TECHNOLOGICAL ASPECTS OF TABLETS CREATION BASED ON FLAMMULINA VELUTIPES BIOMASS DRY POWDER

© T. A. Butkevych¹, M. L. Syatynya¹, V. P. Popovych²

Bohomolets National Medical University², Kyiv
«PTF «Acme» Co. Ltd², Ukrainka
e-mail: but-t@ukr.net

The aim of the work. To study the pharmaco-technological properties of granulate and tablets based on Flammulina velutipes biomass dry powder, to develop the composition and technology of the medication.

Materials and Methods. Research of granules and tablets pharmaco-technological properties (sieve analysis, bulk density, tapped density, compressibility index, Hausner ratio, flowability of tablet mass, average weight, resistance to crushing, friability and disintegration of tablets) was carried out in accordance to the requirements of State Pharmacopoeia of Ukraine 2nd edition.

Results and Discussion. The determined pharmaco-technological parameters of the granulate indicate good values of the bulk density, tapped density, compressibility index, Hausner ratio and flowability. An intermediate product undergoes a tabletting process to produce a qualitative finished product of satisfactory appearance (plain, cylindrical tablets with a facet, yellowish-white color with brown inclusions, with a height of 4 mm, and diameter of 10 mm), a constant average mass (1.0 g), and strength (68 N).

Conclusions. The pharmaco-technological properties of tablet mass (granulate) and Flammulina velutipes biomass dry powder tablets (sieve analysis, bulk density, tapped density, compressibility index, Hausner ratio, flowability, average weight, resistance to crushing, friability and disintegration) were studied. The composition and technology of Flammulina velutipes biomass dry powder tablets have been developed, pharmaco-technological parameters of their quality have been studied, technological block diagram of industrial production has been developed.

Key words: Flammulina velutipes, tablets, pharmaco-technological properties.

Introduction. Nowadays in Ukraine the interest in the usage of medicinal plants and medical mushrooms, as well as the medications received on their basis, is quite high. It is due to the fact that when properly dosed, they are practically non-toxic, harmless, relatively affordable, effective and, in some cases, do not have competitors in complex action [1]. Large resources, availability of raw materials, and the possibility of cultivation make raw materials of natural origin to be a promising object of research in order to develop new medications [2].

On the previous stages of the study, the influence of four groups of excipients on the pharmaco-technological characteristics of Flammulina (F.) velutipes biomass dry powder (BDP) tablets was studied. The optimal representatives of the studied groups of excipients were selected for obtaining the medication by the method of wet granulation [3].

The aim of the work was to develop the composition and technology of F. velutipes BDP tablets.

Materials and Methods
The objects of the study were tablet mass (granulate) and F. velutipes BDP tablets, obtained by the method of wet granulation.

All researches were conducted on the basis of Scientific and Production Association “Ekomed” and at the department of Pharmaceutical and industrial drug technology of O. Bohomolets National Medical University.

Sieve analysis was determined by granulate sifting through SLM-200 sieve No. 1400, 355, 180, 125, and weighing each fraction to an accuracy of 0.01 g. The study of bulk density and tapped density was carried out on the device of “Promprylad” Interval-NO. The compressibility index and Hausner ratio were calculated according to the formula. Flowability of the granulate was determined using a vibration device TK-1TRP 02-M Universal with a diameter of the outlet of the funnel 15 mm. The flow properties of the granulate were determined according to the scale of State Pharmacopoeia of Ukraine 2nd edition [5].

Tablets were compressed on a Single Punch Tablet Press TDP-5 (MINHUA Pharmaceutical Machinery CO., Ltd., China). Resistance to crushing was determined using a YPJ-200A Tablet hardness tester, friability was studied using Tablet friability tester CS-2, disintegration was determined with Disintegration Tester BJ-2 (MINHUA Pharmaceutical Machinery CO., Ltd., China).

Results and Discussion. According to the results of previous studies, excipients for the preparation of F. velutipes BDP tablets were selected and the following composition of the intermediate product – tablet mass (Table 1) was proposed.
Dry components were weighed on technical scales, sieved on sieve and placed in intermediate storage containers. The solution of binder was prepared as follows: 2.0 potato starch was ground with 6−10 ml of purified water and added to 100 ml of boiling purified water, mixed up until homogeneous liquid was formed. *F. velutipes* BDP, powdered sugar and white clay were loaded into a laboratory granulator with a 3 mm hole size of the sieve, than a solution of binder was added. The resulting mass was dried and passed through a sieve with a 1 mm hole size in special equipment, powdered with stearic acid and given for a further study after sifting through a sieve system (Table 2) [5].

As can be seen from the data in Table 2, the fractional composition of the granulate is heterogeneous, but the medium particles fraction content in the size of 0.5–1.0 mm (76.26 %) predominate. The content of the smallest particles fraction (smaller than 0.25 mm) is 4.03 %. The obtained results indicate the possibility of tablets obtaining with a constant average mass based on composition of the intermediate product.

### Table 1. The composition of the tablet mass for creation of a medication based on *F. velutipes* BDP

<table>
<thead>
<tr>
<th>No</th>
<th>Substances</th>
<th>Content, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><em>F. velutipes</em> BDP</td>
<td>80</td>
</tr>
<tr>
<td>2</td>
<td>Powdered sugar</td>
<td>15</td>
</tr>
<tr>
<td>3</td>
<td>White clay</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>Stearic acid</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>2% starch paste</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Total:</td>
<td>100</td>
</tr>
</tbody>
</table>

### Table 2. The results of sieve analysis of tablet mass (granulate) for creation of a medication based on *F. velutipes* BDP

<table>
<thead>
<tr>
<th>Mass of sample, g</th>
<th>Results</th>
<th>Content, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>100,00</td>
<td>Did not pass through the sieve No 1400</td>
<td>1,31</td>
</tr>
<tr>
<td></td>
<td>Did not pass through the sieve No 355</td>
<td>8,55</td>
</tr>
<tr>
<td></td>
<td>Did not pass through the sieve No 180</td>
<td>76,26</td>
</tr>
<tr>
<td></td>
<td>Did not pass through the sieve No 125</td>
<td>9,85</td>
</tr>
<tr>
<td></td>
<td>Equipment for receiving</td>
<td>4,03</td>
</tr>
</tbody>
</table>

### Table 3. Pharmaco-technological parameters of the tablet mass (granulate) for creation of a medication based on *F. velutipes* BDP

<table>
<thead>
<tr>
<th>No</th>
<th>Characteristic</th>
<th>Tablet mass (granulate) (after obtaining)</th>
<th>Tablet mass (granulate) (after 7 days of storage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Bulk density, P (g/ml)</td>
<td>0.437±0.003</td>
<td>0.436±0.001</td>
</tr>
<tr>
<td>2</td>
<td>Tapped density, P_{tapped} (g/ml)</td>
<td>0.491±0.009</td>
<td>0.494±0.003</td>
</tr>
<tr>
<td>3</td>
<td>Compressibility index, (%)</td>
<td>11.01±1.50</td>
<td>11.85±0.43</td>
</tr>
<tr>
<td>4</td>
<td>Hausner ratio</td>
<td>1.13±0.02</td>
<td>1.14±0.01</td>
</tr>
<tr>
<td>5</td>
<td>Flowability, V_{п} (g/sec)</td>
<td>3.60±0.24</td>
<td>3.70±0.16</td>
</tr>
</tbody>
</table>

Note: n=5.

### Table 4. Pharmaco-technological parameters of the tablets based on *F. velutipes* BDP

<table>
<thead>
<tr>
<th>No</th>
<th>Characteristic</th>
<th>Tablets based on <em>Flammulina velutipes</em> biomass dry powder</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Average weight, g</td>
<td>1.011±0.010</td>
</tr>
<tr>
<td>2</td>
<td>Resistance to crushing, N</td>
<td>67.60±3.36</td>
</tr>
<tr>
<td>3</td>
<td>Friability, %</td>
<td>0.36±0.17</td>
</tr>
<tr>
<td>4</td>
<td>Disintegration, min</td>
<td>12.76±0.43</td>
</tr>
</tbody>
</table>

Note: n=5.

The determined pharmaco-technological parameters of the tablet mass (granulate) indicate good values of the bulk density, tapped density, compressibility index, Hausner ratio and flowability (Table 3). Data were studied immediately after obtaining and after 7 days of storage in hermetically sealed containers (labeled with appropriate labels).

The results indicate that this intermediate product has pharmaco-technological parameters that do not significantly change during storage, so it can be tableted to produce a qualitative finished product – tablets based on *F. velutipes* BDP.

The good value of the flowability is important for the rapid and continuous feeding of the tablet mass to the press tool and the uniform filling of the matrix volume, determines the productivity of the pressing process. The obtained results allow us to proceed to the development of tablet technology and to study pharmaco-technological parameters of obtained tablets (Table 4).

The technological block diagram of tablets based on *F. velutipes* BDP production has been developed and proposed (Figure 1). The technological process of...
**Stage 2. Preparation of raw materials and components**

- **F. velutipes BDP**, powdered sugar, white clay, stearic acid, potato starch, purified water

**Stage 2.1. Weighing and measuring of components**

- Scales, measuring equipment, storage containers
- **Weight and volume of components**

**Stage 2.2. Sieving of components**

- Sieve, storage containers
- **Diameter of the sieve holes, quality of sieving**

**Stage 2. Preparation of raw materials and components**

- Tools for the disinfection of processing facilities and equipment, staff

**Stage 1. Preparation of production**

- **Microbiological purity of air, rooms, equipment, staff**

**Stage 3. Obtaining of tablet mass**

- F. velutipes BDP, powdered sugar, white clay, stearic acid, potato starch

**Stage 3.1. Mixing of dry ingredients**

- Mixer, storage containers
- **Number of downloaded components, order of input, duration and mixing speed, surface quality**

**Stage 3.2. Solution of binder preparation**

- Reactor, measuring equipment
- **Number of downloaded components, mass, volume**

**Stage 3.3. Granulation**

- Granulator
- **The order and time of components mixing, the diameter of the sieve holes**

**Stage 4. Tabletting**

- Granulate from stage 3.3.

**Stage 4.1. Tabletting**

- Tablet press, storage containers
- **Formulation parameters, surface quality, uniformity of weight, average weight, control of the half-finished product**

**Stage 4.2. Dust removal**

- A dust collector, scales
- **Dust control mode, semi-finished product control**

**Stage 5. Primary packaging**

- Automatic machine for packing
- **Number of tablets in the package, impermeability**

**Stage 6. Labeling**

- Labeling machines
- **Label quality (correctness of printing, completeness, serial number, expiration date)**

**Stage 7. Secondary packaging**

- Bottles with tablets, packs, instructions, boxes
- **The number of packs in the box, the correct labeling**

**Final product**

- **Quality control**

**Figure 1.** The technological block diagram of tablets based on F. velutipes BDP production
TECHNOLOGICAL ASPECTS: DESIGNING TABLETS BASED ON DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS

TECHNOLOGICAL ASPECTS OF THE CREATING TABLETS ON THE BASIS OF DRY POWDER BIOMASS
сыпучесть таблетичної маси, середня маса, устойчивость к раздавливанию, истираемость и распадаемость таблеток проводили в соответствии с требованиями ГФУ 2 издание.

Результаты и обсуждение. Определены фармацевтические параметры гранулята, которые свидетельствуют о хороших значениях насыпной плотности, насыпной плотности после усадки, показателя сжимаемости, коэффициента Гауснера и сыпучести. Промежуточный продукт подвергается процессу таблетирования с получением качественного готового продукта удовлетворительного внешнего вида (плоскоцилиндрические таблетки с фаской, желтовато-белого цвета с коричневыми вкраплениями, высотой 4 мм, диаметром 10 мм), постоянной средней массой (1,0 г) и прочностью (68 N).

Выводы. Исследованы фармацевтические свойства таблеточной массы (гранулята) и таблеток СПБ F. velutipes (ситовой анализ, насыпная плотность, насыпная плотность после усадки, показатель сжимаемости, коэффициент Гауснера, сыпучесть, средняя масса, устойчивость к раздавливанию, истираемость и распадаемость). Разработан состав и технология таблеток на основе СПБ F. velutipes, изучены фармацевтические показатели качества, разработана технологическая блок-схема их промышленного производства.

Ключевые слова: Flammulina velutipes; таблетки; фармацевтические свойства.

Список литературы

References

Отримано 10.08.2018