



## LETTER TO THE EDITOR

### MANAGEMENT OF CHRONIC VENOUS INSUFFICIENCY: A NEW APPROACH

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#### ABSTRACT

Chronic venous insufficiency (CVI) is a prevalent syndrome in medical practice. Despite efforts in managing its symptoms, CVI remains a significant clinical and surgical challenge, as there is still no curative treatment. Recently, plant-based therapies practiced for centuries have been repositioned using modern pharmacological and clinical research techniques. This randomized, double-blind clinical trial aims to demonstrate the non-inferiority of a combination of *Aesculus hippocastanum* (horse chestnut), *Polygonum acre* (dotted smartweed), *Smilax papyracea* (sarsaparilla), and rutin compared to a combination of diosmin and hesperidin for the symptomatic control of CVI.

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## INTRODUCTION

**Aesculus hippocastanum:** This tree species, native to Western Asia, has been traditionally used for managing CVI symptoms. Its active pharmacological compound, extracted from the dried plant, has side effects such as gastrointestinal discomfort, dizziness, and itching (Dickson, 2004). **Polygonum acre** (dotted smartweed): Traditionally used for various conditions such as joint inflammation, hemorrhoids, and circulatory disorders, this species has no documented side effects (Ministério da Saúde e Anvisa, 2014). **Smilax papyracea** (salsaparilla): Known for its steroidal saponins, this plant has historically been used to manage inflammatory joint disorders. No side effects have been reported for this species (Park, 2014). **Rutin:** A flavonoid found in plants such as *Ruta graveolens* (rue), rutin aids in vitamin C absorption. It has traditional uses in hemorrhoids, capillary fragility, and CVI. Rutin also exhibits antioxidant properties. It has no known side effects (Altınterim Başar, 2014).

**Diosmin and hesperidin:** Extracted from citrus peels, these flavonoids improve venous tone, enhance lymphatic drainage, and reduce vascular permeability. Diosmin is used for the symptomatic treatment of CVI and hemorrhoidal crises. Reported side effects are gastric discomfort, diarrhea, insomnia, and lethargy (Batcharov, 2010).

### CHRONIC VENOUS INSUFFICIENCY

CVI can be caused by several factors, including genetics, age, hormonal influences, obesity, prolonged standing, and sedentarism. The condition is characterized by increased vascular permeability, capillary flow decrease, and venous stasis. Symptoms are pain (due to vascular distension), leg heaviness (local edema), night cramps (due to arteriolar compression), as well as skin thickening and hyperpigmentation (from blood extravasation) (Youn, 2019).

## MATERIALS AND METHODS

This study was a double-blind, non-inferiority, randomized trial evaluating the efficacy and safety of *Aesculus hippocastanum* 10 mg + *Polygonum acre* 10 mg + *Smilax papyracea* 40 mg + rutin 20 mg bid (Group A,  $n_A=60$ ) versus diosmin 450 mg + hesperidin 50 mg bid (Group B,  $n_B=60$ ) in patients with lower limbs CVI. The study's primary objective was to assess venous symptoms severity according to a visual analogic scale. Secondary objectives were to evidence quality of life measured according to CIVIQ-20 (chronic venous insufficiency quality of life questionnaire - 20 parameters) score, physician's assessment score, patient's assessment score, and pharmaceutical swallow ability, over a four-months period. Tolerability was assessed during Visit 2 and Visit 3 (final Visit), when participants reported any adverse events. The study included adult patients aged 18-65, who all provided written informed consent.

## DISCUSSION AND CONCLUSION

CVI has been a long-standing medical challenge, for which an extensive ethno pharmacological body of evidence has been produced. This study is the first to compare the effectiveness and safety of two specific combinations in a randomized, double-blind trial. Group A combination was found to be as effective as Group B combination, both showing significant symptomatic improvement in four endpoints, with Group A tablets providing better swallow ability than Group B. Both treatments were generally well tolerated, although Group A had a slightly higher incidence of adverse events, possibly due to the combination of four active ingredients versus two in Group B (no severe adverse reactions or study withdrawals reported). In conclusion, both combinations were effective in managing CVI symptoms, with Group A showing an advantage in terms of ease of use and faster response time.

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