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INVESTIGATION OF THE ANTI-INFLAMMATORY EFFECT OF THE EXTRACTS FROM THE LEAVES AND RHIZOMES WITH ROOTS OF *ANGELICA ARCHANGELICA*

Introduction. *One of the promising areas for creating safe and effective anti-inflammatory drugs is herbal medicine. According to the literature, plants of the genus Angelica have been used as herbal medicines in all cultures around the world. Given the above, a valuable medicinal plant Angelica archangelica has been used in folk medicine for the treatment of gastrointestinal problems. However, it is established that angelica also possesses anxiolytic, hepatoprotective, antimicrobial, and antioxidant effects. Phytochemical studies have shown that Angelica archangelica contains many important biologically active substances with different pharmacological properties.*

The aim of the study *was to investigate the anti-inflammatory effect using extracts of the leaves and rhizomes with roots prepared from Angelica archangelica.*

Materials and methods of research. *The study of anti-inflammatory action in the model of carrageenan edema in the foot of rats was performed on 47 rats of the Wistar line weighing 150-180 g. The volume of paws was measured using a Plethysmometer (Ugo Basile, Italy), anti-exudative activity of the studied extracts was determined by the degree of swelling subsidence in experimental animals compared with control.*

Research results and their discussion. *With prophylactic administration of extracts from the leaves and rhizomes with roots Angelica archangelica in the dose range of 100–150 mg/kg, a decrease in paw edema was observed in rats when using the test samples at these doses. Analysis of the obtained data showed that the studied extract of the leaves of Angelica archangelica at a dose of 150 mg/kg had a pronounced anti-inflammatory effect. The effectiveness of the extract in the first hours of the dynamics of inflammation suggests its effect on the mediators of the acute phase: histamine, serotonin, and leukotrienes.*

Conclusions. *Statistically significant data on the pharmacological anti-inflammatory activity of extracts from Angelica archangelica leaves and rhizomes with roots in the experiment on rats were determined. Thus, an extract of Angelica archangelica leaves at a dose of 150 mg/kg had a pronounced anti-inflammatory effect in a model of acute paw inflammation in rats caused by carrageenan.*

Key words: *Angelica archangelica, leaves, rhizomes with roots, extracts, anti-inflammatory effect.*

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ДОСЛІДЖЕННЯ ПРОТИЗАПАЛЬНОЇ ДІЇ ЕКСТРАКТІВ З ЛИСТЯ ТА КОРЕНЕВИЩ І КОРЕНІВ ДЯГЕЛЮ ЛІКАРСЬКОГО

Актуальність. *Одним із перспективних напрямків створення безпечних і ефективних протизапальних засобів є фітотерапія. За даними літератури, рослини роду Дягель використовувалися як рослинні лікарські засоби в усіх культурах світу. Враховуючи вищесказане, цінною лікарською рослиною даного роду є дягель лікарський, який використовується в народній медицині для лікування захворювань шлунково-кишкового тракту. Проте, встановлено, що дягель лікарський має також анксіолітичну, гепатопротекторну, антимікробну та антиоксидантну дії. Фітохімічні дослідження показали, що дана рослина містить багато важливих біологічно активних речовин з різними фармакологічними властивостями.*

Метою дослідження *було вивчення протизапальної дії екстрактів з листя та кореневищ і коренів дягелю лікарського.*

Матеріали та методи дослідження. *Вивчення протизапальної дії на моделі карагенінового набряку стопи у щурів проводили на 47 щурах лінії Wistar масою 150–180 г. Об'єм лапок вимірювали за допомогою плетизмометра (Ugo Basile, Італія), антиексудативну активність досліджуваних екстрактів визначали за ступенем спадання набряку у дослідних тварин порівняно з контролем.*

Результати дослідження та їх обговорення. *При профілактичному введенні екстрактів з листків та кореневищ з коренями дягелю лікарського в діапазоні доз 100–150 мг/кг спостерігалося зменшення набряку лапи у щурів при застосуванні досліджуваних зразків у цих дозах. Аналіз отриманих даних показав, що досліджуваний екстракт з листків дягелю лікарського у дозі 150 мг/кг мав виражену протизапальну дію. Ефективність екстракту в перші години динаміки запалення свідчить про його вплив на медіатори гострої фази: гістаміну, серотоніну та лейкотрієнів.*

Висновки. *Визначено статистично достовірні дані щодо фармакологічної протизапальної активності екстрактів з листків та кореневищ і коренів дягелю лікарського в експерименті на щурах. Встановлено, що екстракт з листя дягелю лікарського в дозі 150 мг/кг мав виражену протизапальну дію на моделі гострого запалення лап у щурів, спричиненого карагеніном.*

Ключові слова: *дягель лікарський, листки, кореневища і корені, екстракти, протизапальна дія.*

Introduction. Phytotherapy takes into account the knowledge of folk medicine with the use of herbal drugs as monotherapy and in complex with synthetic drugs (Budniak, 2021a). Plants are sources of biologically active substances, which are used both for the prevention and treatment of various diseases of the human body (Feshchenko, 2021). Today, the issue of optimal healing of skin wounds due to the constant increase in the number of skin defects due to surgeries, burns, and injuries, is especially urgent, so the problem of creating wound-healing and anti-inflammatory drugs remains important. Wound-healing and anti-inflammatory activity of herbal medicines depends on the content of biologically active substances (flavonoids, hydroxycinnamic acids, polysaccharides, etc.) (Marchyshyn, 2021b).

According to the literature, plants of the genus *Angelica* have been used as herbal medicines in all cultures around the world. *Angelica archangelica* is found in the inner valleys of the Himalayas (viz. Kashmir, Chamba, Kullu, Pangi, Lahaul and Kinnaur). *Angelaca archangelica* has been used widely in folk medicine; it was employed as a medicinal herb in Nordic countries (where it was cultivated during the Middle Ages and exported to other parts of Europe) (Sigurdsson, 2004; Budniak, 2022). The most characteristic secondary metabolites of *Angelica archangelica* are essential oils and furanocoumarins, both of which are more abundant in the roots and seeds than in the leaves. The whole plant has been used as a vegetable. In folk medicine *Angelica archangelica* has been used for respiratory catarrh, asthma, flatulent dyspepsia, anorexia nervosa, rheumatic diseases and peripheral vascular diseases (Sigurdsson, 2005; Sowndhararajan 2017).

Angelica archangelica has been used in folk medicine and as a food ingredient. The rhizome with roots is used for the treatment of gastrointestinal problems. However, it is established that angelica also possesses anxiolytic, hepatoprotective, antimicrobial, and antioxidant effects (Yeh, 2003; Prakash, 2015).

Angelica archangelica has many chemical compositions, such as coumarins and essential oil, which determine to the plant's pharmacology activities. Furanocoumarins are components found in large quantities in *Angelica archangelica* and are responsible for antiviral, antibacterial, anti-inflammatory, antidepressant, hepatoprotective, and other actions (Acimovic, 2022; Kaur, 2020; Mišic, 2009).

The aim of the study was to investigate the anti-inflammatory effect using extracts of the leaves and rhizomes with roots prepared from *Angelica archangelica*.

Materials and methods. *Angelica archangelica* leaves and rhizomes with roots were collected in the Ternopil region (Ukraine) in 2021. The identity of the plant was verified by Prof. Svitlana Marchyshyn Department of Pharmacognosy and Medical Botany (TNMU, Ternopil, Ukraine) (Budniak, 2021b).

Preparation of extracts. Approximately 500 g of dried *Archangel angelica* leaves and rhizomes with

roots were ground into powder using a suitable crusher. It was placed in an extractor and extracted using 70% ethanol as a solvent. The extracts were concentrated in a vacuum to half the volume and dried at a temperature of 50±2ºC (Marchyshyn, 2021a).

The study of the anti-inflammatory effect of extracts of *Angelica archangelica* leaves and rhizomes with roots was carried out according to the methodological recommendations of the State Expert Center of the Ministry of Health of Ukraine (Drogovoz, 2001).

Studies of the anti-inflammatory effect of *Angelica archangelica* leaves and rhizomes with root extracts in effective doses of 100 mg/kg and 150 mg/kg were performed on a model of a plane wound in rats. As reference drugs were used diclofenac sodium (8 mg/kg), and quercetin in the form of the drug "Quertin" (PJSC Borshchagivskyi HFZ, Ukraine) in an equivalent dose of 20 mg/kg.

The study was performed on 47 rats of the Wistar line weighing 150-180 g. All animals were inflicted with planar wounds, after which, starting from day 1, purified water (untreated control), studied extracts of *Angelica archangelica* leaves and rhizomes with roots (100 mg/kg and 150 mg/kg), diclofenac sodium (8 mg/kg), and quercetin (20 mg/kg) were administered daily intragastrically. Simulating of planar wounds was performed according to the guidelines caused by subplantar administration of 1% carrageenan solution manufactured by Sigma (USA) (Slobodianiuk, 2021).

The volume of paws was measured using a plethysmometer (Ugo Basile, Italy), and the anti-exudative activity of the studied extracts was determined by the degree of reduction of edema in the experimental animals compared to the control.

Research results and discussion. Given that, *Angelica archangelica* contains a significant amount of compounds of phenolic nature, the anti-inflammatory activity of the obtained extracts from the studied leaves and rhizomes with roots was determined. The results of the study are shown in table.

Thus, the anti-exudative activity of the substance on the model of carrageenan edema indicates its effect on the kinin system, histamine, and prostaglandins. Our research showed that the highest degree of anti-edematous activity in the model of carrageenan edema in rats was found when the animals were given an extract of angelica leaves compared to the rhizomes with roots extract.

In the result of the experiment, it was determined that the comparison drug – sodium diclofenac (8 mg/kg) had a persistent anti-inflammatory effect starting from the first hour of the experiment. The most pronounced anti-inflammatory activity was observed after 3 hours during the release of prostaglandins, which confirmed the anti-cyclooxygenase mechanism of action of the drug. On average, the anti-inflammatory activity of the comparison drug was 50% (table).

For the prophylactic administration of the extract from *Angelica archangelica* rhizomes with roots in the dose range of 100-150 mg/kg, a reduction in paw edema in rats was observed only when the tested sample was used at a dose of 150 mg/kg. In addition, an expressed anti-inflammatory effect was observed in the first 2 hours of the experiment and was at the level of 22.9%. In the later periods of the study, the effectiveness of the sample decreased (table 1).

With the prophylactic use of an extract from the leaves of *Angelica archangelica* in the dose range of 100-150 mg/kg, a decrease in paw edema was observed in rats within

Table 1

Dynamics of anti-inflammatory effect of extracts from *Angelica archangelica* leaves and rhizomes with roots on the model of carrageenan edema in rats (M±m, n=5-7)

The name of the drug	Dosemg/kg	the volume of a healthy limb (mm3)	Observation period					
			60 minutes		120 minutes		180 minutes	
			the volume of the swollen limb (mm3)	AIA, %	the volume of the swollen limb (mm3)	AIA, %	the volume of the swollen limb (mm3)	AIA, %
Control pathology	-	355,95±41,68	460,00±47,83*	-	571,13±42,98*	-	682,26±48,64*	-
ELA	100 mg/kg	310,67±27,74	386,81±27,84	28,9	440,9±19,07*	39,5	455,16±24,98*	55,7
ELA	150 mg/kg	316,11±26,01	404,6±29,30*	17,4	441,37±31,51*	41,8	440,23±26,40*	61,9
ERA	100 mg/kg	334,05±45,80	427,98±41,04*	12,3	488,68±52,50*	28,1	540,20±53,37*	36,8
ERA	150 mg/kg	338,00±41,25	434,33±46,79*	10,1	503,71±44,08*	22,9	512,14±59,91*	46,6
Diclofenac sodium	8 mg/kg	400,37±24,35	489,26±23,08*	19,9	522,41±20,1*7	43,3	494,3±29,78*	71,2
Quercetin	20 mg/kg	374,55±40,65	459,26±42,00	20,9	487,15±31,80*	47,7	552,27±51,16*	45,5

Notes: ELA – the extract from *Angelica archangelica* leaves;

ERA – the extract from *Angelica archangelica* rhizomes with roots;

AIA – anti-inflammatory activity in %;

* – the level of statistical significance difference ($p<0.05$) between healthy and swollen limbs.

60 minutes (table). The dynamics of the development of exudation on the carrageenan-induced edema model depends on the action of various mediators, the release of which occurs at different times of the experiment. Thus, kinins are released in the first 30 minutes of carrageenan inflammation, histamine and serotonin – after 1-1.5 hours, leukotrienes – within 1.5-2 hours, and prostaglandins – after 2-5 hours of the experiment (Di Rosa, 1971).

Conclusions

Statistically significant data on the pharmacological anti-inflammatory activity of extracts from *Angelica archangelica* leaves and rhizomes with roots in the experiment on rats were determined.

So, the extract of *Archangel angelica* leaves at a dose of 150 mg/kg had a pronounced anti-inflammatory effect on the model of acute paw inflammation in rats caused by carrageenan. As for the effectiveness of the studied extract in the first hours of the dynamics of inflammation, this indicates its effect on the mediators of the acute phase of inflammation, namely, histamine, serotonin, and leukotrienes.

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