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# Justification of Medicated Chewing Gum Composition for Weight Control and Overweight Fighting

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**ABSTRACT**

Overweight and its consequences are a major public health problem worldwide. This is a problem for Ukraine also, due primarily to the growth in recent years of the patients' number with this pathology. Being overweight creates not only an aesthetic and psychological problem, but also provokes the development of many diseases. As it is known, all medications for weight loss are designed to suppress appetite or to speed up of metabolism. As objects of the study for the drug developed, we have offered dry extract of Hoodia Gordonii and Bromelain. Today, there are many medicines, capable of reducing body weight, but mostly they are dietary supplements in various dosage forms. Special attention deserves a modern oral dosage form – medicated chewing gum (MCG) which is used to treat many diseases and has a number of advantages over other solid dosage forms for use in the oral cavity. The aim of our work is the choice of excipients and development of composition for the drug in the form of medicated chewing gum for weight control and overweight fighting. As objects of research excipients of the following groups were selected: gum base, moisture-absorbing agents, glidants, binders, flavors. MCG obtaining method is pressing. In order to develop the composition of MCG with Hoodia extract and bromelain the physicochemical and pharmacotehnological studies were conducted. Based on the microscopic analysis of the gum base HiG-01 and its mixture with APIs rational method of MCG manufacture has been selected – pressing with previous granulation. According to the results of microscopic analysis and technological properties of the granules obtained by using various humidifiers as an optimal binder – 20% ethanol was selected. Based on the research of moisture-absorbing capacity and technological properties of tablet mass with the addition of various adsorbents as an optimal adsorbent an amorphous silica (silicon dioxide) Syloid® 244FP, allowing the liquid substance easily converted into powders with good flowability and improve the stability of moisture-sensitive APIs, was chosen. It has been established that the development and implementation into production of the drug in the form of medicated chewing gums will expand the range of domestic products for weight control and the fight against overweight.

**Keywords:** overweight, medicated chewing gums, hoodia gordonii, bromelain, excipients, physicochemical and pharmacotechnological research

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## INTRODUCTION

Overweight and its consequences are a major public health problem worldwide. This is a problem for Ukraine also, due primarily to the growth in recent years of the patients' number with this pathology. Being overweight creates not only an aesthetic and psychological problem, but also provokes the development of many diseases – cardiovascular, diabetes, diseases of the joints, some cancers [1-3].

As it is known, all medications for weight loss are designed to suppress appetite or to speed up of metabolism [1, 2]. As objects of the study for the drug developed, we have offered dry extract of Hoodia Gordonii and Bromelain. Acting on hypothalamic structures, Hoodia sends a signal of the high glucose level, which leads to hunger reduction; at this it helps to avoid overeating, save energy and performance during a diet [4-6, 8]. Bromelain as a proteolytic enzyme helps regulate body weight by optimizing digestion processes and normalizing metabolism. It also has the ability to break down fats and reduce body pollution with slags, which allows including it in weight loss programs [6-8].

Today, there are many medicines, capable of reducing body weight, but mostly they are dietary supplements in various dosage forms [6, 9].

Of particular note is a modern oral dosage form – medicated chewing gum (MCG) which is used to treat many diseases and has a number of advantages over other solid dosage forms for use in the oral cavity [10-12].

The aim of our work is the choice of excipients and development of composition for the drug in the form of medicated chewing gum for weight control and overweight fighting.

## OBJECTS AND METHODS OF RESEARCH

The object of study is medicated chewing gum. As the active pharmaceutical ingredients (APIs) have been selected dry extract of Hoodia Gordonii and Bromelain. As excipients chewing basis HiG-01 (Cafosa, Spain), moisture-absorbing agents – Aerosil 380 (Orisil, Ukraine), amorphous silica (silicon dioxide) Syloid® 244FP (Grace Discovery Sciences, USA) and magnesium aluminometa silicate Neusilin® (Fuji Chemical Industry, Japan), binding agents – a solution of PVP 5 %, ethanol 40 % and 20 %, liquid oily flavour "Melon" (Plant of food chemical aromatics, Russia) have been used. MCG obtaining method – the pressing method.

In order to develop a composition of medicated chewing gum with Hoodia extract and bromelain studied physicochemical (shape and size of the powder, nature of surface and moisture-absorbing capacity) and technological parameters (bulk volume, bulk and tap-density, flowability, angle of repose) [13].

Microscopic analysis of powders was performed using laboratory microscope "Konus Academy", equipped with a video camera ScopeTek. Images have been processed using the software Scope Photo (version 3.0.12.498).

Fluidity has been determined using the device VP-12A by measuring the time of sample powder (100.0 g) flowing out of the funnel.

Bulk density has been determined on the device for bulk volume determination type PT-TD1 (Pharma Test, Germany) (100.0 g).

## RESULTS AND THEIR DISCUSSION

As the basic excipient used in the production of chewing gums and providing technological and consumer indicators is chewing basis HiG-01, which in appearance represents white granules. Table 1 shows the results of pharmacotechnological studies of the base.

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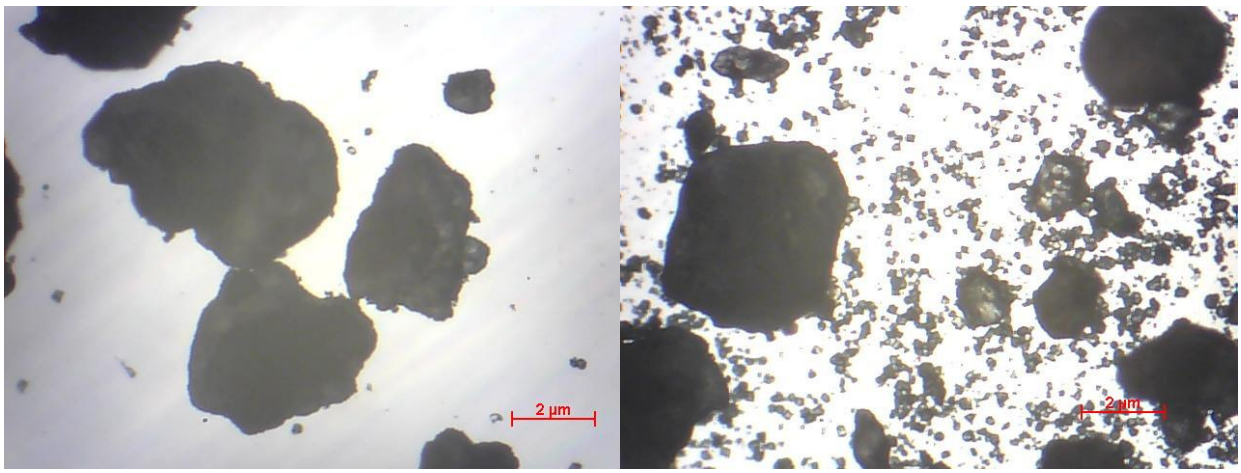
**Table 1: Technological characteristics of the base HiG-01**

| n | Flowability, sec/100 gsample | Angle of repose, ° | Bulk density, g/ml | Tap-density, g/ml |
|---|---|---|---|---|
| 6 | 8,15 ± 0,32 | 31 ± 1 | 0,625 ± 0,015 | 0,694 ± 0,015 |

In determining the base's fluidity used vibration because the base stuck to funnel and did not flow out of it. According to the Table 1, chewing base has good fluidity, confirming information about the possibility of obtaining chewing gums using the base HiG-01 by direct compression[10, 12].

Fig 1: shows the results of microscopic analysis of the chewing base and its mixture with APIs (x20 magnification).




a) b)

**Fig 1: Microscopic analysis:a – base HiG-01, b – mixture of the base with APIs**

According to Fig. 1, the base HiG-01 represents granules of the size6-1,5 µm. The APIs mixture with the base is a polydisperse system with particles of different shape and size that will not allow obtaining a uniform tablet mass.

Considering the fact that when mixed APIs with chewing basis the resulting mixture was not uniform and stratified at stirring, due to the different dispersion of components, we have decided to produce the tabletting mass in the form of granules. To this end, as binding components used PVP solution 5 %, ethanol 40 % and 20 %. The mixture of APIs with the basis moisturized with appropriate solutions, granulated, dried and calibrated [13]. Fig. 2 presents the results of microscopic study of granules obtained.

PVP 5 % Ethanol40 % Ethanol 20 %

**Fig 2: Microscopic study of granules obtained by using different humidifiers**

As the carried studies have shown (Fig. 2), using an aqueous solution of PVP 5 % results in poor quality granules that after drying were very hard (this may be due to the aqueous solubility of active ingredients). The mass moisturized better when added alcohol solution, and granules obtained were homogeneous. At that the drying time of granules was reduced.

For the final choice of a moisturizer, we have conducted technological research of the obtained granules, the results of which are shown in Table 2.

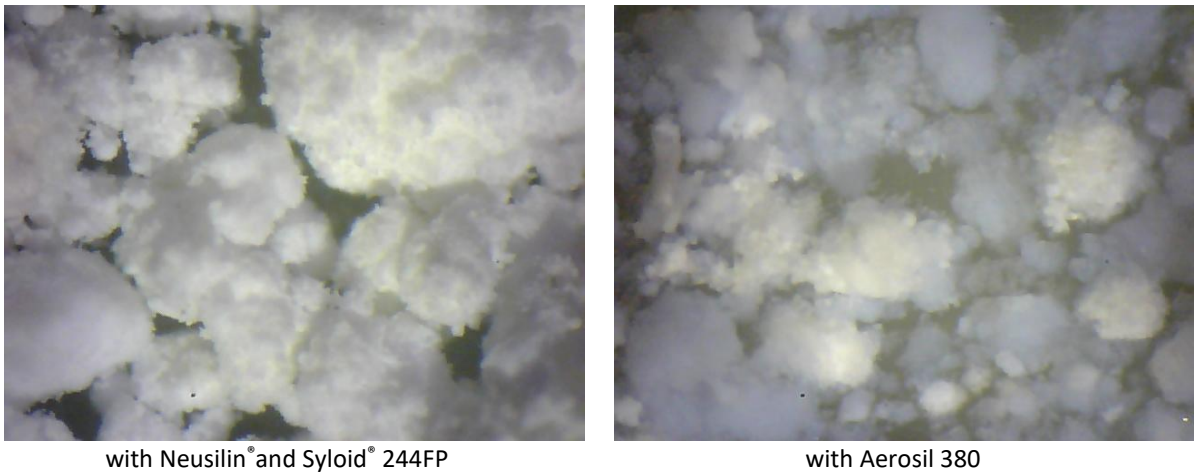
**Table 2: Technological properties of the granules obtained by using different humidifiers**

| Indicator | Binding component | | |
|---|---|---|---|
| | PVP 5 % | Ethanol 40 % | Ethanol 20 % |
| Flowability,sec/100 g | 19,9 ± 1,0 | 18,0 ± 0,7 | 12,4 ± 1,0 |
| Angle of repose, ° | 28 ± 2 | 29 ± 1 | 26 ± 2 |

Considering the results (Table 2), the best binding component alcohol 20 % has been selected.

According to previous studies APIs hygroscopicity has been found [6], which demonstrates the need for the introduction to the MCG excipients to provide a reduction in powders' hygroscopicity and improve the mass flowability. In addition, introduction of liquid oily flavour "Melon" in solid dosage form also requires the use of moisture-absorbing agents that allow easy transformation of liquid APIs in powders with good fluidity. For this purpose, we used Aerosil 380, Syloid® 244FP and Neusilin®. With its unique structure and versatility (adsorption capacity, porosity, particle size, high surface area, etc.) these adjuvants are effective moisture-absorbing agents that increase the stability of moisture-sensitive APIs; and they play the role of glidants which improve the fluidity and homogeneity of the mixture and prevent caking and sticking of tablet mass to pressing tool [8, 12, 13, 14].

The required amount of liquid flavouring sprayed on various adsorbents and thoroughly mixed. The results obtained have shown that each moisture-absorbing agent very quickly adsorbed oil solution forming a dry powdery mixture. But when using Aerosil 380 absorption and colour change took place only in those areas where the solution directly contacted with the adsorbent and the rest remained unchanged, and after stirring the resulting mixture was not uniform. When using Syloid® 244FP and Neusilin® obtained almost identical results – the mixture was homogeneous, there was a weak colour change in all areas of the mass, i.e. oil solution was completely absorbed by the whole mass of adsorbent. These results have been confirmed by microscopic analysis (Fig. 3).



with Neusilin®and Syloid® 244FP | with Aerosil 380

**Fig 3: Microscopic analysis of moisture-absorbing capacity of adsorbents**

Given the fact that the above adsorbents also play the role of glidants in the manufacture of solid dosage forms, we have investigated the fluidity of obtained granules of APIs with chewing basis with the addition of the adsorbent mixture with flavour. Glidants added in various concentrations. The results are

shown in Table 3.

**Table 3: Technological properties of tablet mass with the addition of different glidants**

| Name and brand of the adsorbent | Concentrationsof adsorbents | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 0.5 % | | 1.0 % | | 1.5 % | | 2.0 % | |
| | Flowability, sec/100 g | Angle of repose | Flowability, sec/100 g | Angle of repose | Flowability, sec/100 g | Angle of repose | Flowability, sec/100 g | Angle of repose |
| Aerosil 380 | 12,0 ± 0,7 | 35 ± 2 | 11,6 ± 0,8 | 32 ± 2 | 10,2 ± 0,4 | 27 ± 2 | 10,8 ± 0,8 | 30 ± 1 |
| Syloid® 244FP | 11,6 ± 0,7 | 34 ± 2 | 10,5 ± 0,6 | 32 ± 2 | 8,8 ± 0,5 | 27 ± 3 | 9,7 ± 0,4 | 30 ± 2 |
| Neusilin® | 11,5 ± 1,1 | 33 ± 2 | 9,9 ± 0,5 | 32 ± 2 | 9,3 ± 0,4 | 33 ± 2 | 9,0 ± 0,5 | 29 ± 2 |

As the results have shown, the best fluidity has the mixture with Syloid® 244FP at a concentration of 1.5 %, as confirmed by the angle of repose.

## CONCLUSIONS

1. The analysis of scientific literature has shown that the development and implementation of drug in the form of medicated chewing gum will expand the range of domestic drugs for weight control and the fight against overweight.
2. Based on microscopic analysis of the chewing base HiG-01 and its mixture with APIs rational method of MCG manufacture has been selected – pressing with previous granulation.
3. A selection of optimal binding component – ethanol 20 % has been carried through microscopic analysis and technological properties of the granules obtained by using of different humidifiers.
4. Based on moisture-absorbing capacity research and technological properties of tablet mass with the addition of different adsorbents has been chosen as the best adsorbent amorphous silica (silicon dioxide) Syloid® 244FP, which allows easy transformation of liquids into powders with good fluidity and enhances stability of moisture-sensitive APIs.
5. The next stage of our work is the choice of rational medicated chewing gum sweetener that would have the best corrective ability and anti-caries effect, which is important for a dosage form of oral destination. Another important issue is the choice of lubricant, which would provide a satisfactory pushing-out of compressed gum from a die of tablet machine.

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