RESEARCH ON THE CHOICE OF RATIONAL CONCENTRATION OF THE GEL FORMING AGENT IN THE COMPOSITION OF DENTAL GEL

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Introduction

In inflammatory diseases of the periodontium mucous membrane of the oral cavity is inflamed and is sensitive to food and medicines [1], therefore, the use of a semisolid formulation is the best option for the treatment of such pathologies. Dental gel has several advantages over other dosage forms used in the oral cavity, such as uniform distribution on the mucous membrane, prolonged release of active pharmaceutical ingredients and high bioadhesive properties [2].

In the process of production (mixing in the reactor, dosing in the primary packaging) and use by the patient (squeezing out of tubes and applying to mucous membranes of the oral cavity), the structure of the dental gel is repeatedly subjected to the effects of shear stresses of different strength, which, accordingly, affect its structural and mechanical properties [3, 4]. Therefore, the development of a dental gel is a complex scientific research, which involves solving a range of issues related to providing the necessary biopharmaceutical and rheological properties to the gel composition.

According to the analysis of scientific literature, as well as the preliminary results of microbiological and biopharmaceutical studies of dental gel developed as a gelling agent, we have chosen Carbomer Polacril® 40P (Amedeo Brasca & C. Srl, Italy), which is recommended for use in dental practice, meets the requirements of pharmacopoeia standards and creates high-performance viscosity. In addition, the polymer of this brand is suitable for the creation of water and water-alcohol gels and has a good indicator of the transparency of the final product [5, 6, 7].

The aim of the work is to study the structural and mechanical characteristics of the developed dental gel in order to select the rational concentration of the carbomer Polacril® 40P.

Materials & methods

To determine the rational concentration of Carbomer Polacril® 40P, we prepared 5 gel samples with different amounts of the gelling agent – 1.0, 1.25, 1.5, 1.75 and 2.0 %. In order to determine the plastic viscosity of the specimens, type of flow and yield stress, their structural and mechanical properties were studied.

Measurement of the rheological parameters of the model samples was carried out on a rotary viscometer with coaxial cylinders "Rheolab QC" ("Anton Paar"). The studies were carried out at a temperature of (25 ± 0.1) ºC. For the study, took the weight of the experimental sample (about 20 g) and placed in a container in which the spindle was immersed. Viscometer measurements were recorded at each speed, after achieving stable performance. The determination was carried out with increasing spindle speed and in the opposite direction [4]. According to the results of the study, rheograms were plotted showing the dependence of the shear stress (τ_r) on the velocity gradient (D_r), as well as the graphs of the dental gel's structural viscosity (η) dependence on the concentration of the carbomer at 25 °C with a shear rate of 41.6 s^{-1}, which simulates the stirring speed when obtaining the gel under industrial conditions.

Rheological studies of gels before and after their contact with a solution of artificial saliva, the composition of which is given in Table. 1 have also been performed [8]. The gel was diluted in a ratio of 1:1, taking into account one dose of gel (0.6 g) and an average saliva secretion rate (0.6 ml/min) [9]. After adding this solution to the gel, the mixture was stirred and left at rest to restore the structure of the system. Indications of the structural viscosity of the gel were recorded prior to dilution, as well as after 1 hour and 24 hours of storage. According to research results, rheograms were also plotted.

Table 1. Composition of artificial saliva solution

Composition	**Quantity in 1 litre of water**
Disodium hydrophosphate $12{\cdot}H_2O$, g	28.65
Sodium dodecyl sulfate 99%, g	20
Bi-distilled water, ml	900
Acidity of the solution (regulated by the addition of 5M HCl)	to pH 6.5
Bi-distilled water, ml	1000

Results & discussion

Gels with different concentrations of Carbomer Polacril® 40P (1.0, 1.25, 1.5, 1.75 and 2.0 %) were prepared by dispersing the gel-former in water, with subsequent swelling and neutralization with a 10 % solution of sodium hydroxide to the required pH (5.5-7.5) [2, 9]. After that, API solution was introduced into the prepared gel base: lidocaine hydrochloride and choline salicylate were dissolved in the "Phytodent" tincture. After homogenization, if necessary, adjusted the pH of the gel samples. All samples looked like homogeneous transparent gel-like masses of light-orange colour of varying consistency without mechanical inclusions.

As a reference for comparison, "Dentinox-gel N" (Dentinox Gesellschaft für pharmazeutische Praparate Lenk & Schuppan, Germany), which is also based on carbomer

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and has a similar composition of APIs, contains tincture of VRM and lidocaine hydrochloride, as well as gel "Metrogyl Denta®" (Unique Pharmaceutical Laboratories, India), which is made on carbomer 940 have been chosen [10].

The rheograms representing the dependence of the shear stress (τ_r) on the gradient of the shear rate (D_r) are shown in Figure 1.

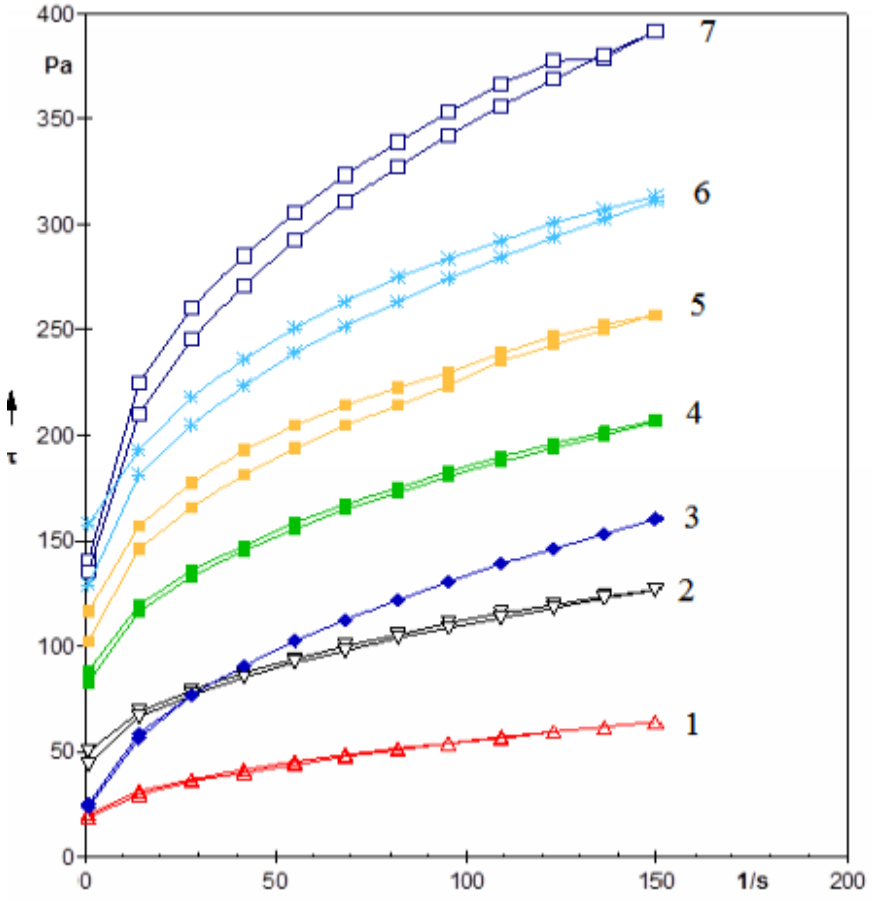

Fig. 1. Rheograms of dental gel, depending on the concentration of carbomer in comparison with reference preparations (at 25 °C)

The results obtained (Fig. 1) show that all gel samples have a non-Newtonian type of flow, that is, they are pseudoplastic systems with pronounced yield strength. In addition, with the increase in the concentration of Carbomer Polacril® 40P, the rheological parameters of the dental gel samples increase, which is confirmed by an increase in the area of the hysteresis loop, which in turn indicates thixotropy of systems – after removing the shear stress, gel samples restore their viscosity, which allows them to provide prolonged effect and enhances bioadhesive properties. The 1.0 % carbomer content sample has a more liquid gel consistency, as evidenced by the smallest area of the hysteresis loop. This, accordingly, can lead to poor fixation of the drug on the surface of the mucous membrane, so this sample was excluded by us from further research.

Also plotted charts the of the structural viscosity of the dental gel dependence on the concentration of the carbomer at 25 °C and the shear rate of 41.6 s^{-1} (Figure 2).

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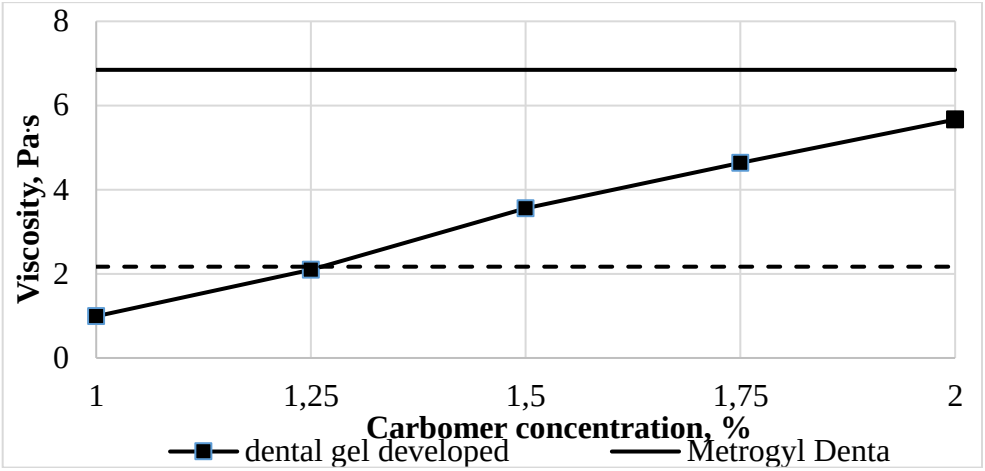
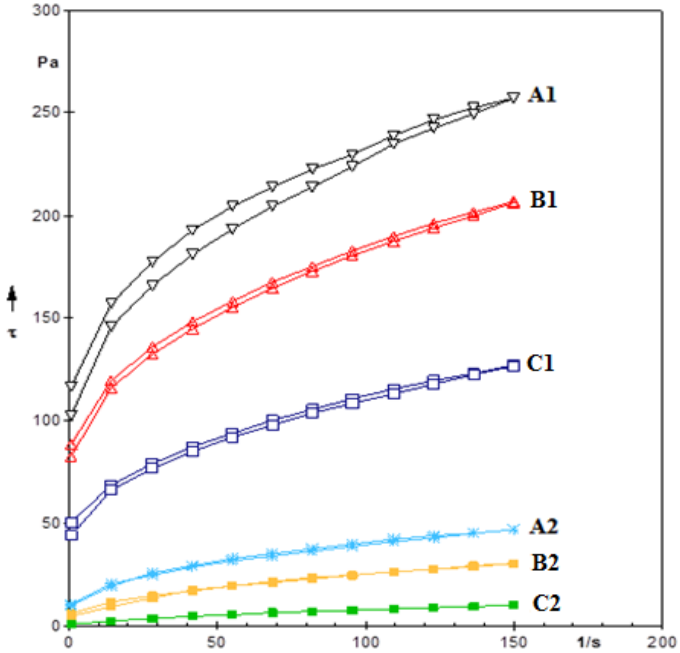


Fig. 2. The dependence of the structural viscosity of the dental gel at a shear rate of 41.6 s^{-1} on the concentration of carbomer in comparison with reference drugs (at 25 °C)

According to the results obtained (Fig. 2), increasing the concentration of carbomer leads to an increase in the structural viscosity values. In the nature of rheograms and structural viscosity the most similar indicators to the drug "Dentinox-gel N" have gels with carbomer concentration of 1.25 % and 1.5 %, and to the drug "Metrogyl Denta®" – 1.75 % and 2.0 %. But the sample of gel with a concentration of carbomer 2.0 % was characterized by unsatisfactory appearance (it was heterogeneous and clumped at stirring), as well as the difficulty in achieving the required pH. Its mechanical strength was greater than in other samples, which could negatively affect the consumer characteristics of the gel and the technological process of its production. Considering the above, this sample was also excluded from the experiment.

For the final choice of the concentration of the selected gel-former, we have conducted rheological studies of gels before and after contact with artificial saliva solution. This characteristic will allow predicting the behaviour of the gel in the oral cavity, namely the rate of its dilution with saliva, and, accordingly, the time of its residence on the mucous surface. Figure 3 shows rheograms of dental gel before and after dilution with saliva in a ratio of 1:1.



A – 1.75 % carbomer;
B – 1.5 % carbomer;
C – 1.25 % carbomer.

Fig. 3. Dental gel rheograms before (1) and after (2) dilution with saliva

According to the rheograms given in Fig. 3, after contact of gels with a solution of artificial saliva, their rheological parameters have reduced. At the same time, the gel with a carbomer concentration of 1.25 % was the most thinned, as evidenced by the smallest area of the hysteresis loop.

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In addition, the structural viscosity of gels before and after dilution with artificial saliva, depending on the shear rate, has been studied. The data are shown in the Table 2.

Table 2. The dynamic viscosity of the dental gel with various concentrations of the carbomer before and after dilution (1:1) with saliva (at 25 °C)

D_r, s^{-1}	Structural viscosity (Pa•s) at 25 °C								
	1.25 % carbomer			1.5 % carbomer			1.75 % carbomer		
	before dilution	1 h after dilution	24 h after dilution	before dilution	1 h after dilution	24 h after dilution	before dilution	1 h after dilution	24 h after dilution
1.00	50.11	-0.389	0.3852	88.24	4.651	4.432	116.3	10.26	9.885
14.55	4.722	0.1459	0.1598	8.226	0.7996	0.6454	10.78	1.432	1.31
28.09	2.811	0.1191	0.1283	4.831	0.5307	0.4876	6.316	0.912	0.9106
41.64	2.093	0.1028	0.1091	3.553	0.4193	0.4162	4.634	0.7035	0.7047
55.18	1.702	0.0932	0.0983	2.872	0.3547	0.3527	3.71	0.5887	0.59
68.73	1.457	0.0863	0.0902	2.437	0.3123	0.3124	3.115	0.5131	0.5124
82.27	1.285	0.0809	0.0848	2.131	0.2822	0.2828	2.707	0.4581	0.4577
95.82	1.155	0.0776	0.0798	1.908	0.2587	0.2591	2.395	0.4178	0.4178
109.4	1.054	0.0736	0.0759	1.735	0.2393	0.2407	2.186	0.3843	0.3836
122.9	0.972	0.0702	0.0724	1.595	0.2239	0.2254	2.007	0.3568	0.3556
136.5	0.9035	0.0674	0.0690	1.477	0.211	0.2129	1.85	0.3341	0.3327
150.0	0.8461	0.0649	0.0662	1.378	0.2001	0.2017	1.715	0.3154	0.3132

Based on the results of the viscosity characteristics of the gel before and after dilution, the structural viscosity (at $D_r = 1.00\ s^{-1}$) of samples with a carbomer concentration of 1.25 % is reduced by 130 times, and with concentrations 1.5 % and 1.75 % of the gel former – 20 and 12 times, respectively. This, in turn, indicates a better adhesion of the gels with Carbomer Polacril® 40P concentrations 1.5 and 1.75 %.

Conclusion

1. Taking into account the results of structural and mechanical studies of gels with and without an artificial saliva solution, as well as in terms of profitability, the optimal concentration of Carbomer Polacril® 40P in the composition of the developed gel has been chosen to be 1.5 %. When using this particular amount of the carbomer, there is a stable behaviour and a quick complete recovery of the volumetric coagulation structure of the dental gel.

2. On the basis of comparative analysis with reference formulations in the form of gels, which are widely used in dental practice, it has been established that the proposed composition of the dental gel being developed has satisfactory structural and mechanical properties.

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Taking into account the wide spreading and

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etiopathogenetic features of the course of inflammatory diseases of periodontium and oral mucosa, it is rational to use semisolid drugs of local action, namely, dental gels. The main issue when developing this dosage form is the choice of the gel former and its concentration. Based on previous studies as the gel basis for the development of a new dental gel with «Phytodent» tincture, choline salicylate 80%, and lidocaine hydrochloride the Carbomer Polacril® 40P, which is authorized for use in dentistry and has the ability to form transparent viscous aqueous-alcohol gels, has been chosen. It is known that rheological characteristics of gels directly affect the processes of release and absorption of active pharmaceutical ingredients from a semisolid dosage form, as well as its consumer properties. The important issue is the convenience and ease of application of a dental gel to inflamed tissues of periodontium and mucous membranes. This process is similar to that occurring during the shift of visco-plastic material in a rotary viscometer. The aim of the work is to study the structural and mechanical characteristics of the developed dental gel in order to select the rational concentration of the carbomer Polacril® 40P. **Materials and methods**. The study objects are gel samples with different concentrations of Carbomer Polacril® 40P – 1.0, 1.25, 1.5, 1.75 and 2.0 %. Measurement of the rheological parameters of the model gel samples was carried out at a temperature (25 ± 0.1) oC on a rotary viscometer with coaxial cylinders "Rheolab QC" ("Anton Paar") before and after contact with a solution of artificial saliva. As standards for comparison dental gels "Dentinox-gel N" (Germany) and gel "Metrogyl Denta®" (India) were selected. **Results and discussion**. It has been found that all gel samples have a non-Newtonian pseudoplastic flow type and are thixotropic systems with pronounced limits of fluidity. The rheological parameters of the dental gel samples increase as the concentration of Carbomer Polacril® 40P increases. In the nature of rheograms and structural viscosity the closest indicators to the drug "Dentinox-gel N" have gels with carbomer concentration of 1.25 % and 1.5 %, and to the drug "Metrogyl Denta®" – 1.75 % and 2.0 %. **Conclusions**. Taking into account the results of structural and mechanical studies of gels with and without an artificial saliva solution, as well as in terms of profitability, the optimal concentration of Carbomer Polacril® 40P in the composition of the developed gel was chosen to be 1.5 %.

Keywords: dental gels, gel former, rheological studies.

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