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**Experimental Studies of the Ability of Pharmacopoeial Excipients to Release Pharmacologically Active Substances when Developing Dental Dressing**

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**Keywords:** formation of dosage forms; wound healing

**Abstract.**

The biopharmaceutical studies have undoubtedly proven that pharmacopoeial excipients based on polyethylene oxide, sodium carboxymethyl cellulose and apple pectin can release pharmacologically active substances and produce pharmacopoeial excipients in the form of ointments and pastes. The dynamics of diffusion of biologically active substances in agar gel within 6 hours of the experiment was practically the same in all samples. The least significant changes in samples consistency and preservation of paste-like consistency were observed in pharmacopoeial excipients based on pectin indicating the advisability of its application in the specific medium of the oral cavity.

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**Problem statement and analysis of the recent research**

The peculiarities of physiological impairment of the oral cavity require from the scientists, dentists and pharmacologists the development of the new means and reasonable pharmacological forms. The urgent problem in local treatment is the prolonged contact of the oral mucosa with the medications if there are any pathologic processes and wounds. In addition, their isolation from aggressive medium of the oral cavity is also of great relevance [10].

Among pharmacological forms pastes are the most efficient in prolonged application. In dentistry pastes based on polymers, derivatives of cellulose, starch are used. In clinical dentistry the prolonged application of paste is called bandage. The bandages are divided into hardening and non-hardening ones [5]. The pastes belong to non-hardening bandages. Hydrophilic excipients including synthetic and natural polymers are the major components of pastes. They are characterized by the functional properties and can improve the technology of soft dosage forms aimed at correlation between efficiency and quality [6].

The objective of the research was to study in vitro the ability of pharmacopoeial excipients to release pharmacologically active substances and advisability of its application as dental bandage.

**Materials and methods**

The first research stage of substantiating the composition of dental bandage was the selection of pharmacopoeial excipients as a type of carrier or the base. Different bases permitted by the MHC of Ukraine were investigated to study the effect of carrier type on drug efficiency [3]. The composition of bases is presented in Table 1. The main requirement for carrier, as a future base of dental bandage, was its ability to make water-soluble ointments and pastes.

<table>
<thead>
<tr>
<th>№</th>
<th>Base type</th>
<th>Base composition, g</th>
<th>Base organoleptic characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No 1</td>
<td>Hydrophilic</td>
<td>PEO-4000 50.0</td>
<td>Homogeneous mass of a thick consistency and white colour with slight characteristic smell</td>
</tr>
<tr>
<td>N*=10</td>
<td>Glycerine 30.0</td>
<td>Purified water 20.0</td>
<td></td>
</tr>
<tr>
<td>No 2</td>
<td>Hydrophilic</td>
<td>Apple pectin 50.0</td>
<td>Homogeneous mass of wet consistency and almond colour with slight characteristic smell</td>
</tr>
<tr>
<td>N =10</td>
<td>Purified water 50.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No 3</td>
<td>Hydrophilic</td>
<td>CMC 5.0</td>
<td>Colourless, transparent, odourless homogeneous mass of viscous gel-like consistency</td>
</tr>
<tr>
<td>N =10</td>
<td>Glycerine 47.5</td>
<td>Purified water 47.5</td>
<td></td>
</tr>
</tbody>
</table>

*N*=10 – number of experimental samples in groups No 1, No 2, No 3

**Polyethylene oxides** (PEO-4000) are polymers of ethylene oxide. The consistency and properties of PEO depend on the degree of polymerization. They range from viscous transparent liquids to solid substances of white colour. PEOs are well dissolved in water and alcohol, low-sensitive to pH changes, stable when storing, and low-toxic. Ointment bases are the mixture of liquid and solid PEOs having viscoplastic consistency.

**Glycerine** (triatomic alcohol) is a colourless transparent viscous liquid with slight characteristic smell. It is well dissolved in water and alcohol, hygroscopic. It is able to absorb water
from the skin. It has beneficial properties as a softener and can be used as a preservative as well as a means preventing drying.

**Apple pectin.** Among all types of pectins used as pharmacopoeial excipients in Ukraine apple pectin is the only one that is certified [7]. Pectins are macromolecular compounds being the polygalacturonic acid by the structure, which is partially etherified with methyl alcohol. Pectin solutions have high gelling properties.

**Sodium carboxymethyl cellulose** (SCMC) is a sodium salt of the glycolic acid ether of cellulose. It is an odourless and tasteless powder of white or greyish colour being able to swell in water. In concentrations of between 4-6% it is used as an excipient in ointments, creams, gels.

There were prepared the mixtures – samples which were placed in Petri dishes. Every sample had its own sequence number as presented in Table 1 (N = 10 in each group). Considering the numbers all samples were heated in the thermostat simultaneously. In every group 5 dishes were closed and 5 dishes were open. The data were recorded with the interval of 15, 30, 45 minutes and 6 hours.

The second stage of the research was the study of the release of medical substances from the experimental samples. The research was carried out in vitro using the standard agar gel diffusion method also known as the agar plate method. Biologically active substances being able to dissolve in water solutions including ascorbic acid, chloramphenicol, lincomycin were additionally placed in every group of experimental samples of pharmacopoeial excipients The criterion for selection of medications was their active absorption by the oral mucosa as well as their accumulation in the osseous structures [2]. The method is based on the creation of the coloured area as a result of interaction between ascorbic acid and 2,6 dichloride carbonate sodium with further pink colouration on blue background. For this purpose a 3% agar gel with addition of a reagent (2,6 - dichloride carbonate sodium) was poured into Petri dishes having horizontal surface of the bottom in two doses of 20 ml. After thickening of the first dose of agar in every dish 3 cylinders of rustproof steel having an outer diameter of 9 mm were placed on its surface. Then, the next layer of agar was poured. After thickening of the second layer the cylinders were taken out. The paste samples (0.2 g) were placed in the holes. There was made 60 experimental samples (20 in every group). The dishes were closed and incubated under 45°C. The data were recorded with the interval of 15, 30, 45 minutes and 6 hours. The diameter of the coloured area was measured for every sample. The results were calculated using the Student’s t-test.

**Results**

The series of experimental samples based on PEO – 4000 in group No 1 before placing into the thermostat were the homogeneous mass of thick consistency and white colour with slight characteristic smell. The consistency of samples allowed us to place them easily on the surface of Petri dishes. The samples based on apple pectin in group No 2 were the homogeneous mass of wet consistency and almond colour with slight characteristic smell. Directly after mixing the samples in groups No 1 and No 2 did not spread out. The series of experimental samples based on SCMC in group No 3 could be characterized as a colourless, transparent, odourless homogeneous mass of viscous gel-like consistency spreading out on the surface. Its transfer to Petri dishes for further research required additional efforts. The samples of group No 1 being placed in thermostat lost their paste-like consistency 15 minutes after the beginning of the experiment. The samples of group No 3 became less viscous (more fluid in appearance) both in closed and open Petri dishes. The samples of group No 2 in closed Petri dishes slightly thickened without drying. In open Petri dishes on all surfaces of the samples, the solidification occurred on the surface of all samples 45 minutes after the beginning of the experiment. Considering the obtained results the additional experiments relating to variability in amount of solvent were carried out in group No 2. The results
demonstrated that despite the fact that their consistency changed to soften mass the samples did not spread out and withstood a 6-hour exposure.

The experimental data obtained in vitro by diffusion in agar gel demonstrated the process of releasing medical substances from the experimental samples. The results given in Table 2 proved that there was almost the same release of biologically active substances in groups No 1, No 2, No 3. In samples of group No 2 within the first 15 minutes the process of release was the slowest. When the experiment was prolonged (6 hours after the beginning of the experiment) the process was accelerated compared to samples in groups No 1 and No 3. When carrying out the biopharmaceutical research there was determined that pastes based on polyethylene oxide with carboxymethyl cellulose in groups No 1, No 3 lost their viscous consistency and became fluidal. The samples based on pectin in group No 2 when heating in closed Petri dishes were denser continuing to release the excipients.

<table>
<thead>
<tr>
<th>No of base group</th>
<th>Time of diffusion in agar gel</th>
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<tbody>
<tr>
<td></td>
<td>15 minutes</td>
</tr>
<tr>
<td></td>
<td>M±m</td>
</tr>
<tr>
<td>No 1  N =20</td>
<td>20.0±0.02</td>
</tr>
<tr>
<td>No 2  N =20</td>
<td>17.6±0.00</td>
</tr>
<tr>
<td>No 3  N =20</td>
<td>20.0±0.02</td>
</tr>
<tr>
<td>*p</td>
<td>p&lt;0.05</td>
</tr>
</tbody>
</table>

*N =20 – number of the experimental samples in groups No 1, No 2, No 3. 
*p<0.05 – statistically significant differences in data obtained when heating compared to those obtained at room temperature.

Our research proved that samples No 1 and No 3 were similar to the ointment base. In order to make the paste-like consistency it was necessary to put the additional excipients. Samples No 2 did not require any additional components to make the paste and can be used for making the dental bandages.

**Discussion**

Modern pharmaceutical medications are a definite type of pharmaceutical system including active pharmacological ingredients and different additional substances. In the scientific literature the conventionality of the boundaries between active and auxiliary substances is defended more often [1]. We support this viewpoint considering the important practical significance of the pharmacological forms for using by dentists when dealing with pathologic processes, wounded surfaces, surgeries and tooth extraction. Pectins belong to the additional substances. In the classification of additional substances they are considered as natural organic means. The advisability of their using in dentistry is also explained by the fact that pectins serve as foods capable of forming colloidal structures. Due to their properties the natural biopolymer apple pectin can be used in dentistry as both active and additional substance.

**Conclusion**

1. According to the results of the biopharmaceutical research there was established that samples of additional substances based on polyethylene oxide as well as on the sodium carboxymethyl cellulose can release the excipients. When heating they lose their viscous consistency and become fluidal. Thus, it is impossible to use them in dentistry in order to make the paste as a pharmaceutical form without using the additional thickeners.
2. The samples based on apple pectin when heating in closed Petri dishes thicken continuing to release the excipients. The additional ingredients are not necessary in order to make the paste. They can be used for making dental bandages.

**Prospects for further research**

The study of the process of releasing active substances by the additional ones is one of the stages of delivering drugs into the organism of the patient. Our further research will clarify the other experimental part of this work. To minimize the use of antibiotics when extracting the tooth the effect of the components of pharmaceutical ingredients and additional substances in different concentrations and one dosage form on the standard microorganisms will be studied in vitro.

**References**

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5. Kosenko SV, Soroka OB. Dental bandage of prolonged action for treating wounds, mucosal defects of various etiology and inflammatory processes of the oral cavity [informational letter No 231]. 2012;