https://doi.org/10.54500/2790-1203-2024-4-124-34-43
UDC 543.645.2; 543.429.2; 547.548.68
IRSTI 31.23.19; 75.31.29

Original article

Polyoxysteroids of plants of the genus Silene L. and their derivatives as potential anti-inflammatory agents

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Abstract

According to literature and our experimental data, plant polyoxysteroids or phytoecdysteroids are found in more than 126 species of Silene L. growing in Kazakhstan (12 endemic species). In the last decade, scientific interest in polyoxysteroids as substances with potentially pharmacologically active properties has led to an increase in the number of studies aimed at their isolation, quantitative determination and chemical modification.

Objective. *Study the anti-inflammatory activity of new derivatives of polyoxysteroids of the genus Silene L. in vivo conditions.*

Methods. *The studies were conducted by the method of supramolecular complexation and mechanochemistry, determination of transmembrane permeability and water solubility.*

Results. *To obtain new water-soluble derivatives with increased bioavailability, solid dispersions and complexes of 20-hydroxyecdysone (20E) with disodium salt of glycyrrhizic acid (Na_2GA) and 2-hydroxypropyl-β-cyclodextrin (2-HP-β-CD) were prepared using mechanochemical methods. Several supramolecular encapsulated complexes based on polyoxysteroids were also synthesized, and their water solubility in different ratios and anti-inflammatory activity at doses of 25 mg/kg and 50 mg/kg were studied. The supramolecular β-cyclodextrin complex of 3-epi-2-deoxyecdysone demonstrated significantly greater anti-inflammatory activity at both doses than sodium diclofenac.*

Conclusion. *The results of the study showed that new supramolecular complexes of polyoxysteroids with α-, β-, γ- and 2-hydroxypropyl – β – cyclodextrins and disodium salt of glycyrrhizic acid and mechanochemically obtained solid dispersions can be recommended for use in the development of an anti-inflammatory herbal medicine origin, due to their high anti-inflammatory effectiveness.*

Keywords: *genus Silene L., polyoxysteroids, supramolecular complexes, mechanocomposites, anti-inflammatory activity.*

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2024; 4 (124): 34-43
Recieved: 21-09-2024
Accepted: 27-10-2024

Introduction

From the perspective of searching for polyoxysteroid containing plants within the Kazakh flora, species of the genus Silene L. (family Caryophyllaceae Juss.) are particularly promising. This genus consists of approximately 700 species worldwide, with 62 species (12 of which are endemic) found in our republic, including 16 species in Central Kazakhstan [1-4]. Currently, literature and our experimental data reveal that polyoxysteroids have been identified in more than 126 Silene species, surpassing the number found in any other plant family. The presence of deoxyecdysteroids primarily characterizes species within this genus. It is likely that the 2-deoxysteroids, 2-deoxyecdysone and 2-deoxy-20-hydroxyecdysone, along with 20-hydroxyecdysone (the major polyoxysteroid in plants), should also be considered key products of biosynthesis [5].

Polyoxysteroids, particularly 20-hydroxyecdysone, exhibit a range of biological activities, including anabolic, adaptogenic, lipid-lowering, antisclerotic, antiradical, antioxidant, and immunomodulatory effects. These effects manifest as a mild activating effect on human leukoconcentrate lymphocytes [1].

They also exhibit antiulcer, antirheumatic, diuretic, antimicrobial, neuroprotective, and insulin-regulating (and hypoglycemic) properties [1,2]. Notably, according to the international database Ecdybase.org [6], more than 335 pharmacological substances based on plant polyoxysteroids have been developed, most of which are biologically active additives, with only two medicines, "Ecdysten" and "Ecdyphyt" having medicine status [3-11]. Unfortunately, modern research on new phytopreparations based on polyoxysteroids is hindered by their low solubility in water, complicating their use as pharmaceutical substances.

The purpose of this study is to evaluate the anti-inflammatory activity of new derivatives of polyoxysteroids from the genus Silene L. and to summarize the results of our research on their potential as anti-inflammatory agents.

Material and methods

The research materials consist of medicinal plant raw materials, including the following species: Silene wolgensis (Hornem) Bess., S.altaica Pers., S.fruticulosa (Pall) Schischk., S.cretaceae L. The materials used in this study include their extracts, isolated polyoxysteroids, and new derivatives derived from them.

Extraction. Extraction of the aboveground parts (leaves, buds, stems) of 1.0 kg of crushed air-dry resinous raw materials was carried out four times using 10 liters of 96% ethanol. The extraction process involved heating the mixture in a water bath at the boiling point of the solvent for 1 to 1.5 hours. The extract was then cooled, drained, and evaporated using a rotary evaporator at a temperature not exceeding 50 °C. To the resulting thick brown syrupy mass, 0.2 liters of ethanol were added.

Next, the ethanol extract was treated with a mixture of petroleum ether and ethyl acetate in a ratio of 2:1 (0.4:0.2 liters) to remove non-polar components. The remaining water-soluble part was then extracted with isobutanol (0.6 liters), resulting in a thick extract. The isobutanol extracts were combined and distilled dry under vacuum, yielding 86.5 grams of ecdysteroids along with accompanying substances in the form of a thick green syrupy mass. The presence of 20-hydroxyecdysone (20E) and minor polyoxysteroids was confirmed through thin-layer chromatography (TLC) and qualitative analysis.

Column chromatography. During repeated column chromatography on Al2O3 (Brockman activity level I, sorbent weight 1.6 kg) and subsequent column elution with a chloroform–ethanol mixture (60:40), a fraction weighing 1.0 g was isolated based on TLC "Sorbfil." This fraction was characterized as a chromatographically pure substance, identified as 20E, while other fractions contained minor 2-deoxysteroids.

Synthesis and production of new derivatives and mechanocomposites. The synthesis and preparation of new derivatives and mechanocomposites involved the formation of supramolecular complexes of 20E and minor polyoxysteroids. These were obtained by reacting equimolar amounts of the compounds with α-, β-, γ-, and 2-hydroxypropyl–β–cyclodextrins. Specifically, a solution of 0.1 mmol of cyclodextrins in 4 ml of distilled water was combined with solutions of 0.1 mmol of polyoxysteroid in 3 ml of absolute ethanol. The mixture was stirred at 50°C for 8 hours. Afterwards, the residue was filtered, washed with ethanol, and dried in a vacuum oven at 40°C.

Mechanochemical composites based on 20E, other polyoxysteroids, and excipients, including the disodium salt of glycyrrhizic acid (Na2GA) and 2-hydroxypropyl–β–cyclodextrin (2–HP–β–CD), were produced through joint mechanochemical treatment in a mass ratio of polyoxysteroid to excipient of 1:10 for 8 hours.

Determination of anti-inflammatory activity. Anti-inflammatory activity was conducted in the pharmacology laboratory of the Joint-Stock Company "Scientific Production Center "Phytochemistry" (Karaganda, Kazakhstan), which holds a state license for work in the field of science and scientific and technical activities “MK No. 004791 dated August 3, 2016”, as well as for pharmaceutical activities related to the manufacture of medicines under industrial production conditions (“№FD65000018 KMPCF” dated February 4, 2010). A technological audit of the pharmaceutical production at JSC “SPC “Phytochemistry” was performed by the engineering company "Glatt Ingenieurtechnik GmbH" (Weimar, Germany), resulting in the issuance of EU certificate No. 1528/2011/004 dated November 29, 2011, confirming compliance with European GMP standards. JSC “SPC “Phytochemistry” is accredited by the Committee for Technical Regulation of the Ministry of Health of the Republic of Kazakhstan for compliance with QMS standards in research, pharmaceutical, and educational activities (certificate no. KZ7500207.07.03.00332 dated September 17, 2019).

The anti-inflammatory effects of the samples were evaluated using an acute exudative reaction model. This model involved inducing acute exudative reaction (peritonitis) through intraperitoneal administration of a 1% acetic acid solution at a volume of 1 ml per 100 g of rat body weight. After 3 hours, the animals were euthanized, the abdominal cavity was opened, and exudate was collected and its volume measured. The studies followed the methodology outlined in the references [12, 13]. The test subjects were administered doses of 25 and 50 mg/kg of the studied objects via oral administration in the form of starch mucus, while the comparison medicine, Diclofenac sodium, was similarly administered at doses of 25 and 50 mg/kg.

Control animals received an equivalent volume of starch mucus. Both the studied objects and the comparison medicine were administered once, one hour before the administration of the 1% acetic acid solution.

Statistical processing of the results was conducted using the Statistica 8.0 software package. The results are presented as "average value ± standard error of the mean." Intergroup differences were assessed using the nonparametric Mann–Whitney U-test. Differences were considered statistically significant at a p-value of less than 0.05.

Determination of transmembrane permeability. Transmembrane permeability was preliminarily assessed using the Parallel Artificial Membrane Permeability Assay (PAMPA) on artificial membranes.

Water solubility study. Water solubility studies were performed at 22°C in air (humidity 63%, pH of distilled water 6.55). Samples (100 mg) were mixed with 1 liter of distilled water in a 2-liter flask. The heterogeneous mixture was continuously stirred in an ultrasonic bath for 1 hour. The solution was then filtered through a glass filter (class 2, 40-100 microns, diameter 0.5 cm). The resulting pure solution was evaporated using a rotary evaporator, and the dry residue was weighed. This experiment was repeated three times.

Results

It is known that it is practically impossible to experimentally investigate any chemical compound for all known types of bioactivity. Even considering the capabilities of modern high-performance bioscreening—conducted about one or more biological targets of medicines deemed promising during a specific period—the comprehensive study of the biological activity of substances can only be effectively achieved through the development of new technologies for mathematical forecasting and virtual bioscreening (docking). These technologies can then be applied to assess the likely types of activity of chemical compounds, followed by testing and confirmation of the predicted activity through in vitro and in vivo bioscreening.

In this context, the use of the PASS online database enables the comparison of the chemical structure of polyoxysteroids with substances stored in various databases, allowing for the prediction of the presence and intensity of specific biological activities with a certain degree of probability. Therefore, to avoid a blind search for new anti-inflammatory substances among polyoxysteroids isolated from plants of the genus Silene L. and to develop a strategy for their targeted production, mathematical modelling of the bioactivity of 20-hydroxyecdysone and the basic 2-deoxysteroids was performed (Figure 1).

As a result of analyzing the structural formulas of the studied basic polyoxysteroids using the PASS online database, several activities were identified that are likely present in 20-hydroxyecdysone and its deoxyanalogs. Specifically, 20-hydroxyecdysone (1) may exhibit anti-ischemic, immunostimulating, antipsoriatic, dermatological, anti-inflammatory (71% probability), hepatoprotective, and antiviral activity. 2-deoxy-20-hydroxyecdysone (2) shows anti-ischemic, antipsoriatic, immunostimulating, dermatological, lipid-lowering, anti-inflammatory (62% probability), hepatoprotective, and antiviral activity. Both 2-deoxyecdysone (3) and its epimer, 3-epi-2-deoxyecdysone (4), display anti-ischemic, hepatoprotective, antipsoriatic, dermatological, antitumor, immunostimulating, antiviral, and anti-inflammatory (52% probability) activities.

As illustrated in Figure 1, for all polyoxysteroids, there is a characteristic trend of increasing potential anti-inflammatory activity by the increasing number of hydroxyl groups: 20-hydroxyecdysone – 6, 2-deoxy-20-hydroxyecdysone – 5, and 2-deoxyecdysone – 4.

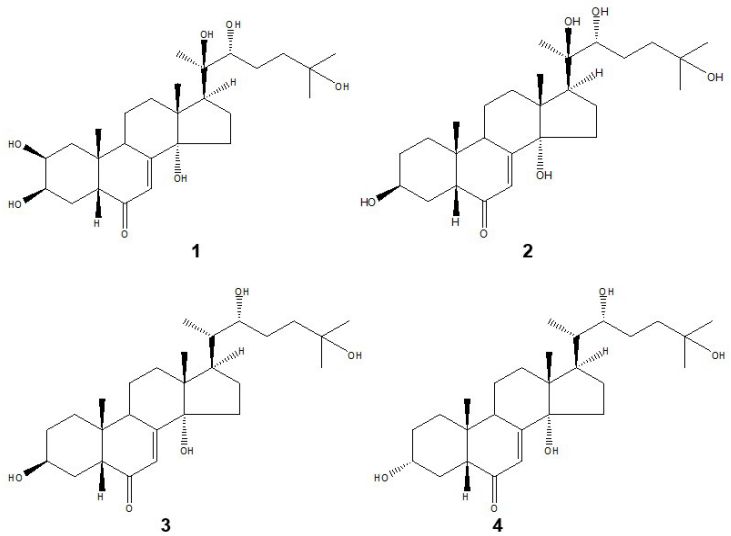

Figure 1 – Structural formulas of 20-hydroxyecdysone and basic 2-deoxysteroids of plants of the genus Silene L

Thus, the results of the bioprognosis of the initial polyoxysteroids significantly guided further research in the search for anti-inflammatory agents and the establishment of structure-activity relationships. To determine the degree of correlation between the results of mathematical modelling and the indicators from experimental studies, a series of experiments were conducted to investigate the anti-inflammatory properties of ethanol extracts from plants of the genus Silene L. (Si-Ex), individual polyoxysteroids (1-4), and their water-soluble derivatives.

The study of anti-inflammatory activity was carried out by all applicable international, national, and institutional guidelines for the care and use of animals, specifically following the Rules of the European Convention for the

Protection of Vertebrates Used for Experimental and Other Scientific Purposes (Strasbourg, 1986) and The decision of the Bioethics Committee of NCJSC "Medical University of Karaganda", Session No. 9, Protocol No 9" Date (D/M/Y) 29.03.2022, Assigned number 32). The obtained research data are presented in Tables 1-3.

Table 1 – Anti-inflammatory activity of samples of extracts of plants of the genus Silene L.: Si.Cl – Ex, Si.Gn – Ex, Si.Br – Ex

The studied indicator	Control n=5	Comparison medicine Diclofenac sodium n=5	Si.Cl – Ex n=5	Si.Gn – Ex n=5	Si.Br – Ex n=5
Dose, mg/kg	-	50	50	50	50
Weight of animals, gr.	269,2±29,1	282±24,6	270±34,25	264,2±26,8	322,6±19,8
Amount of exudate, ml	4,3±1,48	4,18±1,54	5±1,06	5,0±0,31	6,1±1,2
Note:* - p<0,05 compared to the control					

As a result of the experiment, it was revealed that the samples of extracts Si.Cl – Ex, Si.Gn – Ex, and Si.Br – Ex, obtained from the plants of the Silene claviformis Litv., S. guntensis B.Feditsch., S. brahuica Boiss, at a dose of 50 mg/kg did not exhibit anti-inflammatory activity in the model of acute exudative reaction.

Consequently, we decided to investigate ethanol extracts from other plants of this genus, using a lower dose of 25 mg/kg.

Table 2 – Anti-inflammatory activity of samples of extracts of plants of the genus Silene L.: Si.Alt – Ex, Si. Wol – Ex, Si.Fr – Ex and Si.Cr. – Ex

The studied indicator	Control n=5	Comparison medicine Diclofenac sodium n=5	Si.Alt – Ex n=5	Si. Wol – Ex n=5	Si.Fr – Ex n=5	Si.Cr. – Ex. n=5
Dose, mg/kg	-	25	25	25	25	25
Weight of animals, gr.	220±15,0	190,2±17,5*	268,2*±23,7	264,2±28,1	270,4±52,6	232,4±22,0
Amount of exudate, ml	6,7±1,0	3,9±0,6*	6,5±0,6	5,4±1,0	5,4±0,6*	4,9±1,1
Note:* - p<0,05 compared to the control						

The results indicate the presence of Si. Wol – Ex in the samples, as well as Si.Fr – Ex and Si. Cr – Ex, which exhibits weak anti-inflammatory activity at a dose of 25 mg/kg in a model of acute exudative reaction.

When investigating the anti-inflammatory activity of the individual polyoxysteroids isolated from the aforementioned extracts of various plants of the genus Silene L., column chromatography revealed that these compounds also demonstrate weak anti-inflammatory activity at the same dose and in the same model of acute exudative reaction.

Table 3 – Anti-inflammatory activity of samples of individual polyoxysteroids (1-3) isolated from extracts of plants of the genus Silene L

The studied indicator	Control n=5	Comparison medicine Diclofenac sodium n=5	(1) from Si.Wol – Ex n=5	(2) from Si.Fr – Ex n=5	(3) from Si.Cr. – Ex. n=5
Dose, mg/kg	-	25	25	25	25
Weight of animals, gr.	220,0±15,0	190,2±17,5*	245,6±41,9	241,8±38,8	231,4±18,6
Amount of exudate, ml	6,7±1,0	3,9±0,6*	5,2±1,0	5,1±0,7*	5,2±1,3
Note:* - p<0,05 compared to the control					

Considering that the solubility and bioavailability of medicines and substances are typically the main interrelated factors in the development and creation of new potentially effective dosage forms, we have conducted further work in this area. 20-hydroxyecdysone (1), the active component of the phytosteroid preparations "Ecdysten" and "Ecdyphyt" unfortunately exhibits extremely low water solubility, leading to slow and incomplete absorption in the gastrointestinal tract (GIT), which significantly reduces the effectiveness of medicines based on it.

In contrast, the supramolecular inclusion complex of 20-hydroxyecdysone with 2-hydroxypropyl-β-cyclodextrin (20E/2-HP-β-CD) demonstrates improved water solubility and transdermal permeability compared to the original 20E. The oral and transdermal bioavailability of this complex increases by 2.97 and 1.92 times, respectively, compared to free 20E. Glycyrrhizic acid (GA) and its disodium salt (Na2GA) are also effective natural low molecular weight complexing agents with enhanced biodegradability and bioavailability.

To obtain new water-soluble derivatives with improved bioavailability, we mechanochemically produced solid dispersions and complexes of 20E with Na2GA and 2-HP-β-CD, synthesized a number of supramolecular encapsulated complexes based on polyoxysteroids, and investigated their water solubility and anti-inflammatory activity. Transmembrane permeability measurements conducted using the PAMPA method on artificial membranes indicated the potential of mechanochemically obtained supramolecular delivery systems based on intermolecular complexes of 20E with 2-HP-β-CD or the inclusion of its molecules in micelles formed by GA, predicting an increase in their absorption in the gastrointestinal tract and facilitating the creation of new highly effective drugs.

Experimental results also revealed that the mechanochemically obtained complexes of 20E with

2-HP-β-CD and Na2GA displayed water solubility more than 3 and 2.7 times higher, respectively, than that of the original substance 20E. The determination of the water solubility of synthesized supramolecular complexes of 20E (1) with β-cyclodextrin (β-CD) in different ratios, and 2-deoxyecdysone (3) or (2-DE) with α-, β-, and γ-CD, showed that all new derivatives exhibit increased water solubility. The obtained data are presented in Table 4.

Table 4 – Solubility results of 20E(1) and 2-DE(3) and their supramolecular encapsulated cyclodextrin complexes

Samples of polyoxysteroids and their complexes	Solubility mg/ml	Increased solubility (compared to 20E and 2-DE)
20E (1)	0,000084	-
20E/β-CD (1:1)	0,00887	~ 105 times
20E/β-CD (1:2)	0,00931	~ 110 times
2-DE (3)	0,068	-
2-DE/α-CD	7,4	108 times
2-DE/β-CD	8,3	122 times
2-DE/γ-CD	7,9	116 times

Thus, it was found that β-CD complexes 20E (1) in stoichiometric ratios (1:1) and (1:2) exceed the initial substance in water solubility by 105 and 110 times, and α-, β-, and γ-CD complexes 2-DE (3) by 108, 122, and 166 times, respectively. At the same time, it should also be emphasized that the highest degree of water solubility is shown by the complex with β-CD, and its stoichiometric increase also affects this process.The study of the anti-inflammatory activity of synthesized new supramolecular derivatives was carried out according to the above method at the same dose and on the model of acute exudative reaction. At the same time, it should also be emphasized that the highest degree of water solubility is shown by the complex with β-CD, and its stoichiometric increase also affects this process.

The study of the anti-inflammatory activity of synthesized new supramolecular derivatives was carried out according to the above method at the same dose and on the model of acute exudative reaction. The results of the studies are presented in Table 5.

Table 5 – Anti-inflammatory activity of samples of new water-soluble derivatives of 20-hydroxyecdysone (1) (20E/α-CD, 20E/β-CD, 20E/γ-CD)

The studied indicator	Control n=5	Comparison medicine Diclofenac sodium n=5	20E/α-CD n=5	20E/β-CD n=5	20E/γ-CD n=5
Dose, mg/kg	-	25	25	25	25
Weight of animals, gr.	288,8±22,9	288,4±35,5	224,2±27,1*	261,4±20,3	260,4±13,9*
Amount of exudate, ml	5,6±1,1	3,9±0,7*	3,7±0,9*	5,3±0,6	4,6±0,9
Note:* - p<0,05 compared to the control					

As shown in Table 5, among the studied supramolecular complexes 20E (1) with α-, β-, and γ-cyclodextrins, the sample 20E/α-CD at a dose of 25 mg/kg exhibits an anti-inflammatory effect comparable to that of the reference medicine Diclofenac sodium. In contrast, the sample 20E/γ-CD demonstrates a weak anti-inflammatory effect in a model of acute exudative reaction in vivo.

The study of the anti-inflammatory activity of water-soluble complexes encapsulated in α-, β, and γ-cyclodextrins, based on 2-deoxyecdysone (3) or 2-DE, was carried out using similar methods. 2-deoxyecdysone was first isolated from the fern Blechnum minus and later isolated by us from Silene cretacea and Silene wolgensis.

The results of the anti-inflammatory activity study are presented in Table 6.

Table 6 – Anti-inflammatory activity of samples of new water–soluble derivatives of 2 -deoxyecdysone (3) (2-DE/α-CD, 2-DE/β-CD, 20-DE/γ-CD)

The studied indicator	Control n=5	Comparison medicine Diclofenac sodium n=5	2-DE/α-CD n=5	2-DE/β-CD n=5	2-DE/γ-CD n=5
Dose, mg/kg	-	25	25	25	25
Weight of animals, gr.	293,0±15,4	319,5±25,9	246,3±21,7*	232,0±40,6	225,3±20,8*
Amount of exudate, ml	7,0±0,9	4,4±0,7*	4,7±0,4	4,2±1,2*	4,4±0,6*
Note:* - p<0,05 compared to the control					

The studied samples of α-, β-, and γ-CD complexes of 2-DE (3) demonstrated significant anti-inflammatory activity in an experiment modelling acute exudative inflammation (peritonitis) at a dose of 25 mg/kg, comparable to that of diclofenac sodium. In contrast, the starting compound 2-DE (3) at the same dose exhibited weak anti-inflammatory activity in the acute exudative reaction model (Table 3).

The results of the anti-inflammatory activity studies of water-soluble supramolecular α-, β-, and γ-cyclodextrin complexes based on the epimer 2-deoxyecdysone (3) - 3-epi-2-deoxyecdysone (4) and 2-HP-β-CD complexes based on 20-hydroxyecdysone (1) and 2-deoxy-20-hydroxyecdysone (2) are shown in Tables 7 and 8.

Table 7 – Anti-inflammatory activity of samples of new water solubility of derivatives of 3-epi-2-deoxyecdysone (4) (3-E-2-DE/α-CD, 3-E-2-DE/β-CD, 3-E-2-DE/γ-CD)

The studied indicator	Control n=5	Comparison medicine Diclofenac sodium n=5	3-E-2-DE/α-CD n=5	3-E-2-DE/β-CD n=5	3-E-2-DE/γ-CD n=5
Dose, mg/kg	-	25	25	25	25
Weight of animals, gr.	293,0±15,4	319,5±25,9	293,0±11,0	305,0±24,2	283,5±16,5
Amount of exudate, ml	7,0±0,9	4,4±0,7*	4,0±1,2*	2,8±0,5*	6,5±1,4
Note:* - p<0,05 compared to the control					

Table 8 – Anti-inflammatory activity of samples of new water–soluble derivatives of 3 – epi – 2 – deoxyecdysone (4), 20 – hydroxyecdysone (1) and 2 – deoxy - 20 – hydroxyecdysone (2) (3 – E – 2-DE/2 – HP – β – CD, 20E/2 – HP – β – CD, 20 - DE/2 – HP – β – CD)

The studied indicator	Control n=5	Comparison medicine Diclofenac sodium n=5	3-E-2-DE/2-HP-β-CD n=5	20E/2-HP-β-CD n=5	20-DE/2-HP-β-CD n=5
Dose, mg/kg	-	25	25	25	25
Weight of animals, gr.	293,0±15,4	319,5±25,9	252,0±4,9*	254±9,7*	306,5±20,4
Amount of exudate, ml	7,0±0,9	4,4±0,7*	6,0±1,4	3,9±1,2*	6,0±1,9
Note:* - p<0,05 compared to the control					

As shown in Tables 7 and 8, the sample 3 – E – 2-DE/β – CD at a dose of 25 mg/kg exhibits pronounced anti-inflammatory activity in the model of acute exudative reaction. The samples 3 - E - 2-DE/α - CD and 20E/2 -HP - β – CD at a dose of 25 mg/kg, demonstrate anti-inflammatory activity comparable to that of the comparison drug Diclofenac sodium in the same model.

Therefore, it is of interest to conduct an in-depth study of the dose dependence of the sample – β -cyclodextrin complex 3-epi-2-deoxyecdysone (3-E-2-DE/β-CD). The results of the study on the anti-inflammatory activity of the examined sample are shown in Table 9.

Table 9 – Effect of 3–epi – 2 – deoxyecdysone (4) and its supramolecular complex with β-cyclodextrin (3-E-2-DE/β-CD) on the amount of formed exudate in the abdominal cavity

The studied indicator	Control n=5	Comparison medicine Diclofenac sodium n=5	3-epi-2-deoxyecdysone (4) n=5	3-E-2-DE/β-CD n=5
Dose, mg/kg	-	50	50	50
Weight of animals, gr.	246,6±8,32	224,0±6	209,3±33,7	305±24,2
Amount of exudate, ml	6,53±0,37	4,4±0,7*	4,96±0,28	2,8±0,5*
Note:* - p<0,05 compared to the control				

Thus, the data in Table 9 indicate that the supramolecular β-cyclodextrin complex of 3-epi-2-deoxyecdysone (4), administered at a dose of 50 mg/kg, exhibits significant anti-inflammatory activity in the acute exudative reaction model. This activity is 1.6 times greater than that of the comparison drug, Diclofenac sodium. Further research is needed to understand the mechanism by which the 3-api-2-deoxyecdysone (4) molecule, with its equatorially oriented 3-OH group, affects bioavailability and anti-inflammatory activity (Figure 2).

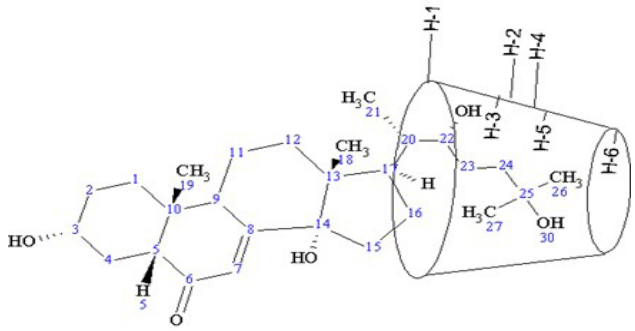

Figure 2 – The structural formula of a supramolecular encapsulated water-soluble complex of 3-epi-2-deoxyecdysone with β-cyclodextrin

Discussion

A series of experiments were conducted to investigate the anti-inflammatory properties of ethanol extracts from plants belonging to the Silene L. genus rich in polyoxysteroids. The examination of polyoxysteroids' biological activity underscores the necessity for contemporary approaches, such as mathematical modeling and virtual bioscreening, in medicine development [14-17]. Utilizing resources like the online PASS database enables the systematic prediction and assessment of compounds' potential activities based on their chemical structures [18, 19].

These simulations not only streamline the quest for novel anti-inflammatory agents but also enhance the efficiency of medicine development [20].

The analysis results indicated that 20-hydroxyecdysone and its deoxyanalogs exhibit diverse biological activities, with significant probabilities suggesting their anti-inflammatory effects [11]. Particularly, 20-hydroxyecdysone displayed a 71% probability likelihood of anti-inflammatory activity, while 2-deoxy-20-hydroxyecdysone, 2-deoxyecdysone, and its epimer 3-epi-2-deoxyecdysone also demonstrated considerable activity (62% and 52% probability respectively). This trend implies that structural modifications, particularly the addition of hydroxyl groups, could boost the anti-inflammatory properties of these compounds. This correlation aligns with prior studies [21] indicating that hydroxylation can notably affect the biological activity of steroid compounds [1-3, 22].

The experiments revealed that extracts Si.Cl – Ex, Si.Gn – Ex, and Si.Br – Ex did not display anti-inflammatory activity in acute inflammation models at a 50 mg/kg dose, however, when the dose was lowered to 25 mg/kg, Si. Wol - Ex, Si.Fr – Ex, and SiCr – Ex exhibited mild anti-inflammatory effects. The comparison of anti-inflammatory activity among polyoxysteroid analogues isolated from extracts similarly showed their mild activity under these circumstances, underscoring the necessity to optimize isolation and synthesis techniques to enhance bioavailability and activity. An essential factor limiting pharmaceutical effectiveness is solubility and bioavailability. In this context, the development of supramolecular complexes has shown significantly improved solubility characteristics compared to the original compounds. The mechanochemical complexes of 20-hydroxyecdysone with 2-hydroxypropyl-β-cyclodextrin increased water solubility by 2.97 times, representing a promising model for new dosage form development [23, 24].

The exploration of the anti-inflammatory activity of supramolecular complexes has substantiated their potential as effective anti-inflammatory agents [25-27]. Specifically, the 20E/α-CD complex exhibited promising results comparable to diclofenac sodium, indicating new possibilities for cyclodextrins in anti-inflammatory drug development. Noteworthy activity was also observed in 3-E-2-DE/β-CD and 20E/2-HP-β-CD, warranting further investigation into their mechanism of action and dosage dependence.

Consequently, this study's outcomes advance efforts in formulating and optimizing compounds to enhance bioavailability and anti-inflammatory activity. These findings may contribute to the development of more effective drugs based on compounds of interest to pharmaceutical science and medicine.

Conclusions

Studies have established that new water-soluble supramolecular derivatives of polyoxysteroids, isolated from plants of the genus Silene L., exhibit anti-inflammatory effects. Given that the quality of phytopreparations currently hinges on their bioavailability and water solubility, we have synthesized a water-soluble encapsulated form of a polyoxysteroid-based substance that surpasses the comparison drug. This investigated water-soluble, encapsulated supramolecular complex shows promise as a potential candidate for further development into an anti-inflammatory drug of plant origin.

No **conflicts of interest** have been declared. This material has not been previously submitted for publication in other publications and is not under consideration by other publishers.

Finding. The work was carried out within the framework of the grant project AP23489639 “New derivatives, mechanocomposites and conjugates of polyoxysteroids: targeted synthesis and biological activity”, funded by the Science Committee of the Ministry of Science and Higher Education of the Republic of Kazakhstan

Authors Contributions. All authors participated equally in writing of this article.

References

1. Тулеуов Б. И. Стероидные соединения растений и лекарственные препараты на их основе. Поиск, химическая модификация и практические аспекты применения / Б.И. Тулеуов. - Караганда: Гласир, 2017. - 208 с.

Tuleuov B. I. Steroidnye soedinenija rastenij i lekarstvennye preparaty na ih osnove. Poisk, himicheskaja modifikacija i prakticheskie aspekty primenenija (Steroid compounds of plants and medicinal preparations based on them. Search, chemical modification and practical aspects of application) [in Russian]. Karaganda: Glasir, 2009; 208 p.

2. Рамазонов Н.Ш., Бобаев И.Д., Сыров В.Н., Сагдуллаев Ш.Ш., Маматханов А.У. Химия, биология и технология получения фитоэкдистероидов // Fan va texnologiya. - 2016. - С. 3-5. [Google Scholar]

Ramazonov N.Sh., Bobayev N.D. Syrov V.N., Sagdullayev Sh.Sh., Mamatkhanov A.U. Khimiya, biologiya i tekhnologiya polucheniya fitoekdisteroidov (Chemistry, biology and technology of obtaining phytoecdysteroids) [in Russian]. Fan va texnologiya. 2016; 3-5. [Google Scholar]

3. Зибарева Л.Н. Фитоэкдистероиды: распространение в мировой флоре, биологическая активность // Фармацевтический бюллетень. - 2015. - №3-4. - С. 40-48.

Zibareva L.N. Fitoekdisteroidy: rasprostraneniye v mirovoy flore, biologicheskaya aktivnost' (Phytoecdysteroids: distribution in the world flora, biological activity) [in Russian]. Farmatsevticheskiy byulleten', 2015; (3,4): 40-48.

4. Тулеуов Б.И. Технология фитостероидных препаратов: монография / Б.И. Тулеуов. - Караганда: Гласир, 2017. - 112 с.

Tuleuov B.I. Tehnologija fitosteroidnyh preparatov: monografija (Technology of phytosteroid preparations: monograph) [in Russian]. Karaganda: Glasir, 2017; 112 p.

5. Володина В.В. Фитоэкдистероиды. - Санкт-Петербург: Наука, 2003. - 293 с.

Volodina V.V. Fitoekdisteroidy (Phytoecdysteroids) [in Russian]. Sankt-Peterburg: Nauka, 2003; 293 p.

6. Lafont R., Harmatha J., Marion-Poll F., Laurence Dinan, Ian D. Wilson. The Ecdysone handbook. 3rd Edition, 2002 continuously updated. Electronic resource. Access mode: https://ecdybase.org/

7. Соколов С.Я. Фитотерапия и фитофармакология: руководство для врачей. - Москва: Мед.информационное агентство, 2000. - 976 с. [Google Scholar]

Sokolov S.Ya. Fitoterapiya i fitofarmakologiya: rukov. dlya vrachey (Phytotherapy and Phytopharmacology: A Guide for Physicians) [in Russian]. Moskva: Meditsinskoye informatsionnoye agenstvo, 2000; 970 p. [Google Scholar]

8. Лагунова О.Н., Ивановский А.А. Лекарственные растения сибирской флоры как источник биологических

активных действий // Матер. 3-4-го междунар. науч. сем'н. «Биотехнология, экология, медицина». - Москва: Киров. 2002. - С. 34-36.

Lagunova O.N., Ivanovskiy A.A. Lekarstvennyye rasteniya sibirskoy flory kak istochnik biologicheskikh aktivnykh deystviy (Medicinal plants of Siberian flora as a source of biologically active actions) [in Russian]. Mater. 3-4-go mezhdunar. nauch. sem'n. Biotekhnologiya, ekologiya, meditsina. Moskva: Kirov. 2002; 34-36.

9. Тимофеев Н.П. Физиологическая активность фитоэкдистероидов и перспективы их использования в медицине. Нетрадиционные природные ресурсы, инновационные технологии и продукты: сб. науч. тр. – Москва: 2001; (95): 108-134.

Timofeyev N.P. Fiziologicheskaya aktivnost' fitoekdisteroidov i perspektiva ikh ispol'zovaniya v meditsine (Physiological activity of phytoecdysteroids and prospects for their use in medicine) [in Russian]. Netraditsionnyye prirodnyye resursy, innovatsionnyye tekhnologii i produkty: sb. nauch. tr. Moskva: 2001; (95): 108-134.

10. Molumed R.S., Saldana M.D.A., Socantaype F.H. et al. Reduction in the cholesterol content of butter oil using supercritical ethane extraction and adsorption on tlumint. J. Suparcrit. Fluids. 2000; (16): 225-233. [Crossref]

11. Lozano P., Delgado D., Gomez D. et al. A non-destructive method to determine the safranal content of saffron (Crocus sativus L.) by supercritical carbon dioxide extraction combined with high-performance liquid chromatography and gas chromatography. J. Biochem. Biophys. Methods. 2000; (43): 367-378. [Crossref]

12. Руководство по экспериментальному (доклиническому) изучению новых фармакологических веществ (под общ. ред. Р.У. Хабриева): учеб. пособие для системы послевуз. проф. образования врачей. Москва: Медицина Шико, 2005. - 826 с. [Google Scholar]

13. Rukovodstvo po eksperimental'nomu (doklinicheskomu) izucheniju novyh farmakologicheskih veshhestv (Guidelines for experimental (preclinical) study of new pharmacological substances) [in Russian]. (pod obshh. red. R.U. Habrieva): ucheb. posobie dlja sistemy poslevuz. prof. obrazovanija vrachej. Moskva: Medicina Shiko, 2005: 826 p. [Google Scholar]

13. Руководство по проведению клинических исследований лекарственных средств (под ред. Мировнова А.Н. и др.). Часть первая. - Москва: Гриф и К, 2012. - 944 с. [Google Scholar]

Rukovodstvo po provedeniju klinicheskih issledovanij lekarstvennyh sredstv (Guidelines for Conducting Clinical Trials of Medicinal Products) [in Russian]. (pod red. Mirovnova A.N. i dr.). Chast' pervaja. Moskva: Grif i K, .2012: 944 p. [Google Scholar]

14. Политова Н.К., Бешли И.В., Пшунетлева Е.А. и др. Лекарственные препараты на основе фитоэкдистероидов / Матер. науч.-практ. конф. «Юбилейные февральские чтения». – Сыктывкар. 2012. - С. 537-545.[Google Scholar]

Politova N.K., Beshley I.V., Pshunetleva Ye.A. i dr. Lekarstvennyye preparaty na osnove fitoekdisteroidov (Medicines based on phytoecdysteroids) [in Russian]. Mater. nauch.-prakt. konf. "Yubileynyye fevral'skiye chteniya". Syktyvkar. 2012: 537-545. [Google Scholar]

15. Щулькин А.В., Якушева Е.Н., Давыдов В.В., Дармограй В.Н. Современные представления о фармакодинамике экдистероидов //Российский медико-биологический вестник имени академика ИП Павлова. – 2012. – №4. – С. 164-169. [Google Scholar]

Shchul'kin A.V., Yakusheva Ye.N., Davydov V.V. i dr. Sovremennyye predstavleniya o farmakodinamike ekdisteroidov (Modern concepts of pharmacodynamics of ecdysteroids) [in Russian]. Ross. med.-biol. vestnik im. akad. I.P. Pavlova. 2012; 4: 164-169. [Google Scholar]

16. Тимофеев Н. П. Новая разработка для рынка БАД. Экдистерон содержащая субстанция из литьевой части левзеи и серпухи // Рынок БАД. – 2013. – №2-С. – С. 30-31. [Google Scholar]

Timofeyev N.P. Ekdisteronsoderzhashchaya substantsiya iz list'yevoy chasti levzei saflorovidnoy i serpukhi ventsenosnoy (New development for the dietary supplement market. Ecdysterone-containing substance from the casting part of Leuzea and Serpukha) [in Russian]. Zhurnal Rynok BAD. 2013; (2):30-31. [Google Scholar]

17. Kutepova T.A., Syrov V.N., Khushbaktova Z.A. et al. Hypoglycemic Activity of the Total Ecdysteroid Extract from Ajuga turkestanica. Pharmaceutical Chemistry Journal. 2001; (35): 608-609. [Crossref]

18. Vazquez M., Silvestre I.S., Provs I.R. Methods Find Exp. Clin. Pharmacol. 2002; (24) No, 8: 515-523.

19. Poroikov V., Filimonov D. Preductive Toxicology. 2005; 459-478.

20. Temirgaziyev B.S., Abulyaissova L.K., Kozhanova A.M. et al. Quantum – Chemical DFT – Approach to The Study of Synthons – 2 – Deoxyecdysone, 2-Deoxyecdysterone and Ecdysterone and their Virtual Bioscreening. Chemical Journal of Kazakhstan. 2020; 4(72): 201-209.[Google Scholar]

21. Temirgaziev B.S., Tuleuov B.I., Romanova M.A. et al. Supramolecular Complexes of 3-Epi-2-deoxyecdysone with Cyclodextrins and Their Anti-Inflammatory Activity. Russ J Gen Chem. 2019; (89): 424–428. [Crossref]

22. Temirgaziyev B.S., Kucakova K., Baizhigit Ye.A., Jurasek M. et al. Bioavailability and Structural Study of 20-Hydroxyecdysone complexes with cyclodextrins. Steroids, 2019; (147): 37-41. [Crossref]

23. Wang L., Li S., Cai H., Liu X., Feng T., Zhao X. Preparation and characterization of ecdysterone/hydroxypropyl – β – cyclodextrin inclusion complex with enhanced oral and transdermal bioavailability. J.Microencapsul, 2022; 39(2): 145-155. [Crossref]

24. Meteleva E.S., Polyakov N.E., Tuleuov B.I. et al. Preparation and Physicochemical Properties of Supramolecular Complexes of Ecdysterone. Khimija rastitel'nogo syr'ja, 2023; (4): 209-217. [Crossref]

25. Chong Y., Galbraith M.N., Horn D.H.S. Isolation of deoxyecrustecdysone, deoxyecdysone, and α-ecdysone from the fern Blechnum minus. Chem. Commun. 1970; (18): 1217-1218. [Crossref]

26. Tuleuov B. I., Temirgaziev B.S., Kozhanova A. M., Seydakhmetova R. B., et al. Supramolecular Complex of 20-Hydroxyecdysone-3-acetate with β-Cyclodextrin and Its Biological Activity. Russian Journal of General Chemistry, 2020; (90): 2258-2263. [Crossref]

27. Kozhanova A.M., Temirgaziyev B.S., Zhanarbek A., Tuleuov B.I., et al. Synthesis of a hydrophilic derivative of ecdysterone and development of its water-soluble form. Bulletin of the University of Karaganda.Chemistry, 2021; 104(4): 138-148. [Crossref]

Сылдыршөп (Silene L.) туысы өсімдіктерінің полиоксистероидтары және олардың туындылары қабынуға қарсы потенциалды агенттер ретінде

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Түйіндеме

Қазіргі кездегі әдеби және біздің тәжірибелік мәліметтеріміз бойынша өсімдік полиоксистероидтары немесе фитоэкдистероидтар Silene L. туысының 126 – дан астам түрінен табылған. Қазақстанда 62 түрі (12 - эндемик) өседі. Соңғы онжылдықта полиоксистероидтарға потенциалды фармакологиялық белсенді қасиеттері бар заттар ретінде ғылыми қызығушылық, оларды бөліп алу, сандық анықтау және химиялық модифицирлеуге бағытталған зерттеулер санының ұлғаюына әкелді.

Зерттеудің мақсаты: In vivo жағдайында Silene L. туысының жаңа полиоксистероид туындыларының қабынуға қарсы белсенділігін зерттеу.

Әдістері. Зерттеулер супрамолекулалық кешен түзілу және механохимия, трансмембраналық өткізгіштігі пен суда ерігіштікті анықтау әдістері арқылы жүргізілді.

Нәтижесі. Биожетімділігі жоғары суда еритін жаңа туындыларды алу үшін механохимиялық әдістермен глицирризин қышқылының (NA_2GA) және 2-гидроксипропил-β-циклодекстриннің (2-HP-β-CD) натрий тұзы бар 20-гидроксиэкдизонның (20E) қатты дисперсиялары мен кешендері алынды. Сондай-ақ полиоксистероидтар негізінде бірнеше супрамолекулалық инкапсуляцияланған кешендер синтезделініп, олардың әртүрлі қатынастардағы суда ерігіштігі және 25 мг/кг және 50 мг/кг дозаларда қабынуға қарсы белсенділігі зерттелді. 3-эпи-2-дезоксиэкдизонның супрамолекулалық β-циклодекстрин кешені "Диклофенак натрий" препаратымен салыстырғанда екі дозада да айтарлықтай үлкен қабынуға қарсы белсенділікті көрсетті.

Қорытынды. Зерттеу нәтижелері, полиоксистероидтардың α-, β-, γ- және 2-гидроксипропил – β – циклодекстриндермен және глицирризин қышқылының динатрий тұзымен жаңа супрамолекулалық кешендері және механохимиялық алынған қатты дисперсияның жоғары қабынуға қарсы тиімділігіне байланысты одан әрі өсімдік тектес қабынуға қарсы препарат әзірлеуде пайдалануға болатынын көрсетті.

Түйін сөздер: сылдыршөп туысы, Silene L., полиоксистероидтар, супрамолекулалық кешендер, механокомпозиттер, қабынуға қарсы белсенділік.

Полиоксистероиды растений рода Смолевки Silene L. и их производные как потенциальные противовоспалительные агенты

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Резюме

В настоящее время по данным литературы и нашим экспериментальным данным полиоксистероиды растений или фитоэкдистероиды обнаружены более чем в 126 видах Silene L. В Казахстане произрастает 62 вида (эндемичных видов - 12). В последнее десятилетие научный интерес к полиоксистероидам как к веществам с потенциально фармакологически активными свойствами привел к увеличению числа исследований, направленных на их выделение, количественное определение и химическое модифицирование.

Цель исследования: изучить противовоспалительную активность новых производных полиоксистероидов рода Silene L. в условиях in vivo.

Методы. Исследования проводили методами супрамолекулярного комплексообразования и механохимии, определения трансмембранной проницаемости и водорастворимости.

Результаты. Для получения новых водорастворимых производных с повышенной биодоступностью механохимическими методами получены твердые дисперсии и комплексы 20-гидроксиэкдизона (20E) с динатриевой солью глицирризиновой кислоты (NA_2GA) и 2-гидроксипропил-β-циклодекстрина (2-HP-β-CD). Синтезировано несколько супрамолекулярных инкапсулированных комплексов на основе полиоксистероидов и изучена их растворимость в воде в различных соотношениях и противовоспалительная активность в дозах 25 мг/кг и 50 мг/кг. Супрамолекулярный β-циклодекстриновый комплекс 3-эпи-2-дезоксиэкдизона продемонстрировал значительно большую противовоспалительную активность в обеих дозах, по сравнению с препаратом «Диклофенак натрия».

Выводы. Результаты исследования показали, что новые супрамолекулярные комплексы полиоксистероидов с α-, β-, γ- и 2-гидроксипропил – β – циклодекстринами и динатриевой солью глицирризиновой кислоты и механохимически полученные твердые дисперсии могут быть рекомендованы к использованию при разработке противовоспалительного лекарственного средства растительного происхождения, в связи с их высокой противовоспалительной эффективностью.

Ключевые слова: род смолевка, Silene L., полиоксистероиды, супрамолекулярные комплексы, механокомпозиты, противовоспалительная активность.