Study of rheological properties of rectal suppositories with phenothiazine

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Abstract
Rheological properties of suppositories on the basis of the original substance phenothiazine-1-methyl-4\(((2\text{-phenethyl})\text{ amino})\text{ carbonyl}\)pyridinium iodide exhibiting pronounced analgesic and antipyretic activity, stimulating effect on the factor of natural resistance – phagocytosis, moderate anti-inflammatory activity and assigned to low-toxic substances have been studied. The dependence of structural viscosity and shear stress of phenothiazine suppository mass on the gradient of shear rate at different temperatures has been studied. Temperature of phenothiazine suppository mass preparation and dispensing has been determined.

Keywords: suppositories, suppository mass, rheology, structural viscosity, phenothiazine.

1. Introduction
One of the major pharmaceutical factors that affect therapeutic efficacy and quality of medicines, is their production technology. At this stage of pharmaceutical development define: the most efficient method of making the drug; optimal parameters of the process, their maximum deviation limits within which manufactured product meets the specified quality; preventive measures to eliminate the causes of poor quality product obtaining. On the basis of experimental data critical aspects of drug production are determined [1].

Suppositories are complicated structured systems that at certain temperatures are characterized by specific structural and mechanical properties - structural viscosity, type of flow, thixotropy and more. The study of these properties is essential for the optimization of technological process [2-4].

The aim of this work was to study the rheological properties of suppositories based on original substance phenothiazine - 1-methyl-4\(((2\text{-phenethyl})\text{ amino})\text{ carbonyl}\)pyridinium iodide exhibiting pronounced analgesic and antipyretic activity, stimulating effect on the natural resistance factor - phagocytosis, moderate anti-inflammatory activity and related to low-toxic substances [5-11].

2. Materials and Methods. Rheological investigation of phenothiazine suppository mass carried out on a rotary viscometer "Rheotest 2" (Germany) on the method of State Pharmacopoeia of Ukraine (2.2.10) [12] in the temperature range (32-36) °C (in which suppository mass is in the liquid state) at a shear rate gradients (D r) 0,3 s\(^{-1}\) to 145,8 s\(^{-1}\). According to data obtained plotted rheograms of the system shown in Fig.1-3.

3. Results and discussion
Of great practical importance are the curves of suppository mass structural viscosity and shear stress against shear rate gradient at different temperatures (Fig. 1-2).

Results of the study indicate that structural viscosity and shear stress of suppository mass depend strongly on the temperature. Within the temperature from 32 °C to 34 °C under study indicators dramatically decrease.
Fig 1: Structural viscosity of suppository dependence on temperature at different shear rate gradients (Dr): 1 - 3 s⁻¹; 2 - 9 s⁻¹; 3 - 27 s⁻¹; 4 - 81 s⁻¹

At increasing the temperature to (34-36) °C yield curves gradually change to straight lines, which indicate a complete destruction of the structure of the system.

From yield rheograms, reflecting the dependence of shear stress on shear rate gradient, determined the type of system flow, presence of thixotropic properties (Fig.3).

Fig 2: The dependence of the suppository mass shear stress over temperature at different shear rate gradients (Dr): 1 - 3s⁻¹; 2 - 9s⁻¹; 3 - 27 s⁻¹; 4 - 81s⁻¹

In the rheograms ascending and descending rheological curves do not match, so the system studied forms hysteresis loops. The ascending part of the hysteresis loop displays thixotropic destruction of the structure, which leads to a drop in viscosity. The downward part of the hysteresis loop characterizes thixotropic restoration of the structure.

When heated to a temperature of 35 °C suppository mass flow type approaches the Newtonian at which there is virtually no area of hysteresis loops, indicating insufficient thixotropy. Low values of the system structural viscosity indicate the destruction of the structure, which could lead to sedimentation of solid phase and create a risk to the homogeneity of the suspension dosing.

Within the temperature from 33 °C to 34 °C hysteresis loop area increases, flow type of the system changes to pseudoplastic.

Suppository mass has the value of structural viscosity at which it is characterized by the optimal fluidity which at the proper mode of mixing can provide production of homogeneous by drug content suppository mass and uniformity of its dosage.

Thus, the temperature range from 33 °C to 34 °C should be considered the most suitable for the preparation and dosing of phenothiazine suppository mass.

4. Conclusions

Rheological properties of suppositories on the basis of the original substance phenothiazine - 1-methyl-4[(2-phenethyl)amino]carbonyl]pyridinium iodide at temperatures (32-36) °C have been studied.

The optimum temperature for preparation and dispensing of phenothiazine suppository mass has been found the temperature range from 33 °C to 34 °C. Results of the research are used in the development and standardization of production technology of phenothiazine suppositories.

5. References


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