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EXPERIMENTAL STUDY OF THE PHARMACOLOGICAL ACTIVITY OF CAPSULES “VOMICIN”

Hop is a valuable medicinal plant. Flavonoids, vitamins, hormones contained in the plant cause a wide spectrum of pharmacological activity of preparations from its raw materials. Following a review of the literature it has been concluded that extracts of hop cones were appropriate for treatment of inflammatory diseases, namely diseases of the gastrointestinal tract. Thus, the aim of our research was to experimentally study anti-inflammatory and anti-ulcer activity of the encapsulated dosage form with a dry hop cones extract codenamed “Vomicin”. Their specific activity has been investigated and it allows to predict Vomicin use as a prophylactic and therapeutic agent in the complex therapy of gastric and duodenal ulcer.

Key words: peptic ulcer; common hop; dry extract

INTRODUCTION

Hop (*Humulus lupulus* L.) is a medical plant that is widely used in both traditional and folk medicine as well as in homeopathy. Hop blossom clusters – female “cones” (*Strobuli Humuli lupuli* or *Strobuli Lupuli*) are the most widely used ones for medical purposes [2].

Hop is a valuable medical plant. Flavonoids, hormones and vitamins contained in the plant provide anti-inflammatory, anti-ulcer, capillary-strengthening, hyposensitization and analgesic properties of an extract from hop cones. Anti-inflammatory, analgesic, bactericidal and anti-allergenic properties of galenic plants provide the therapeutic effectiveness in skin and mucous membrane diseases accompanied with inflammatory affections, allergic reactions, pruritus and other symptoms [3, 7].

After studying the literature concerning the etiology, pathogenesis and treatment of gastrointestinal tract ulcer, we created an experimental medicinal agent in the form of solid gelatine capsules containing a dry hop cones extract under the codename “Vomicin”. Thus, the aim of our research is to study experimentally the anti-inflammatory and anti-ulcer activity of the capsulated pharmaceutical form containing a dry hop cones extract.

MATERIALS AND METHODS

Evaluation of anti-inflammatory properties of a dry hop cones extract (DHCE) was conducted in comparison with diclofenac sodium in dose of 8 mg/kg and plant medicine altan on the model of acute exudative carragenine and formalin inflammation of a rat's paw [5].

Analgesic activity of a dry hop cones extract was evaluated by the ability of the medicine to reduce the number of “writhes” in the investigated group in comparison with the control one and expressed as a percentage. There were 5 white rats weighing 160-200 g in each group of the experiment. An hour before the research the animals of the first control group got distilled water intragastrically, animals of the second group got the comparator – analginum – in its effective dose of 55 mg/kg, animals of the third group got altan and of the fourth one – a DHCE in dose of 15 mg/kg intragastrically. “Writhes” were caused by injecting the 0.75 % aqueous solution of acetic acid intra-abdominally in dose of 0.1 ml per 10 g of animal body weight. Calculation of the “writhes” number was being conducted 20 minutes after the intra-abdominal injection of the acetic acid during the next 30 minutes.

An experiment on studying the effect of the extract on motion activity of gastrointestinal tract of healthy animals was carried out by the method of Sticknay J. S. and the co-authors. White mice weighing 20-22 g had been kept on a starvation diet for 20 hours but without any restriction of water intake. The group of the experimental animals got the investigated medicine in dose of 15 mg/kg orally, the control group of animals got an equivalent amount of water. An hour after the oral ingestion of the medicine, each animal got 0.3 ml of contrast mass orally. 40 minutes later the animals were taken out of the experiment. Total length of the intestine was measured as well as the part covered by the contrast mass along the intestine of each experimental animal in comparison with the group of control animals. As an integral index that characterizes the power of intestinal peristalsis the per-

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Table 1

**ANTI-EXUDATIVE ACTIVITY ON THE MODEL
OF CARRAGENINE EDEMA OF A RAT'S PAW
(M(m), n = 5)**

| Experiment conditions | | Results |
|----------------------------|--------------|--------------|
| Control pathology | ΔV , | 37.6 ± 0.9 |
| Hop extract, 15 mg/kg | ΔV , | 24.4 ± 0.73* |
| | AiA, % | 36.2 % |
| Diclofenac sodium, 8 mg/kg | ΔV , | 19.8 ± 0.64* |
| | AiA, % | 47.3 % |
| Altan, 1 mg/kg | ΔV , | 26.4 ± 0.82* |
| | AiA, % | 29.8 % |

Note: * - deviation is valid in regard to control, $P \leq 0.05$;
AiA - anti-inflammatory activity in comparison with control;
 ΔV - the difference between the edematic and non-edematic paw.

centage of the length of the intestine covered by the contrast mass to the total length of the intestine was taken.

To study the anti-ulcer activity of a hop extract, white rats weighing 180-210 g were used. The animals had been kept on a starvation diet for 12 hours but with free access to water. Gastric ulcer was caused by a single intragastrical injection of prednisolone in dose of 20 mg/kg, dissolved in 80% ethanol in the amount of 0.8 ml per 100 g of body weight. As a comparator altan was used. The hop cones extract in dose of 15 mg/kg and the comparator were injected an hour before the gastric ulcer modeling. 24 hours later all animals were taken out of the experiment. The ulcer area was calculated in numbers (S_u), as well as the percent of animals having ulcer (A_u) and the ulcer index (UI) [4].

Gradation in numbers of ulcer surface was carried out according to the total area of ulcer defects in the following was: area of 1-2 mm² was equivalent to 1 point, 3-5 mm² - 5 points, 6-10 mm² - 10 points and above 10 mm² - 15 points. In case of the animals death from gastric perforation the ulcer area was evaluated as 15 points. We also studied the anti-ulcer activity of capsules with a dry hop cones extract on a model of rats acetylsalicylic ulcer.

While conducting the anti-exudative, analgesic and anti-ulcer activity screening, we discovered that a DHCE in an investigated dose showed a diuretic action. That is why the diuretic activity of capsules containing the extract was studied using 6 rats of both sexes weighing 120-180 g by the method of Berchin E. [1]. The animals had been kept on a vivarium diet. The animals of the first (control) group were injected with water, the animals of the second group were orally ingestioned with the hop extract in the form of aqueous solution in dose of 15 mg/kg and the third group of animals got a comparator - "Nephrophytum" tea in dose of 15 mg/kg. Water load accounted 3% of an animal mass. The amount of urine was taken into account only 4 hours after the last ingestion of the investigated complexes.

Table 2

**HOP EXTRACT ANTI-EXUDATIVE ACTIVITY
ON THE MODEL OF FORMALIN EDEMA
OF A RAT'S PAW (M(m), n = 8)**

| Experiment conditions | | Results |
|----------------------------|--------------|-------------|
| Control pathology | ΔV , | 15.8 ± 1.56 |
| Hop extract, 15 mg/kg | ΔV , | 6.8 ± 1.04* |
| | AiA, % | 56.9 % |
| Diclofenac sodium, 8 mg/kg | ΔV , | 8.4 ± 1.02* |
| | AiA, % | 46.8 % |
| Altan, 1 mg/kg | ΔV , | 7.4 ± 0.91* |
| | AiA, % | 53.2 % |

Note: * - deviation is valid in regard to control, $P \leq 0.05$;
AiA - anti-inflammatory activity in comparison with control;
 ΔV - the difference between the edematic and non-edematic paw.

Table 3

**HOP EXTRACT ANALGESIC ACTIVITY ON THE
MODEL OF ACETIC-ACID "WRITHES" (M(m), n = 5)**

| Type of the experiment | Dose, mg/kg | Number of "writhes" within 30 min | Analgesic activity, % |
|------------------------|-------------|-----------------------------------|-----------------------|
| Control | - | 63.7 ± 0.91 | - |
| Analginum | 55 | 31.01 ± 0.61 | 51.3 % |
| Altan | 1 | 40.2 ± 0.34 | 36.9 % |
| Hop extract | 15 | 33.6 ± 0.53 | 47.3 % |

Note: $P < 0.05$ in comparison with control.

RESULTS AND DISCUSSION

Results of the experiments on the evaluation of anti-inflammatory properties of the medicine containing a dry hop cones extract on the model of acute exudative carragenine inflammation of a rat's paw are shown in Table 1.

The obtained data indicate that the extract shows anti-inflammatory activity and inhibits the edema development by 36.2%. Having conducted the comparative analysis with such reference-medicine as synthetics of diclofenac sodium and plant medicine altan, it should be noted that the anti-inflammatory effect of the extract in dose of 15 mg/kg (36.2%) is a little lower than the NSAID diclofenac sodium has, but is 1.2 times greater than the anti-inflammatory activity of the plant medicine Altan.

Investigation results of the anti-exudative action of capsules containing extract are shown in Table 2.

Table 2 shows on the model of formalin inflammation of a rat's paw that the investigated medicine in dose of 15 mg/kg inhibits the development of inflammation by 56.9% that is 1.3 times greater than diclofenac sodium activity and 1.1 times greater than that of Altan.

Results of the conducted experiment on studying the analgesic activity of capsules "Vomicin" are shown in Table 3.

Table 4

IMPACT OF HOP EXTRACT ON GASTROINTESTINAL TRACT MOTION ACTIVITY OF HEALTHY ANIMALS

| Experiment conditions | Lcc, sm | Li, sm | Lcc/Li × 100 % |
|-----------------------|------------|------------|----------------|
| Control | 32.8 ± 2.6 | 61.0 ± 3.0 | 53.48 ± 1.74 |
| Hop extract | 30.4 ± 1.8 | 61.4 ± 2.8 | 49.54 ± 2.32 |

Note: n = 6, P < 0.5.

Table 5

DETERMINATION OF ANTI-ULCER ACTIVITY OF A HOP EXTRACT

| Experiment conditions | Condition of MCS | | |
|---------------------------|--------------------------------------|----------------|------|
| | S _U , Sx ± S _U | A _U | UI |
| Control group (pathology) | 15.4 ± 3.0 | 100 % | 15.4 |
| Hop extract | 4.6 ± 1.2*/** | 69 % | 3.85 |
| Altan | 7.6 ± 0.8* | 75 % | 5.7 |

Note: * - deviation is valid in regard to the control pathology group; ** - deviation is valid in regard to comparator.

The experimental data indicate that analginum, altan and hop extract in the investigated doses significantly reduce in regard to control the number of "writhes" in rats. Moreover, the analgesic activity of the extract in dose of 15 mg/kg is 1.3 times greater than that of the plant comparator altan and is not inferior to synthetic analginum.

Results of the experiment on studying the impact of a hop cones extract on gastrointestinal tract functional activity of healthy animals is shown in Table 4.

Analyzing the data we may say that an extract does not have a significant impact on gastrointestinal motor activity of healthy animals [6].

Results of the experiment on determining the anti-ulcer activity of the medicine containing hop are shown in Table 5.

Under macroscopic examining of rat's stomachs the lack of abdominal swellings was observed, rugosity was slightly different from the one in the intact group, however, hyperemia was noted as well as petechial hemorrhages and superficial ulcer defects were observed. Under the influence of hop extract the ulcer index gets 4 times lower in comparison with the group of control pathology. At the same time the extract in dose of 15 mg/kg shows a significant anti-ulcer activity and 1.4 times exceeds the comparator activity.

Results of the experiment on studying the anti-ulcer activity of "Vomicin" capsules on the model of rats subchronic acetylsalicylic ulcer are shown in Table 6.

Analyzing the obtained results we may say that the use of hop extract led to the 2.6 times decrease of number of animals with ulcers in comparison with the control pathology group and 5.3 times decrease of Pauls index. On the model of acetylsalicylic ulcer in rats the anti-ulcer activity of the extract made up 52.9 %. Thus, the

Table 6

DETERMINATION OF ANTI-ULCER ACTIVITY OF A HOP EXTRACT ON THE MODEL OF ACETYSALICYLIC ULCER IN RATS

| Experiment conditions | Number of animals with ulcer | Average number of ulcers per 1 animal | UI (Pauls index) | AuA, % |
|---------------------------|------------------------------|---------------------------------------|------------------|--------|
| Control group (pathology) | 100 % | 12.70 | 12.7 | |
| Hop extract | 37.5 % | 0.64* | 0.24 | 52.9 % |
| Altan | 45.7 % | 0.98* | 0.44 | 28.8 % |

Note: * - differences are valid in comparison with the control group; ** - differences are valid in comparison with altan.

Table 7

IMPACT OF HOP EXTRACT ON KIDNEYS EXCRETORY FUNCTION (M(m), n = 6)

| Type of the experiment | Dose, mg/kg | Diuresis within 4 hours, ml/100 g | Activity in % per control |
|------------------------|-------------|-----------------------------------|---------------------------|
| Control | - | 1.73 ± 0.13 | 100 |
| Hop extract | 15 | 4.9 ± 0.28* | 183.2 % |
| "Nephrophytum" | 15 | 2.81 ± 0.28* | 62.4 % |

Note: * - P < 0.05 in regard to control.

hop extract in dose of 15 mg/kg shows apparent anti-inflammatory, analgesic and anti-ulcer activity.

Results of the experiment on studying diuretic activity of the extract are shown in Table 7.

The obtained data show that in comparison with the animals from control group and the ones that got "Nephrophytum", diuresis in the group of animals that got the investigated medicine was 2.8 and 1.7 times higher, respectively.

CONCLUSIONS

Results of the conducted screening research of the pharmacological activity of capsules "Vomicin" show that the investigated medicine possesses a number of pharmacological properties that characterize it as an anti-inflammatory, analgesic, anti-ulcer and diuretic agent. Our research shows that the investigated medicine does not influence the gastrointestinal tract motion activity of healthy animals and therefore does not have a negative impact on gastrointestinal tract motility.

Thus, the investigated experimental medicine due to its proven pharmacological activity is a very promising one for application in gastroenterology, particularly as a prophylactic and therapeutic agent in the complex therapy of gastric and duodenal ulcer.

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ЭКСПЕРИМЕНТАЛЬНОЕ ИЗУЧЕНИЕ ФАРМАКОЛОГИЧЕСКОЙ АКТИВНОСТИ КАПСУЛ «ВОМИЦИН»

Хмель – ценное лекарственное растение. Содержащиеся в растении флавоноиды, гормоны и витамины обуславливают широкий спектр фармакологической активности препаратов из его сырья. После обзора литературных источников был сделан вывод о целесообразности применения вытяжек из шишек хмеля для лечения воспалительных заболеваний, а именно заболеваний ЖКТ. Таким образом, целью наших исследований стало экспериментальное изучение противовоспалительной и противоязвенной активности капсулированной лекарственной формы с сухим экстрактом шишек хмеля обыкновенного под условным названием «Вомицин». Была исследована их специфическая активность, что позволяет прогнозировать применение Вомицина в качестве профилактического и лечебного средства в комплексной терапии язвенной болезни желудка и двенадцатиперстной кишки.

Ключевые слова: язва желудка и двенадцатиперстной кишки; хмель обыкновенный; сухой экстракт

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ЕКСПЕРИМЕНТАЛЬНЕ ВИВЧЕННЯ ФАРМАКОЛОГІЧНОЇ АКТИВНОСТІ КАПСУЛ «ВОМІЦИН»

Хміль – цінна лікарська рослина. Флавоноїди, гормони і вітаміни, які містяться в рослині, зумовлюють широкий спектр фармакологічної активності препаратів з її сировини. Після огляду літературних джерел було зроблено висновок про доцільність застосування витяжок з шишок хмелю для лікування запальних захворювань, а саме захворювань ШКТ. Таким чином, метою наших досліджень стало експериментальне вивчення протизапальної та противиразкової активності капсульованої лікарської форми з сухим екстрактом шишок хмелю звичайного під умовною назвою «Воміцин». Була досліджена їх специфічна активність, що дозволяє прогнозувати застосування Воміцину як профілактичного і лікувального засобу у комплексній терапії виразкової хвороби шлунка та дванадцятипалої кишки.

Ключові слова: виразка шлунка та дванадцятипалої кишки; хміль звичайний; сухий екстракт

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