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SEARCH RESULTS OF AN OPTIMAL COMPOSITION OF THE BASIS FOR DENTAL GEL AMONG THE CELLULOSE DERIVATIVES

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Abstract

Currently, the problem of prevention and treatment of periodontal diseases is highly relevant and has a medical and social importance because of its high prevalence. According to WHO, nearly 95% of the world's adult population and 80% of children have symptoms of the disease. Periodontal diseases are multifactorial, based on microbial aggression. Therefore, drugs should have, first of all, the antibacterial effect and, given the accompanying phenomena, anti-inflammatory and analgesic effect, and shall accelerate tissue regeneration, i.e. should be the combination products. To date, the range of drugs for the treatment of gingivitis is represented by different dosage forms, including gels. This paper is particularly focused on a component of dental gels - the bases. The paper presents the analysis of searches for the bases for a dental gel among the cellulose derivatives.

Keywords: periodontal diseases, basis, cellulose derivatives, Na-carboxymethylcellulose, Hydroxypropylmethylcellulose, Hydroxyethylcellulose.

Introduction

Periodontal diseases occupy one of the leading places in the range of critical problems of modern dentistry. According to WHO, nearly 95% of the world's adult population and 80% of children have any particular symptoms of the disease [1]. Chemotherapeutic drugs, which have a number of side effects and adverse effects on the human body, are most often used for the treatment and prevention of periodontal tissue diseases [2-5]. Therefore, it is important to develop new and effective medicinal compositions and forms for the prevention and treatment of these diseases.

It was found that the most widely applied dosage form among the range of medicines for the treatment of periodontal disease is gels. They have many advantages over other dosage forms: gels are easily applied to mucosal surfaces,

provide a prolonged contact with mucosa, etc. In this regard, the studies aimed at finding the optimum composition of dental gel bases among cellulose derivatives are relevant.

Materials and methods

As the bases for dental gels we investigated:

- Na-carboxymethylcellulose – Na-CMC, Camcel-500 STANDART;
- Hydroxypropylmethylcellulose – HPMC, TopMill® D clear 290.04;
- Hydroxyethylcellulose – HEC, Natrosol 250HX Pharm.

The study was conducted in 4 phases:

1. Preparation of model polymer blends.
2. Study of the covering capacity of tested gels.
3. Study of the kinematic viscosity of the polymers.
4. Study of the microbiological purity of the samples.

During the first phase, we prepared 1-6% Na-CMC solutions, 1-1.5% HPMC solutions, and 1-5% HEC solutions, 50 ml each. To prepare the composition of Na-CMC and HEC, an accurately weighed amount was dissolved in 50 ml of purified water while stirring at room temperature on a magnetic stirrer for 5 min and left for one day, also at room temperature, to form the gel [6,7,8]. Preparation of HPMC gel was conducted in a similar manner, but using hot water [6,9,10].

To test the covering capacity, a slide was used with a small amount of a polymer applied with a spatula on its surface. Gel base viscosity was measured with the use of a glass capillary viscometer VPG-2 with an inner diameter of 1.31 mm, according to standard procedures of the General monograph of the State Pharmacopoeia of the Russian Federation XII 42-0038-07 "Viscosity" [6].

Inoculation was performed on Czapek medium, which has the following composition (g/liter of solution): Sucrose - 30 g; $NaNO_3$ - 3 g; KH_2PO_4 - 1 g; $MgSO_4 * 7H_2O$ - 0.5 g; KCl - 0.5 g; $FeSO_4 * 7H_2O$ - 0.01 g; Agar-agar 15 g [11]. Agar was poured on the bottom of the flask and embedded with salt solution. The flask was placed in an autoclave for sterilization for 20 min. After sterilization, the flask content was mixed on a shaker for uniform distribution of the agar during solidification. The medium was poured in the sterile room into sterile petri dishes [12].

Results and discussion

Results of the “Spreadability” test are shown in Figures 1-3:

Figure 1 - Appearance of 3%-6% Na-CMC solutions

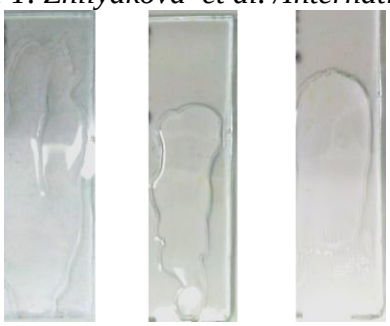

Figure 2 - Appearance of 1.2%-2% HPMC solutions

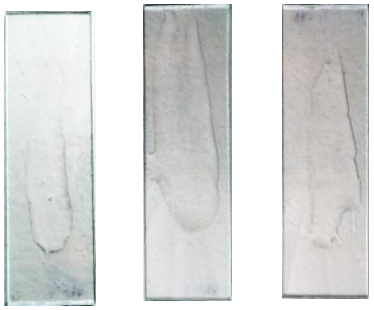

Figure 3 - Appearance of 3%-5% HEC solutions

As can be seen from Figures 1-3, the best covering capacity is shown by 6% Na-CMC solution, 1.2%-2% HPMC solutions, and 4%-5% HEC solutions.

Data on the viscosity of the prepared solutions are presented in Table 1.

Table 1 - Results of the study of the kinematic viscosity of the tested solutions.

No.	Solution concentration, %	Average passing time of the fluid from M_1 to M_2, sec.	Instrument constant, mm^2/sec^{-1}	Kinematic viscosity, mm^2/sec^{-1}
Na-CMC				
1	1	70.00	0.2614	18.298
2	2	128.53		33.598
3	3	206.07		53.867
4	4	900.70		235.44
5	5	1818.00		475.23
6	6	5877.90		1536.48
7	7	21238.20		5551.67
HPMC				
1	1	588.40	0.2614	153.81
2	1.2	1064.50		278.26
3	1.5	2609.50		682.12
4	2	12335.40		3224.47
HEC				
1	1	8.70	0.2777	2.42

2	2	90.80		25.22
3	3	365.90		101.61
4	4	1625.60		451.43
5	5	4482.50		1244.79

Based on the obtained data, the flow curves of polymer solutions viscosity and concentration were built (Figures 4 and 5):

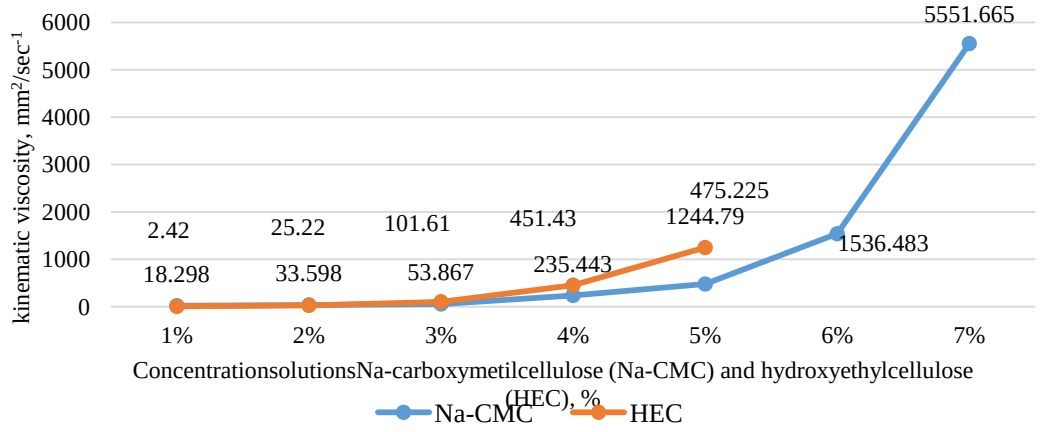

Figure 4 - Flow curve of Na-CMC and HEC solutions.

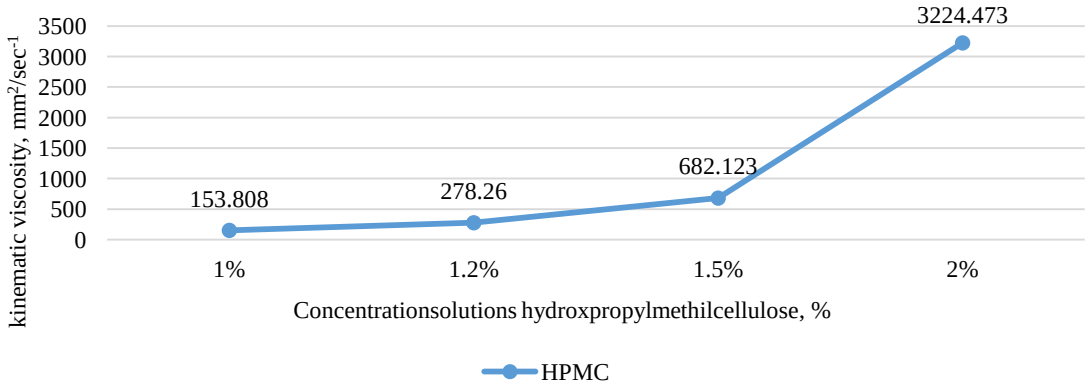

Figure 5 - Flow curve of HPMC solutions.

The results show that the Na-CMC and HPMC solutions are characterized by direct correlation between kinematic viscosity and concentration of the polymer.

Considering that the fundamental characteristic of the drug is the microbiological purity, the fourth phase of the study involved the investigation of microbiological purity of the samples and the identification of the nature of foreign inclusions in the polymer solutions. Since it was found that the most suitable samples are 6% Na-CMC and 4-5% HEC solutions, they were used to study the microbiological purity. HPMC gels were not tested since they showed good stability during storage.

The results obtained on day 4 of the experiment are shown in Figures 6 and 7.

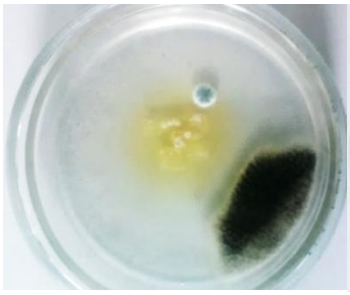

Figure 6 - Appearance of inoculated 6% Na-CMC on day 4 of experiment.

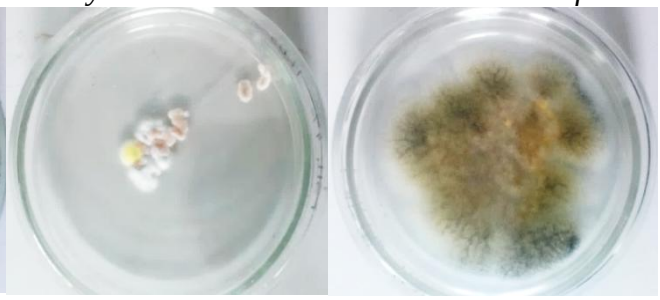

Figure 7 - Appearance of inoculated 4% (left) and 5% (right) HEC on day 4 of experiment.

The results obtained on day 7 of the experiment are shown in Figures 8-10.

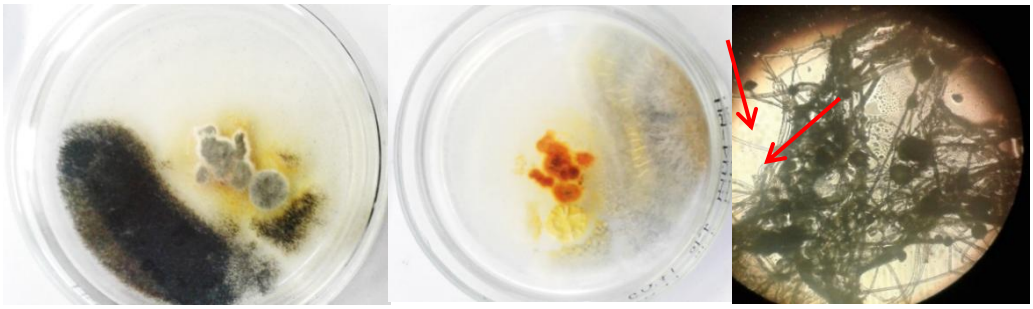

Figure 8 - Appearance of inoculated 6% Na-CMC on day 7 of experiment (top, bottom of Petri dish and under microscope, respectively).

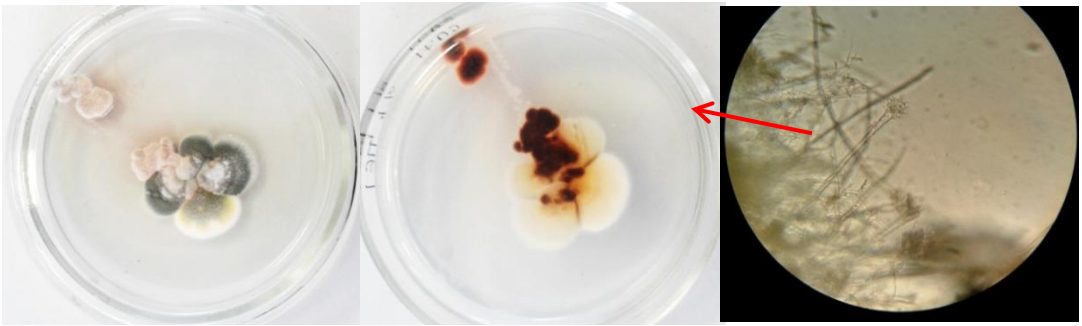

Figure 9 - Appearance of inoculated 4% HEC on day 7 of experiment (top, bottom of Petri dish and under microscope, respectively)

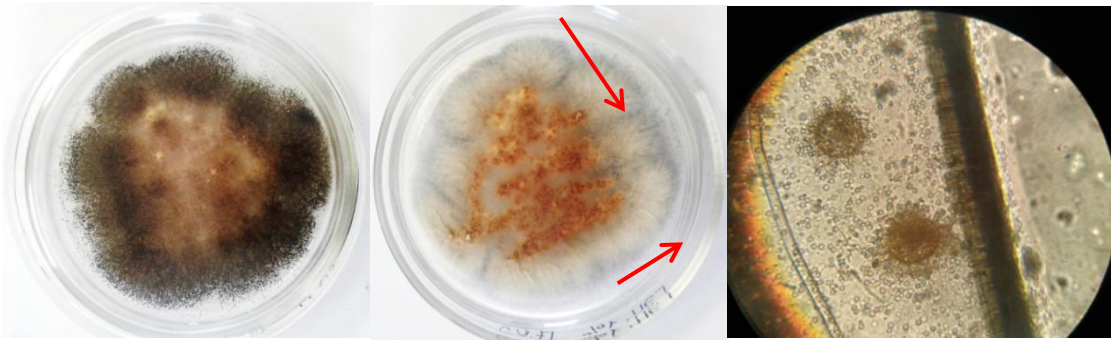

Figure 10 - Appearance of inoculated 5% HEC on day 7 of experiment (top, bottom of Petri dish and under microscope, respectively)

The studies revealed fungi of genus *Aspergillus* in 6% Na-CMC solution, which were identified by the presence of the branching structure in the entire space inside the Petri dish. Under the microscope, the sori with multiple spores were found (accumulation with much spores). Mold fungi of the genus *Penicillium* were found in 4% HEC solution. They were identified by finding the "brushes»") at the ends of the filaments of the fungus. The 5% HEC gel also contained fungi of genus *Aspergillus* found. A confirmation of this species was identification of a capsule with multiple spores inside.

Data on the organoleptic properties of the prepared model samples are combined in Table 2.

Table 2 - Organoleptic properties of Na-CMC model samples.

Composition	Date	Description
Na-CMC		
1% Na-CMC solution Purified water 50 ml Na-CMC 0.5	day 1	Low-viscous homogeneous fluid solution, low-transparent, odorless and tasteless
	day 8	No changes
	day 15	Foreign inclusions appeared in the form of weighted loose particles
	day 22	Bacterial colony growth observed
	day 30	Bacterial colony growth observed
2% Na-CMC solution Purified water 50 ml Na-CMC 1.0	day 1	Low-viscous homogeneous fluid solution, low-transparent, odorless and tasteless
	day 8	No changes
	day 15	Foreign inclusions appeared in the form of weighted loose particles
	day 22	Bacterial colony growth observed
	day 30	Bacterial colony growth observed
3% Na-CMC solution Purified water 50 ml Na-CMC 1.5	day 1	Low-viscous homogeneous fluid solution, low-transparent, odorless and tasteless
	day 8	Foreign inclusions appeared in the form of weighted loose particles
	day 15	Bacterial colony growth observed
	day 22	Bacterial colony growth observed
	day 30	Bacterial colony growth observed
4% Na-CMC solution Purified water 50 ml	day 1	Viscous, plastic, resilient, homogeneous gel with high covering capacity, low-transparent, odorless and tasteless

Na-CMC 2.0	day 8	No changes
	day 15	No changes
	day 22	Foreign inclusions appeared in the form of weighted loose particles
	day 30	Bacterial colony growth observed
5% Na-CMC solution Purified water 50 ml Na-CMC 2.5	day 1	Viscous, plastic, resilient, homogeneous gel with high covering capacity, low-transparent, odorless and tasteless
	day 8	No changes
	day 15	No changes
	day 22	Foreign inclusions appeared in the form of weighted loose particles
	day 30	Bacterial colony growth observed
6% Na-CMC solution Purified water 50 ml Na-CMC 3.0	day 1	Viscous, plastic, resilient, homogeneous gel with high covering capacity, low-transparent, odorless and tasteless
	day 8	No changes
	day 15	Foreign inclusions appeared in the form of weighted loose particles
	day 22	Bacterial colony growth observed
	day 30	Bacterial colony growth observed
7% Na-CMC solution Purified water 50 ml Na-CMC 3.5	day 1	Viscous, plastic, resilient, homogeneous gel with poor covering capacity, low-transparent, odorless and tasteless
	day 8	Foreign inclusions appeared in the form of weighted loose particles
	day 15	Bacterial colony growth observed
	day 22	Bacterial colony growth observed
	day 30	Bacterial colony growth observed
HPMC		
1% HPMC solution Purified water 50 ml HPMC 0.5	day 1	Low-viscous, crystal-clear, homogenous gel with poor covering capacity, odorless and tasteless, without inclusions of air bubbles
	day 8	No changes
	day 15	No changes
	day 22	No changes
	day 30	No changes
1.2% HPMC solution Purified water 50 ml HPMC 0.6	day 1	Low-viscous, crystal-clear, homogenous gel with poor covering capacity, odorless and tasteless, without inclusions of air bubbles
	day 8	No changes
	day 15	No changes
	day 22	No changes
	day 30	No changes

1.5% HPMC solution Purified water 50 ml HPMC 0.75	day 1	Viscous, resilient, plastic, crystal-clear, homogenous gel, sticky to the touch, with high covering capacity, odorless and tasteless, without inclusions of air bubbles
	day 8	No changes
	day 15	No changes
	day 22	No changes
	day 30	No changes
2% HPMC solution Purified water 50 ml HPMC 3.5	day 1	Viscous, resilient, plastic, crystal-clear, homogenous gel, sticky to the touch, with high covering capacity, odorless and tasteless, without inclusions of air bubbles
	day 8	No changes
	day 15	No changes
	day 22	No changes
	day 30	No changes
HEC		
1% HEC solution Purified water 50 ml HEC 0.5	day 1	Low-viscous homogeneous fluid solution, low-transparent, odorless and tasteless
	day 8	Foreign inclusions appeared in the form of weighted loose particles
	day 15	Bacterial colony growth observed
	day 22	Bacterial colony growth observed
	day 30	Bacterial colony growth observed
2% HEC solution Purified water 50 ml HEC 1.0	day 1	Low-viscous homogeneous fluid solution, low-transparent, odorless and tasteless
	day 8	No changes
	day 15	Foreign inclusions appeared in the form of weighted loose particles
	day 22	Bacterial colony growth observed
	day 30	Bacterial colony growth observed
3% HEC solution Purified water 50 ml HEC 1.5	day 1	Low-viscous homogeneous fluid solution, low-transparent, odorless and tasteless
	day 8	Foreign inclusions appeared in the form of weighted loose particles
	day 15	Bacterial colony growth observed
	day 22	Bacterial colony growth observed
	day 30	Bacterial colony growth observed
4% HEC solution Purified water 50 ml	day 1	Viscous, plastic, resilient, homogeneous gel with high covering capacity, low-transparent, odorless and tasteless

HEC 2.0	day 8	No changes
	day 15	Foreign inclusions appeared in the form of weighted loose particles
	day 22	Bacterial colony growth observed
	day 30	Bacterial colony growth observed
5% HEC solution Purified water 50 ml HEC 2.5	day 1	Viscous, plastic, resilient, homogeneous gel with high covering capacity, low-transparent, odorless and tasteless
	day 8	Foreign inclusions appeared in the form of weighted loose particles
	day 15	Bacterial colony growth observed
	day 22	Bacterial colony growth observed
	day 30	Bacterial colony growth observed

Conclusion

Our study revealed that, according to WHO, nearly 95% of the world's adult population and 80% of children have any particular symptoms of the disease. The most widely applied dosage form for the treatment of periodontal disease is gel, due to its advantages. Therefore, we conducted studies aimed at finding an optimal composition of the basis for dental gel among the cellulose derivatives. According to test results for viscosity and covering capacity, the optimum viscosity and the best covering capacity is shown by 6% Na-CMC solution, 1.2%-2% HPMC solutions, and 4%-5% HEC solutions. Considering that the fundamental characteristic of the drug is the microbiological purity, the investigation of microbiological purity of the samples and the identification of the nature of foreign inclusions in the polymer solutions was conducted. As a result, it was found that HPMC solutions are microbiologically stable. We found fungi of genus *Aspergillus* in 6% Na-CMC solution and 5% HEC solution, and fungi of genus *Penicillium* in 4% HEC solution. Thus, the HPMC gel can serve as an optimum basis for promising dental dosage form. The obtained data should be considered in the further development of the composition and the target drug technology.

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