Over the past few decades, a large number of epidemiological, clinical and experimental studies have shown that hypomagnesemia, chronic magnesium deficiency lead to disorders in almost every organ/body. This contributes to the development of new as well as exacerbation of chronic diseases in the human body [1,2,3]. Often, cation availability is not determined or controlled. In this regard, magnesium is called the ‘forgotten’ element [4,5].

Therefore, an important task of pharmacy is to highlight the problem of magnesium deficiency, analyze existing drugs and develop new highly effective cation-based medicines.

We have been theoretically and experimentally substantiated and developed the composition of the oral solution ‘Maglycimet’. The active pharmaceutical ingredients of the drug are organic magnesium salts: aspartate and glutamate. In addition to magnesium salts, active ingredients include glycine and methylcobalamin.

The stability of the drug during storage depends on many factors, such as qualitative and quantitative composition, selection of effective excipients, compatible primary packaging, storage temperature, etc. In this regard, the next stage of our pharmaceutical development was the selection of excipients to ensure the stability of the medicine.

Investigation of the stability of ‘Maglycimet’ oral solution was carried out. The need to add an antioxidant has been confirmed, due to a decrease in the quantitative content of methylcobalamin during storage for 3 months. It is also known, that glycine can enter into the reaction of oxidative deamination as a result of exposure to atmospheric oxygen [6].

The next step of the work was an experimental substantiation of the choice of an antioxidant for the ‘Maglycimet’ oral solution.

One of the representatives of the direct antioxidants group is sodium metabisulphite. It is widely used to stabilize oral, parenteral and other dosage forms. A feature of this excipient is the manifestation of activity in an acidic environment. The pH of the antioxidant is in the range of 3.5-5.0. According to the literature data, the concentration of sodium metabisulphite in the drug should be 0.01-1.0% [7].

Studies on the choice of concentration of sodium metabisulphite for oral solution were conducted. For this, model series of the drug with magnesium salts, glycine, methylcobalamin and an antioxidant in different concentrations were prepared. Indicators such as transparency, color, pH, quantitative content were determined. The research results are presented in Table 1.
The choice of the optimal concentration of the antioxidant sodium metabisulphite in ‘Maglycimet’ oral solution during storage (24 months)

<table>
<thead>
<tr>
<th>Sodium metabisulphite, %</th>
<th>Transparency, color of the solution</th>
<th>pH</th>
<th>Content of active ingredients in solution, mg/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 months 24 months</td>
<td>0 months 24 months</td>
<td>Methylcobalamin</td>
</tr>
<tr>
<td>0.05</td>
<td>T, P</td>
<td>5.45</td>
<td>5.43</td>
</tr>
<tr>
<td>0.10</td>
<td>T, P</td>
<td>5.44</td>
<td>5.42</td>
</tr>
<tr>
<td>0.15</td>
<td>T, P</td>
<td>5.44</td>
<td>5.42</td>
</tr>
<tr>
<td>0.20</td>
<td>T, P</td>
<td>5.46</td>
<td>5.40</td>
</tr>
<tr>
<td>0.25</td>
<td>T, P</td>
<td>5.42</td>
<td>5.39</td>
</tr>
</tbody>
</table>

Notes:
1. T – transparent;
2. P – light pink;
3. Y – yellow;
4. The content in 1 ml of the drug: methylcobalamin – from 0.00225 mg to 0.00275 mg; glycine from 9.50 to 10.50 mg;
5. pH of the oral solution from 5.0 to 6.0;
6. Number of measurements n=5, confidence intervals for P=95% are indicated.

The experimental data in Table 1 revealed that an increase in the concentration of the antioxidant to 0.15% prevented a change in the quantitative content of methylcobalamin and glycine. At a concentration of 0.15 to 0.25% significant changes in the criteria for the quality of the solution was not observed. Therefore, a concentration of sodium metabisulphite of 0.15% was chosen.

Conclusions. The choice of the antioxidant sodium metabisulphite for oral solution based on magnesium salts ‘Maglycimet’ was theoretically and experimentally substantiated. Studies have shown that the excipient should be used in an amount of 0.15%. This prevents changes in the quality of the drug and ensures stability during storage.

References: