BENEFICIAL EFFECTS OF ROSMARINUS OFFICINALIS AND THYMUS NUMIDICUS ON KEY ENZYMES OF CARBOHYDRATE METABOLISM IN ALLOXAN-INDUCED DIABETIC RATS

Abdelkarim Benkhediri, Samira Boussekine, Hichem Sakr, Salim Gasmi, Yasmine Benali

Address(es):
1 Laboratory of bioactive molecules and applications, Faculty of Exact Sciences and Natural Life Sciences, Larbi Tebessi University, 12002 Tebessa, Algeria.
2 Faculty of Exact Sciences and Natural Life Sciences, Larbi Tebessi University, 12002 Tebessa, Algeria.
3 Laboratory of Veterinary Pathological Anatomy and Cytology Laboratory, Veterinary Pathology Microbiology Department, Pasteur Institute of Algeria, Little Stoualé road, Dély-Braham, Algiers, Algeria.

*Corresponding author: Salim.gasmi@univ-tebessa.dz  
https://doi.org/10.55251/jmbsfs.9507

ARTICLE INFO

Received 1. 10. 2022  
Revised 15. 11. 2022  
Accepted 28. 11. 2022  
Published xx.xx.201x

INTRODUCTION

Diabetes mellitus is a major public health problem in the world. The prevalence of which has increased considerably over the past two decades and is expected to affect 592 million adults by 2035 (Paneni et al., 2015; El Gayar et al., 2019). Diabetes mellitus is a metabolic syndrome characterized by the presence of hyperglycemia linked to a dysfunction in insulin secretion or the action of insulin on their receptor or on the post-receptor signal (Vieira et al., 2019; Yong et al., 2021), associated with carbohydrate (at the level of the liver on key enzymes), protein and lipids metabolism disorders which will generate a state of chronic hyperglycemia, combined with secondary complications (Kalra et al., 2021) which are attached with the diabetic patients for a long period. These complications can be: microvascular (affecting the eyes, kidneys...) or cardiovascular (atherosclerosis) or neurodegenerative (Alzheimer’s) (Schalkwijk et Stehouwer, 2020).

Although the prevalence of diabetes is truly growing, an effective treatment is still lacking. Regular administration hypoglycemic agents on the market including insulin and oral drugs (biguanides, sulfonylurea, α-glucosidase inhibitors) (Ild et al., 2020) generate undesirable effects or decreased response after a long period of treatment (Kumar et al., 2017), this led World Health Organization to make it a major public health concern in 2011 and led to the use of traditional medicine for the treatment of diabetes because of their therapy soft. Furthermore, it seems that the conventional treatment is very expensive in developing countries (Bishu et al., 2019), so the use of these plants is affordable and also constitutes a natural reservoir of bioactive compounds (Widyantri et al., 2020).

Nowadays, researchers use all the technological advances to highlight the characteristics and properties of these compounds such as flavonoids, which seem effective in reducing the complications linked to diabetes mellitus (Sundaram et al., 2019; Hussain et al., 2020; Gandhi et al., 2020). Flavonoids were found in several plants of different species, with different quantities and qualities (Testa et al., 2016; Zhou et al., 2020; Jibadil et al., 2021). Based on these observations, we made ethnobotanical investigations in Algeria which allowed us to choose two very used medicinal plants Rosmarinus officinalis and Thymus numidicus. The latter seems to be promising in the therapy of metabolic syndrome (Xie et al., 2017; Rahbhardar et Hosseinzaedeh, 2020; Carresi et al., 2020). Much literature has described Rosmarinus officinalis and cited their antioxidant, anti-inflammatory, hypolipidemic and hypoglycemic power under different aspects (essential oil, aqueous extract, methanolic...) (Karagöz et al., 2019; Othman et al., 2021). On the other hand, the plant Thymus numidicus has been commonly described in essential oil form, while few studies have been carried out on the antidiabetic effect of these plants in vivo, precisely on the key enzymes of carbohydrate metabolism (M Shatia et al., 2019; Baucalì et al., 2019; Landazuri et al., 2021).

The present work studies the effects of the fraction rich in flavonoid compounds of the plant Rosmarinus officinalis and Thymus numidicus on the key enzymes of carbohydrate metabolism in rats rendered diabetic by Alloxan.

MATERIAL AND METHODS

Rosmarinus officinalis and Thymus numidicus were collected in April 2022, during the flowering period from two localities in the east of Algeria, the plant identification was done by a botanist, cleaned, and dried out off the sun. The voucher specimen (05-2022) was deposited in the herbarium of the department of applied biology of Larbi-Tebessi, university, Tebessa-Algeria.

The extraction of the flavonoid fraction was carried out according to the protocol of (Markham, 1982), modified by (Bruneton, 1993). This method includes 2 main phases: a solid-liquid phase and a liquid-liquid phase, the last phase consists of confronting several solvents with the extract to recover different compounds according to their polarity with the solvent, only the ethyl acetate fraction of
Rosmarinus officinalis and Thymus numidicus (RO-EA and TN-EA) was the subject of our study.

Experimental animals

Healthy male Wistar rats of the Rattus norvegicus aged 2 months weighing between 200 and 220g with no prior drug treatment, were used just for the present study, were obtained from the Pasteur Institute, and the animals were acclimatized to laboratory hygienic conditions before 10 days to starting the experiment under these conditions (temperature: 23°C ± 2°C and natural photoperiod: 12h light and 12h dark), they were fed with pellet diet (ONAB-Elharouche, Skikda-Algeria), and water available adlibitum.

Acute toxicity studies

Before starting our study on diabetes an acute toxicity test was done to evaluate our flavonoid fraction, this test was determined according to the guidelines of the OECD n° 420 (organization for economic cooperation and development). Male rats (200-220g) were used and divided into different groups of 6 rats. Each group received different doses of test sample up to 2000 mg/kg b.w, after that the animals were monitored for 14 days to confirm if there are mortalities or detected behavioral response. In the end, no deaths were found up to the dose 2000 mg/kg b.w, Therefore, 300 mg/kg b.w was chosen as the most advanced experimental dose.

Anti-hyperglycemic activity of RO-EA and TN-EA in glucose-loaded normal-animals

The antidiabetic activity of the ethyl acetate fraction was evaluated according to the method of (Jarald et al., 2009) with a slight modification. The animals were randomly divided into 6 groups, 6 rats for each, the negative control received only the vehicle solution 1% Tween 80 dose of 0.5 ml/100g b.w. The other groups were treated with the extract of RO-EA and TN-EA with different doses (150 mg/kg and 300 mg/kg b.w). The animals received their doses orally with a gavage feeding tube number 7. The blood glucose level of the animals was taken after a period of overnight fasting at a time 0. Just after the first measurement, the animals have received all the treatment and remained to receive the dose of glucose 4 mg/kg b.w, and the other blood glucose measurement was taken at ½, 1, 2, 3h after a glucose dose. Blood glucose was estimated with a glucometer (DIAGNO-CHECK smart) from the tail tips of rats.

Hypoglycemic activity of RO-EA and TN-EA in normal fasting animals

The same steps done in the previous test were repeated. However, the rats fasted overnight for 10h, the first group which remained as negative control has received a dose of 0.5 ml/100g b.w of vehicle. The second group received glibenclamide as a reference dose of 5 mg/kg dissolved in water saline (0.9 w/v NaCl). Group 3 up to 6 received the extract of RO-EA and TN-EA (150 mg/kg and 300 mg/kg b.w), as mentioned in the table: 2, the blood sample was taken from the tail tip at a time 0 (before oral administration) and ½, 1, 2, 3h after vehicle, extract and glibenclamide administration. The blood glucose level was done like the previous test.

Dose-dependent effect of extract RO-EA and TN-EA on plasma glucose and insulin level in diabetic rats

Diabetes was induced in the rats (after fasting overnight for 8 hours), with an Alloxan single dose of 120 mg/kg b.w in 0.9 w/v NaCl intraperitoneally. The rats were placed in the cages with bottles filled with 10% glucose for the next 24 h to prevent hypoglycemia. After 72 hours of injection, fasting blood glucose was measured, the rats that showed a blood glucose level more than 300 mg/dl have been accepted for the test. The selected 54 rats were randomly divided into 9 groups, 6 rats for each, as the following table:

<table>
<thead>
<tr>
<th>Treatment groups</th>
<th>Blood glucose concentration (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 min</td>
</tr>
<tr>
<td>N.Control</td>
<td>84,35±1,367</td>
</tr>
<tr>
<td>N+(Gliben 5)</td>
<td>82,26±1,425</td>
</tr>
<tr>
<td>N+TN-EA 150</td>
<td>84,23±1,408</td>
</tr>
<tr>
<td>N+TN-EA 300</td>
<td>86,26±0,573</td>
</tr>
<tr>
<td>N+RO-EA 150</td>
<td>85,50±0,625</td>
</tr>
<tr>
<td>N+RO-EA 300</td>
<td>82,67±1,585</td>
</tr>
</tbody>
</table>

Values were expressed as means ± SEM(n = 6), minimal significant level: P< 0.05, significantly different; “ in respect to N.Control, in respect to N+Gliben, (ANOVA followed with Tukey test), N, normal; Gliben; glibenclamide, TN; Thymus numidicus, RO; Rosmarinus officinalis, EA; ethyl acetate fraction.
Hypoglycemic activity of RO-EA and TN-EA in normal fasting animals

The evaluation of the hypoglycemic activity has clearly shown that extract of the RO-EA fraction exhibited a very significant hypoglycemic activity compared to the control group, and a significantly strong p<0.05 at the dose 300 mg/kg b.w compared to the dose 150 mg/kg b.w, this activity is dose-dependent, it was observed after the 1st 30 min. On the other hand, with the extract of the TN-EA fraction no hypoglycemic activity was recorded with the two-doses, no significant difference p>0.05 compared to the control group (Table 2).

<table>
<thead>
<tr>
<th>Treatment groups (mg/kg b.w)</th>
<th>0 min</th>
<th>30 min</th>
<th>60 min</th>
<th>120 min</th>
<th>180 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>N-Control</td>
<td>84.41±1.991</td>
<td>82.97±1.162</td>
<td>83.45±0.849</td>
<td>81.19±1.551</td>
<td>83.47±1.919</td>
</tr>
<tr>
<td>N+(Gliben 5)</td>
<td>81.45±0.822</td>
<td>80.72±0.670</td>
<td>34.27±1.512</td>
<td>31.35±0.792</td>
<td>32.41±1.435</td>
</tr>
<tr>
<td>N+TN-EA 150</td>
<td>82.34±1.441</td>
<td>81.31±1.454</td>
<td>83.31±0.567</td>
<td>80.22±0.711</td>
<td>81.38±3.401</td>
</tr>
<tr>
<td>N+TN-EA 300</td>
<td>81.37±1.476</td>
<td>83.53±0.748</td>
<td>83.38±0.726</td>
<td>80.38±1.467</td>
<td>80.36±0.601</td>
</tr>
<tr>
<td>N+RO-EA 150</td>
<td>82.43±0.697</td>
<td>74.33±1.419</td>
<td>67.35±0.765</td>
<td>63.03±1.123</td>
<td>59.35±1.501</td>
</tr>
<tr>
<td>N+RO-EA 300</td>
<td>83.40±1.706</td>
<td>67.33±1.347</td>
<td>59.50±1.448</td>
<td>51.51±1.256</td>
<td>45.27±2.236</td>
</tr>
</tbody>
</table>

Table 2 Hypoglycemic activity of RO-EA and TN-EA in normal fasting animals

Values were expressed as means ± SEM (n = 6), minimal significant level; P< 0.05, significantly difference; * in respect to N-Control, † in respect to N+Gliben, (ANOVA followed with Tukey test), N; normal, Gliben; glibenclamide, TN; Thymus numidicus, RO; Rosmarinus officinalis, EA; ethyl acetate fraction.

Dose-dependent effect of extract RO-EA and TN-EA on plasma glucose and insulin level in diabetic rats

Analysis of the results showed a significant increase in the level of serum glucose and a significant decrease in the level of plasma insulin in the diabetic control rats. After 21 days of treatment with RO-EA and TN-EA fraction extract, the rats exhibited good improvement, it prevented the increase in plasma glucose and reversed the serum insulin level when compared to the diabetic rat control, moreover, it was observed that the dose of 300 mg/kg b.w of the RO-EA fraction was more promising compared to the other dose and the other fraction (TN-EA), it significantly prevented the increase in glucose and the decrease in insulin, it was observed that the effect of this dose the most similar to glibenclamide, this dose was fixed as an effective dose for the rest of our study. Regarding the administration of RO-EA and TN-EA fraction extract to normal rats, no significant change was observed in insulin and serum glucose levels when compared to normal control rats (Fig. 1).

Effects of the extract RO-EA fraction in a change in body weight, food, and water intake

The evaluation of the results was shown a significant decrease in body weight in diabetic control rats, and a significant increase in water and food consumption, compared to normal rats, all these changes were significantly restored during treatment with the extract of the RO-EA fraction and glibenclamide. Concerning normal control rats and normal rats treated with the RO-EA fraction no significant change was observed between them (Fig. 2. 3. 4).

Figure 1 Dose-dependent effect of extract RO-EA and TN-EA on plasma glucose and insulin level in diabetic rats.

Figure 2 Effect of RO-EA on body weight in control and experimental rats. Values were expressed as means ± SEM (n = 6), minimal significant level; P< 0.05, significantly difference; * in respect to N-Control, † in respect to Diabetic control, ‡ in respect to D+gliben, (ANOVA followed with Tukey test), N; normal, D; diabetic, Gliben; glibenclamide, RO; Rosmarinus officinalis, EA; ethyl acetate fraction.

Figure 3 Effect of RO-EA on water intake in control and experimental rats. Values were expressed as means ± SEM (n = 6), minimal significant level; P< 0.05, significantly difference; * in respect to N.Control, † in respect to Diabetic control, ‡ in respect to D+gliben, (ANOVA followed with Tukey test), N; normal, D; diabetic, Gliben; glibenclamide, RO; Rosmarinus officinalis, EA; ethyl acetate fraction.
Effect of RO-EA fraction on the level of Hb and HbA1c

Table 3 summarizes the blood Hb and HbA1c levels in the control and experimental rats. This table shows that the diabetic rats suffered a significant decrease in the level of Hb and a significant increase in the level of HbA1c when compared with normal control rats. After treatment with RO-EA extract fraction and glibenclamide, a good improvement was observed with diabetic rats, the blood level of Hb and HbA1c was restored. No significant difference was observed in normal rats treated with the RO-EA fraction at the dose of 300 mg/kg b.wt when compared with normal control rats.

**Table 3** Effect of RO-EA fraction on the level of Hb and HbA1c

<table>
<thead>
<tr>
<th>Groups</th>
<th>Hb (g/dl)</th>
<th>HbA1c (%) Hb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Control</td>
<td>14.4±1.61</td>
<td>5.55±1.43</td>
</tr>
<tr>
<td>N+RO-EA 300 mg/kg b.w</td>
<td>15.50±0.69</td>
<td>5.480±1.35</td>
</tr>
<tr>
<td>Diabetic control</td>
<td>6.41±1.51</td>
<td>12.36±1.46</td>
</tr>
<tr>
<td>D+RO-EA 300 mg/kg b.w</td>
<td>12.50±0.79</td>
<td>7.54±2.12</td>
</tr>
<tr>
<td>D+Gliben 5 mg/kg b.w</td>
<td>12.88±0.66</td>
<td>6.24±1.57</td>
</tr>
</tbody>
</table>

Values were expressed as means ± SEM (n = 6), minimal significant level; P< 0.05, significantly difference; * in respect to N-Control, # in respect to Diabetic control, # in respect to D+gliben, (ANOVA followed with Tukey test), N; normal, D; diabetic, Gliben; glibencamide, RO; Rosmarinus officinalis, EA; ethyl acetate fraction.

Effect of RO-EA fraction extract on activities of carbohydrate metabolic enzymes

The analysis of the results from (Table 4) shows the effect of the RO-EA fraction extract on the activity of carbohydrate metabolism enzymes in the liver of control and experimental rats, we noticed a significant decrease in hexokinase and glucose-6-phosphate dehydrogenase activity and a significant increase in glucose-6-phosphatase and fructose-1,6-bisphosphatase activity in diabetic rats compared to normal rats. It was noted that this activity returned almost to normal when applying treatment with RO-EA fraction extract and also the same was observed with glibenclamide drug. No significant difference was noticed in normal rats treated with RO-EA compared to normal rats.

**Table 4** Effect of RO-EA fraction extract on activities of Hexokinase, Glucose-6 phosphatase Dehydrogenase, Glucose-6-phosphatase, Fructose-1, 6-bisphosphatase, in the liver of control and experimental animals

<table>
<thead>
<tr>
<th>Groups</th>
<th>Hexokinase (unit/g protein)</th>
<th>Glucose-6 phosphatase Dehydrogenase (×10-3 U/mg protein)</th>
<th>Glucose-6-phosphatase (unit/min/mg protein)</th>
<th>Fructose-1, 6-bisphosphatase (unit/h/mg protein)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Control</td>
<td>163±3±0.05</td>
<td>3.87±0.18</td>
<td>0.204±0.012</td>
<td>21.25</td>
</tr>
<tr>
<td>N+RO-EA 300 mg/kg b.w</td>
<td>159±7±5.09</td>
<td>3.95±0.14</td>
<td>0.221±0.016</td>
<td>19.38</td>
</tr>
<tr>
<td>Diabetic control</td>
<td>111±3±8.1</td>
<td>1.30±0.40</td>
<td>0.543±0.019</td>
<td>11.27±0.81</td>
</tr>
<tr>
<td>D+RO-EA 300 mg/kg b.w</td>
<td>149±5±5.41</td>
<td>3.04±0.24</td>
<td>0.327±0.024</td>
<td>7.77±0.71</td>
</tr>
<tr>
<td>D+Gliben 5 mg/kg b.w</td>
<td>153±2±2.23</td>
<td>3.36±0.14</td>
<td>0.307±0.017</td>
<td>7.04±0.95</td>
</tr>
</tbody>
</table>

Values were expressed as means ± SEM (n = 6), minimal significant level; P< 0.05, significantly difference; * in respect to N-Control, # in respect to Diabetic control, # in respect to D+gliben, (ANOVA followed with Tukey test), N; normal, D; diabetic, Gliben; glibencamide, RO; Rosmarinus officinalis, EA; ethyl acetate fraction.

Effect of RO-EA fraction extract on glycogen content, glycogen synthase, glycogen phosphorylase, and liver weight

Table 5 summarizes the variations in liver weight, glycogen content, and the enzymatic activity of glycogen synthase and glycogen phosphorylase in control and experimental rats, a significant decrease in liver weight, glycogen level, and glycogen synthase activity was observed in diabetic rats, while glycogen phosphorylase activity was increased significantly compared to normal rats, so these altered parameters were restored almost to normal upon treatment with RO-EA fraction extract and the same thing was observed with the drug glibenclamide, no significant difference was observed in normal rats compared to normal rats treated.

**Table 5** Effect of RO-EA fraction extract on glycogen content, glycogen synthase, glycogen phosphorylase, and liver weight

<table>
<thead>
<tr>
<th>Groups</th>
<th>Glycogen synthase (µ moles of UDP formed/h/mg protein)</th>
<th>Glycogen phosphorylase (µ moles Pi liberated/h/mg protein)</th>
<th>Liver glycogen (mg/g tissue)</th>
<th>Liver weight (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Control</td>
<td>694.6±26.36</td>
<td>555.6±20.94</td>
<td>65.37±2.46</td>
<td>14.45±2.61</td>
</tr>
<tr>
<td>N+RO-EA 300 mg/kg b.w</td>
<td>700.5±27.17</td>
<td>543.0±12.28</td>
<td>66.45±3.47</td>
<td>13.59±1.68</td>
</tr>
<tr>
<td>Diabetic control</td>
<td>352±21.25</td>
<td>791.7±12.05</td>
<td>33.75±2.16</td>
<td>6.50±1.69</td>
</tr>
<tr>
<td>D+RO-EA 300 mg/kg b.w</td>
<td>612±19.38</td>
<td>601.7±16.08</td>
<td>58.66±3.49</td>
<td>11.48±2.56</td>
</tr>
<tr>
<td>D+Gliben 5 mg/kg b.w</td>
<td>622±23.57</td>
<td>595.6±11.11</td>
<td>60.50±2.68</td>
<td>12.74±2.57</td>
</tr>
</tbody>
</table>

Values were expressed as means ± SD (n = 6), minimal significant level; P< 0.05, significantly difference; * in respect to N-Control vs N+RO-EA, * in respect to Diabetic control vs D+RO-EA, * in respect to Diabetic control vs D+Gliben, (ANOVA followed with Tukey test), N; normal, D; diabetic, Gliben; glibencamide, RO; Rosmarinus officinalis, EA; ethyl acetate fraction.

Liver histomorphometric study

Fig. 5 represents histological sections of the H & E staining of liver tissue, after 21 days of treatment in control and experimental rats, the normal rats represent a normal architecture of the hepatocyte, nucleus, sinusoids, and central veins (A), diabetic rats showed an alteration in the distribution of hepatocytes in radial form, the disappearance of the nucleus, development of necrotic zones around the centrilobular vein with infiltration of inflammatory cells, degeneration of the sinusoids, on the other hand, it was observed that these changes are significantly attenuated in diabetic rats treated with RO-EA or glibenclamide.
conclude that the restoration of insulin level is produced by the effect of the RO-EA fraction that leads to an improvement in glucose control (Rodrigues et al., 2019), probably by inhibition glucogenesis or improvement of peripheral glucose consumption (He et al., 2019; Montaz et al., 2019). Several studies have cited the side effects of diabetes induced by Alloxan in rats, among these effects are polyphagia, polydipsia, wasting, and muscle loss (Elango et al., 2019), the latter due to insulin deficiency which leads to increased protein catabolism, the increase in proteolysis aims to compensate for the role of carbohydrates in the production of energy (Arcaro et al., 2021). The administration of the RO-EA fraction and glibenclamide improves the recovery of body weight, consumption of water and food, the restoration body weight in treated diabetic rats probably due to increased glycemic control which in turn will lead to decreased proteolysis (Rodrigues et al., 2019; Salles et al., 2021; Saravanakumar et al., 2020). Diabetes mellitus has a direct or indirect impact on glucose control, generally by the decrease in insulin release, insulin-dependent enzymes such as hexokinase, glucose-6-phosphate dehydrogenase, and glycerogen synthase will be inhibited (Kalaiyanvi and Sankaranarayanan, 2021; Mabate et al., 2021), which will promote the activity of enzymes of glucoseogenesis and glycogenolysis (glucose-6-phosphatase, fructose-1,6-bisphosphate, glycerogen phosphorylase) (Sundaram et al., 2019), and consequently, hepatic glycerogen will be depleted, and proteolytic increases, which will lead to a decrease in liver weight (Balakrishnan et al., 2019).

In our study, we recorded all these alterations in diabetic rats induced by Alloxan, the administration of the RO-EA fraction and glibenclamide reversed all these alterations, the weight of the liver was recovered following the increase in the enzymatic activity of hexokinase, and glucose-6-dehydrogenase and glycerogen synthase (Zangneh et al., 2018; Vinayagaman et al., 2018; Krishnan et al., 2020), which are insulin-dependent enzymes, play a role in the control and metabolism of glucose, therefore the enzymatic activity of glucose-6-phosphatase, fructose-1,6-bisphosphatase and glycerogen phosphorylase was decreased compared to untreated diabetic rats (Amadi et al., 2021), which in turn leads to an increase in hepatic glycogen levels, this improvement in glucose control probably due to the action of the RO-EA fraction and glibenclamide on the regeneration of pancreatic β cells which increases the insulin level (Sasikala et al., 2019; Jugran et al., 2021), several studies have been described that the RO-EA fraction rich in carnosic acid molecule and carnosol (Lebvre et al., 2021), these molecules directly involved in the activation of AMPK (AMP-activated protein kinase) this protein inhibits glucogenesis and promotes glycogenesis, glycolysis, and glucose uptake (Hasei et al., 2021; Rognhari-Shahraei et al., 2021). The histological study in diabetic rats induced by Alloxan has denied different alterations at the level of hepatic tissue (Ansari et al., 2019) disappearance of the nuclei, areas of necrosis around the central vein, infiltration of the inflammatory cells (Raëta et al., 2020). These hepatic alterations involve the oxidative stress in their development, and this leads to the progression of complications of diabetes mellitus. Our results showed that the treatment of diabetic rats with the RO-EA fraction and glibenclamide attenuate these alterations on the hepatic tissue almost to normal, this improvement shown by the RO-EA fraction could be due to the action of the acid carnosic and carnosol on hepatoprotection (Al-Sharaifi et al., 2020; Singh et al., 2022).

CONCLUSION

In conclusion, the administration of the extract of the RO-EA fraction (300 mg/kg b.w) to diabetic rats induced by Alloxan has an appreciable effect, it significantly modulates plasma glucose and insulin levels, body weight, food consumption, Hb and HbA1c levels, and hepatic glycogen levels, thus this fraction significantly restored the altered activity of key carbohydrate metabolism enzymes almost to normal, this fraction of the RO extract - EA is considered a therapeutic virtue and can be developed as a treatment for the complication of diabetes mellitus. Further studies are needed to reveal the exact mechanism of action of the RO-EA fraction on key carbohydrate metabolism enzymes.

Funding: This research was funded by the Algerian Ministry of Higher Education and Scientific Research and the Directorate General of Scientific Research and Technological Development (DGRSDT).

Conflicts of interest/Competing interests: The authors declare that they have no conflict of interest.

Ethics approval: All of the experimental protocols were approved and performed by the ethics committee of Pasteur Institute of Algeria (PIA) under the ethical code: No.2505/3.2016.

REFERENCE


