Selection of disintegrants for wet granulation method of “Angiolin” tablets

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Key words: Angiolin, Disintegrants, Tablets, Wet Granulation.

Every year there are about 9.4 million people who die from cardiovascular diseases. Among them, 51% of people are dying from stroke, and 45% – from coronary heart disease. Today disease of the cardiovascular system is the number 1 problem in the world and in Ukraine. Annually cardiovascular disease kills more than 500 thousands of Ukrainians; it is about 1370 people every day. According to the State Statistics Service, about half of the deaths in 2016 in Ukraine had been caused by cardiovascular diseases. In comparison with 2015, the death rates have not changed in Ukraine. This shows low culture of prevention, diagnosis and treatment of cardiovascular disease among Ukrainians.

Aim of our work is the selection of disintegrants to produce tablets “Angiolin” by wet granulation method with an active compound content of 200 mg.

Materials and methods. 6 Disintegrants have been studied, most of which were presented in market only in recent years and were not used in the pharmaceutical tableting technology.

Results. The disintegrants were studied in the experiment: a1 – potato starch, a6 – carboxymethyl starch sodium, a3 – polyplasdone XL 10, a4 – microcrystalline cellulose (MCC) burst, a5 – likotab P. The effect of disintegrants on the technological characteristics of “Angiolin” tablets has been studied and the possibility of their use by wet granulation method has been confirmed.

Conclusion. The selected disintegrant, namely sodium carboxymethylcellulose has showed better results and will be used for “Angiolin” tabletting by wet granulation method in the future.
Every year there are about 9.4 million people who die from cardiovascular diseases. Among them, 51% of people are dying from stroke, and 45% – from coronary heart disease. Today the disease of the cardiovascular system is number 1 problem in the world, and in Ukraine. Annually cardiovascular disease kills more than 500 thousands of Ukrainians; it is about 1370 people every day [7]. According to the State Statistics Service, about half of the deaths in 2016 in Ukraine had been caused by cardiovascular diseases. In comparison with 2015, the death rates have not changed in Ukraine. This shows low culture of prevention, diagnosis and treatment of cardiovascular disease among Ukrainians [7].

For the last 3 years the cardiovascular diseases make up 66% in general structure of mortality among Ukrainians while in most European countries, this figure does not exceed 50% [9].

Ukraine is among the countries of the international community, which set a goal to reduce mortality from cardiovascular diseases in 2025. The disease of the cardiovascular system is number 1 problem in the quarter in 2025.

We use the newest and modern equipment to determine the uniformity of the tablet mass, friability, hardness, disintegration time and the production of tablets. The 6 disintegrants have been studied, most of which were presented in market in recent years and were not used in the pharmaco-technological indices [5,6]. But due to the fact that some pharmaco-technological indices of selected tablet series were at threshold limit, we proposed to introduce disintegrant into these series [1].

Therefore, aim of our study is the selection of disintegrants in “Angiolin” tabling by wet granulation method.

### Materials and methods
We use the newest and modern equipment to determine the uniformity of the tablet mass, friability, hardness, disintegration time and the production of tablets.

### Results and discussion
Ingredients per tablet: 0.2 of Angiolin, 0.0256 of powdered sugar, 0.0128 of MCC burst, 0.0528 of disintegrant, 0.0128 of disintegrant, 0.0128 of 3-methyl-1,2,4-triazolyl-5-thioacetate.  

<table>
<thead>
<tr>
<th>N</th>
<th>Disintegrant</th>
<th>y_1</th>
<th>y'_1</th>
<th>y''_1</th>
<th>y_2</th>
<th>y'_2</th>
<th>y''_2</th>
<th>y_3</th>
<th>y'_3</th>
<th>y''_3</th>
<th>y_4</th>
<th>y'_4</th>
<th>y''_4</th>
<th>y_5</th>
<th>y'_5</th>
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<th>y_6</th>
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<th>y''_6</th>
<th>y_7</th>
<th>y'_7</th>
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<td>5</td>
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<td>5</td>
<td>5</td>
<td>5</td>
<td>2.20</td>
<td>2.46</td>
<td>2.01</td>
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<td>40.1</td>
<td>43.5</td>
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<td>0.36</td>
<td>0.35</td>
<td>13.3</td>
<td>13.5</td>
<td>14.5</td>
<td></td>
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<tr>
<td>2</td>
<td>Croscarmellose sodium</td>
<td>4</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>4.04</td>
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<td>3.87</td>
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<td>25.0</td>
<td>28.0</td>
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<td>0.77</td>
<td>0.78</td>
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<td>5.5</td>
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<tr>
<td>3</td>
<td>Polyplasdone XL 10</td>
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<td>5</td>
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<td>2.72</td>
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<td>34.0</td>
<td>37.0</td>
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<tr>
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<td>Carboxymethyl starch sodium</td>
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<td>4</td>
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</tbody>
</table>

Notes: y_i, y'_i, y''_i – process of pressing tablets in first, second and third series of experiments, respectively, points; y_2, y'_2, y''_2 – tablets appearance in first, second and third series of experiments, respectively, points; y_3, y'_3, y''_3 – uniformity of tablets mass in first, second and third series of experiments respectively, %; y_4, y'_4, y''_4 – hardness of tablets in first, second and third series of experiments respectively, H; y_5, y'_5, y''_5 – friability of tablets in first, second and third series of experiments respectively, min.
The 6 disintegrants have been studied in the experiment: a1 – potato starch, a2 – croscarmellose sodium, a3 – polyplasdone XL 10, a4 – carboxymethyl starch sodium, a5 – microcrystalline cellulose (MCC) burst, a6 – likotab P. The experimental design matrix for one-way balanced plan scheme and the study results of powder and tablets mass are shown in Table 1. The analysis of variance was conducted according to the experimental studies results (Table 1) [4].

On the basis of the analysis of variance we came to the conclusion about the effect of the studied disintegrants on pharmaco-technological properties of the powder mass and “Angiolin” tablets [8].

The figure shows the effect of disintegrants on the uniformity of “Angiolin” tablet mass.

The best indexes were observed using potato starch, which takes precedence over MCC burst, carboxymethyl sodium, polyplasdone XL 10, likotab P, croscarmellose sodium. It should be noted that the uniformity of obtained tablets mass met the pharmacopoeia standards for all species of studied disintegrants (Fig. 1).

Next, we considered the effect of disintegrants the on the tablet hardness.

The analysis of figure showed that the effectiveness of disintegrants can be illustrated by the following several advantages: likotab P, MCC burst, sodium carboxymethyl, potato starch, polyplasdone XL 10, croscarmellose sodium. The likotab P is the leader among the substances of the studied group (Fig. 2).

The study of the effect of disintegrants on tablet friability was conducted.

The analysis of figure showed that studied excipients can be placed according to the effect on tablet friability in the following sequence: MCC burst> likotab P> polyplasdone XL 10> sodium carboxymethyl> potato starch> croscarmellose sodium. MCC burst showed the best results, while sodium croscarmellose showed the highest percentage of tablet friability (Fig. 3).

Next, we considered the effect of disintegrants the on the disintegration.

“Angiolin” tablets, which contain croscarmellose sodium, were fastest disintegrated. The mentioned disintegrant has a significant advantage over others such as likotab P, MCC burst, sodium carboxymethyl, starch potato, polyplasdone XL 10 (Fig. 4).

Findings:
1. The effect of disintegrants on the technological characteristics of “Angiolin” tablets was studied and the possibility of their production by wet granulation was confirmed.
2. The selected disintegrant, namely sodium croscarmellose showed better results and will be used for “Angiolin” tabletting by wet granulation method in the future.

Challenges for further study: in future we will select and develop quantitative formula of the “Angiolin” tablets.

Conflicts of Interest: authors have no conflict of interest to declare.

References

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