

To the pharmacology of "St. John's herb" (St. John's wort - *Hypericum perforatum*).
Message 2: Comparative assessment of the wound-healing properties of drugs

Hypericum

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Pharmacological properties of St. John's wort (*Hypericum perforatum*). The second report: The comparative estimation of wound healing properties of *Hypericum* preparations

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SUMMARY

The results of the primary comparative assessment of the wound-healing effect of preparations from St. John's wort on a model of long-term non-healing wounds in mice are presented. The most effective treatment of wounds with a decoction and dusting with herb powder, which acts positively in all 3 phases of wound healing. Enteral administration of a decoction of the herb is also effective. A similar local and enteral application of roots ends with a wound-healing effect, but not so pronounced. The similar activity of novoimanin and lyophilized decoction of the herb has been proven when applied topically. Dry alcoholic extract of herbs and roots applied topically are ineffective. The legitimacy of the use of "St. John's Herb" for wound healing in traditional medicine is obvious.

Key words: phytopharmacology, St. John's wort, wound healing properties.

RESUME

The results of the comparative assessment of the primary wound healing action of *Hypericum perforatum* preparations on the model of long-term healing of wounds in mice are presented. The most effective treatment of wounds was by decoction of herb and applying plant's powder acting positively in all 3 phases of wound healing. Enteral administration of decoction of herb is also effective. A similar local and enteral application of root causes wound-healing effect, but not so manifested. Similar activity novoimaninum and freeze-dried decoction of herb when applied topically was proved. Dry spirit based extract of herb and roots, when used locally are not effective. The use of "St. John's wort" for wound healing in folk medicine is obviously legitimate.

Keywords: phytopharmacology, *Hypericum perforatum*, wound healing properties.

Introduction

St. John's wort got its name after distorting the Kazakh "djerbay" - a healer of wounds. In traditional and folk medicine, the aerial part of St. John's wort, both fresh and dried, has been used locally for centuries to accelerate the healing of ulcers, wounds, especially infected, purulent, non-healing for one reason or another. The high efficiency of St. John's wort, its "oil" has been known since the times of Hippocrates, Dioscorides, Pliny [1, 2], but it was included in the domestic pharmacopoeia a little late - only in 1968, High antibacterial activity of essential oil, juice, various substances, extracts of St. John's wort established long ago, including in Russia [3, 4, 5], which served as the basis for the creation of numerous topically applied drugs, we have novoimanin. Meanwhile, antibacterial activity alone is not enough to effectively heal wounds,

The experience of studying the effect of numerous phytopreparations on wound healing in experimental animals [6] suggested the need to compare local action

those from both the aboveground and underground parts of the plant. The red roots of St. John's wort have not been studied; in the available literature, information on their use cannot be found. When interviewing the Vepsians of the Mezhozerie, the healers themselves, it was possible to find out that they used a decoction of herbs with roots for various diseases (often with diarrhea). The roots were washed without removing, and with local application of St. John's wort, sometimes combining it with other plants (plantain, woodlice, birch, meadowsweet). Subsequently, such an application received some justification, since tannins have a higher anti-exudative effect, the content of which in the roots is higher and reaches 11%. It was of interest to some extent to simulate the centuries-old local application of the herb and roots of St. John's wort in the form of a common powder, decoction. One of the convenient dosage forms for use, not completely mastered by the domestic pharmaceutical industry is a lyophilized decoction of the plant. This dosage form has not been evaluated experimentally for its effectiveness. The only difficulty is the need for constant sealing of the dishes with the lyophilized extract.

The name "St. John's Grass" [7] in North America and other English-speaking countries, as well as the popularity in medicine of different nations, is associated with the high efficiency of its herbal preparations for numerous diseases (according to M.N. Nosal and I.M. 99 diseases) [8]. However, there is no information on the effect on wound healing, for example, of a decoction of St. John's wort when administered enterally. It is known that not only grass, fresh or dry, in the form of a powder, steamed, but also a decoction, "St. John's wort oil" is successfully used externally, and the latter is used internally for gastric ulcer and duodenal ulcer, with ulcerative colitis. These are peculiar clues of the positive effect of St. John's wort preparations on the regeneration process. There is hardly a logical tendency to ascribe a wound-healing

In connection with the foregoing, the purpose of the research was considered to be a comparative assessment of the effect of the combined local application of decoctions and powders of herbs, as well as the roots of St. "St. John's wort oil" cannot be used for group keeping of animals, because animals lick, gnaw it from the surface and from the scab of the wound.

Material and research methods

A 1:10 broth of the aboveground or underground part of St. in terms of air-dry raw materials). A dry alcoholic extract, in which hyperforin, hypericin, hyperoside and a number of other, insoluble or limitedly water-soluble substances [10], should be predominantly, were obtained by the method of repercolation, drying, and grinding to a state of powder. A lyophilized decoction of the aboveground or underground part of St. John's wort was provided by the technology group of the Plant Resources Laboratory of the Botanical Institute of the Russian Academy of Sciences. The dry aboveground or underground part of St. John's wort was ground to a powder state (mortar, coffee grinder). The reference drug was Novoimanin: 2 drops per wound. In the control group for a wound or a scab,

A method for modeling long-term non-healing wounds in mice was developed by us earlier [6] for a comparative assessment of the wound-healing properties of phytopreparations. An indispensable condition for extending the healing time of wounds is the removal of the scab every other day at the beginning of the experiment and even every day thereafter (it is determined specifically by the situation). Removing the scab allows you to often apply the drug directly to the wound. On days when the scab was not removed, it was soaked with a decoction and applied to the soaked scab with a powder-powder. The experiments were carried out on old 38–40 g male SHR mice with delayed regeneration. Under hexenal anesthesia (70–80 mg / kg intraperitoneally), the back of the mice was epilated, the epilator was thoroughly washed off with a 3% solution

acetic acid was applied with a round stamp (13 mm in diameter) to the contours of the wound. With synechial scissors, a full-thickness skin wound was applied along the contour, which was always larger in size than the contour of the stamp and was, on average, the same in all groups. The area of the wounds was characterized daily by multiplying the transverse and longitudinal dimensions. Immediately after the operation, the test or control preparation was applied to the wound. Subsequently, they were applied to the scab, and after removing it every other day - to the wound. Decoctions were administered enterally daily. Dry extracts, lyophilized broth were used to powder wounds or scabs. The wound (scab) was powdered with crushed grass or roots after moistening them with a decoction. Each group consisted of 30-40 mice. Animals intended for histological studies are not included in this number. Since there can be no aseptic conditions for group keeping animals, all wounds are considered infected. On a day, even 1 experimenter is able to measure and treat 300 wounds (10 groups). We compared the averaged areas of lesions by day to identify the activity of drugs in 3 phases: cleansing, contraction of wounds, granulation, epithelialization, as well as the timing of complete epithelialization, the number of festering wounds, animals that died from wound disease. Histology: the sections were stained with hematoxylin-eosin, comparing the general overview of the regeneration processes. The results are processed according to the criteria: Fischer-Student t and χ^2 . We compared the averaged areas of lesions by day to identify the activity of drugs in 3 phases: cleansing, contraction of wounds, granulation, epithelialization, as well as the timing of complete epithelialization, the number of festering wounds, animals that died from wound disease. Histology: the sections were stained with hematoxylin-eosin, comparing the general overview of the regeneration processes. The results are processed according to the criteria: Fischer-Student t and χ^2 . We compared the averaged areas of lesions by day to identify the activity of drugs in 3 phases: cleansing, contraction of wounds, granulation, epithelialization, as well as the timing of complete epithelialization, the number of festering wounds, animals that died from wound disease. Histology: the sections were stained with hematoxylin-eosin, comparing the general overview of the regeneration processes. The results are processed according to the criteria: Fischer-Student t and χ^2 .

Research results

Given in table. 1, the results of a comparative assessment of St. John's wort once again confirm the effectiveness of novoimanin, which significantly reduced the number of suppurating wounds and animals that died from wound infection, as well as as a result of reducing the time of complete epithelialization of wounds by 18%. In the dynamics of reducing the area of wounds, we observe its effectiveness only in the stage of complete epithelialization. Novoimanin did not affect the primary contraction of wounds. Differences from the control in terms of the average area of wounds at the stage of granulation and their secondary contraction were also not noted, although visually the granulation tissue was more pronounced than in the control, which was subsequently confirmed histologically. The lyophilized broth applied topically to the wound acted in almost the same way. There are no significant differences between novoimanin and lyophilized broth in any indicator, although the latter did not reduce the number of festering wounds in comparison with the control. Since powders with dry alcoholic herb or St. John's wort extracts were ineffective, it is impossible to recommend these dosage forms. There were no significant differences either in the number of suppurations, dead mice, or the timing of healing and the dynamics of the area of wounds. Visually, the extracts even promoted relaxation, i.e. some widening of the wounds. neither the timing of healing and the dynamics of the area of wounds was noted. Visually, the extracts even promoted relaxation, i.e. some widening of the wounds. neither the timing of healing and the dynamics of the area of wounds was noted. Visually, the extracts even promoted relaxation, i.e. some widening of the wounds.

Table 1

Comparative grade wound healing properties drugs St. John's wort perforated

| Препарат, способ применения | Количество мышей | | | Сроки полной эпителизации ран | | Дни, в которые площадь ран была достоверно меньше, чем в контроле |
|---|------------------|---------------|------|-------------------------------|-------|---|
| | Всего | с нагноениями | пало | в днях | в %% | |
| Контроль. Тальк. Местно | 40 | 18 | 15 | 39,2 ± 6,0 | 100 | |
| Новоиманин. Местно | 30 | 4* | 3* | 32,1 ± 4,0 | 81,9 | 27, 30, 31, 33-35 |
| Лиофилизированный отвар. Местно. | 30 | 6 | 3* | 31,8 ± 3,9* | 81,1 | 12, 17, 20, 32-35 |
| Местно. Сухие спиртовые экстракты: надземные части корней | 30 | 10 | 7 | 41,0 ± 6,8 | 104,6 | |
| | 30 | 12 | 9 | 43,8 ± 5,4 | 111,7 | |
| Отвар и присыпка надземные части корней | 30 | 5* | 3* | 26,3 ± 4,8* | 67,1 | 2, 4, 6, 10, 12-18, 22-30. |
| | 30 | 6 | 4* | 32,0 ± 3,5* | 81,6 | 2-5, 13, 21, 27-34 |
| Отвары внутрь: надземные части корней | 30 | 6 | 4* | 29,8 ± 4,2* | 76,0 | 12, 14, 17, 21, 25, 27-33 |
| | 30 | 7 | 5 | 32,6 ± 5,3 | 83,2 | 15, 19, 28 |

The most effective was the treatment of the wound with a decoction and then dusting it with fine

powder of the aerial part of St. John's wort. Here we observe a powerful primary contraction of the wound, which cannot be explained only by the local irritating effect of the powder itself, a foreign body, since talc also has such a control. Obviously, the smaller the area of the wound after its reduction, the shorter the time required for its complete healing, which was observed in dynamics. This result supports the popular use of St. John's wort poultices, the application of steamed dry herb to wounds, and finally the use of powders. In no way can we exclude the importance of the resorptive action of St. John's wort, since the wound surface is ideal for the entry into the blood of both toxins (microbial and others) and natural compounds that have a positive effect on regeneration. This is confirmed by the death of animals when strychnine solutions are applied to the wound (test for the consistency of the inflammation barrier). Highly effective was the effect of the topically applied decoction and powder of St. John's wort in the second stage of wound healing with the formation of filling it with granulation tissue, the forerunner of the scar. The pink granulations observed in the experiment, moderately bleeding when removing the scab (as well as when removing the dried dressing in the clinic), granulations are considered an indicator of a normal, optimally proceeding wound healing process. This process results in the third stage - epithelization, the last days of complete healing, which usually proceeds rapidly in rodents. Highly effective was the effect of the topically applied decoction and powder of St. John's wort in the second stage of wound healing with the formation of filling it with granulation tissue, the forerunner of the scar. The pink granulations observed in the experiment, moderately bleeding when removing the scab (as well as when removing the dried dressing in the clinic), granulations are considered an indicator of a normal, optimally proceeding wound healing process. This process results in the third stage - epithelization, the last days of complete healing, which usually proceeds rapidly in rodents. Highly effective was the effect of the topically applied decoction and powder of St. John's wort in the second stage of wound healing with the formation of filling it with granulation tissue, the forerunner of the scar. The pink granulations observed in the experiment, moderately bleeding when removing the scab (as well as when removing the dried dressing in the clinic), granulations are considered an indicator of a normal, optimally proceeding wound healing process. This process results in the third stage - epithelization, the last days of complete healing, which usually proceeds rapidly in rodents.

The most effective was the local application of a decoction and powder of the aerial part of St. John's wort. The wound healing time was reduced by 1/3 in comparison with the control. Against the background of such treatment, the number of festering wounds and dead mice significantly decreased. A decrease in the area of damage to wounds was observed at all stages of their healing. It is significant that already from the first days (primary contraction) it was less than in the control. The legality of using in folk medicine not only herbs, but also the roots of St. John's wort, was confirmed in the experiment. The decoction and powder from the roots did not differ significantly from those of the herb. The effect on the primary contraction of the wound is distinct, less pronounced, judging by the dynamics of the area of the wounds, in the stage of granulation. The effect of decoction of roots in the resulting stage of epithelization is demonstrative. The value of the resorptive action of a water-soluble complex of natural compounds of herbs and roots of St. John's wort has been proven when their decoctions are introduced into the stomach through a tube. The root decoction was less active in all respects in comparison with the control. The effect of the herbal decoction when administered enterally was manifested in the stage of granulation and epithelization, judging by the dynamics of wound areas. The decoction reduced the period of epithelialization of wounds by 24%.

When assessing the wound healing process, we followed the generally accepted rules of statistical comparison, but practitioners, surgeons, traumatologists, of course, are also interested in nuances and trends. In this regard, the best condition of the wounds was observed against the background of local application of a decoction and powder from the aerial part, which manifested itself not only in powerful primary contraction, but in the formation of a more pronounced, dense protective scab, faster and more complete formation of the wound boundaries. Granulation and thin epithelium creeping on them also looked fresher in this group of animals.

Survey histological sections made it possible to note a more powerful leukocyte shaft in the first days of treatment with local application of the herb and roots of St. ... The better vascularization of granulations and wound edges in these groups is demonstrative, observed already from the 5th-6th day after the reduction of the granulation shaft, which creates conditions for faster healing.

Taking into account the timing of complete epithelialization of wounds, St. John's wort preparations can be arranged in the following row in decreasing efficiency: decoction and herb powder locally \geq grass decoction inside \geq lyophilized decoction topically \geq local decoction and root powder \geq local novoimanin \geq root decoction inside.

The discussion of the results

One of the results that are significant for practice is the registration of the effectiveness of the decoction of St. John's wort with enteral application. Most experienced herbalists, healers recommend, for example, not only baths with succession, chamomile, St. John's wort for atopic

dermatoses, but also ingestion of their infusions. S. Hahnemann [11] noted that skin diseases are often a manifestation of internal diseases, "and they all rub off." The same can be said about wound disease, when wound healing depends not only on local treatment, but also on the mobilization of the reparative reserve with the help of simple extemporal and other medicinal plant preparations. The ability of many herbal remedies to limit the volume and severity of lesions (primary and secondary contraction of wounds), have an antidestructive effect, and mobilize regeneration (in our case, the rate of granulation and epithelialization) was previously proven by me using the example of damage to various organs and tissues [6]. Obviously, it is possible to mobilize the reparative reserves of the body by prescribing an infusion, a decoction of St. John's wort, but it is better with the help of water extracts from multicomponent collections with the inclusion of classical phytoadaptogens and a number of other plants. Traumatologists and surgeons, unfortunately, in most cases do not use the most popular means of Indian, Tibetan traditional medicine - mummy.

Today, hardly a lyophilized broth can compete with novoimanin (has no advantages) and claim to be put into practice due to the peculiarities of its storage, but the possibilities of practical use of lyophilisates (packing, packaging, sealing, small fractional doses) have not yet been evaluated. Novoimanin is more convenient to use.

When collecting wild St. John's wort, it is sometimes taken with the roots (which is wrong), removing them later. We have proven the wound-healing effect of roots with local and enteral application, and therefore an increase in the phytomass of raw materials could be of practical importance. The prospects for topical application of powder of herbs and roots of St. John's wort after treatment of the wound with a decoction are rather vague. The results obtained, however, are of theoretical importance, confirming the little-known discovery of myofibroblasts in granulation tissue [12], which are involved in secondary wound contraction. It is obvious that phytopreparations, when applied locally and even when applied enterally, mobilize the protective function of myofibroblasts, leading to a decrease in the area of the wound. Mobilization of the body's defenses, optimization of the reparation and regeneration processes as classical phytoadaptogens, and many other plants - this is the essence of the theory of nonspecifically increased body resistance, created by the great Russian pharmacologist N.V. Lazarev and his school [13]. Myofibroblasts in vitro showed all the properties of smooth muscle organs in relation to the reaction to contractile (acetylcholine, histamine, barium) and muscle relaxant agents (myotropic antispasmodics, M-anticholinergics). Since it is well known that infusions and decoctions of the overwhelming majority of plants, including St. John's wort, act contractilely on isolated smooth muscle organs, it is logical to expect such an effect in case of wound disease. Analysis of the phase process of wound healing allows us to recommend moderate irritative therapy mainly in the 1st and 2nd phases, i.e. before the start of active epithelialization (3rd phase).

conclusions

1) In a comparative assessment of the wound-healing properties of St. John's wort preparations, it was confirmed the effectiveness of novoimanin, the effectiveness of a lyophilized decoction of the herb when applied topically has been established. Dry alcoholic extracts are ineffective.

2) The most effective local application of decoction and powder of St. John's wort, as well as enteral application of a decoction of the herb, which makes it possible to recommend it in practice. Preparations from the roots of St. John's wort were less effective in comparison with the control, but also had a wound healing effect.

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