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INVESTIGATIONS OF RHEOLOGICAL PROPERTIES OF DICLOFENAC SODIUM GEL PREPARATION

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It is well-known that the majority of non-steroidal anti-inflammatory drugs (NSAIDs) are ulcerogenic. Gel or ointment preparations of NSAIDs are free from this side-effect, which is a prerequisite for the increase of aforementioned forms of NSAIDs. A major quality indicator of gels and ointments are rheological properties. Along with determining the quality of preparation, they influence manufacturing, expiration date and terms of storage.

This article demonstrates the results of investigation of rheological indices of 3% gel preparation of diclofenac sodium such as plasticity, structural viscosity, and thixotropy.

Obtained results confirm that the developed gel preparation has thixotropy, plasticity and is classified as a Bingham system.

Keywords: Diclofenac sodium, rheological properties of gel, thixotropy, dynamic viscosity, hysteresis loops

UDC: 615.454

Introduction

Structural-mechanical properties of ointment and gel preparations influence various therapeutic and customer characteristics such as packaging, extrusion from tube, comfort and easiness of application on skin, drug releasability, etc. Investigation of rheological indices, allows evaluation of influence of accessory and active substances on structural-mechanical and elastic-viscoplastic properties of gel preparations. According to the rheological concept - study of deformation and flow of various substances - structural-mechanical properties of ointment preparations include plasticity, structural viscosity and thixotropy. Evaluation of these properties can be used as an objective data for quality control of manufacturing and storage (Malkin, 2007; Percev, Gutorov and Haleyeva, 2002; Bolshakova, Litvinova, Jmurina, and Burceva, 2012; Moreira, Pereira de Sousa and Pierre, 2010).

The purpose of this research is the study of rheological properties of the diclofenac sodium NSAID gel. This preparation has been developed in Tashkent Pharmaceutical Institute in collaboration with "Remedy Group" Ltd. Determination of structural changes of gel during deformational flow presents a big interest for practical application of this type of preparations. Considering the abovementioned, the current study revealed such features as maximal tension of shear, effective viscosity and thixotropy depending on temperature (Ahmetova and Egorova, 2008; Chawla and Saraf, 2012).

Materials and methods

The object of the study is 3% diclofenac sodium gel preparation. The study was performed on "Rheotest-2" viscosimeter (Germany) - dual system equipment containing cylindrical measuring device, in which the substance is in ringlike space of coaxial cylinder system. The following temperatures have been used 25°C, 40°C, 55°C, 70°C. Three measurements were taken which were subsequently averaged.

A sample of the gel (15-20g) was placed in the reservoir of the device. The twelve speeds of internal cylinder rotation were used in sequence. Once the maximal tangent tension was achieved the rotational speed was reduced in the same sequence.

Tension of shear was calculated using the following formula:

$$\tau = Z \times \alpha,$$

where, τ - tension of shear; Z - constant of a cylinder equal to 5.59 Pa; α - reading of the measuring device.

Dynamic viscosity was calculated using the following formula:

$$\eta = \frac{\tau}{\gamma}$$

where, η - dynamic viscosity, Pa*c; τ - tension of shear, Pa; γ - velocity gradient of shearing flow, c^{-1};

FIGURE 1. DEPENDENCE OF LOGARITHM OF EFFECTIVE VISCOSITY FROM VELOCITY GRADIENT OF SHEARING FLOW

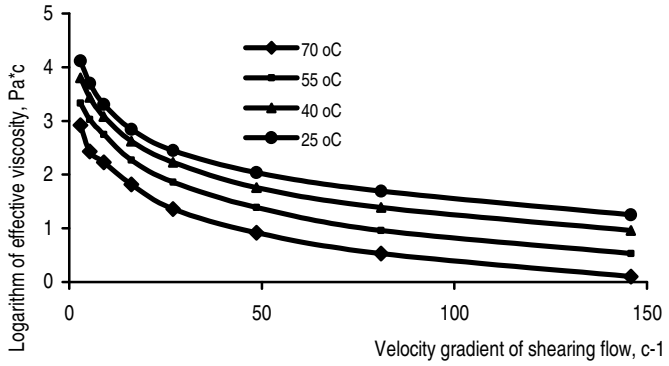
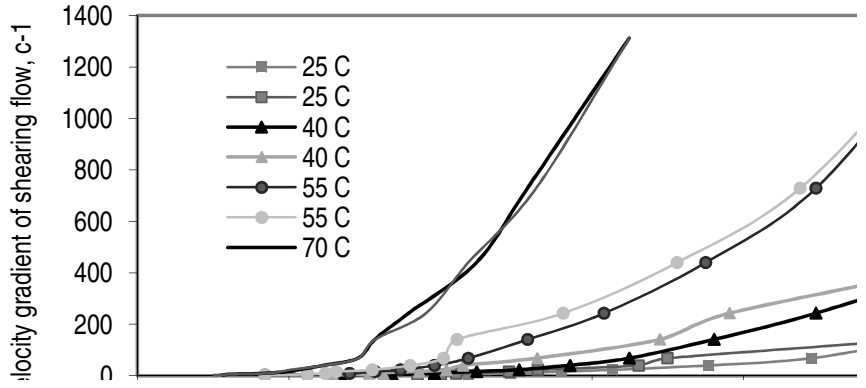
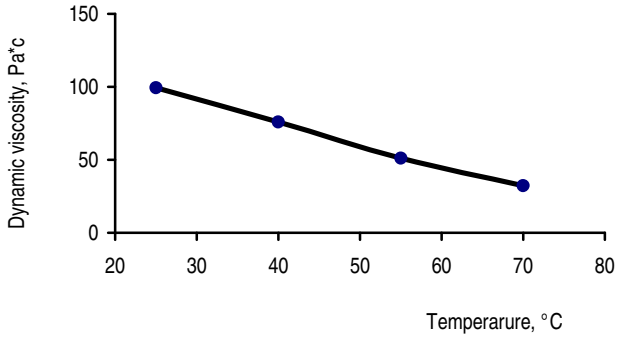


FIGURE 2. DEPENDENCE OF VELOCITY GRADIENT OF SHEARING FLOW FROM TENSION OF SHEAR



On the basis of obtained results the charts were composed, which characterize deviations of logarithm of effective viscosity (ln η_{eff}) from velocity gradient of shearing flow (γ) (Figure 1), dependence of velocity gradient of shearing flow from tension of shear (τ) (Figure 2), dependence of dynamic viscosity from temperature (Figure 3).

FIGURE 3. DEPENDENCE OF DYNAMIC VISCOSITY FROM TEMPERATURE



Results and discussion

Figure 1 shows that increase of velocity gradient of shearing flow, i.e. velocity of deformation leads to gradual decrease of gel viscosity. A major factor reducing viscosity is temperature of the experiment, i.e. temperature rise moves the chart in the area of lower readings of viscosity. As an example, when temperature is equal to 25°C changes of velocity gradient of shearing flow from γ=3 c^{-1} to γ=145.8 c^{-1} entails decrease of the logarithm of effective viscosity of the gel 3.3 times. Similarly, changes at temperatures equal to 40°C, 55°C, and 70°C consisted of 3.96, 6.28, and 29.2 respectively. The fastest decrease in gel viscosity at all four temperatures occurred till the velocity gradient of shearing flow equal to γ=81 c^{-1} after which the process would slow down. The obtained data confirm the presence of structure formation feature in diclofenac sodium gel preparation.

Figure 2 demonstrates dependence of velocity gradient of shearing flow on tension of shear. This chart shows "flow rheograms" which are non-linear and are described with two "ascending and descending" lines. These lines form hysteresis loops. The width of loops is a relative assessment of degree of structure formation processes in ointment and gel preparations for external application (Shram, 2003; Lyapunov and Volovik, 2001). The increase of temperature of the experiment narrows down the width of hysteresis loops which is due to increase of thermal motion of the components, i.e. diminished interaction of constituent elements. The presence of ascending and descending curves forming hysteresis loops indicate that diclofenac sodium gel preparation possesses thixotropic properties which means it is easily applied to skin spreadability and well expressed from tubes.

On Figure 3 we can see that increase of temperature causes all the structural-rheological characteristics of ointments to decrease. For example, the increase of the temperature from 25°C to 40°C (1.6 times) leads to reduction of dynamic viscosity from 99.4 Pa*c to 75.9 Pa*c (1.31 times). At temperatures 55°C and 70°C the dynamic viscosity diminished 1.95 and 3.09 times respectively in comparison to the reading at 25°C. The research results empower us to forecast storage conditions of 3% diclofenac sodium gel preparation.

Conclusion

The results of investigation of rheological characteristics of diclofenac sodium gel preparation allowed the following summary: the developed gel possesses thixotropy, plasticity and is classified as a Bingham system.

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