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V E N O U S I N S U F F I C I E N C Y



## Chronic Venous Insufficiency (CVI)

Recent studies demonstrated that about one third of female population is affected by Chronic Venous Insufficiency at different stages, indicating that CVI may be considered one of the most common diseases. Similar prevalence has been observed in men.

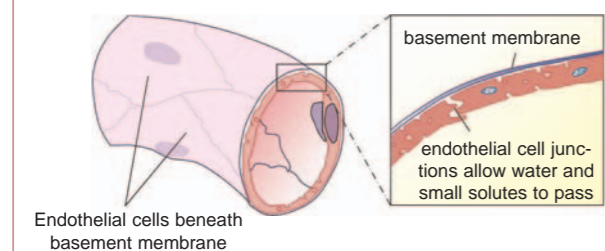
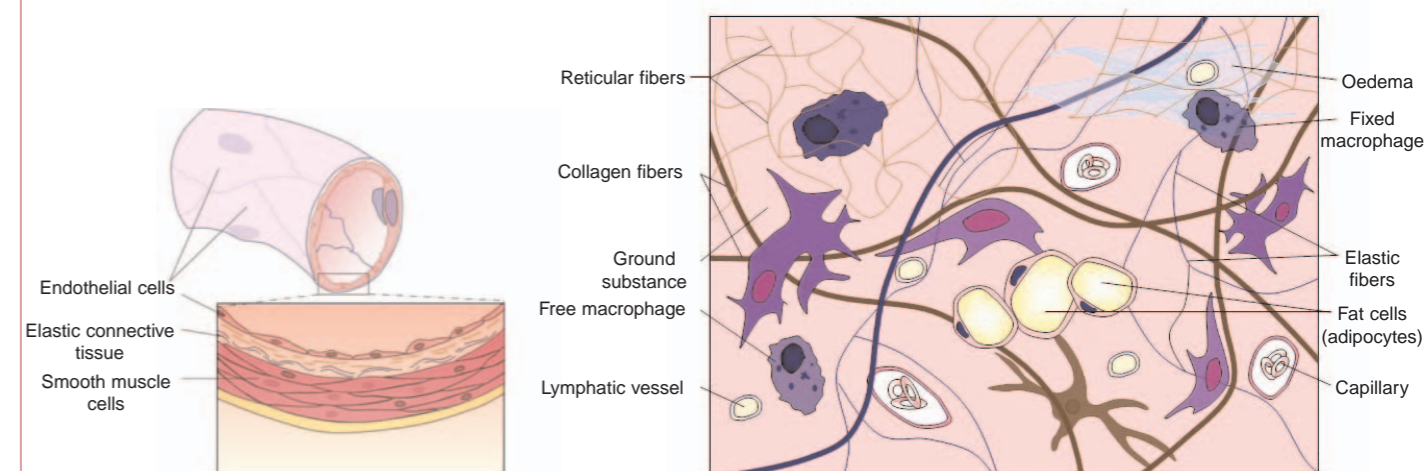
Typical symptoms of this pathology are leg discomfort (pain, pressure, burning, itching, dull aches, heaviness), cold feet, cramps.

Other signs, commonly considered mere aesthetic defects, such as spider veins and oedema, actually represent the first steps in the onset of CVI.

The causes of CVI are the degeneration of the venous walls, the dysfunction of the valves and of the lymphatic system, both mixed together and alone. Different biological pathways are involved in these problems.

An effective response to the initial causes of CVI comes from Indena: several products, acting at different sites and by means of different mechanisms of action, contribute in reducing the main symptoms of CVI. Clinical trials have demonstrated the efficacy, and the safety, of the products indicated.

They also may be combined in order to better exploit their single characteristics, thus obtaining a synergistic and complementary action.



### REINFORCEMENT VENOUS WALL

**Centella Asiatica Selected Triterpenes\***: exerts its activity on vascular and perivascular connective tissue by stimulating collagen biosynthesis. This results in an improvement of tone and elasticity of venous wall and reduction of abnormal capillary permeability.

Oral 30-60 mg/die  
Topical up to 1%

**Esculoside**: it is a glycosidated coumarin endowed with capillary protection profile related to its inhibitory activity on catabolic enzymes such as hyaluronidase and collagenase, thus preserving the perivascular connective tissue integrity. In addition, an antioxidant and anti-inflammatory profile has been reported.

Oral 60-120 mg/die  
Topical up to 3%

**Leucoselect®\* (grape seed extract)**: ever since considered one of the most effective extracts for vascular protection, for its ability in preventing all oxidation damages in vessels, protecting vascular system against atherosclerosis and improving the plasma total antioxidant capacity. Its anti-proteases activity helps to maintain vascular integrity.

Oral 150-300 mg/die  
Topical up to 1%

**Mirtoselect® (anthocyanosides)**: it strengthens capillary walls by linking with endothelial cells membranes, thus increasing their resistance, and reduces capillary permeability by stimulating the synthesis of perivascular tissue constituents. A blood microcirculation improvement is also observed, due to phosphodiesterases inhibition.

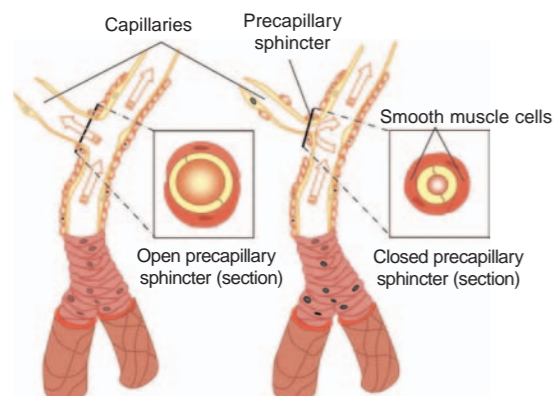
Oral 80-160 mg/die  
Topical up to 1%

**Proanthocyanidin A<sub>2</sub>\***: this pure molecule extracted from *Aesculus hippocastanum* normalizes impaired capillary permeability and resistance thanks to the ability of inhibiting proteolytic enzymes, contributing to maintain the vessel integrity. Its antioxidant activity prevents vascular damages.

Oral 150-300 mg/die  
Topical up to 1%

**Asiaticoside**: it is a triterpene from *Centella asiatica*. It is known to stimulate vascular and perivascular collagen biosynthesis, with a particular activity on collagen type I, whose reduction is significant in aging. The result is an improvement of tone and elasticity of vascular wall and reduction of abnormal capillary permeability.

Oral 30-60 mg/die  
Topical up to 1%



### VASOKINETICS

**Ginkgolect®\***: it acts on many levels of the cardiovascular system, including arteries, veins, capillaries, blood components. It stimulates arterial blood flow, capillary perfusion and venous return. Other actions have been described, including endothelial protection, antioxidant and microvasculokinetic activity.

Oral 120-240 mg/die  
Topical up to 0.5%

**Hawthorn\***: the extract lowers the blood pressure by inhibiting the Angiotensin Converting Enzyme and enhances the blood flow, by reducing the peripheral resistance. It binds with endothelial phospholipids and inhibits hydrolases, thus reducing vessels fragility.

Oral 300-750 mg/die  
Topical up to 1%

**Butcher's broom**: it acts on smooth muscle cells in venous system. This is due to the activation of postjunctional  $\alpha_1$  and  $\alpha_2$  adrenergic receptors. Besides, it stimulates the release of noradrenaline in the venous wall, inducing a vasoconstriction that reduces venous stasis.

Oral 100-200 mg/die  
Topical up to 5%

**Ruscogenins C**: this group of highly purified molecules extracted from *Ruscus aculeatus* exerts vasoconstricting effect by promoting smooth muscle contraction. The observed anti-elastase activity is useful for blood vessels functionality. In addition, the product exerts a strong anti-inflammatory activity.

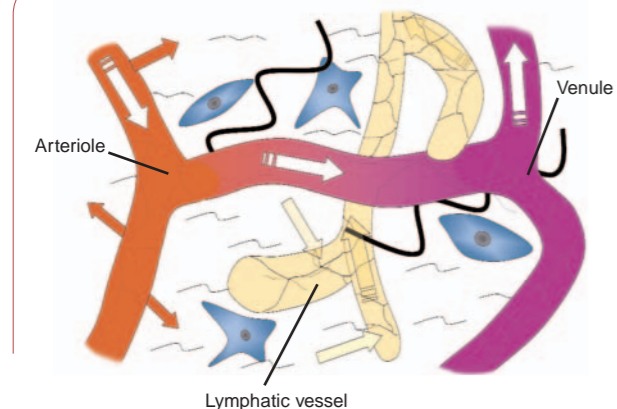
Oral 10-20 mg/die  
Topical up to 1%

**Visnadine\***: has a strong vasokinetic activity, not associated with vasodilating properties. Its efficacy is due to the enhancement of the inotropic activity of the wall myocytes in microcirculatory vessels.

Topical up to 1%

**Ginkgo Biloba Dimeric Flavonoids\***: acts on capillary blood flow. It inhibits cAMP-phosphodiesterase and stimulates the rhythmic contraction of precapillary arterioles. This is due to a specific microvasculokinetic action, increasing smooth muscle cells contraction.

Topical up to 3%



### ANTIOEDEMA

**Lymphaselect® (coumarin)**: shows a marked action on lymphatic system, thanks to its myotropic activity resulting in a stimulation of the rhythm and tonus of the lymphatic vessels. At the venous system level, Lymphaselect® increases blood flow, improves the venous return quality reducing the oedema.

Oral 20-50 mg/die  
Topical up to 2%

**Escin\***: from *Aesculus hippocastanum*, acts principally on capillaries. Its mechanism of action is mainly related to the modification of the vascular permeability. Escin reduces the number and the diameter of the small pores of the capillary walls through which water exchange normally occurs. The final result is a strong reduction of oedema.

Oral 100-150 mg/die  
Topical up to 0.4%

**Sericoside\***: it is a triterpene extracted from *Terminalia sericea*. It has a capillary protecting activity and antioedema properties. This is due to a remarkable reduction of capillary permeability. In addition, significant anti-inflammatory properties have been demonstrated in experimental models.

Topical up to 0.5%

**Horse chestnut**: the extract acts principally on capillaries. Its mechanism of action is mainly related to the presence of escin. Horse chestnut extract shows, as well, antioxidant properties, as it inhibits enzymatic and non-enzymatic lipoperoxidation. This way, it improves all CVI symptoms (oedema, cramps, heaviness, pain, fatigue).

Oral 500-750 mg/die  
Topical up to 2%

**\*Also in more bioavailable Phytosome® formulations.**

Visnadex® and PA<sub>2</sub> AFFILENE™ are the Brand Names for Visnadine and Proanthocyanidin A<sub>2</sub> Phytosome® complexes.