

Review Article

**STUDY OF ANTIBACTERIAL PROPERTIES OF A NEW DEVELOP DENTAL DRUG
«DENTA ALOE»**

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Abstract

The variety of clinical forms of stomatitis and a large number of etiological factors and pathogenetic chains of the development of inflammatory and dystrophic diseases in the oral mucosa actualize the problem of prevention and treatment of stomatitis for a practical solution. The multifactorial nature of the development of the disease, the chronization of the process, difficulties in achieving positive results of complex treatment, the emergence of resistant forms of microorganisms require the creation of new drugs for the local treatment of lesions of the oral mucosa. A promising direction is considered to be the development of medicines for the treatment of oral diseases based on medicinal plants, in particular Aloe arborescens mill. This article presents the results of studying the antimicrobial activity of the drug «Dent Aloe». This article discusses the characteristics of the sensitivity of microbes to the newly created drug «Dent Aloe» in vitro.

Keywords: stomatitis in children, microbiology, drug «Denta Aloe», Plant-based substances, microorganisms, oral mucosa, oral hygiene, sensitivity, wound healing, fungi.

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INTRODUCTION

It is known that many drugs contain substances that can inhibit the growth of a number of microorganisms. The effectiveness of these substances is due to the content of a number of chemically complex and variously active substances. Plant-based substances contain alkaloids, amino acids, antibiotics, vitamins, glycosides, tannins, organic acids, fats, trace elements, pigments, mucus, resins, volatile, essential oils, etc [2,3,6,21].

They are able to influence the microbial, aseptic effect in the production of drugs. In this regard, the study of the medicinal properties of many plants of wild flora with antimicrobial properties has recently become relevant. A microbiological purity test is required to evaluate the quality of medicinal forms [7,8,12,23].

Before the analysis, it is recommended that the antimicrobial effect of the drug be determined under the conditions of the test in relation to the test of microorganisms specified in the general pharmacopoeial articles for microbiological purity. For the quantitative determination of aerobic bacteria and fungi, the European Pharmacopoeia recommends: if a suitable method or combination of methods does not remove the inhibitory effect of the drug against a particular microorganism test, it can be assumed that the drug has an antimicrobial effect against this microorganism and there is little chance of contamination [1,8,10,20,22].

However, it is possible that the drug inhibits only the test microorganisms involved in the test in determining the antimicrobial activity, but does not show antimicrobial activity in relation to other microorganisms that are not used as the test microorganisms. In this case, the test is performed at the maximum dilution of the test subject, taking into account microbial growth and acceptable criteria.

Stomatitis is an inflammatory lesion of the oral mucosa, which is an urgent problem in modern dentistry. The mechanism for the occurrence of stomatitis has not yet been fully identified, but most likely this is a reaction of the immune system to irritants. Local factors, such as poor oral hygiene, are also

considered the cause [2,11,14,17,24].

With this disease, oral mucosa becomes edematous, painful, and may be covered with white or yellow plaque. Hypersalivation is noted (increased salivation). There may be unpleasant breath noted. There are allergic, aphthous, vesicular, herpetic, catarrhal, traumatic, ulcerative varieties of stomatitis.

LITERATURE SURVEY.

Recurrent aphthous stomatitis is one of the most common diseases of the oral mucosa. Prevalence of recurrent aphthous stomatitis (RAS) greatly differs among different populations [Neville B.W., 2010, Yang S., 2017]. According to recent studies, it varies from 5 to 66%, with an average value of 20% [Momen-Beitollahi J., 2010].

Aphthous stomatitis refers to systemic pathology with a complex genesis, is characterized by a long course and resistance of therapy. Currently, there are many methods for treating lesions of the oral mucosa. The complex treatment includes topical drugs with analgesic and anti-inflammatory, antimicrobial and keratoplastic properties.

Multi-varieties of disease, development of chronic process, difficulty in achieving a positive outcome of complex treatment, the appearance of resistant microorganisms require the creation of new drugs for the local treatment of lesions of the oral mucosa.

Diagnosis of stomatitis and determination of the cause are made based on history and physical examination; specific tests may be conducted in cases where stomatitis is likely a result of systemic disease or infection (eg, inflammatory bowel disease, celiac disease, nutritional deficiency, HIV infection, HSV infection). No cure exists for aphthous stomatitis and ulcers typically remit without drug therapy; topical anesthetics such as lidocaine provide relief. Stomatitis caused by specific infection may be treated with the appropriate antimicrobial (eg, nystatin or fluconazole for candidiasis; acyclovir for HSV). In cases associated with a systemic inflammatory or autoimmune disease, treatment of the underlying condition often results in

reduction in the frequency and severity of stomatitis. Cases associated with trauma (eg, dentures, orthodontic appliances) can often be managed with mechanical modifications; good oral hygiene is also essential, including disinfection of dentures and removal of dentures during sleep. Stomatitis due to radiation therapy or cancer chemotherapy can sometimes be prevented or mitigated with cryotherapy, laser therapy, or cytoprotective agents; the latter may also be used therapeutically. Cases associated with nutritional deficiency are treated with repletion. Secondary infection, malnutrition, and dehydration are possible complications of stomatitis; in immunocompromised patients, stomatitis may act as a portal for systemic bacterial infection. Prognosis depends on the cause, but in many patients, recurrence is common; avoidance of known triggers and control of underlying conditions may reduce the frequency and severity of relapses and recurrences. [3,9,13,14,24]

Methodology.

A promising area is the development of prolonged-release drugs that provide local and uniform release of the active substance from the medicinal form, creating its high therapeutic concentration at the site of exposure without any effect on the level of the drug in the systemic circulation.

In this regard, the development of a domestic drug in the form of a powder for the prevention and comprehensive treatment of inflammatory and dystrophic - inflammatory diseases of the oral cavity is relevant. Designed in Uzbek Scientific - Research Chemical - Pharmaceutical Institute product, code-named «Denta Aloe» is intended for the treatment of inflammatory dental diseases.

The object of research was to study the characteristics of the sensitivity of microbes to the newly created drug «Denta Aloe» in vitro.

Material and methods of research.

To achieve this goal, we initially conducted in vitro experiments to study the sensitivity of 12 strains of microbes (the most common inhabitants in the oral cavity) to the «Denta Aloe» antiseptic drug.

Experimental results

«Denta Aloe» is a dental powder for rinsing the oral cavity, combined preparation for local use. It has anti-inflammatory, wound healing, and local anesthetic effects and also improves the regeneration of oral tissue.

The composition of the dental preparation «Denta aloe» in 3 g:
Active substances:

- Aloe dry extract of leaves (*Aloe arborescens* mill) - 1.0 g;
- Menthol (Mentol) - 0.05 g;

Excipients:

- Sodium chloride (*Natrii chloridum*) - 0.54 g;
- Sodium bicarbonate (*Natrii hydrocarbonas*) - 1.4 g;
- Benzoate sodium (*Sodium benzoate*) - 0.01 g;

Developer: Uzbek Scientific Research Chemical - Pharmaceutical Institute, Uzbekistan.

Aloe extract has anti-inflammatory and wound healing effects: during biostimulation in cells, aloe forms biogenic stimulants that stimulate the vital activity of cells, which turn on the activation of the metabolic process and the process of tissue repair and healing achieved. The local anesthetic menthol, which is part of the drug, acts on the receptors of the skin and mucous membranes of the mouth and gums, helps to quickly reduce pain, refreshes, and causes a feeling of coolness. Sodium bicarbonate increases the alkaline reserves of the blood relieves the effects of tissue acidosis, reduces the reaction. Sodium benzoate is a surface- active substance that improves dispersion and maintains the stability of active substances. Sodium chloride component with antitoxic and anti-inflammatory effect allows to stimulate a complex system of tissue regulation of water-salt metabolism.

According to recent data in the literature (Tsarev V.N., 2010; Y. Levinson, 2015) the sensitivity of microorganisms to chemicals is determined by two methods:

1. Disc - diffuse method, based on diffusion into agar using paper disks impregnated with chemicals.
2. The method of serial dilutions of chemicals in dense or liquid nutrient media with the introduction of microbes in them.

Among these methods, disc - diffusion is the most common spread. Frequency of use of this method is related its benefits such as reliability of the testing process, low cost, flexibility, high reproduction of results in compliance with the testing conditions and preparing expenses materials [15,18,19].

For the setting this research method, we initially prepared fresh (18 hours) culture of microbes for test. After that, 1-2 ml of the test culture according to the turbidity standard of 1×10^6 microbes were uniformly distributed by shaking the cups on the surface of the dried Müller Hinton culture medium in Petri dishes, and the excess was removed with a pipette in a disinfectant solution. At the same time, in certain penicillin vials, chemical preparations of certain concentrations (0.1 - 0.5 - 0.75 - 1.0%) were prepared to be tested. We used these concentrations of the drug to treat sick children.

After seeding, Petri dishes were dried at room temperature for 10-15 minutes, then prepared paper disks (like anti-biotic ones) were taken with sterile tweezers, soaked in prepared chemicals and applied at different distances from each other and 2 cm from the edge of the cup on the surface of the nutrient medium seeded with a certain culture (no more than 6 discs per cup), the plates were closed and placed in a thermostat at a temperature of 37 °C, incubated for 18-24 hours. At the end of the incubation period, the plates were removed from the thermostat and, to take into account the results obtained, the plates were placed on a dark matte surface and the diameter of the microbial growth inhibition zone around the disks was measured using a special ruler, including the diameter of the disks themselves with an accuracy of 1 mm.

DISCUSSION

The results of microbiological studies on the sensitivity of microbes to the drug "Denta Aloe" in various concentrations (0.1 - 0.5 - 0.75 - 1.0%) in vitro are presented in table No. 1.

The table shows that the drug "Denta Aloe" was quite high antibacterial activity in respect of microbes belonging to Gram-positive cocci, but also Menno all strains belonging to the streptococci and staphylococci.

It is interesting to note that with an increase in the concentration of the «Denta Aloe» drug, the degree of antibacterial activity also increases. It is interesting to note that among all the studied cocci, the most sensitive were the strains: *Staph. aureus* and *Str. salivarius*, and the least sensitive of the strains is *Str. mitis*. It could be noted as well, high antibacterial activity «Denta Aloe» to microbes pertinent camping fungi genus of *Candida*.

At the same time, the antibacterial activity of this drug to gram-negative microbes is not enough expressed. It should be noted that an increase in the concentration of the drug mail does not change the antibacterial effect.

Analyzing the obtained results, the differences in the antibacterial activity of the drug on relation to gram-positive and gram- negative microbes depend on the mechanism of action of this drug.

It is known that the human oral cavity is a unique system, which is explained by the habitat of more than 800 species of microbes in the areola, among which the leading role, both quantitatively and qualitatively, belongs to the gram-positive flora, namely to streptococci and staphylococci, at the same time. Gram-

negative flora and other groups are more relevant to the transit flora.

Thus, based on the conducted microbiological studies in which the antibacterial activity of the Denta Aloe drug is evaluated, the following conclusions can be drawn:

1. According to statistical data, dysbiosis in the oral cavity is most often due to quantitative and qualitative violations of

microbes such as streptococci, staphylococci and fungi of the genus *Candida*. On this base, the drug «Denta Aloe» can be widely used for diseases of the oral mucosa.

2. Given the antibacterial activity of the drug «Denta Aloe» depending on the concentration of the drug, it is recommended in the treatment of children with diseases of the oral cavity, in a concentration of 1.0%.

Table 1. Antibacterial activity of the drug «Denta Aloe» under conditions in vitro ($M \pm m$) m.m.

No.	Microbial groups	Drug concentrations				
		0.1 %	0.5 %	0.75 %	1,0 %	R
1	<i>Str. salivarius</i>	12,0 ± 0,1	14,0 ± 0,3	18,0 ± 0,3	21,0 ± 0,4	
2	<i>Str. mutans</i>	15,0 ± 0,3	16,0 ± 0,4	21,0 ± 0,5	20,0 ± 0,5	
3	<i>Str. Mitis</i>	11,0 ± 0,2	14,0 ± 0,2	17,0 ± 0,3	19,0 ± 0,3	
4	<i>St aph. aureus</i>	17,0 ± 0,3	18,0 ± 0,3	19,0 ± 0,4	20,0 ± 0,4	
5	<i>St.epidermidis</i>	10,0 ± 0,1	12,0 ± 0,2	14,0 ± 0,1	16,0 ± 0,1	
6	<i>St.saprothiticus</i>	14,0 ± 0,4	16,0 ± 0,3	18,0 ± 0,1	21,0 ± 0,4	
7	<i>Esch. coli lp</i>	10,0 ± 0,1	12,0 ± 0,1	13,0 ± 0,1	15,0 ± 0,2	
8	<i>Esch. coli ln</i>	8,0 ± 0,1	12,0 ± 0,3	14,0 ± 0,2	15,0 ± 0,3	
9	<i>Prot. vulgaris</i>	13,0 ± 0,4	14,0 ± 0,3	16,0 ± 0,2	17,0 ± 0,2	
10	<i>Klebsiella</i>	10,0 ± 0,1	13,0 ± 0,3	14,0 ± 0,3	15,0 ± 0,3	
11	<i>Pseudomonas</i>	14,0 ± 0,4	15,0 ± 0,3	17,0 ± 0,3	18,0 ± 0,2	
12	<i>Candida albicans</i>	16,0 ± 0,3	17,0 ± 0,4	18,0 ± 0,3	20,0 ± 0,5	

Note: units are given in mm of microbial growth inhibition zone.

A series of works to determine the antibacterial activity in studying the sensitivity of microbes living in the oral cavity to the Denta Aloe drug: the sensitivity of the microbes to the Denta Aloe drug was studied at a concentration of 0.1%, 0.5%, 0.75%, 1.0% (children's dose) .

As seen from Table 1, investigated concentrations drug «Denta Aloe» possess antibacterial activity and can be widely applied in diseases of the oral mucosa in children

Table 2. Characterization of the sensitivity of microorganisms to the drug «Denta Aloe» ($M \pm m$) m.m.

No.	Microbial groups	Drug concentrations					
		1%	3%	5%	10%	R	TO
1	<i>Str. Salivarius</i>	14,0 ± 0,2	15,0 ± 0,1	19,0 ± 0,3	22,0 ± 0,5		
2	<i>Str. Mutans</i>	13,0 ± 0,2	17,0 ± 0,3	16,0 ± 0,2	21,0 ± 0,4		
3	<i>Str. Mitis</i>	12,0 ± 0,2	15,0 ± 0,2	18,0 ± 0,3	20,0 ± 0,4		
4	<i>St aph. aureus</i>	18,0 ± 0,3	20,0 ± 0,3	19,0 ± 0,3	23,0 ± 0,4		
5	<i>St.epidermidis</i>	17,0 ± 0,3	19,0 ± 0,3	18,0 ± 0,1	21,0 ± 0,4		
6	<i>St.saprothiticus</i>	16,0 ± 0,4	14,0 ± 0,3	14,0 ± 0,2	18,0 ± 0,3		
7	<i>Esch. coli lp</i>	10,0 ± 0,1	11,0 ± 0,1	12,0 ± 0,1	12,0 ± 0,1		
8	<i>Esch. coli ln</i>	13,0 ± 0,3	15,0 ± 0,3	12,0 ± 0,2	14,0 ± 0,3		
9	<i>Prot. Vulgaris</i>	13,0 ± 0,2	14,0 ± 0,2	14,0 ± 0,3	14,0 ± 0,3		
10	<i>Klebsiella</i>	13,0 ± 0,3	12,0 ± 0,2	14,0 ± 0,3	14,0 ± 0,4		
11	<i>Pseudomonas</i>	8,0 ± 0,1	8,0 ± 0,1	14,0 ± 0,2	13,0 ± 0,2		
12	<i>Candida albicans</i>	15,0 ± 0,4	12,0 ± 0,3	18,0 ± 0,3	21,0 ± 0,5		

Note: units are given in mm of microbial growth inhibition zone.

As can be seen from table 2, the results show that the preparation «Denta Aloe» in high concentrations has the same tendency as with small, that is, gram-positive microbes are sensitive to it, most often it is streptococci and staphylococci. With streptococcus red, *Str. salivarius*, and the least sensitive was the culture of *Str. mitis*. At the same time among staphylococci drug «Denta Aloe» had a significant antibacterial effect on the culture of *St. aureus*, and the culture of *St. saprothiticus* was the least sensitive.

Drug «Denta Aloe» has antibacterial effect on gram-negative flora, but this action is lower extent compared to gram-positive one, under the action of the drug on the gram-negative flora.

Recommendation

Investigated concentrations drug «Denta Aloe» possess antibacterial activity and can be widely applied in diseases of the oral mucosa.

«Denta Aloe» preparation in high concentrations has the same tendency as with small, that is, gram-positive microbes are sensitive to it, most often it is streptococci and staphylococci. Drug «Denta Aloe» has antibacterial effect on gram-negative flora, under the action of the drug on the gram-negative flora.

CONCLUSION

Thus, based on the obtained microbiological data, it is possible to draw the following conclusions:

1. As can be seen in tables 1-2, the studied drug «Denta Aloe» exhibits antibacterial activity to all clinical strains of microorganisms.
2. With an increase in the concentration of the «Denta Aloe» drug, the degree of antibacterial activity also increases. It is interesting to note that among all the studied cocci, the most sensitive were the strains: Staph. aureus and Str. salivarius, and the least sensitive of the strains is Str. mitis. It should be noted as well, and high antibacterial activity «Denta Aloe» to microbes belonging to the fungi of the genus of Candida.
3. Disposes are often created in the oral cavity, due to quantitative and qualitative disorders of microbes such as streptococcus, staphylococcus and fungi of the genus Candida. On this base, the drug «Denta Aloe» can be widely used for diseases of the oral mucosa.
4. The drug «Denta Aloe» also had an antibacterial effect on gram-negative flora.
5. Drug «Denta Aloe» has a pronounced antibacterial activity to gram-positive coccus microbial flora in the oral cavity, and it is recommended for wide use in dentistry, both for children and for adults.

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AUTHORS CONTRIBUTIONS

All the authors have contributed equally

CONFLICT OF INTERESTS

Author(s) have no conflict of interest

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