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**NON-STEROIDAL ANTI-INFLAMMATORY
DRUGS "CELEXIB" AND "DIBUTALIASTIN" EFFICACY IN INDUCED
INFLAMMATION IN RATS**

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Abstract. *Non-steroid Anti-Inflammatory Drugs (NSAIDs) are the most widely used analgesics in veterinary medicine. Induced inflammation in laboratory animals is one of the most common methods to determine the anti-inflammatory and analgesic properties of new drugs. We studied the anti-inflammatory properties of the drugs "Celecoxib", with the celecoxib (100 mg in 1 ml) active pharmaceutical ingredient and "Dibutalastin" ointment (1 g of the drug contains 61.0 mg of methyl salicylate). The studies resulted in the following, after supplantation of 1% carrageenan solution into laboratory rats, animals of the control and experimental groups developed an acute inflammatory process (swelling, increased volume of the paw, hyperemia, and tenderness). The most significant changes were observed in rats of all groups three hours after carrageenan administration. It was found that rats of the control group that did not receive anti-inflammatory drugs had the volume of the paw increased on the 4th and 6th hours of the experiment. The animals of experimental E₁ and E₂ groups, after 4 hours showed decreased intensity of the inflammatory process under the influence of "Celecoxib" and "Diclofenac" anti-inflammation drugs. The volume of the paw was 25.6, 8.2, and 14.3% less in the E₁, and E₂ groups of animals, compared to the period before induction of inflammation. By the 6th hour of the study, the animals of group E₁ had virtually no visible clinical signs of the inflammatory process caused by carrageenan, which confirms the anti-inflammation effectiveness of the "Celecoxib" drug. It was found that inflammation induced by allyl isothiocyanate and formalin in rats, the investigated drug "Dibutalastin" ointment also showed peculiar analgesic properties. It was observed that its analgesic and anti-inflammatory effects were like the reference drug "Dolaren-gel".*

Keywords: Celecoxib, Dibutalastin, carrageenan-induced inflammation, white rats, analgetic and anti-inflammatory effect

Increasing the effectiveness of treatment of diseases in animals that occur with inflammation is one of the challenges in veterinary medicine.

Inflammation is connected with a range of biochemical and immunological processes, their control is conditioned by a large number of humoral mediators, among which a prominent place belongs to low-molecular-weight proteins called cytokines.

Pain, as an unpleasant sensation accompanying the inflammation process, often performs an alarming function, warning the body of danger and protecting it from possible damage. Special neural structures – nociceptors are responsible for the perception and analysis of the pain signals in animal bodies, they are mainly sensitive to pathological marks or to marks of the pathologies after prolonged exposure. The pain syndromes are associated with the activation of nociceptive receptors in trauma, inflammation, or damage to the structures

of the central or peripheral nervous systems involved in the transportation of pain signals (Bennet and Villa, 2000; Laporte et al., 2004).

Non-steroid Anti-Inflammatory Drugs (NSAIDs) are the most widely used analgesics in veterinary medicine. After the discovery of preferential and selective cyclooxygenase – 1, 2 inhibitors (COX-1, -2), these inhibitors became even more extended due to their anti-inflammatory, analgesic, and antipyretic effects (Brune et al., 2015; Blanca-Lopez et al., 2019).

More than 1000 types of drugs containing NSAIDs, or their active ingredients are used in humane and veterinary medicine. They have been primary analgesics in pain therapy in animals' musculoskeletal disorders for many years. Typically, NSAIDs exert their analgesic effect by inhibiting the cyclooxygenase (COX) enzyme, which is involved in the synthesis of prostaglandins from arachidonic acid in animal bodies. The discovery of selective COX-2 inhibitors was caused by the adverse effects (gastrointestinal and renal dysfunction) of COX-1 (Kukanich et al., 2012; Salazar Alcala et al., 2019). Modern drugs of this group include meloxicam, nimesulide, diclofenac, ibuprofen, ketoprofen, etc. Recently, newer NSAIDs under the 'coxib' generic name (celecoxib, cimicoxib, deracoxib, firocoxib, mavacoxib, robenacoxib, etc.) have been approved and appeared on the pharmaceutical market (Reinoso et al., 2001). It is believed that the new anti-inflammatory drugs should be focused not so much on improving efficacy but on enhancing their safety, since in Ukraine NSAIDs are the cause of 50% of all complications from pharmacotherapy.

The adverse effects of anti-inflammatory drugs also depend on the dose and the delivery. Topical NSAIDs have almost the same analgesic effect as oral administration, but their systemic effect on the body and adverse effects are less.

In human medicine, NSAIDs with various active ingredients are often used as topical therapies. They include soft drugs with methyl salicylate as the active ingredient. Such as Bom-Benge ointment, Capsin, Saliniment, and others. Methyl salicylate is a derivative of salicylic acid and has a local irritating effect. Methyl salicylate irritates the skin receptors, causing the formation and release of many active substances into the blood that regulate pain sensitivity. This releases a substance from the neurons. Reduced accumulation of this substance in the nerve endings leads to a decrease in pain sensitivity. Besides, methyl salicylate, which is a non-steroidal anti-inflammatory ingredient (NSAID), inhibits prostaglandin synthesis by inhibiting cyclooxygenases (COX-1, 2), which reduces swelling and infiltration of inflammatory tissues (Li et al., 2016; Yeoh and Goh, 2022).

The common non-steroidal anti-inflammatory drugs are widely used in veterinary medicine. However, the problem is there are few drugs approved or licensed specifically for the treatment of animals, which can create certain therapeutic and legal issues. Therefore, in our opinion, the development of new safe, and effective NSAIDs for veterinary medicine is urgent and requires prompt resolution.

The purpose of the study is to substantiate and develop a formulation of new NSAIDs for veterinary medicine, and to study their adverse effects and efficacy in the treatment of musculoskeletal diseases in animals.

Materials and methods. Inducing an inflammatory process in laboratory animals is one of the most common methods to determine the analgesic and anti-inflammatory properties in developing new drugs or synthesizing substances. The study on the effect of non-steroidal anti-inflammatory drugs (NSAIDs) "Celexib" and "Dibutalastin" was conducted in the vivarium and laboratory of the Department of Pharmacology and Toxicology of Stepan Gzhytskyi National University of Veterinary Medicine and Biotechnologies Lviv, Ukraine, on laboratory rats of 3-4 months old, with body weight 260-290 g. The laboratory animals were selected on the analogue principle by way of randomization. The housing and feeding of laboratory rats met the established requirements. The air temperature in the room was 20-24 °C, the humidity – 45-65%, and the lighting regime was comfortable for the animals. The animals were kept in

cages (3 animals each), with regular ventilation and disinfection with a UVC germicidal lamp. The access to food and water was constant. The laboratory rats were fed with granular meal.

Before the research procedures, the laboratory animals had a preparation and acclimation period. The animals were kept in a separate room, had daily examinations and behavior assessments, their body temperature was measured, and their functional characteristics, reflex activity, etc. were monitored for a week.

The studies were conducted in compliance with the rules and requirements of the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Purposes (Strasbourg, 1986).

For the study, we substantiated and developed the formulation, technological aspects of preparation, and preliminarily studied acute and chronic forms in laboratory rats, analyzed the toxicity and cumulation of two new NSAIDs, "Celexib", a solution for injections with celecoxib (100mg in 1ml) active ingredient, and "Dibutalastin" ointment for external use (1g of the drug contains 61.0 mg of methyl salicylate).

The study was conducted in several stages. First, we studied the anti-inflammatory effect of the new celecoxib-containing drug "Celexib" in three groups of white rats (six animals each): The Control (C) and two Experimental (E₁ and E₂). Animals of all groups were clipped and shaved on the thigh area of the right hind paw. The rats of the Control group were administered 0.15 ml of 0.9% sodium chloride solution intramuscularly, the rats of the Experimental groups had: first group – 0.15ml of "Celexib" and the second group – 0.15ml of diclofenac. After 1 hour, all rats involved in the study were induced with an inflammatory process by subplantar (under the plantar aponeurosis of the right hind paw) injection of 1% carrageenan solution (with 0.9% sodium chloride solution) (Morris, 2003). The anti-inflammatory pharmacological effect was assessed by measuring the paw thickness (at the widest point) using an electronic caliper (before and after 1, 2, 3, 4, 6-hour time after carrageenan administration).

In the second stage, like the previous procedure, the anti-inflammatory effect of another NSAID the topical drug "Dibutalastin", was investigated. White rats of the control group (C₂) were treated with petroleum ointment rubbed on the shaved thigh area of the right hind paw, the III experimental group (E₃) with "Dibutalastin" ointment and the IV experimental group (D₄) with the reference drug "Dolaren-gel". In 30 min, animals of all groups were subplantar administered with 0.15ml of allyl isothiocyanate (AITC) solution in 1.2-propylene glycol. Inflammation signs were assessed visually (redness, swelling, higher body temperature) and changes of the paw volume before and in 1, 3, 6, 12, and 24 hours after induction of inflammation in laboratory animals by subplantar administration of allyl mustard oil. During each measurement of the paw thickness, it was additionally lubricated with petroleum ointment and the ointment and gel under study.

The analgesic effect of experiment ointment was also studied in rats when the inflammation was induced with formalin. Petroleum ointment, "Dibutalastin" ointment, and "Dolaren-gel" were applied to the prepared thigh area in the Control and 2 Experimental groups, respectively. In 30 min animals of all three groups were subplantar administered with 0.15ml of 2% formalin solution (in 0.9% sodium chloride), to induce the inflammatory process. The effect of the experimental drugs was assessed by the time animals spent licking the paws with inflammation.

To determine whether "Dibutalastin" ointment has analgesic activity, white rats of the control (C₄) and experimental groups (E₇, E₈) were shaved the thigh area of the right hind paw, a "hot plate" test was performed. With that, the animals of Experimental groups E₇ and E₈ were pre-applied with "Dibutalastin" ointment and "Dolaren-gel", and the rats of the Control group were rubbed with petroleum ointment. In 30 min the rats were alternately placed on a metal plate heated to 50-55 °C. The analgesic activity of "Dibutalastin" and "Dolaren-gel" was

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assessed by their ability to change the threshold of pain sensitivity, namely by assessing the period, or the time until the animal would try to lick the paw.

After 24 hours, the animals were decapitated under light chloroform anesthesia, and their blood was taken for morphological studies. The study was performed on a Dymind DF51 hematology analyzer.

Results. It was found that after subplantation of 1% carrageenan solution into laboratory rats, animals of Control and Experimental groups E₁ and E₂ developed an acute local inflammatory process with signs in the thigh area of the hind right paw. The thigh swelled, increased in volume and thickness, and had significant redness. The rats felt pain while being palpated, and this area was hotter when touched.

In the time range of the study, it was noted that during the continuous 6 hours of observation in the control group of rats, the pattern of inflammation hadn't changed significantly. As for the rats of Experimental groups E₁ and E₂, which before the administration of carrageenan were injected intramuscularly with the experimental anti-inflammatory drugs "Celexib" and the reference drug "Diclofenac", it was found that the pain in the area of experimentally induced inflammation, swelling and temperature were slightly lower than in the rats of the control group.

Fig. 1 shows the results of measuring the thickness of the paws with inflammation of the control and experimental groups rats.

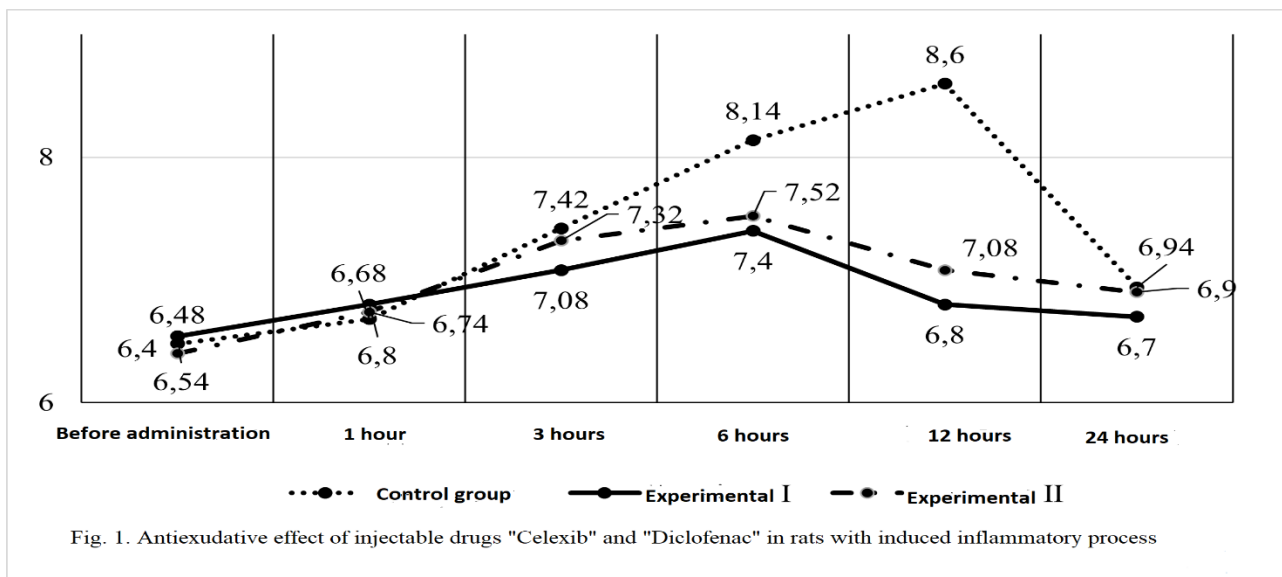


Fig. 1. Antiexudative effect of injectable drugs "Celexib" and "Diclofenac" in rats with induced inflammatory process

We found that the most peculiar changes in the paw's thickness were observed in rats of all groups three hours after carrageenan administration. The thickness of the paws, at this time of the procedure, in the rats of groups C, E₁, and E₂ was more than the values obtained before the drug administration by 25.6, 8.2, and 14.3%, respectively. It was found that rats of the control group that did not receive anti-inflammatory drugs had the volume of the paw increased on the 4th and 6th hours of the experiment. Regarding the experimental groups, we noted that after 4 hours the intensity of the inflammatory process decreased.

According to the evaluation of the Anti-Exudative Effect Index (AEEI), which is the factor of the thickness of the paw during the relevant study period and the size before the drug that induced the inflammation administration, we found that the experimental non-steroidal anti-inflammatory drugs "Celexib" and "Diclofenac" had a certain anti-inflammatory effect (Table 1). From the 4th hour of observations, the AEEI decreased and by the 6th hour, it was 0.22 and 0.30, respectively. During this period of observation, there were practically no visible clinical signs of the inflammation induced by carrageenan, the rats of the experimental groups

reluctantly allowed palpation of the thigh area of the hind right paw, pain and hyperemia were already not significant.

The efficacy of the drug "Celexib" developed by us for veterinary medicine, in terms of anti-inflammatory effect, was comparable to the anti-inflammatory and pain-relieving effect of the non-steroidal anti-inflammatory drug "Diclofenac", which has been widely used in medicine for a long time.

We have also studied the morphological composition of the blood of control and experimental groups' laboratory rats with induced inflammation. (Table 2).

Table 1

Anti-Exudative Effect Index (AEEI) of "Celecoxib" and "Diclofenac" in rats with carrageenan-induced inflammation, $M \pm m$, $n=6$

#	Group of rats	NSAID	Anti-Exudative Effect Index after carrageenan administration (hours)				
			1	2	3	4	6
1	Experimental I (E_1)	Celexib	0.4 ± 0.08	0.36 ± 0.08	0.57 ± 0.04	0.49 ± 0.08	0.22 ± 0.06
2	Experimental II (E_2)	Diclofenac	0.47 ± 0.6	0.50 ± 0.06	0.67 ± 0.04	0.53 ± 0.02	0.30 ± 0.08

Table 2

The effect of "Celecoxib" and "Diclofenac" drugs on the morphological composition of the blood of laboratory rats with induced inflammations, $M \pm m$, $n=6$

#	Values	Units of measurement	Groups of rats		
			C	E_1	E_2
1	WBC	$10^9/l$	13.0 ± 0.6	$8.40 \pm 0.22^{**}$	$8.2 \pm 0.32^{**}$
2	RBC	$10^{12}/l$	6.88 ± 0.22	6.77 ± 0.36	6.9 ± 0.26
3	Hb	g/l	140.1 ± 2.4	137.0 ± 12.4	146.0 ± 7.8
4	HCT	%	37.0 ± 0.9	35.2 ± 0.52	33.2 ± 0.88
5	Thrombocytes	$10^9/l$	560 ± 40.2	573 ± 28.6	592 ± 40.2
6	MCV	fl	53.7 ± 1.3	52.0 ± 2.4	54.4 ± 3.3
7	MCH	pg	20.4 ± 0.7	20.2 ± 0.64	20.8 ± 0.82
8	MCHC	g/l	380.0 ± 12.4	388.0 ± 16.6	398.6 ± 24.2

Note in this Table: $** - P < 0,01$

It was found that in the blood of the rats of the Control group during the first 6 hours of the study, the leukocyte counts significantly increased, which is a strong confirmation of the development of an inflammatory process. The number of WBCs in rats that did not receive "Celexib" or "Diclofenac" (control group) was 68 and 74% higher ($P < 0.01$) than in the blood of rats of the first and second groups. It is important to note that there were no peculiar changes in the qualitative composition of WBC during this period of the experiment (6 hours) (Table 2). However, in 24 hours after carrageenan-induced inflammation, it was found that the percentage of eosinophils in the blood of the control group rats increased from 3 to 8%, the level of segmented neutrophils was 17.8% higher compared to the blood of the rats that did not receive NSAIDs, and the number of lymphocytes decreased by 13.6%.

Table 3

Blood leukogram of rats with carrageenan-induced inflammation, $M \pm m$, $n=6$

#	Values	Units of measurement	C	E ₁	E ₂
1	Eosinophils	%	8±0.01	3±0.01	3±0.01
2	Neutrophils with a drum-sticks shaped nucleus	%	4±0.01	3±0.01	2±0.01
3	Segmented neutrophils	%	53±2.6	37±4.0	40±3.4
4	Lymphocytes	%	29±2.2	51±4.8	47±6.0
5	Monocytes	%	6±0.8	7±0.4	5±0.2

The analysis of the parameters showed that in the rats of the experimental groups that had non-steroidal anti-inflammatory drugs "Celecoxib" and "Diclofenac", no significant changes in the blood were observed.

Thus, based on the results of the experiment, it can be stated that "Celecoxib" has anti-inflammatory and analgesic properties. The mechanism of this effect is not simple. Here, it is necessary to assume that the carrageenan-induced inflammation was characterized not only by local manifestations but also had a generalized character because the content of leukocytes in the blood of the experimental rats increased. The infiltration of tissues by inflammatory cells (neutrophils, monocytes, lymphocytes) at the area of administration is the critical feature of any inflammation. Such inflammatory cells release many enzymes (proteases, elastases, collagenases, acid hydrolases, phosphatases, lipases) and chemical mediators (eicosanoids, cytokines, chemokines) and induce tissue damage and the development of inflammation.

We had an experimentally induced inflammation and it resulted in tissue damage. Toll-like receptors (TLRs), NOD-like receptors (NLRs), and receptors for advanced glycation end products (RAGE) responded to tissue injury. These receptors, as J. White et al. (2010) L. Moilanen think when binding to pathogenically active molecules, stimulate and, through signal transduction, accelerate transcription factors, in particular nuclear factor – κ B (NF- κ B) and activate protein – 1 (AP-1), where there is expression of an anti-inflammatory gene. Nuclear factor- κ B (NF- κ B), according to the authors, regulates the expression of genes for anti-inflammatory cytokines, chemokines, inflammatory enzymes, adhesion molecules, receptors, and microRNAs (John et al., 2010; Lauri et al., 2012).

We have investigated the anti-inflammation effect of another drug developed by us – "Dibutalastin" ointment in white rats with evoked inflammation by allyl isothiocyanate (AITC) injection. Methyl salicylate is the active ingredient of this ointment, international classification says that it is a non-steroidal anti-inflammatory drug. We found out that after subdermal injection of AITC in the laboratory rats of the control and experimental groups E₃ and E₄, an acute inflammatory process developed in the thigh area of the right hind paw. Likes in a carrageenan-induced case, it had the clinical signs of inflammation from the 1st hour of observation and was characterized by an inflammatory reaction and swelling, increased paw volume, hyperemia, higher body temperature, and significant pain. However, the dynamics of inflammation in the control group and experimental E₃ and E₄ rats were different (Fig. 2).

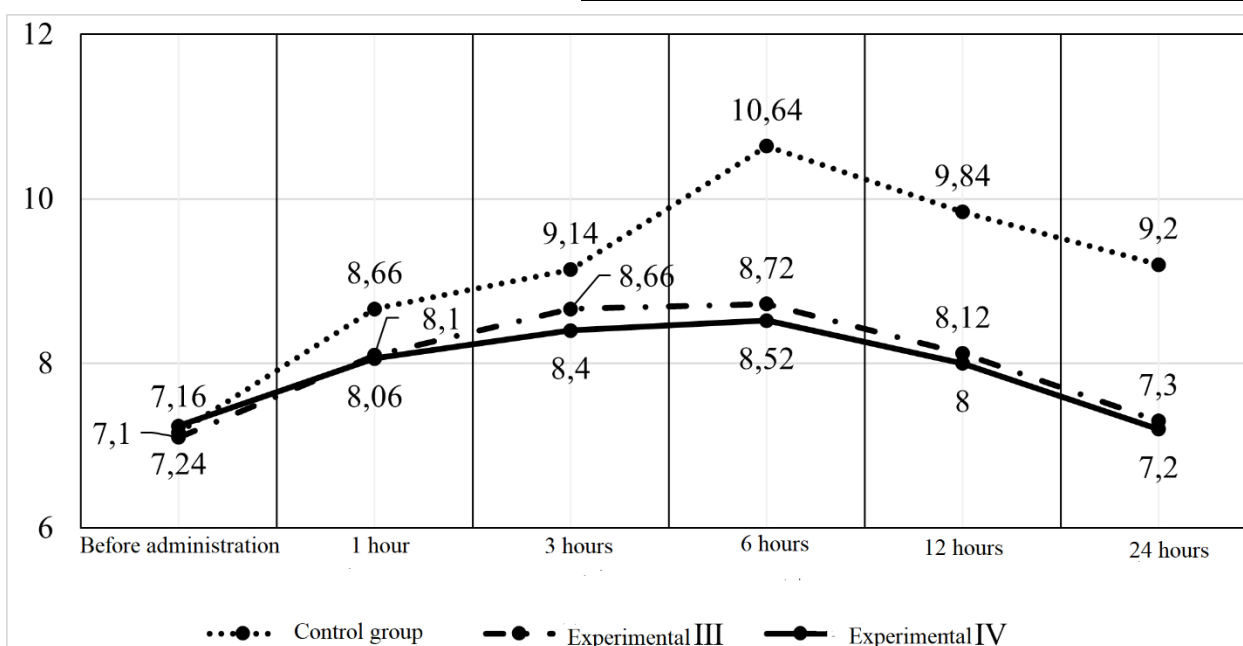


Fig. 2. Efficacy of NSAIDs in AITC-induced experimental inflammation

The diagram shows that the thickness of the paws with signs of inflammation in the Control group was the largest at the 6th hour of the study and was more than the normal (before AITC administration) by 40.6%. It can be assumed that the intensity of the inflammation process tended to decrease, although it remained quite high (after 24 hours, the thickness of the paws was 20.9% more).

With the effect of anti-inflammatory drugs "Dibutalastin" ointment and "Dolaren-gel", a significant decrease in the intensity of the inflammatory process was observed. As Table 4 shows the anti-exudative effect of the investigated drugs can be assessed by evaluating their indices.

Table 4

Comparative efficacy of non-steroidal anti-inflammatory drugs according to the anti-exudative effect index in rats, $M \pm m$, $n=6$

#	Groups of rats	AEEI after AICT administration (hours)				
		1	3	6	12	24
1	E ₃	0.67±0.08	0.78±0.02	0.65±0.02	0.41±0.03	0.27±0.06
2	E ₄	0.48±0.04	0.59±0.08	0.52±0.08	0.36±0.04	0.11±0.08

Thus, "Dibutalastin" ointment and "Dolaren-gel" can be asserted that these NSAIDs, when applied to the inflamed area, AEEI started decreasing from the 6th hour of observation, and 24 hours after it was the lowest. It can be stated as a conclusion that the investigated soft drug showed a high anti-inflammation effect, apparently due to the same active ingredient – methyl salicylate.

The analgesic effect of "Dibutalastin" and "Dolaren-gel" was also investigated in a rat model of formalin-induced inflammation (Table 5).

It was found that the time spent by the animals of the control group on licking the paw with signs of inflammation in the first phase, when the pain was apparently because of the formalin irritating effect on sensitive receptors, was 68 seconds. In the later period (20-30 min)

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after formalin administration, i.e. when we could observe the development of inflammation in the tissues, the time was 120 seconds. In the rats of groups E₅ and E₆, which were treated with "Dibutalastin" ointment and "Dolaren-gel" before formalin administration, the time spent on licking the paw with inflammation was less compared to the control group: in the first phases 24 and 38 seconds less and 54 and 64 seconds less in the second phase of the investigation. The results verify the analgesic effect of the investigated drugs.

Table 5

Analgesic effect of a new methyl salicylate "Dibutalastin" ointment and "Dolaren-gel" in formalin-induced inflammation in rats, $M \pm m$, $n=6$

#	Groups of rats	Evaluation by the time of response (sec.)	
		I phase 0-5 min.	II phase 20 -30 min.
1	Control (C ₃)	68	120
2	Experimental V (E ₅)	44	66
3	Experimental VI (E ₆)	30	56

The "hot plate" test also showed that soft drugs containing methyl salicylate "Dibutalastin" and "Dolaren-gel" have analgesic properties (Table 6)

Table 6

Investigation of analgesic effect of non-steroidal anti-inflammatory drugs in the "hot plate" test, $M \pm m$, $n=6$

#	Investigated drug	Reaction time (sec.)
1	Control (C ₄)	20±4.0
2	Experimental VII (E ₇)	42±2.8
3	Experimental VIII (E ₈)	46±3.6

It was found that the response time of rats before the onset of the defense reflex, after putting them on the "hot plate", ranged from 20±4.0 to 46±3.6 seconds. It was observed that when using the investigated soft drugs with analgesic effect, the response time was 22 and 26 seconds more, respectively, compared to the control group.

Conclusions. 1. Celecoxib, when administered intramuscularly in white rats with carrageenan-induced inflammation, has anti-inflammatory effects (reduces swelling, pain, and hyperemia in the inflammation area). Its effectiveness is comparable to the Diclofenac reference drug.

2. The anti-inflammatory and analgesic effect of "Dibutalastin" ointment is similar in effectiveness to the "Dolaren-gel" reference drug.

The next stage of our scientific experiments will be the study of the effectiveness of "Celexib" and "Dibutalastin" in pets with musculoskeletal disorders.

REFERENCES

1. Bennett, A., & Villa, G. (2000). Nimesulide: an NSAID that preferentially inhibits COX-2, and has various unique pharmacological activities. Expert opinion on pharmacotherapy, 1(2), 277–286. <https://doi.org/10.1517/14656566.1.2.277>
2. Laporte, J. R., Ibáñez, L., Vidal, X., Vendrell, L., & Leone, R. (2004). Upper gastrointestinal bleeding associated with the use of NSAIDs: newer versus older

- agents. Drug safety, 27(6), 411–420. <https://doi.org/10.2165/00002018-200427060-00005>
3. Brune, K., & Patrignani, P. (2015). New insights into the use of currently available non-steroidal anti-inflammatory drugs. Journal of pain research, 8, 105–118. <https://doi.org/10.2147/JPR.S75160>
4. Blanca-Lopez, N., Soriano, V., Garcia-Martin, E., Canto, G., & Blanca, M. (2019). NSAID-induced reactions: classification, prevalence, impact, and management strategies. Journal of asthma and allergy, 12, 217–233. <https://doi.org/10.2147/JAA.S164806>
5. KuKanich, B., Bidgood, T., & Knesl, O. (2012). Clinical pharmacology of nonsteroidal anti-inflammatory drugs in dogs. Veterinary anaesthesia and analgesia, 39(1), 69–90. <https://doi.org/10.1111/j.1467-2995.2011.00675.x>
6. de Salazar Alcalá, A. G., Gioda, L., Dehman, A., & Beugnet, F. (2019). Assessment of the efficacy of firocoxib (Previcox®) and grapiprant (Galliprant®) in an induced model of acute arthritis in dogs. BMC veterinary research, 15(1), 309. <https://doi.org/10.1186/s12917-019-2052-0>
7. Reinoso, R. F., Farrán, R., Moragón, T., García-Soret, A., & Martínez, L. (2001). Pharmacokinetics of E-6087, a new anti-inflammatory agent, in rats and dogs. Biopharmaceutics & drug disposition, 22(6), 231–242. <https://doi.org/10.1002/bdd.258>
8. Yeoh, S. C., & Goh, C. F. (2022). Topical delivery of salicylates. Drug delivery and translational research, 12(5), 981–1001. <https://doi.org/10.1007/s13346-021-00988-5>
9. Li, J., Yin, Y., Wang, L., Liang, P., Li, M., Liu, X., Wu, L., & Yang, H. (2016). Synthesis, Characterization, and Anti-Inflammatory Activities of Methyl Salicylate Derivatives Bearing Piperazine Moiety. Molecules (Basel, Switzerland), 21(11), 1544. <https://doi.org/10.3390/molecules21111544>
10. Morris C. J. (2003). Carrageenan-induced paw edema in the rat and mouse. Methods in molecular biology (Clifton, N.J.), 225, 115–121. <https://doi.org/10.1385/1-59259-374-7:115>
11. White, J. P., Cibelli, M., Rei Fidalgo, A., Paule, C. C., Noormohamed, F., Urban, L., Maze, M., & Nagy, I. (2010). Role of transient receptor potential and acid-sensing ion channels in peripheral inflammatory pain. Anesthesiology, 112(3), 729–741. <https://doi.org/10.1097/ALN.0b013e3181ca3179>
12. Moilanen, L. J., Laavola, M., Kukkonen, M., Korhonen, R., Leppänen, T., Högestätt, E. D., Zygmunt, P. M., Nieminen, R. M., & Moilanen, E. (2012). TRPA1 contributes to the acute inflammatory response and mediates carrageenan-induced paw edema in the mouse. Scientific reports, 2, 380. <https://doi.org/10.1038/srep00380>

ЕФЕКТИВНІСТЬ НЕСТЕРОЇДНИХ ПРОТИЗАПАЛЬНИХ ПРЕПАРАТІВ “ЦЕЛЕКСИБ” І “ДІБУТАЛЯСТИН” ЗА ІНДУКОВАНОГО ЗАПАЛЕННЯ В ЩУРІВ

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Резюме. Нестероїдні протизапальні засоби є найбільш широко використовуваними анагетиками в практиці ветеринарної медицини. Одним з поширених методів з'ясування протизапальних і анагетичних властивостей нових препаратів є індукування в лабораторних тварин запального процесу. Нами в умовах експерименту було вивчено протизапальні властивості препаратів “Целексиб”,

діючою речовиною якого є целекоксиб (в 1 мл 100 мг) і мазі “Дібуताлястин” (в 1 г препарату міститься 61,0 мг метилсаліцилату). В результаті проведених досліджень з’ясовано, що за субплантарного введення лабораторним щурам 1% розчину каррагінану у тварин контрольної і дослідних груп розвивався гострий запальний процес (набряк, збільшення об’єму і товщини кінцівки, гіперемія, болючість). Найбільш характерними були зміни в щурів усіх груп через три години після введення каррагінану. Відзначено, що у щурів контрольної групи, які не отримували протизапальні засоби об’єм лапки збільшувався і на, 4-ту та 6-ту години досліду. У тварин дослідних груп Д₁ і Д₂ вже починаючи з 4-ої години, на тлі дії протизапальних засобів “Целексиб” і “Диклофенак”, інтенсивність розвитку запального процесу зменшувалась. Товщина лапки, при цьому, була, порівняно з періодом до індукування запалення, у тварин К, Д₁ і Д₂ меншою на 25,6, 8,2 і 14,3%, відповідно. На 6-ту годину досліджень у тварин групи Д₁ видимі клінічні ознаки запального процесу, викликаного каррагінаном, були практично відсутні, що підтверджує протизапальну ефективність досліджуваного препарату “Целексиб”. Встановлено, що в щурів за умови індукування запального процесу алізізотіоціанатом і формаліном досліджуваний засіб у формі мазі “Дібуताлястин” також проявляв характерні анагетичні властивості. Відзначено, що протизапальна та знеболювальна його дія була подібною за ефективністю до препарату-порівняння “Доларен-гель”.

Ключові слова: “Целексиб”, “Дібуталястин”, каррагінан-запалення, щури білі, протизапальна, анагетична дія

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