

A topical combination of blackberry, *Centella asiatica*, sodium hyaluronate, vitamin E and Melilotus to relieve legs symptoms of venous insufficiency

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Abstract

Chronic Venous Insufficiency (CVI) is a clinical condition characterized by several legs symptoms: telangiectasias, reticular veins, varicose veins, edema, pigmentation, eczema, lipodermatosclerosis, white atrophy and ulcers. These symptoms are often associated with tired and heavy legs, leg pain, itching, legs and ankles swelling. This report analyzes the usefulness of a cream based on blackberry, *Centella asiatica*, sodium hyaluronate, vitamin E and Melilotus (Flavofort 1500® legs cream) to relieve leg symptoms in CVI. A group of 35 subjects (7 men and 28 women) with legs symptoms applied Flavofort 1500® legs cream on the legs, twice a day for 10 days. The symptoms were evaluated with a patient questionnaire at 4 steps: T0 (before cream application), T1 (just after first application), T2 (5 days after first application) and T3 (10 days after first application). A reduction of subjects (%) with legs symptoms was observed both after 5 day and after 10 days.

Introduction

Venous insufficiency is a widespread condition characterized by an abnormal function of the valve system, in the presence or absence of an obstacle to venous return, which involves the superficial and / or deep venous system, which generally affects the lower limbs.¹

Phytotherapy is helpful in countering signs and symptoms of venous insufficiency of the lower limbs.¹

Among the various natural extracts and natural substances, used both topically and

orally, there are: i) *Aescin* from horse-chestnut seed extract with antiedematous, anti-inflammatory, and venotonic properties that may be attributable to the decreased vascular permeability;¹ ii) *Ginkgo biloba* extract which is important in peripheral circulation and microcirculation because of its antioxidant properties;¹ iii) *Centella asiatica* extracts with vasoprotective action, in particular phlebotonic and microcirculation stimulating properties;² iv) blackberry, *Vaccinium myrtillus*, with protective properties on the basal endothelium, because of its anti-oxidant activity;³ v) Melilotus, *Melilotus officinalis*, that favors capillary permeability reduction and the increase in venous wall resistance;⁴ vi) vitamin E that performs antioxidant activity at cell membranes level and favors collagen synthesis for the normal blood vessels functions;⁵ vii) hyaluronic acid that is a polysaccharide of all the living organisms where it plays a key structural function. This active is able to improve capillary resistance.⁶

Materials and Methods

We evaluated Flavofort 1500® legs cream (Blackberry, *Centella asiatica*, Sodium Hyaluronate and Melilotus) in patients with legs symptoms, analyzing the reduction of symptoms and the patient opinion.

Patients (n=35) with a diagnosis of venous insufficiency of different degree [from C0s to C4a according to Clinical, Etiology, Anatomy, and Pathophysiology (CEAP) classification; not detected data] with bilateral leg symptoms (tired and heavy legs/leg pain/itching and tingling/cramps/legs and ankles swelling/telangiectasias or reticular veins/ankles pigmentation/ varicose veins) and no comorbidities were enrolled.

All patients underwent ultrasound examinations, of both legs, to assess superficial and deep veins of the lower limbs.

This exam was performed using multi-frequency 7.5-10 MHz Doppler ultrasound probes (Sonos 1500B; Hewlett Packard, Palo Alto, CA). The room temperature was maintained between 18°C and 22°C.

In detail 7 men and 28 women were recruited. Their baseline characteristics are reported in the Table 1. The 14% of patients were aged between 26 and 35 years old, the 34% were aged between 36 and 50 years old and the 52% were over 50 years old.

Informed consent was obtained from all individual participants included in this analysis. All patients applied Flavofort 1500® legs cream (3 mL for each application; corresponding to the size of a nut) for

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Informed consent: Informed consent was obtained from all individual participants included in the study.

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5 minutes of a gentle superficial massage in circulatory motion on the affected area (both calves and ankles), twice a day for 10 days. Patients were evaluated at 4 steps: T0 (baseline), T1 (just after first application), T2 (5 days after first application) and T3 (10 days after first application). At each step an evaluation of symptoms was conducted, while at the beginning and at the end of local treatment a patient judgment on skin characteristics (hydrated, bright, elastic, soft or velvety) was recorded. All patients filled in an assessment questionnaire at each step, assigning a score from 0 to 4 to the symptoms based on the severity of the symptom (score: 1=at all; 2=a little; 3=enough; 4=very much).

Results

The % of patients with legs symptoms (tired and heavy legs/leg pain/itching/cramps/legs and ankles swelling/telangiectasias or reticular veins/ankles pigmentation/varicose veins) decreases after 5 days of cream application and further after 10 days of cream application (Table 2, Figures 1 and 2).

Data showed that Flavofort 1500® , after 10 days of cream application, decreases the % of patients with: tired and heavy legs [−85%; P<0.05], leg pain [−67%; P<0.05], itching and tingling [−85%; P<0.05], cramps [−78%; P<0.05] (Table 2 and Figure 1), legs and ankles swelling [−82%; P<0.05], telangiectasias and reticular

veins [-91%; $P<0.05$], ankles pigmentation (redness and dark spots) [-87%; $P<0.05$], visibility and perceptibility of varicose veins (Table 2 and Figure 2) [-100%; $P<0.05$] (Table 2 and Figure 2). The data shown are related to the patients who assigned a score 4 to their symptoms, based on the severity of the symptom.

Most patients expressed a positive judgment on the pleasantness of the cream. After the treatment, the skin was smooth, soft, bright and hydrated.

Conclusions

The observations in this study show that Flavofort 1500® legs cream application can produce local benefits. The beneficial effects of local treatment with Flavofort cream may be seen by symptomatic evaluation of patients.

These findings, as preliminary data, suggest the usefulness of a formulation based on the association of Blackberry, Centella asiatica, Sodium Hyaluronate, Vitamin E and Melilotus to relieve legs symptoms of venous insufficiency. The association of a cream formulated by combining these substances with other phlebotonic agents opens a window of opportunities to be evaluated in more prolonged and larger studies.

Table 1. Baseline characteristics (T0).

	Patients (N=35)
Sex, N (%) male/female	7 (20) / 28 (80)
Age distribution, N (%)	
26-35 years	5 (14%)
36-50 years	12 (34%)
>50 years	18 (52%)
BMI	21-27
Legs symptoms	N (%) patients
Tired and heavy legs	7 (20%)
Leg pain	3 (9%)
Itching and tingling	7 (20%)
Cramps	5 (14%)
Legs and ankles swelling	12 (34%)
Telangiectasias and reticular veins	12 (34%)
Ankles Pigmentation	8 (23%)
Varicose veins	8 (23%)

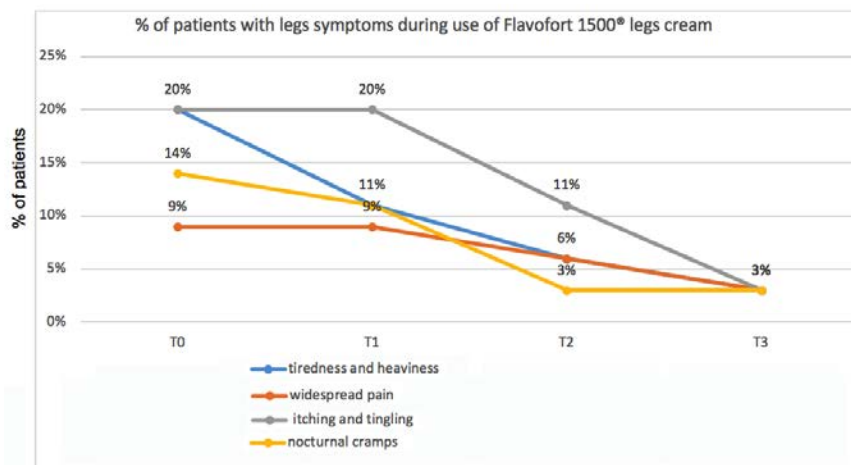


Figure 1. Percentage of patients with legs symptoms (tiredness and heaviness, widespread pain, itching and tingling and nocturnal cramps) during use of Flavofort 1500® legs cream. The data shown are related to the patients who assigned a score 4 to their symptoms, based on the severity of the symptom. T0=baseline; T1=after the first application; T2=5 days after treatment; T3=10 days after treatment.

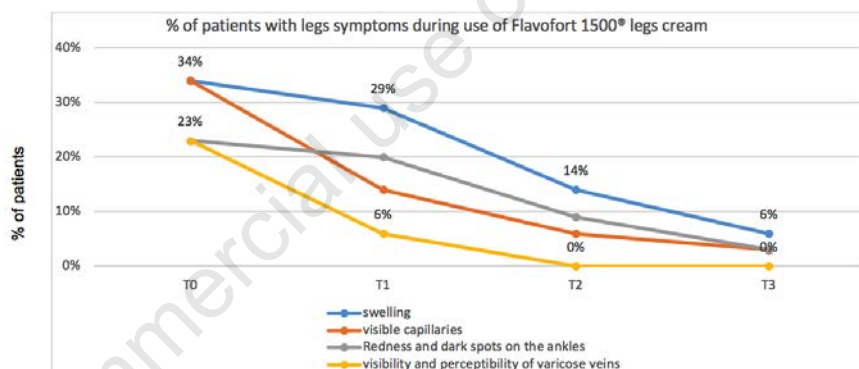


Figure 2. Percentage of patients with legs symptoms (swelling, visible capillaries, redness and dark spots, visibility and perceptibility of varicose veins) during use of Flavofort 1500® legs cream. The data shown are related to the patients who assigned a score 4 to their symptoms, based on the severity of the symptom. T0=baseline; T1=after the first application; T2=5 days after treatment; T3=10 days after treatment.

Table 2. Number and Percentage of patients with legs symptoms after: the first application (T1), 5 days of application (T2) and 10 day of application (T3) of Flavofort 1500® legs cream.

Symptoms	N (%) patients at T1	N (%) patients at T2	N (%) patients at T3
Tired and heavy legs	4 (11)	2 (6)	1 (3)
Leg pain	3 (9)	2 (6)	1 (3)
Itching and tingling	7 (20)	4 (11)	1 (3)
Cramps	4 (11)	1 (3)	1 (3)
Legs and ankles swelling	10 (29)	5 (14)	2 (6)
Telangiectasias and reticular veins	5 (14)	2 (6)	1 (3)
Ankles pigmentation (redness and dark spots)	7 (20)	3 (9)	1 (3)
Varicose veins (visibility)	2 (6)	0 (0)	0 (0)

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