skin discoloration are common side effects with this procedure, results which are dramatically reduced using concomitant oral enzyme preparations (7). Spider veins (Idiopathic telangiectases) can be treated in a similar manner (sclerotherapy) with good results.

### Surgery:

The complete removal of an incompetent vein is often referred to as vein stripping. Since the advent of bypass grafting of the coronary and peripheral arteries, every effort is made to preserve the saphenous veins (8). Some studies have shown that the risk of recurrent varicose veins may be associated with surgery of superficial insufficiency (9). There are few studies that have assessed the beneficial effects of surgery on objective end-points and in a random and controlled way.

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## A Natural Approach

### Diet:

A fundamental element of the diet for patients suffering from venous insufficiencies is fiber. Low-fiber diets tend to make the stools smaller and harder, making them more difficult to pass. This strain increases the abdominal compression on the major veins, increasing the pressure and the likelihood of varicosities and edema in the legs. Difficult bowel movements also increase the likelihood of hemorrhoids. By increasing the soluble fiber content of the diet, which may include the addition of psyllium, pectin, or guar gum fiber supplements; the patient will greatly decrease the abdominal pressure required to expel the stool. Increasing the amount of water will also greatly help in this respect.

A second dietary consideration would be the consumption of flavonoids. This group of phytochemicals is responsible for the color of most fruits, especially the berries. Increasing the intake of fresh fruits such as cherries, raspberries, blackberries, currants, blueberries (or bilberries), hawthorn berries, etc will greatly increase venous, capillary, and arterial tonicity. Flavonoids are also excellent as antioxidants for the lipid membranes along these vessels, preventing them from losing their tone and becoming brittle from oxidative damage.

Foods that increase the fibrinolytic activity of the blood have been shown to be helpful, as fibrin is often deposited near varicose veins. Decreased fibrinolytic activity is associated with increase risk of thrombus formation, thrombophlebitis, and pulmonary embolisms. Foods such as onions, garlic, ginger and cayenne will increase fibrinolytic activity as well as promote other benefits to the overall circulation.

### Horsechestnut:

The Horsechestnut tree (*Aesculus hippocastanum* L.) has been planted through the northern hemisphere as an ornamental and shade tree, although it is native to the Balkan peninsula. The seed is primarily used medicinally, having as its major known active component the group of saponins known as aescin (or escin). Other components include, quinones, flavones, sterols, and a variety of fatty acids. The extract of the seeds of Horsechestnut, and specifically aescin, have antiinflammatory, antiedema, antiexudative, and venotonic activity (10). Many of these activities have been described since about 1960 and have been the focus of many studies related to chronic venous insufficiencies and varicose veins.

One of the modes of action associated with aescin

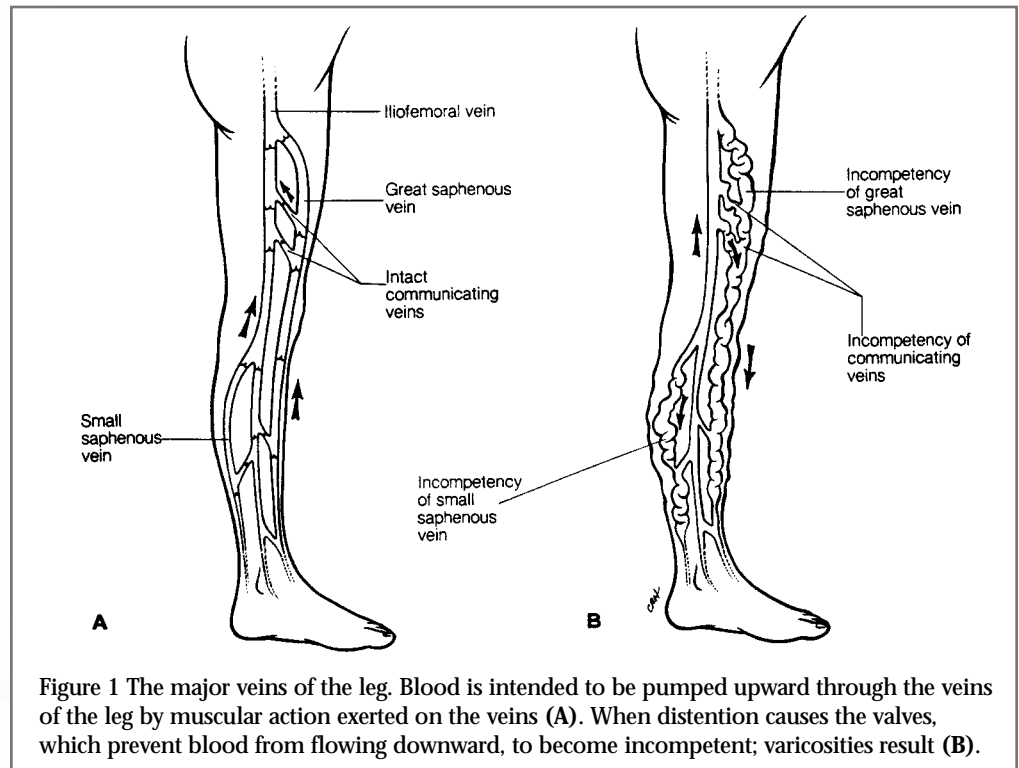


Figure 1 The major veins of the leg. Blood is intended to be pumped upward through the veins of the leg by muscular action exerted on the veins (A). When distention causes the valves, which prevent blood from flowing downward, to become incompetent; varicosities result (B).

appears to be mediated by prostaglandin F alpha, attributing an anti-exudative activity (11). Its anti-edema properties are attributed to its ability to decrease transcapillary filtration (12). Several enzymes that decrease the tone of vessels (hyaluronidase and several lysosomal proteoglycan destructing enzymes) are inhibited by escin or horsechestnut extracts (13,14). This venotonic activity has been confirmed in animal models (15,17), as well as human vessel *in vitro* studies on saphenous veins (16).

A review article published in 1996 (18) summarizes a case observation study of more than 800 practitioners and more than 5,000 patient with chronic venous insufficiency, treated with a standardized horsechestnut extract. They conclude that "all the symptoms investigated- pain, tiredness, tension and swelling in the leg, as well as itching and the tendency toward edema- all improved markedly or disappeared completely." They conclude it to be a therapeutic 'pillar', and include that it is additionally beneficial because compliance is much higher than compression stockings. These conclusions can be seen in double-blind placebo controlled studies using standardized horsechestnut extract at 50 mg aescin, twice daily (19, 20, 21). The safety and efficacy of this natural product is sure to be recognized in greater measure in the United States as more information continues to confirm these phenomenal results.

### Butcher's Broom:

Butcher's Broom (*Ruscus aculeatus* L.) is a short evergreen shrub, native to the Mediterranean region. It is the root (rhizomes) of this plant, also referred to as box holly or knee holly, that is used medicinally. This plant has recorded medicinal use as early as the first century, but has been a focus of studies in venous disease primarily in the past 40 years. Like horsechestnut, saponins play a major role in the

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activity of butcher's broom. In this case it is the saponins ruscogenin and neuruscogenin. They apparently function as vasoconstricting agents through the  $\alpha$ -adrenergic receptors, a property that is diminished by decreased temperature (22). Extracts of butcher's broom have also been shown to inhibit elastase, an enzyme involved in the decreased tone of veins (13). Several experiments with animal models have confirmed the microcirculatory, venous constricting, and the anti-edema (inhibition of venous permeability) effects of butcher's broom extracts (23,24,25,26).

*"This is quite exciting because [troxerutin has] a mechanism unlike that of the saponin components... The synergistic potential may have great benefits..."*

Several human studies have confirmed its effective use for venous insufficiencies alone, as well as in combination with the flavonoids and ascorbic acid (27,28,29). Results included rather immediate changes in symptoms and direct measurements (28), improvement of venous tone as measured by venous occlusion plethysmography (27), and a decrease in capillary filtration rate, tissue volume of the foot and ankle, and a reduction of the blood volume in the lower leg (29). Dosages range from 100 mg of extract per day, all the way to 100mg of the extract (standardized to 9-11% ruscogenin) taken 3 times per day. Again butcher's broom is considered extremely safe and has minimal adverse reactions.

**Gotu Kola:**

The fresh-dried leaves of the Gotu Kola plant (*Centella asiatica* L.) have been used medically for a variety of concerns throughout China, East Asia, and Africa for many years. The saponin component again, in this case asiaticoside and others, are thought to be the most active components. Like aescin, the triterpenic fraction of Gotu Kola extracts is able to inhibit some of the lysosomal enzymes thought to participate in the etiology of varicosities and venous insufficiencies (30).

Other factors attributed to Gotu kola is its ability to enhance connective tissue, increasing the tone of vessels. This activity has been confirmed in several clinical trials, in which edema, pain, decreased capillary permeability, and improved microcirculation were all improved significantly without adverse effects (31,32,33,34). These data show that the response is dose dependent up to 60 mg three times daily. Interestingly, those patients with normal capillary filtration rates and no edema were not significantly affected by the Gotu kola extract treatment (34). The use of this herb, sometimes called Indian Pennywort, is becoming more frequent for a number of connective tissue, vascular, and wound healing protocols. The safe use of this herb and its extracts has been confirmed by many studies.

**Rutin and Its Derivatives:**

Rutin is a flavonoid glycoside containing quercetin as the aglycone portion and rutinose as its sugar portion, and is found widely distributed in the plant kingdom. Rutin has been used for many years for its ability to decrease capillary permeability and fragility (one of the group called vitamin P, from years ago).

A group of rutin derivatives collectively known as troxerutin (O-(beta-hydroxyethyl)-rutosides) has become a very useful ingredient in the treatment of

chronic venous insufficiencies. Its effectiveness and safety has been evaluated in both elderly patients (35), as well as pregnant women (36), with excellent results. While the complete mechanism is not understood, troxerutin has been reported to have both anti-erythrocyte aggregation effects and a favorable effect on blood fibrinolytic activity (37). These authors claim that "Abnormal increase of erythrocyte aggregation and reduction of profibrinolytic activity are the two most frequent biological perturbations found in chronic venous insufficiency." This is quite

exciting because this is a mechanism unlike that of the saponin components previously described. The synergistic potential may have great benefits in the treatment of CVI (21). Dosages of troxerutin as a single ingredient were around 900-1000 mg per day in divided doses (35,38).

**Other ingredients:**

There are a whole host of ingredients one could list that have been used for the conditions described here. We will briefly overview a few that may be of some benefit, this is by no means an exhaustive or exclusive list.

Witch hazel (*Hamamelis virginiana* L.) has been used both internally, but primarily externally for concerns of varicosities (especially hemorrhoids). Among its activities are anti-inflammatory, alpha glucosidase inhibition, elastase inhibition, as well as anti-edema properties (39). Its use is not wide-spread and has not been confirmed in many double-blind controlled studies.

A tea preparation of buckwheat (*Fagopyrum esculentum*) was used in a double-blind, placebo-controlled clinical trial with good results in patients with leg edema and CVI (40). Interestingly, buckwheat is very high in rutin and this may account for this activity.

Most of the other natural remedies would include extracts of the flavonoid-rich fruits such as hawthorn berries (*Crataegus* sp.), blue berries or bilberries (*Vaccinium* sp.), currants (*Ribes* sp.), etc. In general the proanthocyanadin compounds in these extracts have been shown to reduce capillary fragility, increase venous wall integrity and muscular tone, and prevent the break of the extracellular matrices of blood vessel. In this respect, grape seed extracts would be efficacious for similar reasons.

**Conclusion:**

As this brief review has shown, chronic venous insufficiencies and its associated outcomes is a serious and wide-spread problem in the United States. Once thought of as only a cosmetic difficulty, these conditions signal a deep underlying change in physiology of the venous system. The prevention and treatment of these conditions has been difficult under the current paradigm of treatments, although the use of natural ingredients in these conditions is quite promising. Many of the ingredients (or several combined) are sure to become standard treatments for venous conditions here in the United States within the next several years.

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# IN MY OPINION

This is in response to the New England Journal of Medicine editorial, dated September 17, 1998. I would suggest reading the issue, as it is quite clear a concerted effort was made to discredit and even vilify the use of alternative medicines.

The title speaks volumes about the authors' views about alternative medicine; "Alternative Medicine- The risk of untested and unregulated remedies". They propose to debate the question: "What is there about alternative medicine that sets it apart from ordinary medicine?" They answer their own question by saying: "What most sets alternative medicine apart, in our view, is that it has not been scientifically tested and its advocates largely deny the need for such testing." To say that these statements reveal their ignorance of much of alternative medicine is obvious to most of our readers. The rest of the article reveals more than ignorance is involved, but a distinct bias against such remedies.

They assert that FDA has no control over supplement manufacturers, while failing to mention that FDA is in the process of approving a set of Good Manufacturing Procedures (GMPs) specifically for the supplement industry, or the new labeling laws that go into effect in March of 1999. The notion that alternative therapies and herbal medicines are defined by trial and error, while conventional medicines are tested with double-blind, placebo-controlled, FDA approved clinical trials is a gross over-simplification and ignores 30 years of data collected from around the world. This points out two glaring inconsistencies.

First, the assumption that FDA approval is not a highly politicized and lobbied process is laughable. The authors' own journal and profession is underwritten by pharmaceutical companies that have a vested interest in the failure of any unpatentable alternative to their own lucrative products. The fact is that FDA refuses to use data from Germany, France, Italy, England, etc in the case of botanical medicine, while it quite readily will accept pharmaceutical company trial information from these countries. Add to this their position that non-FDA approved products are inherently dangerous is rather interesting when you consider the voluntary dispensing of FDA approved drugs for non-FDA approved conditions; an action which is wide spread by conservative measures and not discouraged by pharmaceutical companies.

We do not mean to imply by these comments that unscrupulous vendors of dietary supplements should be unregulated. We are merely defending the fact that a vast field of research has given us credible data to support the use of numerous different natural products and alternative therapies. Furthermore NEJM does a disservice to their readers when they make a concerted effort to smear the field of alternative medicine as founded on "assertions, speculation, and testimonials". The concerted effort is magnified by the inclusion of five other articles (in the same issue) casting doubt on the safety, effectiveness, and adulteration of herbal or alternative products. Let us remind our readers that over 100,000 deaths per year are attributed to adverse reactions to FDA approved drugs, taken at proper doses, for approved conditions.

Until the bias is removed from those in control of such editorial positions, healthcare professionals and their patients must look elsewhere for credible information on these therapies and ingredients. Unfortunately this industry, like many others, is full of individuals all too ready to take advantage of these people who have "strayed from the fold". I would suggest that we be aware that the benevolent concerns of pharmaceutical companies and the medical establishment may be no more than a wolf in shepherd's clothing.

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