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THE INFLUENCE OF PRODUCTION PROCESS CONDITIONS ON THE RHEOLOGICAL PROPERTIES OF PASTES

WPŁYW WARUNKÓW PROCESOWYCH, W TOKU WYTWARZANIA, NA PARAMETRY REOLOGICZNE MATERIAŁÓW PASTOWATYCH

Abstract

Pastes are multiphase systems which are frequently encountered in the food, cosmetics and pharmaceutical industries. Their production is a difficult process, due to their non-newtonian character and also because of limited stability of many active substances which have to be included in the commercial product. Therefore highly intensive and prolonged mixing is not recommended for their production. In this work investigation of process condition influence on the rheological parameters of final product have been carried on. The results obtained using pharmaceutical ointment bases as a test fluids, show importance of the preparation method.

Keywords: pastes, pharmaceutical mixer, rheology

Streszczenie

Pasty są wielofazowymi układami często spotykanymi w przemysłach spożywczym, kosmetycznym i farmaceutycznym. Ich wytwarzanie jest trudnym procesem, wynikającym z ich nienetonowskiego charakteru, jak również z ograniczonej stabilności wielu substancji aktywnych, które wchodzą w skład handlowego produktu. W związku z tym długotrwałe i intensywne mieszanie powinno być ograniczane podczas ich wytwarzania. W niniejszym artykule przeprowadzono badania wpływu warunków procesowych na parametry reologiczne końcowego produktu, maści farmaceutycznych wykonanych za pomocą miksera recepturowego. Wyniki uzyskane z wykorzystaniem baz maściowych wskazują na duże znaczenie metody ich przygotowania.

Słowa kluczowe: pasty, mikser recepturowy, reologia

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1. Introduction

Pastes are typically understood as a highly concentrated suspensions, which rheological properties are close to newtonian with the adequate correction. Unfortunately pasteous substances especially those encountered in food, cosmetics and pharmaceutical industries have much more complicated internal structures, ranging from the packing of submicrometric particles, to the soft drops and bubbles. Even more critical is the fact that most such materials contain a wide range of elements of various sizes and interaction patterns which causes their behavior highly unpredictable [1]. Medical and cosmetic ointments, gels, creams, and liniments are usually intended for prolonged action, which is provided by increased viscosity and enhanced structure. These properties are provided by adding densifying agents [2]. Physiological accessibility of the medicinal expedients in the soft medicinal forms is substantially influenced by the dispersity of the substance the nature of the auxiliary additives and the method of adding the substance in the preparation of the ointment. Therefore physical characteristics of the pharmaceutical forms, and particularly its rheological properties, play an important role in the current topical drugs administration [3, 4].

Producing a homogenous pasteous mixture still poses a difficult task. In spite of a new mixer constructions, as well as new and more precise control systems, the mixing of semisolid materials is a great problem for many branches of industry. Very rigorous conditions have to be met in pharmaceutical products [5]. Apart of an uniform distribution of an active particles, the process must be sterile. Another feature in the technology of manufacturing the medicinal forms is connected with rather low thermal stability of the many active agents, therefore the mixture temperature, should be kept low (for antibiotics no more than 32°C) and highly intensive mixer system cannot be used.

Apart from commercial products, in many cases the medicine is prepared by pharmacist according to individual prescription. Not so far ago, the basic method of manufacturing small amounts of ointments was manual mixing in mortar and its final quality was dependent on skill and experience of pharmacy technician. Presently most of pharmacies are equipped with automatic mixers which enable to prepare various formulations using several preset programs.

As a small scale apparatus, used practically entirely by pharmacists, and due to its complicated hydrodynamics, that device was not investigated from the engineering point of view. Especially the effect of programmed procedures on the product quality was not systematically analyzed. In this work comparison of typical ointment bases obtained with various procedures of Unguator® 2100 pharmaceutical mixer were performed, using rheological measurements.

2. Experimental

UNGUATOR® Mixing System [6] was designed by german pharmacist Albrecht Konietzko in the nineties, to facilitate the small scale preparation of pharmaceutical, cosmetic, veterinary and other semi-solid formulations. At the moment, there are several models of Unguators® produced by firma GAKO, which differ in the power and degree of automation. The main advantage of those devices is a combination of mixer rotation, with oscillatory

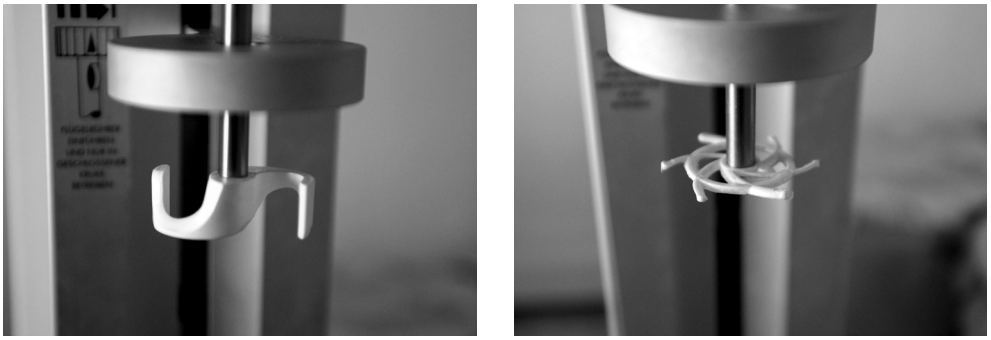

Fig. 1. Standard (left) and disposable (right) blades

Rys. 1. Łopatki standardowe (L) i jednorazowe (P)

movement of a jar. The Unguator® 2100 model which was used in experiments is fully automatic internal microprocessor enables its independent work, but special software enables its control by computer. Pre-programmed mixing parameters (time, speed, jar oscillation) are automatically adjusted depending on a jar size and mixture type, which are stated before the mixer starts. The device uses two types of mixing blades, standard and disposable. Both are of scraper type, but the standard type is more stiff and the scraping blades has wider edges. Fig 1. The mixing blades are slightly larger in diameter than its corresponding jar (taking the advantage of elastic jar walls), to optimize shear and total ingredient incorporation during the mixing process. The disposable blades can be used with smaller jars (up to 200 ml).

There are several jar sizes available: 15, 20, 30, 50, 100, 200, 300, 500 and 1000 ml, depending on the amount of ointment needed. Small jars are designed as disposable container to serve simultaneously as measuring, mixing, dispensing and storage jar. The biggest can be washed, sterilized and reused. After selecting a jar, the procedure should be chosen from the menu list (normal, emulsion, emulsion+, suspension <2%, suspension >2%, gel) or after selecting manual, programmed individually. During the procedure actual rotational speed is shown, and after furnishing its time, total number of rotations and number of up-down cycles is shown.

Mixing was performed using mixtures of popular ointment bases and additives, namely petrolatum, lanolin, lekobaza and water. To test the applicability of standard procedures, various amount of mixture were processed using this same program settings. The mixing effect was evaluated visually, which enabled for elimination of bad samples, then rheological measurements were performed. Using HAAKE RS 75 rheometer. The cone-plate 20 mm, 0.3° measuring sensor was used, and the basic test was flow curve determination.

3. Results

Obtained results are presented graphically. On Fig. 2 flow curves, obtained with this same procedure (ointment-cream), using two jar sizes (100 and 200 ml) and two mixing blade types (standart and disposable), are put together. The strong discrepancy between them can be seen.

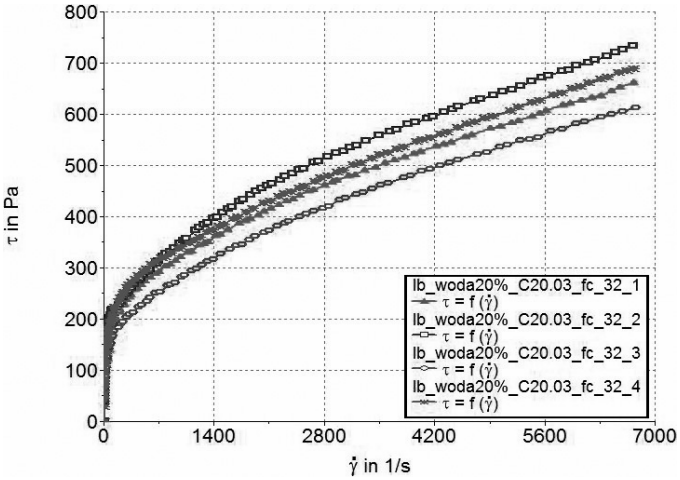

Fig. 2. Flow curves of lekobaza-water (20%) mixtures, at 32°C, obtained with two jar sizes and two blade types; 1-jar 200 ml, blade standard, 2- jar 200 ml, blade disposable, 3-jar 100 ml, blade standard, 1-jar 100 ml, blade disposable

Rys. 2. Przebieg zależności mieszanin lekobaza-woda (20%) przy temperaturze 32°C, dwóch pojemnościach słojów i dwóch typach łopatek: 1-słój 200 ml, łopatka standardowa, 2-słój 200 ml, łopatka jednorazowa, 3-słój 100 ml, łopatka standardowa, 4-słój 100 ml, łopatka jednorazowa

This can be attributed to non-sufficient mixing in the case of bigger jar, since total mixing parameters:

Jar size	Time	Rotations	Cycles
200	3.44	7237	43
100	2.04	4352	43

show that there is this same number of cycles while the height of vessel is doubled in case of 200ml jar, also total number of rotations is smaller, then can expected. The differences in curves may be attributed to various dispersion of water during mixing of the four systems.

On the next picture the comparison between three procedures for the same system is shown. Since current definitions of cosmetic and pharmaceutical products are in many case not very concise and their names can vary depending on literature source, market history or traditional use, so it is not always possible to adapt right procedure. Here effect of procedures emulsion and emulsion+ are collated together with the ointment-cream. All were obtained in 100ml jar with standard blade. Their mixing parameter were as follows:

Procedure	Time	Rotations	Cycles
Ointment-cream	2.04	4352	43
Emulsion	2.25	4829	66
Emulsion+	17.08	4856	258

It can be seen, that both emulsion programs gave different results, so the effect of unsuitable procedure can result in spoiled product. It was found, that when using higher water content, after any procedure part of water remained undispersed. The manual preparation in mortar-pestle system, by skilled pharmacist, enabled full water introduction, so preprogrammed procedures have also limitations, and this should be taken into account.

That influence is even more obvious, when mixing is performed with materials of dense consistency. On the Fig. 4 the flow curves of 50-50% petrolatum-lanolin mixture was obtained using various procedures.

It can be seen that the differences between hard (petrolatum, lanoline), and soft ointment bases can markedly influence product quality. The important aspect is also heating during mixing. The typical final temperature of mixture surpasses 30°C and in the case of highly viscous substances can easily exceed even 50°C. Such temperatures can spoil some active substances, and should be avoided.

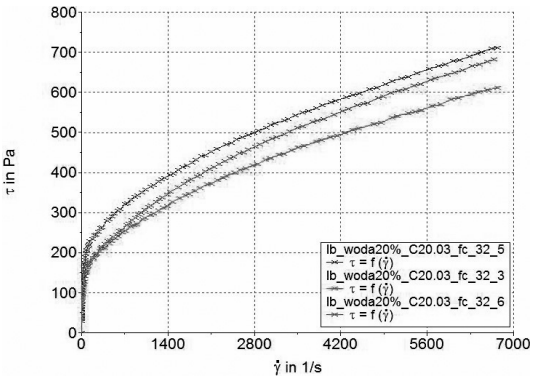

Fig. 3. Flow curves of lekobaza-water (20%) mixtures, at 32°C,
obtained with three procedures 3 ointment-crème, 5-Emulsion, 6-Emulsion+

Rys. 3. Przebieg zależności mieszanin lekobaza-woda (20%) przy temperaturze 32°C
w trzech procedurach 3-maść-krem, 5-emulsja, 6-emulsja+.

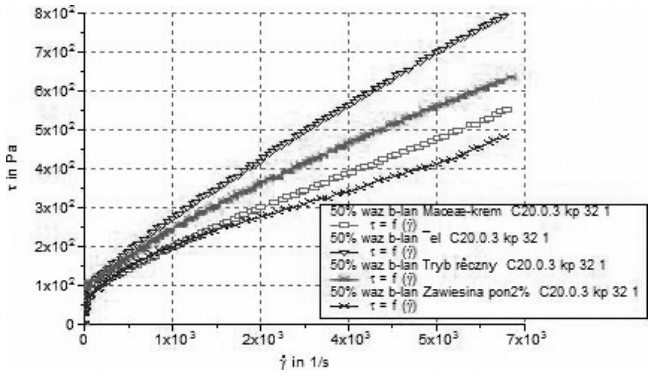

Fig. 4. Flow curves of petrolatum-lanolin mixtures obtained with various procedures

Rys. 4. Przebieg zależności mieszanin wazelina-lanolina w różnych procedurach

4. Conclusions

In general pharmaceutical mixer provides good homogenization of pastes, suspension and emulsions. The factory preprogrammed procedures have certain limitation, which may be of minor importance for the pharmacists, nevertheless, some modifications may be needed, anyway there is also manual setting option, in case of simpler models as a basic one. Unfortunately it requires certain experience, and obeying of producers instructions. Rheological tests are important tools in comparing performance of semisolids.

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