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STUDY THE ANTI-INFLAMMATORY AND WOUND-HEALING ACTIVITY OF THE DRY EXTRACT OF THE HERB *CYPERUS ESCULENTUS* L.

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Abstract

One of the promising areas for creating safe and effective anti-inflammatory drugs is herbal medicine. In recent years, interest in herbal medicines has grown. Given the above, a valuable medicinal plant earthnut (*Cyperus esculentus* L.) is of great interest today; chufa is a perennial herbaceous plant of *Cyperaceae* family, which is grown to produce edible tubers. Phytochemical studies have shown that earthnut contains a number of important biologically active substances with different pharmacological properties. Therefore, the purpose of our research was to study the anti-inflammatory and wound-healing activity of the dry extract of the herb *Cyperus esculentus* L. Studies of the anti-inflammatory effect of earthnut extract (chufa) in a conditionally effective dose (200 mg/kg) and diclofenac sodium (8 mg/kg i.g.) were performed on a model of a plane wound in rats. Thus, in the model of planar wounds, the presence of a pronounced anti-inflammatory and wound-healing effect was found in the extract from the herb of *Cyperus esculentus* L., which was comparable to the effect of diclofenac sodium. It can be suggested that the extract of chufa herb has moderate anti-inflammatory properties.

Keywords: *Cyperus esculentus* L., tubers extract, hypoglycemic effect, diabetes mellitus, dexamethasone, Arfazetin, Metformin, inulin

Introduction

Today, plants are acknowledged as a form of folk remedies due to their wide therapeutic potential and, in turn, minor side effects and good toleration with patients regardless of age [1-5]. Combinations of different medicinal plants need special attention as such herbal mixtures have a variety of biologically active substances [6-9]. Medicinal plants play a main role in the development of traditional medicine, as well as actual pharmaceuticals [10-12]. Pharmacotherapy increasingly takes into importance the centuries-old experience of folk medicine with the application of phytopreparations [13, 14]. The plant medicines are well tolerable, often used in the fight against many diseases, and have minor side effects [15-19]. Phytotherapy has a number of advantages over traditional therapy with using oral synthetic agents, namely, has a mild pharmacological effect and possibility to be used for long periods of time, is well combined with synthetic drugs, and has a complex activity through many biologically active compounds [20-24]. The methods of treatment using plants have become increasingly common too [25-27].

Nowadays, the issue of optimal healing of skin wounds due to the constant increase in the number of skin defects due to surgeries, burns, injuries, ulcers, etc. is especially urgent, so the problem of creating wound-healing and anti-inflammatory drugs remains important [28]. Wound-healing and anti-inflammatory activity of herbal medicines depends on the content of biologically active substances (flavonoids, hydroxycinnamic acids, polysaccharides, etc.) [29, 30]. One of the promising areas for creating safe and effective anti-inflammatory drugs is herbal medicine. In recent years, interest in herbal medicines has grown.

Given the above, a valuable medicinal plant earthnut (*Cyperus esculentus* L.) is of great interest today; chufa is a perennial herbaceous plant of *Cyperaceae* family, which is grown to produce edible tubers. According to the professional literature, tubers contain 20–35 % of lipids, 12–25 % – sugars, 25–30 % – starch, up to 2–7 % protein, 7–14 % – fiber, trace elements, vitamins [31-33]. Tubers are consumed raw, fried and boiled, they are used to make flour, sugar, starch, alcohol, oil. They are considered promising for the production of children's, dietary and special products, used in medicine for the treatment, prevention of hypertension, diabetes, stress, varicose veins, AIDS and more [34-36]. The leaves are used to make mats, paper, insulation material [31, 36]. Chufa is one of the few species of the family *Cyperaceae* introduced into the culture. In Ukraine, the culture of chufa has been known since the early XX century. Earthnut (*Cyperus esculentus* L.) belongs to a promising, but uncommon and poorly studied culture. Phytochemical studies have shown that earthnut contains a number of important biologically active substances with different pharmacological properties [37-39]. A mandatory characteristic of medicinal plant substances, along with high pharmacological activity, should be their safety.

Therefore, the purpose of our research was to study the anti-inflammatory and wound-healing activity of the dry extract of the herb *Cyperus esculentus* L.

Materials and Methods

Plant Materials

Herb of the *Cyperus esculentus* L. was collected at the experimental sites of the New Cultures Department of M. M. Hryshko National Botanic Garden of the National Academy of Sciences of Ukraine in Kyiv [40]. The aerial part was harvested during a mass flowering period in 2018. The raw material was authenticated by Prof. Dzhamal Rakhmetov [41, 42]. A voucher specimen was deposited in the herbarium at the Department of Pharmacognosy and Medical Botany, TNMU, Ternopil, Ukraine [43-45]. The study plant material was dried using conventional method and stored in paper bags in a dry place [46-49].

Preparation of extract

About 200 g of dried *Cyperus esculentus* L. herb were powdered with the help of a suitable crusher. It was taken in an extractor and extracted using 40 % ethanol as a solvent. The extract was concentrated under vacuum to half under volume and dried at a temperature of 50±2° C [50, 51].

Animal models

The experiments were performed on 21 white Wistar rats weighing 290–320 g. All animals were kept on a standard vivarium diet [52]. The animals were kept in a room having a temperature 20-22 ° C, and relative humidity of 55-70% under 12/12 hour light and dark cycle with standard laboratory diet and water was given ad libitum (feeding was stopped 12 hours before blood sampling) [53-56]. Pharmacological studies have been conducted in accordance with the rules and requirements of the "General Principles for the Work on Animals" approved by the I National Congress on Bioethics (Kyiv, Ukraine, 2001 and agreed with the provisions of the "European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes" (Council of Europe No 123, Strasbourg 1985), and the Law of Ukraine "On the Protection of Animals from Cruelty" of 26.02.2006 [57-60].

The removal of animals from the experiment was carried out under light inhalation anesthesia by decapitation [61].

Study of the anti-inflammatory and wound-healing activity of Cyperus esculentus L. herb extract

Studies of the anti-inflammatory (antiphlogogenic) effect of earthnut extract (chufa) in a conditionally effective dose (200 mg/kg) and diclofenac sodium (8 mg/kg i.g.) were performed on a model of a plane wound in rats.

The study was performed on 21 rats weighing 290–320 g, which were divided into 3 groups of 7 individuals each. All animals were inflicted with planar wounds, after which, starting from day 1, purified water (untreated control), studied dry extract of earthnut (200 mg/kg) and diclofenac sodium (8 mg/kg) were administered daily intragastrically. Simulating of planar wounds was performed in accordance with the guidelines [62]. Rats underwent general anesthesia (ketamine, 10 mg/kg), epilation was performed in the middle of the back, a square measuring 2x2 cm was marked, after which a piece of skin with subcutaneous fat with a total area of 400 mm^2 was cut with scissors. The wound remained open throughout the observation period. Visual assessment of the wound condition and skin edges around the wound was performed, and the wound area was measured by applying a transparent film with a millimeter mark. Observations were performed for 28 days, recorded the number of animals with complete wound defect healing in each period of the study, calculated the rate of wound healing. The presence of antiphlogogenic action was evaluated by the reduction of visual signs of inflammation of the wound edges, as well as by the acceleration of complete closure of the skin defect in comparison with animals without treatment.

Statistical analysis

All the tests were carried out five times. Obtained results were presented as mean ± SEM [63-65]. Results were determined using Statistica v 10.0 (StatSoft I nc.) program. Statistical significance of differences between mean values was assessed by the Student's t-test [66, 67]. The level of significance was mounted at *p<0.05 [68,69].

Results and Discussion

As a result of the study, it was found that signs of inflammatory reaction: redness, swelling of the wound edges, some purulent foci developed in the animals of the control group on day 2–5. The wound was covered with crust, which is easily damaged, it exuded liquid exudate. There was a slight increase in the wound defect (by 1.6 %, 5.1 % and 3.2 % on days 2, 3 and 4 after the experimental injury). Beginning from day 5, gradual wound healing was recorded. On day 28, all wound defects were completely epithelialized.

In animals treated with chufa extract, the macroscopic signs of a local inflammatory reaction in the early period were much less pronounced: the wound edges were less swollen, redness and exudation were observed in only 3 of 7 animals. No increase in the area of the wound defect was detected, and from day 3 after wound simulation, its area in treated animals was statistically significantly smaller (28.9 %) compared to baseline. On day 21, in 3 rats complete wound healing was recorded, in other animals the average area of skin defect was closed by 99.6 %. All this indicates in favor of the existing anti-inflammatory and wound-healing effects in the studied extract of earthnut.

In rats treated with the reference non-steroidal anti-inflammatory drug sodium diclofenac in its average effective dose, no signs of inflammation were found in the area of the plane wound (wound edges were smooth, not swollen, no redness, no exudate), the wound area began to change unfavorably. already from day 2, and on day 3 and the rest of the observation period it decreased statistically relative to the initial level. When analyzing the rate of wound healing, it should be noted that on days 2, 3, 4, 5, 7 and 14 in this group it exceeded the same indicator in the group of the studied extract, but later healing slowed down, and on day 21 its area decreased by only 77.8 % relative to the initial level. On day 28, only one animal had the wound completely closed and the average wound area decreased by an average of 96.6 %, which may be due to the antiproliferative effect of diclofenac sodium (Table 1).

Conclusions

Thus, in the model of planar wounds, the presence of a pronounced anti-inflammatory and wound-healing effect was found in the extract from the herb of earthnut, which was comparable to the effect of diclofenac sodium. It can be suggested that the extract of chufa herb has moderate anti-inflammatory properties. And although the anti-inflammatory effect of the studied extract is inferior to diclofenac sodium, but the level of toxicity, significantly exceeds it, because it belongs to class toxicity VI, almost harmless substances. The use of earthnut extract consisting of anti-inflammatory therapy will reduce the dose and reduce the side effects of classic nonsteroidal anti-inflammatory drugs.

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Table 1. Dynamics of planimetric parameters in rats with planar wounds in the treatment with earthnut extract and diclofenac sodium (M ± m, n = 7)

Observation period	Control group (without treatment)		Earthnut extract herb (200 mg/kg)		Diclofenac sodium (8 mkg)	
	Wound area, mm^2	Rapid healing rate	Wound area, mm^2	Rapid healing rate	Wound area, mm^2	Rapid healing rate
Initial values	391.7±7.2	0	399.3±4.7	0	398.9±5.5	0
Day 2	398.0±7.5	-0.016	388.4±3.7	0.027	383.1±5.7	0.039
Day 3	411.6±4.5	-0.051	346.1±2.3*	0.133	336.3±4.8*	0.157
Day 4	404.1±7.7	-0.032	284.0±6.0*	0.289	272.6±5.6*	0.317
Day 5	386.1±7.3	0.014	234.3±4.6*	0.413	210.0±3.0*	0.473
Day 7	353.4±3.6*	0.098	181.0±4.4*	0.547	143.6±6.2*	0.639
Day 14	180.6±14.7*	0.539	110.0±6.9*	0.724	108.1±3.1*	0.729
Day 21	100.7±15.7*	0.753	2.4±0.9*	0.994	88.7±4.6*	0.778
Day 28	0.0±0.0*	1.0	0.0±0.0*	1.0	13.4±2.6*	0.966