Application of guar gum biopolymer in the prescription of tablets with sodium ibuprofen – quality tests and pharmaceutical availability 

in vitro

Aneta Berner-Strzelczyk, Justyna Kołodziejksa, Marian Mikołaj Zgoda

Department of Drug Form Technology, Applied Pharmacy Faculty
Medical University in Lodz

Summary

The increasing interest of the technology of drug form in natural biopolymers has become the reason for undertaking investigations on the possibility of guar gum application in the prescription of oral solid form of a drug. Alternative compositions and technology of the production of tablets of regulated in time sodium ibuprofen release were worked out for children. Two series of tablets were prepared with guar gum (5 and 10% content) and a series without the biopolymer. The tablet mass in each case contained keryostatic sorbitol and bioadhesive polyvinylpyrrolidone. All tablets were tested as regards the quality of production, compliance with the requirements of Polish Pharmacopoeia VI and potential therapeutic usefulness, manifestation of which is pharmaceutical availability of the therapeutic agent (sodium ibuprofen).

The tests demonstrated that the produced tablets with sodium ibuprofen have proper physicochemical properties, in compliance with Polish Pharmacopoeia VI requirements. Application of biopolymer of guar gum type as adjuvant substance contributes to the improvement of the tablet hardness parameters and prevents technological problems (lining mixture of powders to tableting machine punch). The designed tablets demonstrate proper pharmaceutical availability of over 80%. Introduction of guar gum into their prescription prolonged their disintegration time and the rate of sodium ibuprofen release, which
predisposes the produced form of a drug to have the function of a tablet with slowed-down release.

**Key words:** guar gum, matrice tablets, sodium ibuprofen, pharmaceutical availability

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**INTRODUCTION**

Guar gum, a natural polysaccharide composed of galactan and mannan units, is a natural polymer of significant economic and technological importance [1]. Its application is mainly in food industry where it is used as the so called additive forming the structure of food products [2-4]. Guar gum properties of an emulsifier, thickener and stabilizer decide on its application in the technology of a drug form. It is used in the production of ointments, hydrogels, for modification of solutions viscosity, stabilisation of emulsion and also as a binding and blowing agent for the production of tablets [5-10]. Due to specific parameters of structural viscosity, biopolymers of guar gum type applied in the technology of tablets production have a direct effect – owing to bioadhesiveness – on the rate of therapeutic agent penetration through a net of blood vessels to the central compartment [11, 12]. The fact that guar gum is hydrolysed in digestive tract to basic saccharic alcohols forming its polymeric structure is an unquestionable advantage in case of application.

In this study investigations were undertaken on the introduction of guar gum into the prescription of a drug form for children of analgesic, anti-inflammatory and antifebrile activity. Tablets were produced with regulated time of sodium ibuprofen release in three alternative compositions: with 5% and 10% content of the biopolymer and without guar gum in the prescription. The aim of the study was to carry out quality tests of model drug form and comparative estimation *in vitro* of pharmaceutical availability of sodium ibuprofen from tablets from various series produced according to own prescription.

**MATERIAL AND METHOD**

**Reagents**
- sodium ibuprofen (Fischer Chemicals AG);
- guar gum (Sigma) (fig 1);
- sorbitol (Fluka);
- polyvinylpyrrolidone XL 10 (ISP Technologies Inc.);
- magnesium stearate (POCH Gliwice);
- ethyl alcohol 95\(^0\), (POCH Gliwice).

**Apparatus**

- tableting striking machine EKO (Erweka);
- hardness tester YBH-200 TD (Erweka);
- friabilator F2 (Research-Development Centre for Pharmaceutical Industry Mechanization “Polfa”);
- electronic slide caliper (Mitutoyo (UK) Ltd);
- apparatus for testing the time of tablet disintegration ZT 53 (Erweka);
- apparatus for testing therapeutic agent release from tablets MUS IB 386 (Research-Development Centre for Pharmaceutical Industry Mechanization “Polfa”);
- spectrophotometer Nicolet Evolution, version 1.0 (Spectro Lab);
- general laboratory balance (Precision Engineering Plant “Radwag”);
- analytical balance (Precision Engineering Plant “Radwag”).

**Formulation of tablets with sodium ibuprofen**

Three alternative compositions of tablets with sodium ibuprofen were produced on polymer matrice. Series I tablets contained 10\%, while series II tablets – 5\% of guar gum in their prescription. Tablets of analogical prescription components were also prepared but without guar gum (series III).

Prescription amount of sodium ibuprofen, sorbitol, polyvinylpyrrolidone (PVP) and guar gum (series I and II) were introduced into a high-speed mixer.

At slow rotations of the stirrer (35-45 rpm) the formulation components were mixed thoroughly until stable and repeatable bulk density of the tablet mass was obtained. The powdered mass was then unified by passing through sieve Ø = 1,2 mm. Before tableting, magnesium stearate (lubricating agent) was added and these were mixed uniformly.

The tablets without guar gum in the prescription were made with wet granulation. Ethanol 95\(^0\) was used to mix the granulate.

All tablets were compressed with the punches of Ø10 mm checking periodically the bulk density stability and appropriate tablet mass resulting from the suggested prescription.

**Morphological tests of the produced tablets** [15, 16].
Mean mass \((m_t[\text{mg}])\), diameter \((D[\text{cm}])\) and height \((h[\text{m}])\) were determined for 20 tablets of each series and then, their real density \((d_{rezecz}[\text{g/cm}^3])\) and mean tablet surface \((P_{rezecz}[\text{cm}^2])\). Furthermore, hardness was tested for ten tablets from each series \((P[\text{N}])\) and stress \((T_s[\text{MPa}])\) was calculated as well as the \% of plasticity. The time of disintegration was tested for 6 tablets from each series.

**Testing pharmaceutical availability of sodium ibuprofen** [16, 17].

The testing of the therapeutic agent rate of release from the produced tablets was performed with the spatula method recommended by Polish Pharmacopoeia VI. To evaluate sodium ibuprofen pharmaceutical availability, the samples of solutions obtained in release tests were subjected to spectrophotometric analysis. Absorbance of the tested solution was measured at the wave length 223 nm in comparison with the standard obtained by producing placebo tablets.

Total amount of the therapeutic agent dissolved after time \(t\) was calculated according to the formula:

\[
C_0 - C_t = \frac{V}{v} \cdot C_t + m_i,
\]

where:

\(C_0 - C_t\) – total amount of the substance dissolved after time \(t\), \(V\) – fluid volume in which the tablet is immersed, \(v\) – the volume of solution taken for analysis, \(C_t\) – amount of substance determined in sample \(v\), \(m_i\) – total amount of substance determined in samples collected previously.

In order to standardize and to compare the results with the results of other studies of similar subject meter, basing on the regulations resulting from literature, the amount of the therapeutic agent was calculated into \% release coefficient \(Q\) expressed by the formula:

\[
Q = \frac{C}{D} \cdot 100,
\]

where:

\(Q\) – release coefficient expressed in \%, \(C\) – amount of therapeutic agent released to the solution in grams, \(D\) – declared content of therapeutic agent in a tablet in grams [15].

**RESULTS AND DISCUSSION**

Basic physicochemical values of the produced tablets are presented in table I. From the technological point of view, the application of guar gum as a substance conditioning the time of disintegration of the designed tablets appeared to be beneficial. The process of direct
tableting, that is omitting granulation, was efficient and without any technological problems. The powder mass for tableting was characterized by constant weight, no “spraying” or mixture lining to punches. Obtaining proper thickness and bulk density of the tablet mass reflected in uniform and homogenous pouring the mixture into the matrice, which enabled getting tablets of demanded, resulting from the suggested prescription, mass \( m_t \) (g) and density (appropriate tablet size in relation to its mass).

In the case of tablets without guar gum in the prescription, a slight lining of the mixture of powders (tablet mass) to the elements of tableting machine was observed.

The effect of flowing in a beaker during release test was not observed in all the tested tablets of all series. The produced tablets in each series had smooth surface, uniform shape and colour (no stains). There were no chips or mechanical defects, which was confirmed testing the tablets mechanical resistance to abrasion (the loss of total mass did not exceed 1% in all cases) and mechanical strength. In the case of the production of tablets with sorbitol (series I, II, III) the problem of technological nature is usually obtaining a drug form of proper hardness which prevents from crushing during extracting from the blister niche. The above is explained by the existence of the so called crystallographic memory of polyhydroxide saccharic alcohols (xylitol, sorbitol). The measurements of basic physciochemical values of the tested series of tablets demonstrated certain differences in the hardness dependently on the content of guar gum in the prescription. The tablets with guar gum (series I and II) were characterized by higher hardness parameters (128 N and 108,3 N, respectively) than the tablets from series III without guar gum (67,9 N) (tab. I).

The graphic interpretation of the dependence of the release coefficient \( Q = f(t) \) for the tested tablets with sodium ibuprofen is presented in figure 2.

All produced series of tablets had high sodium ibuprofen pharmaceutical availability of 80% (fig. 1). In the case of tablets which did not contain guar gum in prescription (series III) the amount of the released therapeutic agent calculated in relation to \( Q \) coefficient was 80% already after about 20 min from the beginning of the release. The increase of guar gum content in the prescription of a model tablet affects \textit{in vitro} the rate of therapeutic agent diffusion to a model dialysis fluid (fig. 2). And thus, formulation I reached the value of \( Q \) coefficient (80%) after 45 min, while formulation II insignificantly earlier – after about 35 min of exposure (fig. 2). The above results were reflected in the testing of the time of disintegration of tablets from three produced series: in the case of tablets with guar gum (series I, II) it was longer than 30 min (fig. 3).
Both, the disintegration time of the alternative series of tablets with guar gum (series I and II) and the observed dependence of therapeutic agent release coefficient on time, are the base for further studies on the possibility of the application of the worked out drug form in pharmacotherapy, effectiveness of which is based on slowed-down release of sodium ibuprofen (maintenance of therapeutic concentration of drug in blood). Due to bioadhesive properties of guar gum, better contact of the tablet with gastric mucosa (formation of the so-called absorption space) may be the result of guar gum application in the prescription of the designed tablet. Prolonged exposure time to sodium ibuprofen may be of importance in the reduction of the dose and frequency of administration of anti-inflammatory, analgesic and antifebrile drug designed for children.

CONCLUSION

1. The designed tablets with sodium ibuprofen are characterized by proper physicochemical parameters in accordance with the requirements of Polish Pharmacopoeia VI. Introduction of guar gum biopolymer into the prescription of paediatric drug contributes to the improvement of hardness parameters and prevents granulometric problems (lining of the mixture of powders to tableting machine punches).

2. Model tablets with sodium ibuprofen demonstrate the expected prolonged in time pharmaceutical availability of over 80% after 45 min of exposure in model dialysis fluid.

3. Application of guar gum polymer as adjuvant substance prolongs the disintegration time and the rate of sodium ibuprofen release which predispose the produced drug form to be a tablet with slowed-down release. The above may be the cause of the reduction of dose and frequency of administration of this paediatric drug of anti-inflammatory, analgesic and antifebrile activity.