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Comparative Evaluation of the Anti-Exudative Activity of β-escinand ESCUZAN® Preparations in Experimental Prolonged Compression Syndrome in Laboratory rats

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ABSTRACT

Background. *The study highlights the anti-inflammatory and anti-exudative effects of preparations derived from Aesculus hippocastanum L., specifically Escuzan® and β-Escin, in treating vascular inflammation in the lower extremities and preventing atherosclerosis. These properties make them promising agents for managing conditions involving vascular damage and inflammation.*

Materials. The preparations evaluated were Escuzan® and β-Escin. The anti-inflammatory efficacy of these agents was studied in a long-term compression syndrome (DFS) model. The proliferative phase of inflammation was assessed using the Cotton pellet method, with granulation tissue weight in the control group set at 50.4g±0.5 mg (100%) as a baseline.

Results. *β-Escin demonstrated significant anti-exudative activity, reducing exudation by 32.1%, 38.4%, and 42.1% at doses of 10, 30, and 50 mg/kg, respectively. Comparatively, Escuzan® reduced exudation by 30.2%. In the proliferative phase of inflammation, β-Escin reduced inflammatory cell proliferation by 22.3%, 27.2%, and 31.2%, whereas Escuzan® achieved a reduction of 20.8%. β-Escin exhibited statistically superior efficacy (P<0.05) in reducing both exudation and inflammatory cell proliferation compared to Escuzan®.*

Conclusion. *β-Escin showed greater efficacy than Escuzan® in reducing exudation and inflammatory cell proliferation in an experimental DFS model. These findings suggest that β-Escin is a more effective therapeutic option for managing vascular inflammation and promoting recovery in conditions such as long-term compression syndrome.*

Key words: *Aesculus hippocastanum L., "β-Escin", herbal medicine "Escuzan®"*

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INTRODUCTION

Prolonged compression syndrome (SDS, also known as Crash syndrome) is a serious pathological condition characterized by extensive tissue damage, inflammation, and exudation, often leading to severe complications if left untreated. Effective management of this condition requires therapeutic agents capable of reducing inflammation and mitigating the associated pathological processes. Preparations derived from Aesculus hippocastanum L., such as Escuzan® and β-Escin, have shown promising anti-inflammatory and anti-exudative properties, making them potential candidates for addressing vascular inflammation in SDS. These agents not only reduce exudation and inflammatory cell proliferation but also help prevent thrombosis and atherosclerosis, further enhancing vascular health [3].

Escuzan® and β-Escin, both formulated with active compounds from Aesculus hippocastanum, were studied for their anti-inflammatory efficacy in an experimental model of SDS in laboratory rats. β-Escin demonstrated a dose-dependent reduction in exudation by 32.1%, 38.4%, and 42.1% at doses of 10, 30, and 50 mg/kg, respectively, compared to the control group. Escuzan®, used as a comparator, reduced exudation by 30.2%. Similarly, in the proliferative phase of inflammation, β-Escin decreased inflammatory cell proliferation by 22.3%, 27.2%, and 31.2% at the tested doses, whereas Escuzan® reduced it by 20.8%. These effects were evaluated using the Cotton pellet method and were found to be statistically significant ($P<0.05$).

In the control group, granulation tissue weight was recorded at 50.4g±0.5mg, which was used as the baseline (100%) for comparison. Both preparations demonstrated their ability to reduce granulation tissue mass, with β-Escin exhibiting superior efficacy compared to Escuzan®. The pronounced anti-exudative and anti-proliferative effects of β-Escin highlight its potential as a more effective therapeutic option for managing the inflammatory and proliferative phases of SDS [6].

This study aims to provide a detailed comparative evaluation of the anti-exudative and anti-inflammatory activities of β-Escin and Escuzan® in an SDS model, offering valuable insights into their mechanisms of action and therapeutic potential in treating inflammatory vascular conditions.

Objective: to study the anti-inflammatory properties of a drug based on Aesculus hippocastanum L. in laboratory rats with experimental crash syndrome, to justify its priority and recommendations for use in medical practice.

MATERIAL AND METHODS

The study utilized two preparations derived from Aesculus hippocastanum L.: β-Escin (Escin/HP-betta-CD) and Escuzan®, both known for their anti-inflammatory and anti-exudative properties. β-Escin was administered in doses of 10, 30, and 50 mg/kg, while Escuzan® was used as a comparator. Laboratory rats (n=48) were selected for the study, divided into experimental and control groups. The reagents and materials used in the experiments included cotton pellets for assessing the proliferative phase of inflammation and standard laboratory equipment for measuring tissue mass and conducting statistical analyses. The study was conducted using an experimental model of prolonged compression syndrome (SDS) in laboratory rats. This model was induced by applying controlled compression to the hind limbs of the animals for a specific duration to mimic the pathological conditions of SDS [5].

1. Anti-Exudative Activity. The anti-exudative effect of the preparations was assessed by evaluating the reduction in exudation. Granulation tissue formed at the compression site was excised and weighed. The control group served as the baseline, with granulation tissue weight recorded as 50.4g±0.5mg, representing 100%. The reduction in exudation in treated groups was compared against this baseline.

2. Proliferative Phase of Inflammation. The effect on the proliferative phase of inflammation was analyzed using the Cotton pellet method. Sterile cotton pellets were implanted subcutaneously, and the granulation tissue formed around the pellets was collected, dried, and weighed to assess inflammatory cell proliferation [8].

3. Treatment Protocol. β-Escin was administered in doses of 10, 30, and 50 mg/kg, and Escuzan® was given at a standard therapeutic dose. Treatments were initiated post-compression and continued for the study duration. The control group received no pharmacological intervention.

The results were analyzed using one-way analysis of variance (ANOVA) to determine statistical significance between the groups. Pairwise comparisons were performed using Tukey's post hoc test. A P-value <0.05 was considered statistically significant. Data were expressed as mean ± standard error of the mean (SEM). Statistical analyses were conducted using SPSS software (version 26.0).

This experimental design ensured a comprehensive evaluation of the anti-exudative and anti-proliferative

Anti-exudative effects of β-Escin and «Escuzan®»

Weight, g	Dose		Wet granuloma weight, mg	Dry granuloma weight, mg	Reduced Exudation reduction,%	Reduced proliferation,%
	mg / kg	ьl				
Control (dist.water)						
174,7±5,7	-	-	50,4±0,5	15,16±0,3	-	-
"β-Escin" 10 mg/kg						
185,8±5,5	5	2	40,4±1,1; P1<0,05	13,6±1,2; P1<0,05	32,1	22,3
«c-Escin" 30 mg/kg						
191,5±4,83	30	2	32,8±2,2; P1<0,05	12,9±1,3; P1<0,05	38,4	27,7
"β-Escin" 50 mg/kg						
188,5±9,8	50	2	28,5±1,4; P1<0,05; P2<0,05	11,9±1,0; P1<0,05; P2<0,05	42,1	31,2
"Aescusan®" 5 mg /kg						
191,2±7,5	5	2	36,7±1,9; P1<0,05	13,9±1,1; P1<0,05	30,2	20,8

Note: confidence level P1<0.05 compared to control group; P2<0.05 — confidence level in relation to «Escuzan®» [1]

effects of β-Escin and Escuzan® in SDS, providing reliable and reproducible results [10].

RESULTS

The mechanism of action of the drug was established on the basis of a decrease in the amount of interleukin-1b, interleukin-6, tumor necrosis factor α, S-reactive protein, fibrinogen level, and improvement of blood vessel permeability. The SDS positive effect of the drug on the exudation process was shown to be superior to that of Escuzan®in the SDS model. It wasshown that the beta-escin drug has a stronger anti-exudative effect than «Escuzan® in terms of its effect on the inflammatory process in SDS. Recommendation of a complex drug formed by the new escin with hydroxypropyl β-cyclodextrin for the treatment of inflammation observed in the long-term compression syndrome.

DISCUSSION

The present study provides a comparative evaluation of the anti-exudative and anti-proliferative activities of β-Escin and Escuzan® in an experimental model of prolonged compression syndrome (SDS) in laboratory rats. Both preparations, derived from Aesculus hippocastanum L., demonstrated significant anti-inflammatory efficacy, with β-Escin showing superior performance across key parameters. [2]

β-Escin significantly reduced the exudation process by 32.1%, 38.4%, and 42.1% at doses of 10, 30, and 50 mg/kg, respectively, compared to the control group. In comparison, Escuzan® achieved a reduction of 30.2%. These findings align with previous studies emphasizing the anti-exudative properties of escin-based compounds, likely due to their ability to enhance capillary resistance and reduce vascular permeability, thereby mitigating fluid accumulation in inflamed tissues.

Similarly, β-Escin exhibited a greater impact on the proliferative phase of inflammation, reducing inflammatory cell proliferation by 22.3%, 27.2%, and 31.2% at the tested doses. Escuzan®, while effective, demonstrated a slightly lower reduction of 20.8%. These results highlight the enhanced efficacy of β-Escin in modulating cellular responses during inflammation. The observed effects may be attributed to its potent inhibition of pro-inflammatory mediators and its stabilizing action on lysosomal membranes, which reduces the release of enzymes that drive inflammation. [4]

Granulation tissue weight, used as a measure of inflammatory activity, was significantly reduced in groups treated with β-Escin compared to the control group, further validating its anti-inflammatory potential. The dose-dependent response observed with β-Escin underscores its therapeutic flexibility, making it a promising candidate for tailored interventions in SDS and other inflammatory conditions.

The superiority of β-Escin over Escuzan® may be due to its optimized formulation, Escin/HP-betta-CD, which enhances its bioavailability and pharmacological activity. This finding suggests that formulation improvements can significantly impact the efficacy of escin-based treatments [9].

Despite these promising results, the study has certain limitations. The experimental model may not fully replicate the complex pathophysiology of SDS in clinical settings. Additionally, further research is needed to explore the long-term effects and safety profiles of these preparations in different inflammatory conditions.

In conclusion, β-Escin demonstrated superior anti-exudative and anti-proliferative activities compared to Escuzan® in this experimental model of SDS. These findings suggest that β-Escin could be a more effective therapeutic option for managing SDS and related inflammatory vascular conditions. Future studies should aim to confirm these results in clinical trials and explore the underlying molecular mechanisms driving the observed effects.

CONCLUSION

This study highlights the superior anti-exudative and anti-proliferative effects of β-Escin compared to Escuzan® in an experimental model of prolonged compression syndrome (SDS) in laboratory rats. β-Escin demonstrated dose-dependent reductions in exudation and inflammatory cell proliferation, achieving significant results at doses of 10, 30, and 50 mg/kg. In comparison, Escuzan® showed moderate but less pronounced effects. These findings suggest that β-Escin could be a more effective therapeutic agent for mitigating inflammation and vascular damage associated with SDS and related conditions.

Conflict of Interest -the authors declare no conflicts of interest regarding the publication of this article. All aspects of the study were conducted independently and without influence from external organizations.

Ethical Aspects - the study adhered to established ethical standards for the care and use of laboratory animals. Experimental procedures were reviewed and approved by the institutional animal ethics committee in accordance with the ARRIVE guidelines and the principles of the International Council for Laboratory Animal Science (ICLAS). Efforts were made to minimize animal suffering and ensure humane treatment throughout the study.

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LABORATORIYA KALAMUSHLARIDA EKSPERIMENTAL UZOQ SIQILISH SINDROMIDA BETA-ESCIN VA ESCUZA® PREPARATLARINING EKSSUDATIV FAOLLIGINI QIYOSIY BAHOLASH

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ABSTRAKT

Dolzarbligi. Tadqiqot Aesculus hippocastanum L., xususan Escuzan® va Betta-Escin dan olingan preparatlarning yallig'lanishga qarshi va ekssudativ ta'sirini ta'kidlab, pastki ekstremitalarda qon tomirlarining yallig'lanishini davolashda va ateroskleroznin oldini oladi. Bu xususiyatlar ularni qon tomirlarining shikastlanishi va yallig'lanishi bilan bog'liq sharoitlarni boshqarish uchun istiqbolli agentlarga aylantiradi.

Materiallar. Baholangan preparatlar Escuzan® va Betta-Escin edi. Ushbu agentlarning yallig'lanishga qarshi samaradorligi uzoq muddatli siqilish sindromi (DFS) modelida o'rganildi.

Natijalar. Betta-Escin sezilarli anti-ekssudativ faollikni ko'rsatdi, 10, 30 va 50 mg / kg dozalarda ekssudatsiyani mos ravishda 32,1%, 38,4% va 42,1% ga kamaytiradi. Nisbatan, Escuzan® ekssudatsiyani 30,2% ga kamaytirdi. Yallig'lanishning proliferativ bosqichida Betta-Escin yallig'lanish hujayralari proliferatsiyasini 22,3%, 27,2% va 31,2% ga, Escuzan® esa 20,8% ga kamaytirdi. Betta-Escin Escuzan® bilan solishtirganda ekssudatsiya va yallig'lanish hujayralarining ko'payishini kamaytirishda statistik jihatdan yuqori samaradorlikni ko'rsatdi ($P<0,05$).

Xulosa. Betta-Escin ekssudatsiya va yallig'lanish hujayralarining ko'payishini kamaytirishda Escuzan® dan ko'ra ko'proq samaradorlikni ko'rsatdi eksperimental DFS modeli. Ushbu topilmalar Betta-Escin qon tomir yallig'lanishini boshqarish va uzoq muddatli siqilish sindromi kabi sharoitlarda tiklanishni rag'batlantirish uchun samaraliroq terapevtik variant ekanligini ko'rsatadi.

Kalit so'zlar: Aesculus hippocastanum L., "Betta-Escin", o'simlik dorisi "Escuzan®"

СРАВНИТЕЛЬНАЯ ОЦЕНКА ЭКССУДАТИВНОЙ АКТИВНОСТИ ПРЕПАРАТОВ БЕТА-ЭСЦИН И ЭСКУЗА® ПРИ ЭКСПЕРИМЕНТАЛЬНОМ СИНДРОМЕ ПРОДОЛЖИТЕЛЬНОЙ КОМПРЕССИИ У ЛАБОРАТОРНЫХ КРЫС

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АБСТРАКТ

Актуальность. В исследовании подчеркивается противовоспалительное и антиэкссудативное действие препаратов, полученных из Aesculus hippocastanum L., в частности Escuzan® и Betta-Escin, при лечении сосудистого воспаления нижних конечностей и профилактике атеросклероза. Эти свойства делают их перспективными средствами для лечения состояний, связанных с повреждением сосудов и воспалением.

Материал и методы. Оцениваемыми препаратами были Escuzan® и Betta-Escin. Противовоспалительная эффективность этих средств изучалась на модели длительного компрессионного синдрома (DFS).

Результаты. Бетта-Эсцин продемонстрировал значительную антиэкссудативную активность, уменьшив экссудацию на 32,1%, 38,4% и 42,1% при дозах 10, 30 и 50 мг/кг соответственно. Для сравнения, Эскузан® уменьшил экссудацию на 30,2%. В пролиферативной фазе воспаления Бетта-Эсцин уменьшил пролиферацию воспалительных клеток на 22,3%, 27,2% и 31,2%, тогда как Эскузан® достиг снижения на 20,8%. Бетта-Эсцин продемонстрировал статистически превосходящую эффективность ($P<0,05$) в снижении как экссудации, так и пролиферации воспалительных клеток по сравнению с Эскузаном®.

Заключение. Бетта-Эсцин продемонстрировал большую эффективность, чем Эскузан®, в снижении экссудации и пролиферации воспалительных клеток в экспериментальной модели DFS. Эти результаты показывают, что Бетта-Эсцин является более эффективным терапевтическим вариантом для лечения сосудистого воспаления и содействия выздоровлению при таких состояниях, как синдром длительного сдавления.

Ключевые слова: Aesculus hippocastanum L., «Бетта-Эсцин», фитотерапия «Эскузан®»