

Treatment of venous leg ulcers with an ointment containing yarrow (*Achillea millefolium*) extract

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Abstract

Traditional medicine credits yarrow (*Achillea millefolium*) with the ability to accelerate wound healing. The purpose of this research was to determine the effects of yarrow on the epithelization of the lower leg venous ulcers. The study included 39 patients with venous leg ulcers. They were divided into two groups: the first (experimental) group of patients were treated with an ointment containing 7.5% of yarrow extract. In the second (control) group, saline solution dressings were applied to ulcers, within the period of three weeks. In the experimental group, at the beginning of the therapy, the total surface of all the ulcers was 44736 mm². After three weeks, the total surface of all the ulcers was 27000 mm² (a decrease of 39.64%). In the control group, at the beginning of the therapy, the total surface of all the ulcers was 46116 mm². At the end of the study (21 days) the total surface of all the ulcers was 39153 mm² (a decrease of 15.1%). Herbal preparations are suitable for application in the therapy of venous ulcers, but their efficiency in wound healing is still to be investigated.

According to the World Health Organization statistics, disorders of the venous circulation are among the most frequent diseases affecting the world population. It is estimated that 15% of the whole adult population has some type of chronic venous insufficiency (1, 2, 3). According to various epidemiological studies, it is evaluated that the prevalence of lower leg ulcers in adult population is about 2%. The etiological factor of the vast majority (70-90%) of these ulcers is chronic venous insufficiency (4, 5).

Any topical preparation that accelerates wound healing is of great help. Because of this, modern medicine is frequently using traditional methods.

Yarrow (*Achillea millefolium* L., Asteraceae) is a widely distributed medicinal plant. The herbal drug (*Millefolii herba*) is believed to possess antiphlogistic, spasmolytic, stomachic, carminative and cholagogue

activities. Topically, it is used in the treatment of skin disorders, especially inflammation of skin and mucous membranes, as well as a trophic protective agent (6). Recent investigations also point to the antimicrobial (7, 8, 9) and antioxidant activities (8) of yarrow. Yarrow is also well known for its wound healing properties, particularly in staunching blood flow. An infusion of the leaf, stems, and flowers will speed the healing of rashes, hemorrhoids, and skin ulcers (10).

Its pharmacological activity is attributed to particular plant constituents. *A. millefolium* contains essential oil which, depending on the origin, contains no, or up to 50% of chamazulene (produced during the distillation process of proazulene). The presence of prochamazulene is correlated with the chromosome number in the plant. Only tetraploid plants contain prochamazulene and blue sesquiterpene (chamazulene) in essential oil. Most

common oil compounds are camphor, sabinene, 1,8-cineole, etc. The plant contains several classes of sesquiterpene lactones: guaianolides, germacranolides, dihydroparthenolides. These substances have been proven to take part in the antiseptic and antiphlogistic action of yarrow. However, although *Millefolii herba* is widely used in phytotherapy, its use is sometimes restricted, because it may cause allergic contact dermatitis (11, 12). Guaianolide peroxides and sesquiterpene lactones, and with azulenes in the essential oil, are believed to be responsible for itching and inflammatory skin changes with formation of vesicles (11). Beside terpenoids, yarrow contains considerable amount of plant phenolic compounds, of which the most important are flavonoids: apigenin, luteolin and their 7-O-glycosides, 6-methoxylated or di- and trimethylated flavonols (pectolarigenin, 3-methylbetuletol, etc). Flavonoids are presumed to be responsible for the well-known anti-inflammatory effects of yarrow's herbal medicines (13).

Purpose

The aim of this research was to determine the therapeutic efficiency of yarrow (*Achillea millefolium*) extract on the epithelization of the lower leg venous ulcers.

Material and methods

The experiment was carried out on 39 patients with venous leg ulcers. All patients were treated at the Clinic of Dermatovenereology Diseases of the Clinical Center of Vojvodine in Novi Sad, Serbia. All patients were randomly assigned into the investigation in regard with their arrival to the Clinic. Arterial etiology of ulcers was excluded by measuring the ankle-brachial pressure index (ABPI). The average value of ABPI was 0,98. Prior to being included into the study, all patients were tested with originally made 1%, 3% or 10% ether extract of yarrow, in order to exclude contact sensitivity due to previous sensitization to compositae-containing herbal remedies and cosmetics (14). Patch tests were performed according to international guidelines (15). They were applied to the patients' back using Curatest® (Lohmann-Rauscher, Neuwied, Germany). All patients were divided into two groups.

Potential adverse effects of the therapy were explained to all patients in detail, and all signed a written consent form for participation in the research.

Experimental group

In the first group, patients were treated with an ointment with yarrow extract.

Plant material

The herbaceous part of the cultivated *Achillea millefolium* L. (Asteraceae) was collected in June of 2003, in the Province of Vojvodina. Voucher specimens were confirmed and deposited at the Herbarium of the Botany Department, Faculty of Sciences, University of Novi Sad.

Plant extract preparation

Sixty-five grams of dry plant material was subjected to the Soxhlet extraction with absolute ethanol for 3 hrs. After that, the solvent was evaporated under vacuum, and the obtained dry residue (4 g) was subsequently dissolved in propylene glycol. A 7.5% concentration of yarrow extract was added to a neutral basis, Galsana® (Galenika, Belgrade, Serbia).

Treatment protocol

The first group, included a total of 20 patients: 6 males and 14 females, of an average age of 63.05, with a total number of 32 venous ulcers. Local therapy was applied twice a day, for three weeks.

Control group

The second group was the control group. It included 19 patients, 15 females and 4 males, of an average age of 68.35, with a total number of 31 venous ulcers. This group was treated with saline solution dressings which were applied to ulcers, for the period of three weeks.

Results were recorded by measuring the ulcer area, as well as semi-quantitative parameters (granulation, epithelization and dermatitis) once a week, throughout the treatment.

The study was approved by the Institutional Review Board and the Ethics Committee of the University of Novi Sad and the Ministry of Science and Environment Protection of the Republic of Serbia.

Results

At the beginning of the therapy the total surface of all ulcers in the experimental group (treated with ointment containing yarrow extract) was 44736 mm², that is 1398 mm² on average. After the first week there was a 14.07% decrease of ulcer size, 26.80% after the

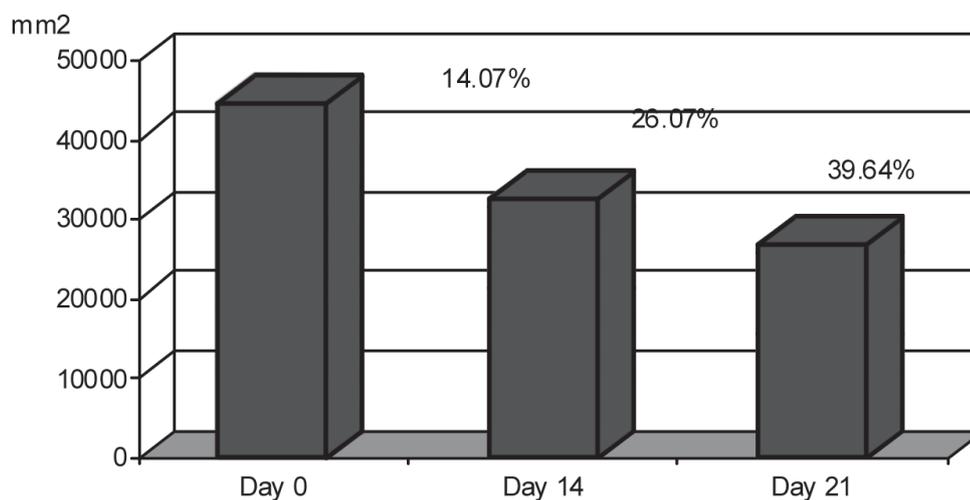


Figure 1. Decrease in total ulcer surface in patients treated with topical preparation with yarrow extract

second and after the third week the total surface of all ulcers was 27000 mm² (a decrease by 39.64%) (Figure 1). In 3 cases a complete epithelization was achieved (Figure 2, Figure 3).

All of the registered semi-quantitative parameters (granulation, epithelization and dermatitis) were significantly improved when compared to the

beginning of the treatment. During the experiment, there were no systemic or local side effects.

In the control group, at the beginning of the therapy the total surface of all ulcers was 46116 mm², 1487 mm² on average. After 7 days, a 3.93% decrease was established, 10.11% after 14 days, and at the end of the experiment (21 days) the total surface of all



Figure 2. Before treatment



Figure 3. After treatment

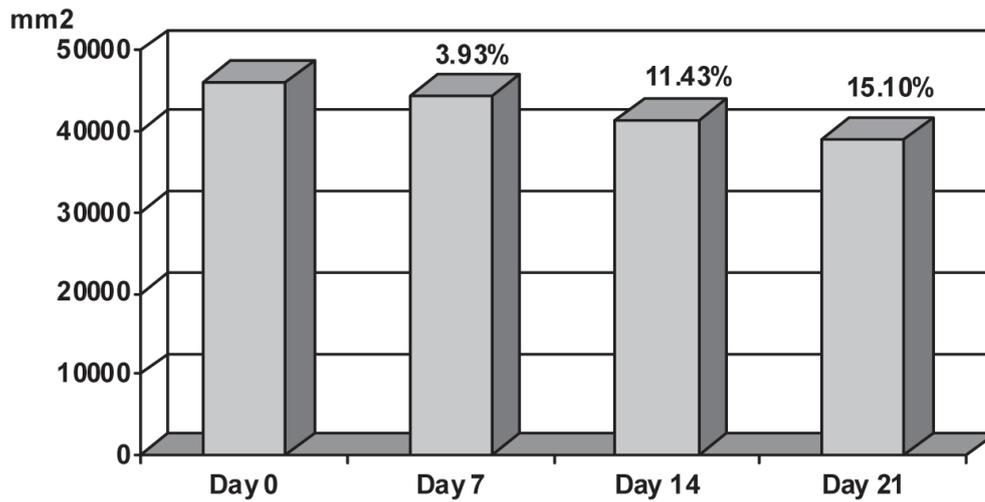


Figure 4. Decrease in total ulcer surface in the control group

ulcers was 39153 mm² (a 15.10% decrease) (Figure 4). In 4 cases a complete epithelization was achieved.

After statistical evaluation (student t-test) of results between the experimental and control groups, the group treated with ointment containing yarrow extract showed no statistically significant acceleration of wound healing ($p > 0.05$) (Figure 5).

Discussion

In contemporary literature, no previous researches concerning the effects of yarrow preparation on venous ulcers healing were found. In general, there are very few controlled clinical studies concerning the effects of medicinal plants on wound healing.

The obtained results of the study point to a faster epithelization of venous ulcers after the application of the cream with yarrow extract, in comparison with the control group (decrease of ulcer surface by 39.64% in comparison with 16.75%), although without statistical significance.

However, the previous investigation, in which we analyzed the influence of the cream with 7.5% marigold extract on the healing of venous ulcers, a statistically significant acceleration of the healing process ($p < 0.05$) was established (16).

Nevertheless, the evaluation of semi-quantitative parameters (granulation, epithelization and dermatitis) showed better results in the group treated

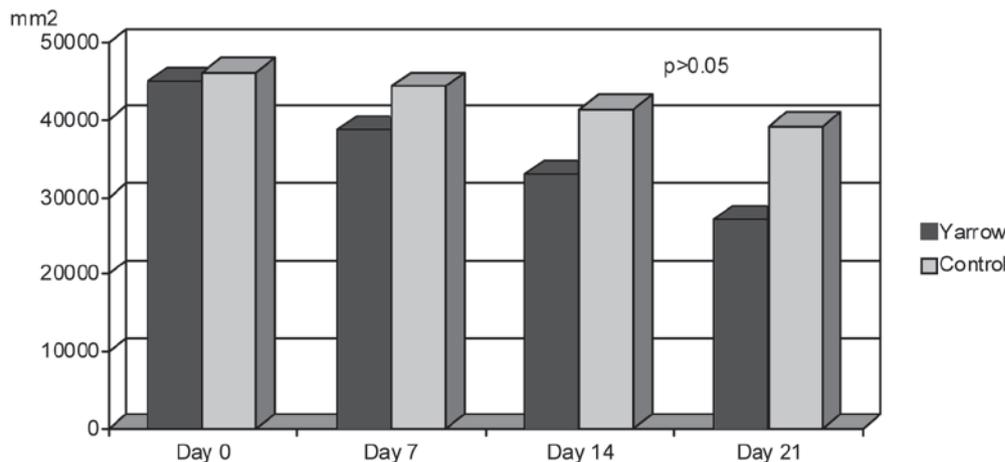


Figure 5. Decrease in the wound surface during the study in experimental and control groups (comparative review)

with yarrow extract, especially concerning reduction of dermatitis. On the basis of these findings, one can conclude that, even though both of these plants are known for their capacity to accelerate wound healing, their effects are achieved at different levels. Therefore, a combination of several medicinal plants probably exerts a synergistic effect. This is in accordance with yet another of our previous investigations, in which a preparation containing 4 different medicinal herbs (*Calendula officinalis*, *Achillea millefolium*, *Symphytum officinale*, *Salvia officinalis*) showed the best results (17). In this investigation we treated 40 patients with a total number of 66 venous ulcers. After a 3-week therapy, a 58.55% decrease of ulcer surface was established. A complete epithelization was recorded in 22 ulcers.

Conclusion

Our investigation showed no significant acceleration of wound healing after application of cream with yarrow extract. However, based on this research and our previous investigations, we can conclude that herbal preparations are safe and suitable for application in the therapy of venous ulcers. Better results may be achieved by appropriate combination of different medicinal herbs and by utilization of their synergistic effect. Yet, this calls for good knowledge of herbal medicines and venous pathology.

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Primena preparata sa ekstraktom hajdučke trave (*Achillea millefolium*) u lečenju venskih ulkusa potkolenice

Sažetak

Uvod: U Tradicionalnoj medicini hajdučka trava (*Achillea millefolium*) je dobro poznata po svojoj sposobnosti da ubrzava zarastanje rana.

Cilj: Cilj ovog istraživanja bio je da ispitamo uticaj hajdučke trave na zarastanje venskih ulkusa potkolenice.

Materijal: U našem istraživanju lečeno je ukupno 39 pacijenata sa venskim ulkusima. Bili su podeljeni u dve grupe. U prvoj (eksperimentalnoj grupi) pacijenti su lečeni preparatom u obliku krema koji je sadržao 7,5% ekstrakta hajdučke trave. U drugoj (kontrolnoj) grupi su na ulkuse primenjivani oblozi fiziološkog rastvora, tokom perioda od 3 nedelje.

Rezultati: Na početku ispitivanja u eksperimentalnoj grupi ukupna površina ulkusa iznosila je 44 736 mm². Posle tri nedelje terapije ukupna površina ulkusa bila je 27 000 mm² (smanjenje za 39,64%). U kontrolnoj grupi ukupna površina ulkusa na početku eksperimenta je bila 46116 mm². Na kraju ispitivanja (21 dan) ukupna površina ulkusa bila je 39 153 mm² (smanjenje za 15,1%).

Zaključak: Primena biljnih preparata pogodna u terapiji venskih ulkusa, ali efikasnost njihovog dejstva na zarastanje ulkusa tek treba da bude detaljnije ispitana.