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VERIFICATION OF ANGIOPROTECTIVE AND ANTI–INFLAMMATORY PROPERTIES OF *VACCINIUM MYTILLUS, VACCINIUM ARCTOSTAPHYLOS* IN EXPERIMENT

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SUMMARY

The dental system is a complex mechanism that includes a number of connective tissue structures that have specific properties and perform a number of functions, in particular, protective. One of the main barrier elements of the oral cavity is the mucous membrane lining it, throughout its length, having a different morphological structure. The most frequently pathological process is the periodontal tissue, which consists of attached and non-attached gums, bone alveoli, cementum of the tooth root and periodontal ligament of the tooth. At present, all periodontal diseases are usually divided into inflammatory and primary dystrophic, while a number of authors have found that in its pure form, the dystrophic process is detected no more than 1–8% of all diseases and is characterized as a generalised process against the background of general somatic pathology. The frequency of occurrence of periodontal diseases varies from 60 to 85% in the working population, which determines the relevance of studying therapeutic measures aimed at their relief and is the purpose of this study.

The aim of the study *was to investigate the angioprotective and anti-inflammatory properties of Vaccinium mytillus, Vaccinium arctostaphylos in experiment.*

Materials and methods. *In this experimental work, the authors developed a model of periodontal damage in experimental animals (Vistar rats, weight – 25–300 g) under the conditions of drug loading with chloral hydrate, in accordance with the Directive on the Protection of Vertebrate Animals of 2000 and extracts from the act of Local Ethical Committee. The model was created by inflicting a single injury with a sharp object in the projection of the interdental space in the frontal segment of the mandible. The proper pathological condition was recorded on the 5–7th day; the verification of the morphological changes in some of the animals was being made by fragmenting the frontal segment of the lower jaw, followed by a pathological and histological examination. Then, the control group of animals was treated applied gel, made of Vaccinium mytillus, Vaccinium arctostaphylos to stop the process for 2 weeks. For comparison, the main group was treated with a gel without the inclusion of a drug component. At the end of the course of conservative therapy, according to the design of the study, biopsy specimens were taken again in both groups to evaluate the results of the conservative therapy provided.*

Results. *According to the patho-histological study in the biopsy specimens of the damaged periodontium, the animals, revealed morphological disorders corresponding to chronic periodontal disease. At the stage of treatment in the control group, positive dynamics was noted both according to the clinical examination and after the pathological and histological examination of biopsy specimens in the comparison groups.*

Conclusions. *The obtained results indicate the presence of anti-inflammatory and angioprotective effect of medicament compositions based on Vaccinium mytillus, Vaccinium arctostaphylos, which will be further tested in clinical trials.*

KEYWORDS: *medicinal composition, modeling of the pathological process, biopsy specimens.*

CONFLICT OF INTEREST. *The authors declare no conflict of interest.*

ВЕРИФИКАЦИЯ АНГИОПРОТЕКТИВНЫХ И ПРОТИВОВОСПАЛИТЕЛЬНЫХ СВОЙСТВ VACCINIUM MYTILLUS, VACCINIUM ARCTOSTAPHYLOS В ЭКСПЕРИМЕНТЕ

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РЕЗЮМЕ

Зубочелюстная система является сложным механизмом, включающим в себя ряд соединительнотканных структур, обладающих специфическими свойствами и выполняющими ряд функций, в частности защитной. Одним из основных барьерных элементов полости рта является выстилающая ее слизистая оболочка, на всем протяжении, имеющая различное морфологическое строение. Наиболее часто патологическому процессу подвергаются ткани пародонта, который состоит из прикрепленной и неприкрепленной десны, костной альвеолы, цемента корня зуба и периодонтальной связки зуба. В настоящее врем все заболевания пародонта принято делить на воспалительные и первично-дистрофические, при этом рядом авторов, установлено, что в чистом виде дистрофический процесс выявляется не чаще 1–8 % от всех заболеваний и характеризуется, как генерализованный процесс, на фоне общесоматической патологии. Частота встречаемости заболеваний пародонта варьирует от 60 до 85 % у работоспособного населения, что определяет актуальность изучения терапевтических мероприятий, направленных на их купирование и является целью настоящего исследования.

Целью исследования *было изучение ангиопротекторных и противовоспалительных свойств Vaccinium mytillus, Vaccinium arctostaphylos в эксперименте.*

Материалы и методы. *В настоящей экспериментальной работе авторами разработана модель повреждения пародонта у животных, участвующих в эксперименте (крыс рода Vistar, весом 25–300 гр.) в условиях медикаментозной нагрузки препаратом хлоралгидрат, согласно директиве о защите позвоночных животных от 2000 г., и выписки из акта локального этического комитета ПМФИ № 10 от 02.03.2023 г. Модель создалась посредством нанесения однократной травмы острым предметом в проекции межзубного пространства во фронтальном сегменте н/ч. Получение должного патологического состояния регистрировали на 5–7-е сутки, для верификации морфологических изменений у части животных, участвующих в эксперименте, забирали фрагмент тканей пародонта, путем фрагментации фронтального сегмента нижней челюсти, с последующим пато-гистологическим исследованием, после чего в течение 2-х недель ежедневно контрольной группе животных с целью купирования процесса наносили гель на основе vaccinium mytillus, vaccinium arctostaphylos, для сравнения основной группе наносили гелевую основу без включения медикаментозного компонента. По окончанию курса консервативной терапии согласно дизайну исследования проводили повторный забор биоптатов, как в контрольной, так и основных группах для оценки результатов оказываемой консервативной терапии.*

Результаты. *По данным патогистологического исследования в биоптатах поврежденного пародонта животных выявлены морфологические нарушения, соответствующие хроническому заболеванию пародонта. На этапе лечения в контрольной группе была отмечена положительная динамика как по данным клинического обследования, так и после патологоанатомического и гистологического исследования биоптатов в группах сравнения.*

Выводы. *Полученные результаты свидетельствуют о наличии противовоспалительного и ангиопротекторного действия лекарственных композиций на основе Vaccinium mytillus, Vaccinium arctostaphylos, которые будут дополнительно протестированы в клинических испытаниях.*

КЛЮЧЕВЫЕ СЛОВА: *медикаментозная композиция, моделирование патологического процесса, биоптаты.*

КОНФЛИКТ ИНТЕРЕСОВ. *Авторы заявляют об отсутствии конфликта интересов.*

Introduction

Vaccinium mytillus, Vaccinium arctostaphylos – common blueberry and Caucasian blueberry plants of the heather family (*Ericaceae*) are mostly distributed in mountainous areas, in coniferous, mixed and marshy forests [1]. The lack of wide distribution in the use of medicinal purposes is determined by the impossibility of cultivation. Despite this fact, since the 16th century, plants of the genus *Vaccinium* have been used as medicinal plants for such diseases as cholelithiasis, scurvy, tuberculosis, dysentery, as well as in the treatment of inflammatory diseases of the oropharynx with relevant evidence-based results of effectiveness [2, 3]. Relevant research today is the study of angioprotective properties associated with vascular ophthalmic pathology, vascular complications of diabetes mellitus and inflammatory periodontal diseases [4]. The chemical residue of medicinal plants varies depending on the part used. For fruits, the characteristic composition includes sugars (6–10 %), citric, succinic, quinic, oxalic, lactic and malic acids (1–1.3 %), ascorbic acid, thiamine, riboflavin, nicotinic acid, carotenoids, pectin substances (0,14–0.69 %), essential oil, tannins (12 %), arbutin, flavonoids, triterpenoids, anthocyanin glycosides, as well as easily digestible manganese and iron compounds [5, 6]. The leaves, in turn, contain tannins, arbutin, flavonoids, phenolic glycoside. For fruits, the characteristic composition includes sugars (6–10 %), citric, succinic, quinic, oxalic, lactic and malic acids (1–1.3 %), ascorbic acid, thiamine, riboflavin, nicotinic acid, carotenoids, pectin substances (0,14–0.69 %), essential oil, tannins (12 %), arbutin, flavonoids, triterpenoids, anthocyanin glycosides, as well as easily digestible manganese and iron compounds [5, 6]. The leaves, in turn, contain tannins, arbutin, flavonoids, phenolic glycoside. For fruits, the characteristic composition includes sugars (6–10 %), citric, succinic, quinic, oxalic, lactic and malic acids (1–1.3 %), ascorbic acid, thiamine, riboflavin, nicotinic acid, carotenoids, pectin substances

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The main elements with pharmacological activity are anthocyanides, which have high antioxidant activity, the ability to stabilize collagen molecules and accelerate its biosynthesis, reduce the permeability and fragility of the capillary link [7]. In addition, anthocyanides block the biosynthesis of pro-inflammatory mediators – histamine, prostaglandins and leukotrienes, thereby possessing anti-inflammatory activity. A number of scientists have identified antiallergic, antimicrobial, antiviral, antimutagenic, antiproliferative actions. Penarrola R., 1980 et al. [8], who studied microcirculation parameters such as vascular permeability, vascular wall thickness, linear blood flow velocity as in the experimental conditions, as well as in clinical practice, confirms the studied anti-inflammatory and angioprotective properties. Thus, in 47 patients with diagnosed venous insufficiency [9], blueberry extract contributed to the restoration of microcirculation, elimination of stagnation and stasis of blood in the vessels of the lower extremities.

Multiple therapeutic effects of the studied medicinal plant, in particular anti-inflammatory and angioprotective properties determined the purpose of this study: to study the properties and effectiveness of medicinal compositions based on *Vaccinium mytillus, Vaccinium arctostaphylos* in inflammatory periodontal diseases in the experiment.

The aim of the study was to investigate the angioprotective and anti-inflammatory properties of *Vaccinium mytillus, Vaccinium arctostaphylos* in experiment.

Materials and methods

On the base of the PMFI vivarium, a branch of the Federal State Budgetary Educational Institution of Higher Education «VolgSMU» of the Ministry of HealthCare of the Russian Federation, 18 animals (white mice of the Vistar breed) were selected for the experiment, randomly divided into 3 experimental groups. Randomisation was performed by pulling alternately random numbers of animals. The weight of the animals did not exceed 300 g, keeping conditions: room temperature 22±2 °C, relative air humidity 55±5 °C. The maintenance of animals, the European Convention, 2002, and the local ethical committee No. 17 of February 10, 2023 carried out invasive manipulations in accordance with the Directive on the Protection of Vertebrate Animals. The division into groups was carried out as follows, in the first control group (n=6) the medicinal composition is represented by a gel without an active substance, second group (n=6) drug composition based on *Vaccinium mytillus*, third group (n=6) drug composition based on *Vaccinium arctostaphylos*. Modeling of the pathological process (inflammatory periodontal disease) was carried out in all animals under the conditions of a drug load of chloral hydrate to achieve controlled short-term sedation. To obtain a pathological process in the periodontal tissues, the animals were subjected to a mechanical injury in the projection of the frontal incisors by inserting a 16G catheter into the interdental space. After infliction of injury for 7 days, dynamic monitoring of the progression of the pathological process was carried out. Next, the approbation of drug compositions and the application of the gel base for subsequent comparative analysis began. The application was performed once, daily, for 14 days.

Results and discussion

In 18 animals, by 7 days of observation from the modeling of the pathological process, the phenomena of hyperemia, edema, formation of a periodontal pocket in the projection between the central incisors, a depth of 3 ± 0.06 mm, with the presence of purulent detachable. The central incisors in 4 animals had mobility of the second degree (vestibulo-oral and mesio-distal directions), in 14 animals – the first degree (vestibulo-oral direction). The general condition of the animals did not suffer at the same time; the functional activity remained at the proper level, while there was difficulty in the usual volume in 4 animals, due to the mobility of the frontal group of teeth of the lower jaw. At the stages of approbation of medicinal compositions by the third day in the control group of animals, n=6 inflammatory phenomena remained in the same volume, in 2 cases progression of periodontitis was registered, with tooth mobility of the third degree (vestibulo-oral, mesio-distal, vertical). In the control groups, n=12, there was no progression of the pathological process. By the 7th day, in the animals in the main group, the phenomena of an inflammatory nature underwent a positive trend, the diameter of hyperemia decreased, and pathological mobility remained at the same level. In the main group, n=6 (second group), the periodontal pocket was reduced to 2 mm according to the metric measurement with a periodontal probe, the mobility of the frontal group of teeth remained the same. In the main group, n=6 (third group), the periodontal pocket was reduced to 2 mm according to the metric measurement with a periodontal probe,

By the 14th day in the control group of animals, the state of periodontal tissues was without pronounced dynamic changes, there was no discharge, while the mobility of the frontal group of teeth was in the 5th degree (vestibulo-oral, mesio-distal, vertical directions). In the animals, the main group n=12 has intact periodontium, a periodontal pocket up to 1 mm deep, and stable dentogingival attachment.

Conclusions

The obtained results indicate the presence of anti-inflammatory and angioprotective effect of medicament compositions based on *Vaccinium mytillus, Vaccinium arctostaphylos*, which will be further tested in clinical trials.

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