Screening of Bearberry leaves extracts hypoglycemic effect and study of acute toxicity

Diabetes mellitus type 2 (DM2) is a global health problem. The plant origin medicinal preparations revealed different mechanisms of antidiabetic action. Despite a wide range of plants that have already been studied, other species are of interest. Particularly, Bearberry (Arctostaphylos uva-ursi) attracted our attention because its leaves are rich with biologically active compounds, but hypoglycemic activity has not been studied yet.

The aim of our experiment was studying acute toxicity and hypoglycemic activity of Bearberry extracts on non-diabetic standard models.

Materials and methods. It was conducted the screening of hypoglycemic effect in healthy rats, oral glucose tolerance test in healthy rats and study of acute toxicity. The object of study were water and alcohol polyphenol extracts of Bearberry leaves (extractor – alcohol 50 % and 90 %).

Results and discussion. Screening and comparative study shows that the maximal hypoglycemic activity revealed Bearberry leaves alcohol extract (extractor – 50 % ethanol, PE50) in dose 100 mg/kg. The least pronounced effect was observed for the introduction of water extract administration.

Conclusions. The results indicate the practicability of this Bearberry leaves extract further study for renewal the range of medicinal products that revealed hypoglycemic activity.

Key words: Bearberry (Arctostaphylos uva-ursi); acute toxicity; hypoglycemic activity; oral glucose tolerance test.
INTRODUCTION

Diabetes mellitus type 2 (DM2) is a global health problem. More than 230 million people worldwide are affected, and it is expected to reach 350 million by 2025 [1–2]. For the DM2 pharmacological correction clearly are used hypoglycemic drugs of synthetic origin but the naturally compounds complexes obtained from plants are quite popular. That is because there action involved different mechanisms and allows to prevent complications, which always occurs under the DM2 development [3–4]. Despite a wide range of plants that have already been studied, other species are of interest. In this respect our attention was attracted by Bearberry (Arctostaphylos uva-ursi), which leaves are rich with biologically active compounds and has been used for a long time in medical practice. However, this plant hypoglycemic activity was not studied [5]. For this purpose, we conducted Bearberry leaves extracts hypoglycemic screening in healthy (non-diabetic) rats and under glucose load (glucose tolerant test, GTT).

The aim of our experiment was studying acute toxicity and hypoglycemic activity of Bearberry extracts on non-diabetic standard models.

MATERIALS AND METHODS

Hypoglycemic study in healthy rats [6]. For screening of hypoglycemic activity were used inbred albino male rats (14 weeks age) weighing 180-200 g. Animals were divided into groups (n = 4) depending on the aim of the experiment: 1 - intact control (IC) healthy animals, which were administered physiological solution; 2 - animals administered water polyphenol extract of Bearberry leaves (PEW) in doses 50, 100, 500 mg/kg; 3 - animals administered 50 % Bearberry leaves ethanol extract (PE50) 50, 100, 500 mg/kg; 4 - animals administered Arphasetin infusion (AI) in recommended dose recalculated for rats (18 ml/kg). The test extracts were administered to overnight fasted animals orally with the help of gastric catheter sleeved to syringe. Blood glucose concentration were determined with the help of glucometer “One Touch Select” (LifeScan, USA) at the 0, 15, 30, 60 and 120 minutes after glucose load, samples were collected by gingival vein puncture [7].

Oral glucose tolerance test (OGTT) in healthy rats [6]. In order to study hypoglycemic activity using the OGTT we reused inbred albino male rats (14 weeks age) weighing 180-200 g. Animals were divided into groups (n = 6) depending on the aim of the experiment: 1 - intact control (IC) healthy animals, which were administered physiological solution; 2 - animals, which were administered glucose solution in dose 5 g/kg body weight per os (glucose load, for other group of animals 30 min after drug administration); 3 - animals after glucose load and administered PEW; 4 - animals after glucose load and administered PE50; 5 - animals after glucose load and administered PE90; 6 - animals after glucose load administered AI (18 ml/kg); 7 - animals after glucose load administered metformin (15 mg/kg). The test extracts were administered to overnight fasted animals orally with the help of gastric catheter sleeved to syringe in dose 100 mg/kg. Blood glucose concentration were determined with the help of glucometer “One Touch Select” (LifeScan, USA) at the 0, 15, 30, 60 and 120 minutes after glucose load, samples were collected by gingival vein puncture [7].

RESULTS AND DISCUSSION

The first stage of the experiment was done in order to screening and select the most effective extract and dose in non-diabetic rats for the assessment of hypoglycemic effect. We have found that more pronounced hypoglycemic effect was after 6 hours after treatment agents administration (Table). Nevertheless, it was indicated that studied extracts showed a hypoglycemic activity, its distinctiveness significantly depended on the extractor and dose used. Thus, hypoglycemic effect of PEW was not significant during all the time of observation. The significant decrease in blood glucose level was determined for PE50 in doses 50 mg/kg (8.1 % from the baseline), 100 mg/kg (14.4 % from baseline) and 500 mg/kg (7.2 % from baseline). As for PE90 introduction the maximal decrease in blood glucose content was observed also after 6 h from the extract administration, but only in the dose 100 mg/kg. As a reference drug was selected Arphasetin, as, currently in the Ukraine pharmaceutical market, it is the only popular. That is because there action involved different classes and allows to prevent complications, which always occurs under the DM2 development [3–4]. Despite a wide range of plants that have already been studied, other species are of interest. In this respect our attention was attracted by Bearberry (Arctostaphylos uva-ursi), which leaves are rich with biologically active compounds and has been used for a long time in medical practice. However, this plant hypoglycemic activity was not studied [5]. For this purpose, we conducted Bearberry leaves extracts hypoglycemic screening in healthy (non-diabetic) rats and under glucose load (glucose tolerant test, GTT).

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one plant origin preparation – plant species with anti-diabetic activity. In our experiment, we administered to laboratory animals the recommended dose recalculated for rats. The results showed the significant blood glucose rate reduction after 6 h after AI administration by 18.1%. Thereby in normoglycemic study we have observed that glucose reduction rate was more prominent at a dose 100 mg/kg for PE50.

For further hypoglycemic activity study OGTT was carried out. Fig. depicts the result of OGTT in healthy rats after extracts oral administration.

As shown in Fig. the baseline levels of blood glucose did not differ among the groups. It was found that glucose load caused hyperglycemia by 60.3% after 60 min. The administration of PEW did not have a significant effect on the glycemia dynamics. On the contrary, PE50 administration caused a reliable glycemia after 30 minutes by 18.7%, after 60 min by 26.8% (Fig.). PE90 reduced glucose level in animals by 41.1% in 60 min. Along with Arphasetin as reference preparation was used Metformin in dose 15 mg/kg.

As a result, determine the ability of Bearberry leaves extracts to reduce hyperglycemia after glucose load found that PE50 provides a significant reduction in glycaemia by 16.8. Thus, the most promising for further study should consider, therefore further investigation of antidiabetic properties.

As for acute toxicity study, the obtained results showed that rats under administration of the PE50 study-doses the animal death and signs of intoxication were

### Table

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>Dose (on kg of body weight)</th>
<th>Blood glucose, mmol/l</th>
<th>0</th>
<th>2 h</th>
<th>4 h</th>
<th>6 h</th>
<th>8 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NaCl, 0.9%</td>
<td>1 mg</td>
<td>3.97 ± 0.23</td>
<td>3.92 ± 0.22</td>
<td>4.04 ± 0.26</td>
<td>3.83 ± 0.18</td>
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<td>2</td>
<td>PEW</td>
<td>50</td>
<td>3.91 ± 0.18</td>
<td>3.96 ± 0.23</td>
<td>3.87 ± 0.22</td>
<td>3.91 ± 0.21</td>
<td>4.02 ± 0.14</td>
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</tr>
<tr>
<td>3</td>
<td></td>
<td>100</td>
<td>4.04 ± 0.13</td>
<td>4.03 ± 0.19</td>
<td>4.01 ± 0.19</td>
<td>3.89 ± 0.19</td>
<td>3.87 ± 0.15</td>
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<tr>
<td>4</td>
<td></td>
<td>500</td>
<td>3.96 ± 0.19</td>
<td>3.89 ± 0.21</td>
<td>3.79 ± 0.14</td>
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<tr>
<td>5</td>
<td>PES0</td>
<td>50</td>
<td>4.05 ± 0.17</td>
<td>3.93 ± 0.17</td>
<td>3.81 ± 0.23</td>
<td>3.74 ± 0.24*</td>
<td>3.90 ± 0.21</td>
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<tr>
<td>6</td>
<td></td>
<td>100</td>
<td>4.01 ± 0.11</td>
<td>3.88 ± 0.24</td>
<td>3.61 ± 0.22*</td>
<td>3.43 ± 0.17*</td>
<td>3.72 ± 0.24</td>
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</tr>
<tr>
<td>7</td>
<td></td>
<td>500</td>
<td>3.99 ± 0.24</td>
<td>3.94 ± 0.16</td>
<td>3.78 ± 0.19</td>
<td>3.70 ± 0.21*</td>
<td>3.81 ± 0.19</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>PE90</td>
<td>50</td>
<td>3.93 ± 0.15</td>
<td>3.84 ± 0.21</td>
<td>3.72 ± 0.24</td>
<td>3.65 ± 0.19</td>
<td>3.84 ± 0.18</td>
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</tr>
<tr>
<td>9</td>
<td></td>
<td>100</td>
<td>3.89 ± 0.10</td>
<td>3.72 ± 0.18</td>
<td>3.67 ± 0.18</td>
<td>3.41 ± 0.14*</td>
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</tr>
<tr>
<td>10</td>
<td></td>
<td>500</td>
<td>4.06 ± 0.16</td>
<td>3.94 ± 0.22</td>
<td>3.71 ± 0.21</td>
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</tr>
<tr>
<td>11</td>
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<td>18 ml</td>
<td>4.02 ± 0.22</td>
<td>3.63 ± 0.21</td>
<td>3.42 ± 0.24*</td>
<td>3.33 ± 0.21*</td>
<td>3.82 ± 0.14</td>
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</tr>
</tbody>
</table>

Notes: * – p < 0.05 – Intact control vs treatment groups.

**Fig.** Effect of Bearberry leaves extracts on blood glucose level (mmol/l) in loaded normoglycemic rats

Notes: * – p < 0.05 – intact control vs treatment groups; ** – p < 0.05 – treatment groups vs glucose load
not observed. Thus, the substance belongs to the class of relatively non-toxic substances with intragastric administration according to the classification of toxicity [6].

CONCLUSIONS

Screening and comparative study shows that the maximal hypoglycemic activity revealed Bearberry leaves alcohol extract (extractor – 50% ethanol, PE50) in dose 100 mg/kg. PE50 belongs to the class of relatively non-toxic substances with intragastric administration.

The results indicate the practicability of this Bearberry leaves extract further study for renewal the range of medicinal products that revealed hypoglycemic activity.

Conflict of Interests: authors have no conflict of interests to declare.

REFERENCES


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