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STUDY OF THE PHYSICOCHEMICAL AND TECHNOLOGICAL PROPERTIES OF THE BASE FOR HEALTH IN GUM® MEDICAL CHEWING GUM

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Medicinal chewing gum is a dosage form that is gaining popularity due to the ease of use (does not require water), the gradual release of medicines in the oral cavity, reducing the risk of side effects due to the lack of direct contact with the gastric mucosa and other benefits. This study demonstrated the physicochemical and technological properties of the base for the preparation of Health in Gum® PWD-04 chewing gum (gum bases) by direct compression. The analysis of the resulting data is carried out and the conclusion is made about the applicability of the direct compression process for the studied brand of gum base.

Keywords: medicinal chewing gum, gum base, base for medicinal chewing gum, Health in Gum®, technological properties, particle shape and size

The oral route of administration of medicines is the most preferred among patients and physicians due to some advantages over other dosage forms (DF). One of the reasons is the ease of administration and the possibility of use for people suffering from dysphagia, in addition, some active substance (AS) are absorbed in the oral cavity [1–3]. Medicines with significant buccal absorption, such as oro-dispersible tablets, chewing tablets, and chewing gum, provide a rapid therapeutic effect compared to DF for oral administration.

Chewing tablets and chewing gums are especially actively used in pediatrics as more preferred dosage forms compared to oral liquids and tablets. In addition, chewing gums are kept in the oral cavity for a long time, which provides local use for some medicines. According to SP XIV, "medicinal chewing gum is a solid dosage form of "rubber-like" consistency intended for chewing for a certain period of time without subsequent ingestion in order to provide local action in the oral cavity and throat or systemic action." Therefore, due to the presented features and ease of use, a medicinal chewing gum is a promising dosage form for oral use.

The purpose of this work is to describe the excipients used in the production process for medicinal chewing gum, as well as to study the physical, chemical and technological properties of one of the brands of bases for medicinal chewing gum (gum bases).

MATERIALS AND METHODS

During the research, the physicochemical and technological properties of the base for Health in Gum® PWD-04 medicinal chewing gum (Cafosa®, Spain) were studied according to the following characteristics.

Assessment of the flow character and measurement of the angle of repose (OFS.1.4.2.0016.15 SP XIV) was performed using an Erweka GDT vibrating funnel. Optical microscopy (OFS.1.1.0015.15, SP XIV) was carried out using a microscope (Nikon, Eclipse E200). Weight loss during drying (OFS.1.2.1.0010.15, KV XIV) was measured using a Sartorius MA-35 moisture meter. Compressibility was checked using a PRG-50 manual hydraulic press. Tablet compression test (OFS.1.4.2.0011.15, SP XIV) was performed using a TBF 1000 mechanical strength tester (Copley Scientific®). The bulk weight (bulk density) was measured using an Erweka SVM 221 instrument. The Carr's index was calculated using the formula:

$$Ic = [(\rho_2 - \rho_1) / \rho_2] \times 100\%;$$

the Hausner coefficient was calculated using the formula:

$$k_H = \rho_2 / \rho_1,$$

where $\rho_1 = M/V_1$ is the bulk density, and $\rho_2 = M/V_2$ is the bulk density after compaction. The true density was determined using a pycnometer for powdered substances (volumeter) filled with liquid, according to the formula:

$$\rho = \frac{m \times \rho_l}{m + m_1 + m_2},$$

where m is the mass of the substance, g; ρ_l is the density of the liquid, g/cm^3; m_1 is the mass of the volumeter with the substance, g; m_2 is the mass of the volumeter with the liquid and substance, g. The porosity was calculated based on the density and bulk density values:

$$П = (1 - P/\rho) \times 100\%,$$

where П is the porosity, %; P is the bulk density, g/cm^3; ρ is the density, g/cm^3.

RESULTS AND DISCUSSION

Chewing gum is a mixture of natural or synthetic resins and resins sweetened with sugar, corn syrup, artificial sweeteners, and may also contain colorants and flavors.

Chewing gum consists of two parts:

1. Water-insoluble chewing gum base.
2. Water-soluble constituent.

1. The water-insoluble base of chewing gum usually contains polymers (elastomers), resins, fats, oils, and inorganic fillers [4].

a) Elastomers are polymer compounds with high elasticity properties. The elastomer provides flexibility to tear and break and controls the regular texture.

There are natural and synthetic types of elastomers, the most commonly used are natural resins, such as: Jelutong, LechiCaspi, Perillo, Chicle.

b) Plasticizers are necessary to obtain a variety of desired textures and consistency properties, reduce brittleness, and facilitate the mixing of other components. Excipients such as glycerin, lanolin, palmitic acid, oleic acid, stearic acid, potassium stearate, microcrystalline waxes, propylene glycol, terpene resins derived from α-pinene and/or d-limonene are used.

c) Fillers or texturizers form the texture, improve the chewable properties, provide a reasonable size of a chewing gum with a low dose of a pharmaceutical substance. Commonly used fillers are magnesium and calcium carbonate, ground limestone, magnesium and aluminum silicate, aluminum hydroxide, talc, titanium oxide, and calcium mono -, di -, and triphosphate.

2. Water-soluble excipients consist of sweeteners, flavors, emulsifiers, dyes and antioxidants [5].

In addition, the composition for compression includes excipients, improving the flowability and anti-adhesive properties of the mixture for tableting (lubricants and glidants): silicon dioxide, magnesium stearate, talc can be used in medicinal chewing gum.

In addition to the independent selection of these components, there is an alternative direction in the production of medicinal chewing gum, which consists in the use of a ready-made base for chewing gum, which contains the main components of the formulation. An example of such a base is Health in Gum® (Cafosa®), which was used to study physical, chemical and technological properties.

This combined mixture of excipients is an inert and insoluble product used as a base for chewing gum [6]. Health in Gum® belongs to the group of free-flowing resin-like substances for direct compression developed by Cafosa Gum SAU. The presented bases for production of medicinal chewing gum contain a high percentage of inert soft thermoplastic elastomers, a mixture of polyols (sorbitol/xylitol/mannitol), sugars, plasticizers and anti-adhesives. When compressing the Health in Gum®, chewing gums are produced, which are similar in appearance to tablets for oral use. They have a higher hardness and friability than medicinal chewing gum, made by the traditional method of extrusion. Health in Gym® has three varieties: HiG PWD-01, HiG PWD-03 и HiG PWD-04, which contain 25, 35 and 30% of elastomeric base, respectively.

The results of studies of the physico-chemical and technological parameters of the HiG PWD04 base are presented in Table. 1 and in Figures 1 and 2.

Health in Gum® is a mixture of anisometric particles with different shapes or (Fig. 1) in the form of conglomerates of particles with the sizes of the main fractions from 500 to 1000 μm (<50%) and 100–300 μm (<70%) (Fig. 2). Based

Table 1

PHYSICO-CHEMICAL AND TECHNOLOGICAL PARAMETERS OF THE BASE FOR HEALTH IN GUM® MEDICINAL CHEWING GUM

Parameter	Units	Values
Description	White with a yellowish tint, inhomogeneous amorphous powder	
Flowability	g/s	4.02±1.05
Compressibility (fractural strength)	N	4.56±0.17
Angle of repose	Degrees	40±13
Residual moisture	%	1.03±0.60
Bulk weight before compression	g/cm^3	0.608±0.012
Bulk weight after compression	g/cm^3	0.621±0.021
Carr's index	%	2.13±0.01
Hausner coefficient		1.02±0.02
Porosity	%	54.302±3.503
True density	g/cm^3	1.3304±0.0032

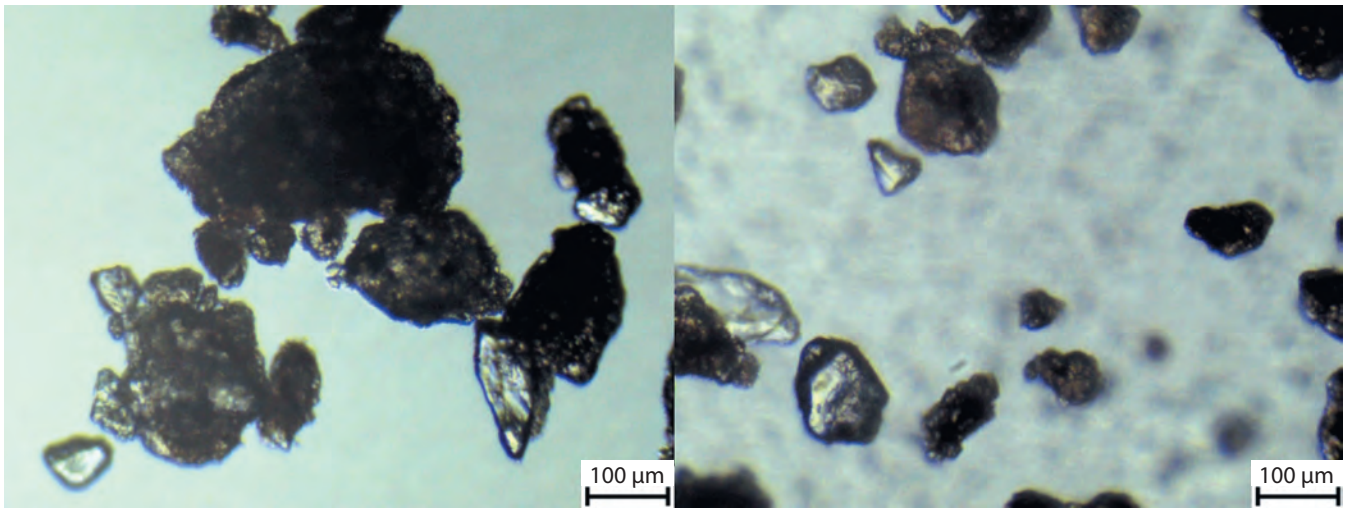

FIG. 1. *Micrographs of the particles of the base for Health in Gum® medicinal chewing gum (magnification 160×)*

on the results of optical microscopy, it can be concluded that the particles of the gum base are heterogeneous in shape and size. There are several main fractions and the largest particles are translucent equilateral agglomerates with pitted surface and inclusions. The remaining fractions are described as translucent angular rough equilateral or transparent angular smooth plate-like particles.

Despite the relatively large distribution of particles in size and shape, gum base has a very good (excellent) degree of flowability, which is also specified by the Hausner coefficient, whose values do not exceed 1.26.

Due to the presence of elastomers in the base for medicinal chewing gums, through the compression a tablet with high elastic-plastic properties is produced, which is indirectly confirmed by a low Carr's coefficient and a low compressibility value. In addition, the tablets are characterized by a low ejection force (<1 kN), but sometimes the base may stick to the punches due to the heating of part of the elastomers. Gum base is also characterized by a moderate degree of porosity and low moisture content. Based on the resulting characteristics, we have identified the applicability of the Health in Gum® base in direct compression technology.

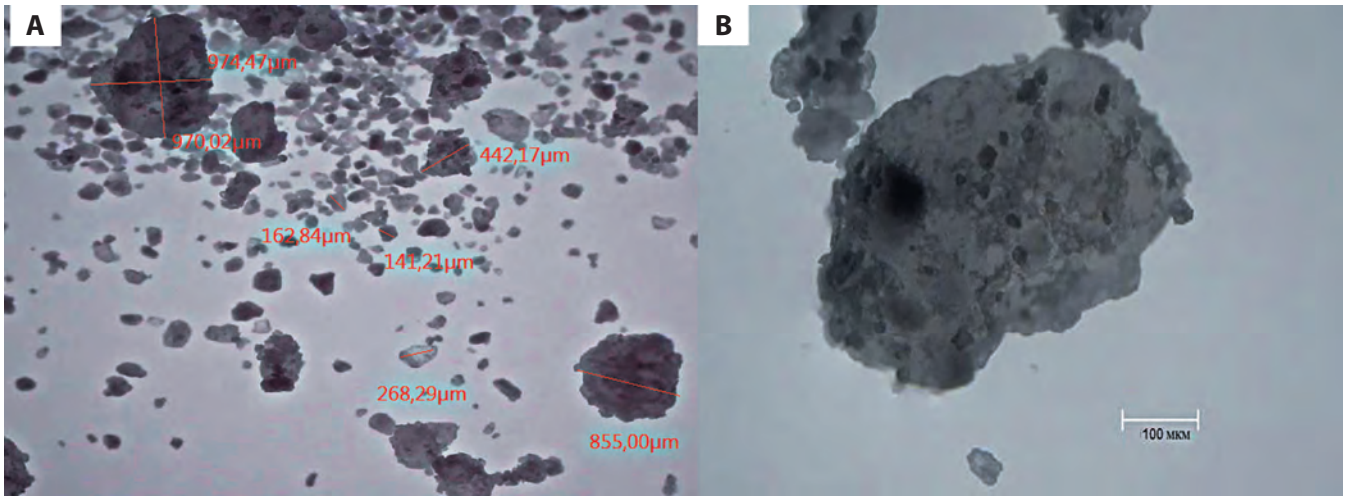

FIG. 2. *Micrographs of the particles of the base for Health in Gum® medicinal chewing gum: A) magnification 30×; B) magnification 195×*

CONCLUSIONS

As a result of the studies, it can be concluded that the base for Health in Gum® medicinal chewing gums has optimal physical, chemical and technological properties, which characterize it as a highly free-flowing powder with a wide particle size distribution, a low degree of compressibility, moderate porosity, low moisture content, and elastic-plastic properties when tableting. Based on its characteristics, this gum base can be used in direct compression technology.

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