Endocrine and Metabolic Science 16 (2024) 100191

Contents lists available at ScienceDirect

Endocrine and Metabolic Science

journal homepage: www.elsevier.com/locate/endmts

Portulaca oleracea (purslane) aqueous extract reduced the adverse metabolic outcomes and favored liraglutide activities in streptozotocin-induced cardiometabolic disorders of male Wistar rats

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ARTICLE INFO

Keywords:
Cardiovascular diseases
Diabetes
Purslane
GLP-1R
Liraglutide
Wistar rats

ABSTRACT

Cardiometabolic diseases including Diabetes mellitus accounts >400 million deaths globally. *Portulaca oleracea* (Purslane) noted for its rich antioxidants, is a perennial herbaceous plant widely cultivated across countries. This study aimed to determine the ameliorative effect of ethanolic extract of *Portulaca oleracea* (EPO) on cardiometabolic diseases of streptozotocin (STZ)-induced diabetic male Wistar rats. Twenty-five male Wistar rats weighing between 120 and 150 g were randomly distributed into five groups and treated respectively as; Control (CTR): normal chow + vehicle (normal saline; orally), EPO; 400 mg/kg orally, STZ; 60 mg/kg intraperitoneally + vehicle, (STZ; 60 mg/kg + EPO; 400 mg/kg orally), STZ+ EPO+ Liraglutide (LG); 0.2 mg/kg subcutaneously. After four weeks, animals were anesthetized by 1 % chloroform inhalation for 5 min (5.0 ppm) and blood was collected by cardiac puncture. Plasma, cardiac and adipose tissue homogenate were analyzed, and data expressed as mean ± SEM; $p < 0.05$ were accepted as significant. The diabetic rats showed decreased body weight, reduced blood glucose and AMP-activated protein kinase (AMPK), adipose mass, insulin ($p < 0.05$). *Portulaca oleracea* resulted in reduced plasma fasting blood glucose (FBG), interleukin 6 (IL-6), tumor necrosis factor-alpha (TNF- α) and increased pancreatic beta cell functions (HOMA-B) compared to the diabetic rats ($p < 0.05$). Also, plasma AMPK, insulin and glutathione (GSH) increased in the purslane, and liraglutide treated ($p < 0.05$), which is a known glucagon-like peptide-1 receptor (GLP-1R) agonist. In conclusion, purslane possess GLP-1R agonist activities and improved glucometabolic activities and this presents a great advantage in the management of cardiovascular risks associated with diabetes.

1. Introduction

Cardiometabolic diseases are complications that can be caused by a variety of factors, such as alterations in dietary habits, lifestyles, and surroundings as well as genetic and epigenetic factors (Ndisang and Rastogi, 2013). Genetic defects, however, are implicated in many cardiometabolic diseases including hypertension and diabetes (Kataoka et al., 2013). Globally, cardiometabolic diseases (CMDs) constitute the leading cause of death and comprises of chronic renal failure, diabetes, and cardiovascular disease (CVD) among others (de Waard et al., 2019). Cardiometabolic disease is associated with increased inflammatory episodes via expression of proinflammatory markers as well as dyslipidemia (Ndisang and Rastogi, 2013). Cardiometabolic problems have increased in frequency and prevalence in tandem with the rise in obesity, diabetes, and hypertension. One of the main contributors to cardiometabolic problems is diabetes.

Diabetes mellitus is a chronic metabolic disorder characterized by elevated blood glucose resulting from impaired insulin secretion or insulin action (Ghulam et al., 2015). It is a multifactorial disease characterized by hyperglycemia, altered lipoproteins, increased basal metabolic rate, deficiency in reactive oxygen species scavenging enzymes, and severe oxidative stress-induced damage to pancreatic beta cells (Sabeeha and Nahida, 2018). It is associated with cell glucotoxicity which suggests that prolonged exposure to high glucose might have a negative or toxic effect on a cell's ability to function. Diabetic glucotoxicity plays a role in driving secondary β cell failure in both type 1 and

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https://doi.org/10.1016/j.endmts.2024.100191
Received 24 March 2024; Received in revised form 26 July 2024; Accepted 12 August 2024
Available online 14 August 2024
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type 2 diabetes (Wu and Yan, 2015). Type 1 diabetes is associated with autoimmune damage and in Type 2 diabetes, insulin resistance and other factors can all contribute to beta cell malfunction (American Diabetes Association, 2019). Diabetes increases the prevalence of cardiovascular morbidity and mortality. Cardiovascular (CV) risk factors such as obesity, hypertension and dyslipidemia are common in patients with DM putting them at increased risk for cardiac events (Leon and Maddox, 2015).

In diabetic patients, transient episodes of hyperglycemia cause a variety of cell types to experience an aberrant metabolic environment, which results in cell- and tissue-specific metabolic reprogramming and macro- and microvascular complications (Grohová et al., 2019). Diabetes being a difficulty that continues to afflict a vast majority of people, numerous animal models are constantly developing to examine the pathogenic mechanism and therapeutic approaches associated with diabetes.

Streptozotocin (STZ) is a chemical which been commonly used for the induction of diabetes in experimental models of mice and rodents. It promotes metabolic alterations that induce the development of cardiovascular diseases. Numerous research has utilized STZ in various combinations to induce diabetes (Akinlade et al., 2021). Type 1 diabetes can be induced in rodents with a single injection of STZ. However, type 2 diabetes can be brought on using at least three different methods, including a low-dose STZ injection after nicotinamide high fat diet (HFD) feeding, a low-dose STZ injection after nicotinamide feeding, and other methods (Wu and Yan, 2015).

Glucagon-like peptide-1 (GLP-1) is an incretin gut hormone released into the bloodstream by intestinal L cells in response to food consumption (Andreozzi et al., 2016). The glucagon-like peptide-1 (GLP-1) hormone impedes islet cell death and slows stomach emptying in addition to controlling insulin production and glucose absorption. Despite being thought of as a potential therapeutic target for the management of diabetes, dipeptidyl peptidase IV (DPP4) readily breaks down GLP-1, making it ineffective for use in diabetes treatment. The human GLP-1 analogue liraglutide demonstrates the pleiotropic functions of GLP-1 and it's difficult to degrade, liraglutide is helpful in the clinical treatment of diabetes (Fan et al., 2018). Liraglutide has glucose-lowering effects and can exert cardiovascular protective effects related to diabetes mellitus (Baylan et al., 2022). GLP-1 binds with GLP-1 receptor (GLP-1R) in the beta cells and regulates biosynthesis and release of insulin in the management of diabetes (Koole et al., 2012).

Portulaca oleracea commonly known as purslane is an annual succulent herb widely distributed across countries. Purslane has several medicinal benefits, particularly for preventing certain cardiovascular illnesses and preserving a strong immune system. It is well known for its antibacterial, anti-inflammatory, antioxidant properties and control of lipid and glucose metabolism in the body (Bai et al., 2016). Its rich flavonoids promote anti-inflammatory, anti-microbiological, antiviral, antioxidant, and anti-diabetic properties (Mingyang et al., 2022; Wang et al., 2018). Bioactive substances such as: dopamine, coumarins, alkaloids and saponins, polyphenols, and flavonoids found in purslane, may affect glucose metabolism via inhibition of carbohydrate digestion and glucose absorption in the intestine, stimulation of insulin secretion from the pancreatic β-cell, modification of glucose release from the liver, and activation of insulin receptors and glucose uptake in the tissues (Abdalla Jr, 2010).

Portulaca oleracea (Purslane) is a high fiber plant with anti-diabetic properties. It acts as a GLP-1R agonist to improve pancreatic beta cell function and increase insulin secretion (Heidarzadeh et al., 2013). While the activities of GLP-1R agonist to reduce the risk of cardiovascular diseases in diabetic individuals was previously reported by Helmstädter et al., 2022, there are paucity of literature on the effect of EPO on cardiometabolic diseases and its probable mechanism of action. This study therefore aimed to determine the effect of ethanolic extract of *Portulaca oleracea* (EPO) on cardiometabolic diseases and GLP-1R agonist in streptozotocin (STZ) treated male Wistar rats.

2. Materials and method

2.1. Animals

Twenty-five adults male Wistar rats weighing between 170 ± 5 g were obtained from the animal house of the College of Health Sciences, University of Ilorin (Ilorin, Nigeria). The rats were fed ad libitum with standard rat chow and had unlimited access to tap water. Rats were maintained in the animal house under environmental conditions of temperature (22–26 °C), relative humidity (50–60 %) and 12-h dark/light cycle.

The ethical approval for the experiment was given by the University of Ilorin Research Ethical Committee after the recommendation of the Faculty of Basic Medical Sciences Ethical Review Committee, University of Ilorin, Ilorin, Nigeria with ethical approval number (UERC/ASN/2018/357).

2.2. Plant material and authentication

Portulaca oleracea was purchased from Mr. Ajayi, Tanke, Ilorin, Kwara state. The identification of the plant leaves was carried out in the Department of Plant Biology of University of Ilorin, Kwara state, Nigeria, with a voucher specimen (UILH/001/1655/2023), and a specimen was deposited in the Herbarium of the Department. The aerial part of the plant was washed, cut into smaller parts (for easy drying), shade-dried for two weeks and finely powdered with a mechanical grinder and kept in a plastic container before the commencement of the study.

2.3. Plant extraction

500 g of the powdered plant sample was soaked in a stoppered container with 2 l ethanol (95 %) for three days (72 h) with frequent agitation. After the three days, the mixture was passed, filtered, and concentrated using a water bath at a temperature of 40 °C (Okafor et al., 2021). A dark green extract weighing 72.43 g (14.486 %) was obtained.

2.4. Drugs and chemicals

Liraglutide (Victoza), a product of Novo nordisk (USA). Streptozotocin (STZ) was purchased from Sigma-Aldrich in St. Louis, Missouri, USA.

2.5. Animal grouping and diabetes induction

After a week of acclimatization, the animals were randomly assigned to five groups ($n = 5$ rats/group. Group 1 (CTR): normal chow + vehicle; normal saline), Group 2: purslane ethanolic extract (EPO; 400 mg/kg body weight, orally), Group 3: STZ (60 mg/kg bw) + normal saline, Group 4: STZ; 60 mg/kg bw + EPO (400 mg/kg bw, orally), Group 5: STZ; 60 mg/kg bw + EPO; 400 mg/kg orally +Liraglutide (LG) 0.2 mg/kg subcutaneously and all treatments lasted for four weeks. The rats were fasted overnight before induction of diabetes. The rats were induced with diabetes by a single intraperitoneal injection of freshly prepared streptozotocin in 0.1 M citrate buffer (PH 4.5) (Bai et al., 2016) at the dose 60 mg/kg body weight (Wankeu-Nya et al., 2014) and to attenuate the effect of STZ, the animals were administered a single intraperitoneal injection of 100 mg/kg of nicotinamide 15 min before diabetes induction (Brahmanaidu et al., 2017). Seventy-two hours post STZ injection, blood was collected from the tail vein of each rat and diabetes was confirmed using one touch ultra-blood glucometer (lifeScan USA). Rats with blood glucose level higher or equal to 12 mmol/L were used for the study according to the work of Yakubu et al., 2011. A total of five rats (71 %) from the treated groups were made diabetic with blood glucose levels ranging from 200 to 250 mg/dl.

2.6. Collection of blood sample

At the end of four-weeks treatment, the animals were anesthetized by exposure to chloroform vapor. A state of deep anesthesia was achieved following an acute exposure to 1 % (0.05 ml/l of container volume) of chloroform. (Aledani et al., 2020). Blood was collected by cardiac puncture into heparinized tube and was centrifuged at 3000 rpm for 5 min at room temperature. Plasma was stored frozen until needed for biochemical assay.

2.7. Preparation of cardiac tissue and adipose tissue homogenates

After dissection, the heart and adipose tissue (perirenal, retroperitoneal, and abdominal fat pad) was excised, cleared of adhering connective tissues, blotted, and weighed. An average of 100 mg of the tissues were homogenized in 2 ml of 0.1 M phosphate-buffered solution (PBS) with a glass homogenizer and centrifuged at 10,000 rpm for 10 min at 4 °C and the supernatant was collected and assessed for biochemical parameters.

2.8. Determination of plasma and cardiac AMP-activated protein kinase AMPK

AMP-activated protein kinase (AMPK) concentration was determined using ELISA Kit from Elabscience with Catalog number: E-EL-R0738.

2.9. Determination of interleukin-6 and tumor necrosis factor alpha

Plasma and cardiac concentration of interleukin-6 and TNF-α was determined by the quantitative standard sandwich ELISA technique using monoclonal antibody specific for these parameters with rat kits obtained from Elabscience Biotechnology Inc. (Wuhan, Hubei, P.R.C., China).

2.10. Determination of plasma and cardiac nitric oxide

The plasma and cardiac nitric oxide were determined by rats ELISA kits obtained from Elabscience Biotechnology Inc. (Wuhan, China) and following the manufacturers' procedures.

2.11. Determination of homeostasis model assessment of β-cell function (HOMA-B)

HOMA-B was determined from the insulin and blood glucose level using the method in Khalili et al., 2023. Insulin level was determined using rat Insulin ELISA kit from Elabscience (Catalog number: E-EL-R3034).

$$\text{HOMA-B} = \frac{\text{Insulin} * 20}{\text{Blood glucose} - 3.5}$$

2.12. Statistical analysis

The data was presented as Mean ± SEM for all of the variables. GraphPad Prism software version 8.0 for Windows (Graphpad Software, San Diego, CA, USA). The mean values of variables were compared using one-way analysis of variance (ANOVA). *Post-hoc* Tukey test was used to determine the significance of mean values among the groups. The *p*-value ($P < 0.05$) was used to determine significant differences. *P < 0.05 vs CTR; #P < 0.05 vs STZ (Fig. 1.

3. Results

3.1. Effect of EPO on body weight in STZ-induced cardiometabolic disorders

There was no significant change in body weight in the EPO group compared to the control. However, following induction of streptozotocin (STZ), body weight reduced significantly in the Diabetic (D), D + EPO and D + EPO + LG groups. At day 28, there was an observable increase in body weight in the treatment groups compared to the diabetic untreated (Table 1).

Table 1
Effect of administration of ethanolic extract of PO (EPO) on body weight in STZ-induced diabetic rats (*p < 0.05 vs control, #p < 0.05 vs D).

Groups	Initial body weight (g)	Final body weight (g)	% body weight gain (g)
Control	174.50 ± 6.30	232.66 ± 7.29	33.32 ± 0.75 %
Diabetic untreated (D)	175.00 ± 2.35	163.50 ± 4.80*	−6.57 ± 1.04 %*
EPO	165.14 ± 5.35	262.57 ± 10.20#	58.99 ± 1.25 %#
D + EPO	160.57 ± 4.82	189.57 ± 22.27#	18.06 ± 10.35 %#
D + EPO + LG	170.83 ± 9.62	200.33 ± 23.91#	6.09 ± 7.30 %#



Fig. 1. A diagram showing *Portulaca oleracea* (Purslane) plant.

3.2. Effect of EPO on HOMA-B and adipose mass in STZ-induced cardiometabolic disorders

A significant decrease in HOMA-B was observed in the diabetic when compared with the control (Fig. 2A). However, EPO group showed significant increase in HOMA-B when compared to control and EPO increased HOMA-B in the diabetic treatment groups compared to the diabetic alone (Fig. 2A). In Fig. 2B, adipose mass was significantly reduced in the diabetic untreated when compared to control and elevated with EPO in comparison with control. EPO and LG also significantly increased adipose mass tissue in the diabetes rats.

3.3. Effect of EPO on FBG in STZ-induced cardiometabolic disorders

There was no significant difference in weekly blood glucose in the EPO group when compared with the control (Fig. 3A). Blood glucose level was shown to increase significantly in the diabetic untreated and the treatment groups at week 1. However, at week 3 blood glucose level reduced significantly in the diabetes treated group compared to the diabetic alone. This trend is similar with the addition of liraglutide which showed a further decrease in FBG (Fig. 3). Furthermore, insulin levels reduced significantly in the diabetic untreated when compared to the control (Fig. 3B). However, EPO administration reverses this trend and showed a significant increase in insulin when compared to the diabetic alone (Fig. 3B).

3.4. Effect of EPO on plasma and cardiac AMPK and NO in STZ-induced cardiometabolic disorders

Plasma and cardiac AMPK increased significantly in the EPO group when compared to the control group (Fig. 4A and B). AMPK reduced significantly in the diabetic untreated group compared to the control. However, EPO and Liraglutide treatment showed significant increase in AMPK when compared with control and diabetic alone (Fig. 4A). Furthermore, plasma and cardiac nitric oxide was reduced in the diabetic untreated when compared to the control (Fig. 4C and D), while EPO alone and with liraglutide increased nitric oxide significantly when compared with control and this effect was mitigated in the diabetes treated group (Fig. 4C and D).

3.5. Effect of EPO on plasma and cardiac TNF- α and IL-6 in STZ-induced cardiometabolic disorders

Plasma and cardiac TNF- α increased significantly in the diabetes untreated when compared with the control (Fig. 5A and B). Administration of EPO reduced plasma and cardiac TNF- α albeit insignificantly compared with control. There was also an observable decrease in TNF- α levels in the diabetes treated with EPO when compared to the diabetic alone. However, EPO + LG treated reduced plasma TNF- α levels significantly when compared to the diabetic and D + EPO groups (Fig. 5A). In addition, plasma and cardiac IL-6 increased in the diabetic untreated rats compared to control while EPO reduced plasma and cardiac IL-6 compared with the control. This is effect is replicated with LG treatment causing significant reduction in plasma and cardiac IL–6 when compared with the diabetes group (Fig. 5C and D).

3.6. Effect of EPO on plasma and adipose GSH and insulin in STZ-induced cardiometabolic disorders

Both plasma and adipose GSH decreased significantly in the diabetes when compared with the control (Fig. 6A and B) while EPO with or without Liraglutide increased GSH when compared with control and diabetes only (Fig. 6A and B). Changes in adipose tissue and glutathione are strong regulator of cellular and cardiovascular health.

4. Discussion

The present study demonstrates the effect of streptozotocin and EPO administration on markers of cardiometabolic disorders. In this study, STZ rats showed elevated blood glucose levels and inflammatory responses (TNF α and IL-6) with reduction in body weight, serum insulin, nitric oxide, and beta cell functions (HOMA-B). However, administration of EPO to diabetic rats increased body weight, AMPK, glucometabolic activities and adipose mass while causing a reduction in inflammatory markers and improved antioxidant defense. Also, combined administration of liraglutide and EPO to diabetic rats ameliorated cardiometabolic risk markers associated with diabetes (Fig. 7).

In this study, EPO was shown to increase significantly the body weight of diabetic rats (Table 1), a finding akin to the work of Bai et al. (2016) where crude *Portulaca oleracea* was seen to improve body weight in diabetic rats. It was also observed from this study that diabetic rats showed a marked increase in fasting blood glucose and EPO administration reduced blood glucose and improved insulin sensitivity when compared with the control (Fig. 3A). Studies by Liu et al., 2016 showed that diabetic models often show increase in fasting blood glucose levels, and observable abnormal changes in glucose metabolism, including decreased glycolysis, impeded glycogenesis, and increased gluconeogenesis. Chronic hyperglycemia in diabetic individuals can also be complicated by cardiovascular diseases (CVDs), atherosclerosis,

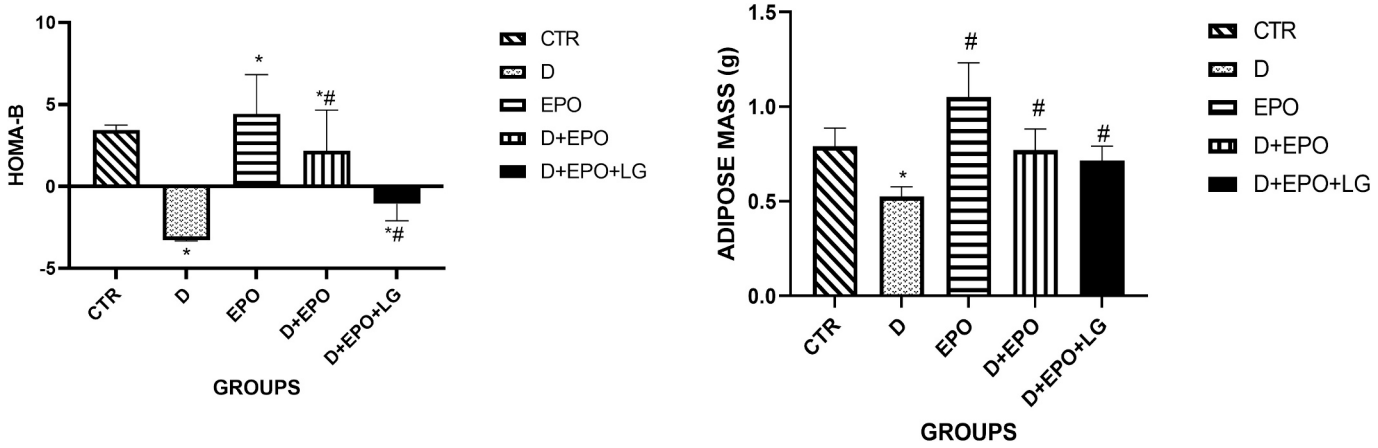

Fig. 2. Effect of ethanolic extract of *Portulaca oleracea* (EPO) on HOMA-B and adipose mass in streptozotocin (STZ)-induced rats (*$p < 0.05$ vs CTR, #$p < 0.05$ vs D). Data were analyzed by one-way ANOVA followed by Bonferroni's Post hoc test. Values are expressed as mean ± SEM of 5 rats per group and $P < 0.05$ was taken as statistically significant.

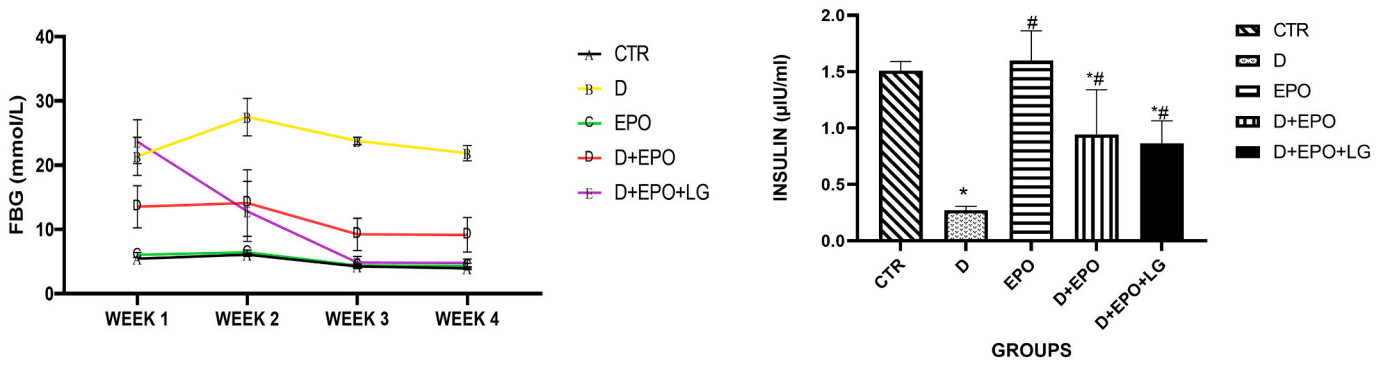

Fig. 3. Effect of ethanolic extract of *Portulaca oleracea* (EPO) on FBG in streptozotocin (STZ)-induced rats (*p < 0.05 vs CTR, #p < 0.05 vs D). Data were analyzed by one-way ANOVA followed by Bonferroni's Post hoc test. Values are expressed as mean ± SEM of 5 rats per group and P < 0.05 was taken as statistically significant.

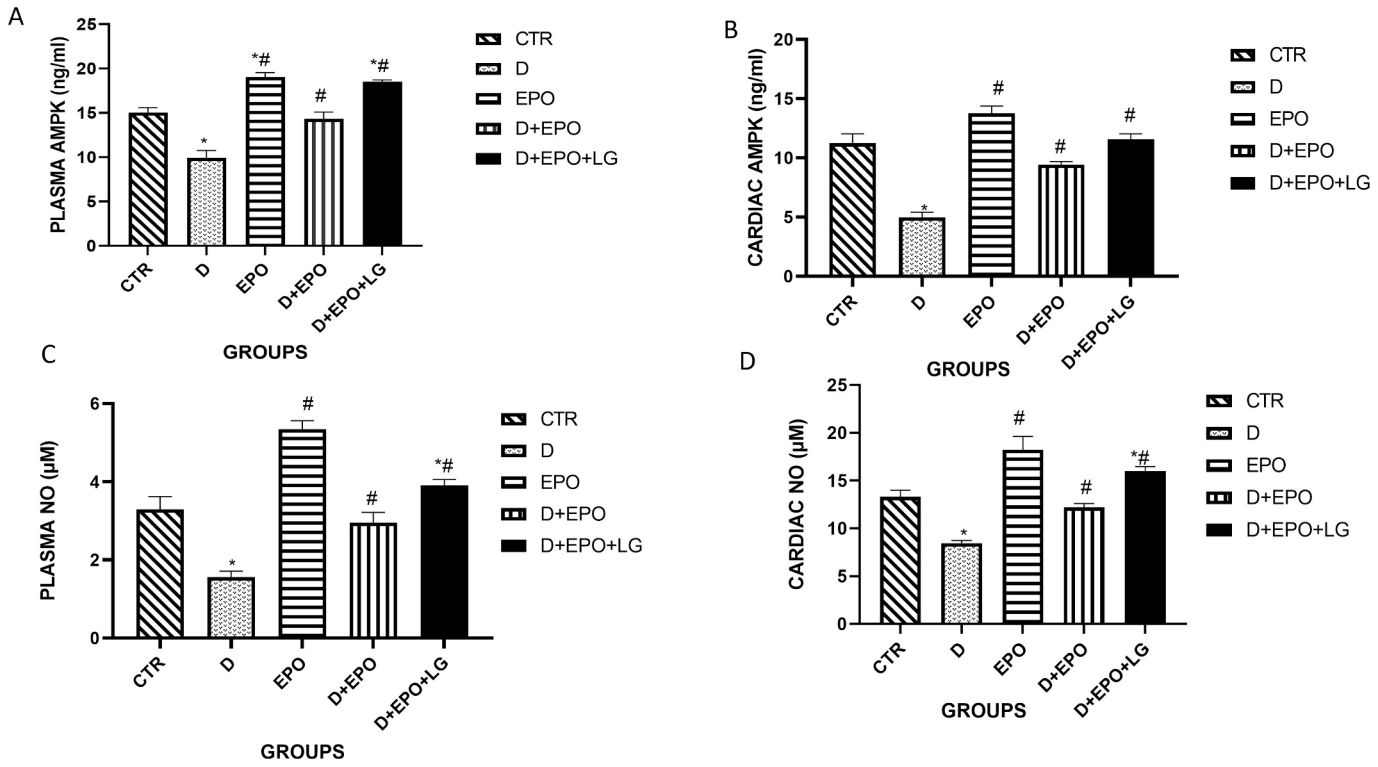

Fig. 4. Effect of ethanolic extract of *Portulaca oleracea* (EPO) on AMPK and nitric oxide in streptozotocin (STZ)-induced rats (*p < 0.05 vs CTR, #p < 0.05 vs D). Data were analyzed by one-way ANOVA followed by Bonferroni's Post hoc test. Values are expressed as mean ± SEM of 5 rats per group and P < 0.05 was taken as statistically significant.

hypertension, microvascular problems affecting the eyes, kidneys, nerves, and this in turn increased the rate of morbidity and mortality (Ebrahimian et al., 2022).

Portulaca oleracea in this study, acts similarly to Liraglutide, a glucagon-like peptide 1 receptor (GLP-1R) agonist to reduce blood glucose levels in the diabetics. GLP-1R agonist activities helps to improve pancreatic beta cell functions (Heidarzadeh et al., 2013). Co-administration of EPO with liraglutide a known candidate drug used in the treatment of diabetes was shown to cause more reduction in blood glucose levels and improved beta cell functions. Congruently, HOMA-B activity was reduced in diabetic treated groups, and this significant reduction may be due to lack of functional pancreatic beta cells associated with STZ action. The addition of EPO with or without LG however, showed a significant increase in HOMA-B and expression of HOMA-B has also been associated with improve beta cell function and improved insulin production in response elevated blood glucose (Al-Jaghthmi and Zeid, 2020).

Although, the coordination of intricate multicellular interactions between pancreatic cells and immune cells, have been directly linked to the pathophysiology of type 1 diabetes (T1D), making them prospective immunotherapeutic targets for this condition (Lu et al., 2020).

Other studies established that AMPK enhances glucose uptake in muscle cells via glucose transporter 4 (GLUT 4). It promotes beta cell functions and reduces hyperglycemia. Interestingly from this study, EPO increases AMPK, and this effect was replicated with the addition of Liraglutide (Fig. 4A, and B). It has an additive effect with GLP-1R agonist liraglutide to increase the activities of AMPK as liraglutide had been shown to work through certain downstream receptors such as AMPK and PI3K. (Yang et al., 2018). So, EPO increasing AMPK in this study is noteworthy to its liraglutide-like activities.

Nitric oxide contributes to endothelium-dependent relaxation in the carotid artery. Diabetes impairs nitric oxide mediated vasorelaxation

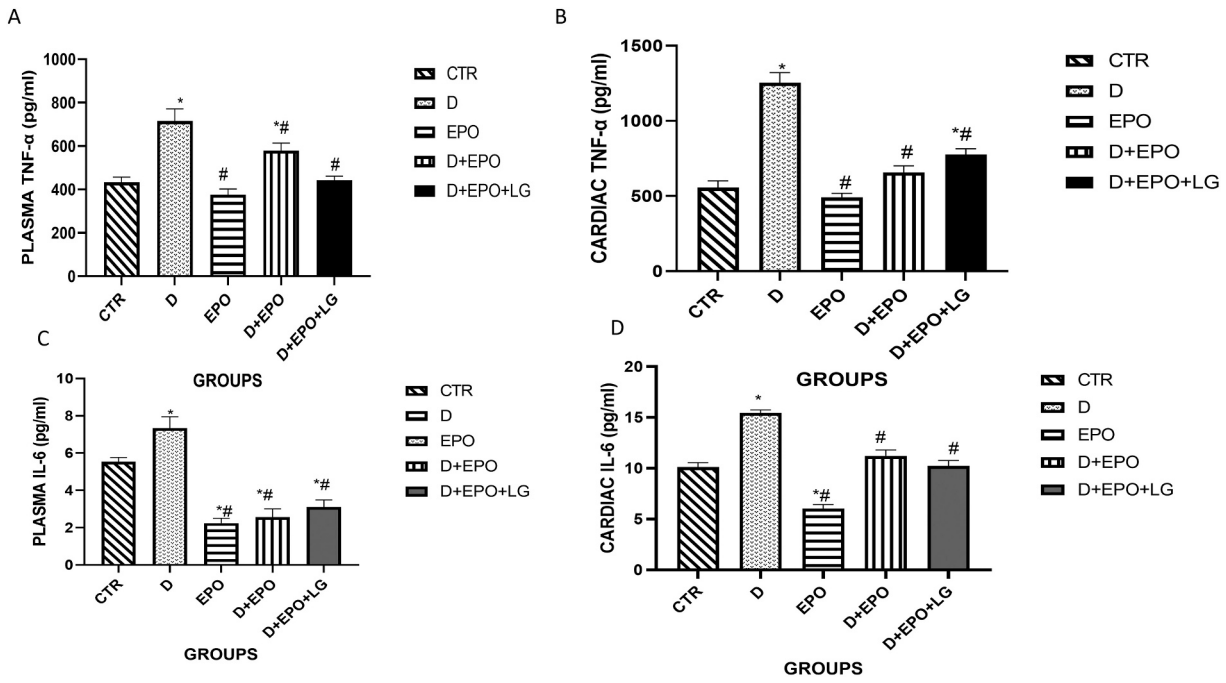

Fig. 5. Effect of ethanolic extract of *Portulaca oleracea* (EPO) TNF- α and IL-6 in streptozotocin (STZ)-induced rats (*p < 0.05 vs CTR, #p < 0.05 vs D). Data were analyzed by one-way ANOVA followed by Bonferroni's Post hoc test. Values are expressed as mean ± SEM of 5 rats per group and P < 0.05 was taken as statistically significant.

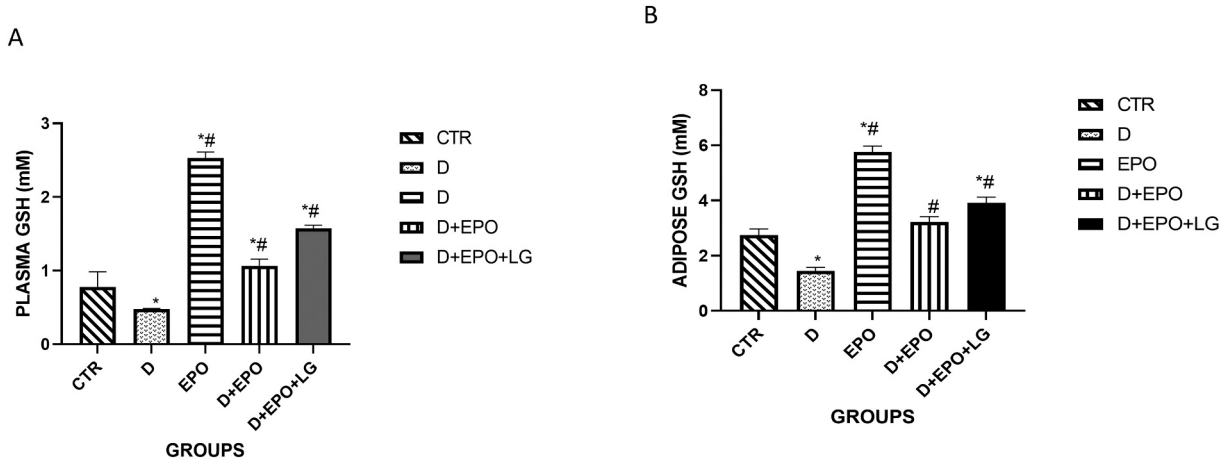

Fig. 6. Effect of ethanolic extract of *Portulaca oleracea* (EPO) GSH and Insulin in streptozotocin (STZ)-induced rats (*p < 0.05 vs CTR, #p < 0.05 vs D). Data were analyzed by one-way ANOVA followed by Bonferroni's Post hoc test. Values are expressed as mean ± SEM of 5 rats per group and P < 0.05 was taken as statistically significant.

and the release of nitric oxide. Decrease in nitric oxide production promotes vascular complications associated with diabetes mellitus such as endothelial dysfunction and coronary artery disease (Li et al., 2021). STZ treated rats in this study showed reduced nitric oxide level and EPO significantly increased NO when compared with the control and diabetes only group. Nitric oxide was also increased in diabetes rats in combination with liraglutide (Fig. 4C and D).

Portulaca oleracea also from this study significantly reduced plasma and cardiac TNF-α and IL-6 when compared to the control and diabetes treated. A significant increase in plasma IL-6 and TNF-α level was also observed in diabetes group compared with the control which suggests the anti-inflammatory and anti-diabetic effect of EPO (Fig. 5A and B).

An increased synthesis of IL-6 is a strong predictive value in the progression of cardiometabolic diseases (Oyabambi et al., 2022) and the risks of cardiovascular diseases such as vascular damage and atherosclerosis are high with Inflammation (Entezari et al., 2022). Interestingly, AMPK signaling has shown to reduces pro-inflammatory cytokines TNF-α and IL-6 and improved antioxidant activities (Entezari et al., 2022) and the upregulation of AMPK by EPO in this study and the reduction of proinflammatory markers is remarkable. A finding similar to the work of Narimani et al., 2023 where *Portulaca oleracea* root activates AMPK, regulates energy homeostasis and prevents metabolic dysfunction in adipocytes.

Previous research has shown that pathogenesis and complications of diabetes are greatly influenced by oxidative stress which greatly leads to the development of metabolic disorders (Oyabambi et al., 2019). Oxygen free radicals are produced in excess because of hyperglycemia, and this contributes to the onset of diabetes and its consequences (Samarghandian et al., 2017). Inflammatory processes induce oxidative stress and reduce cellular antioxidant capacity (Khansari et al., 2009).

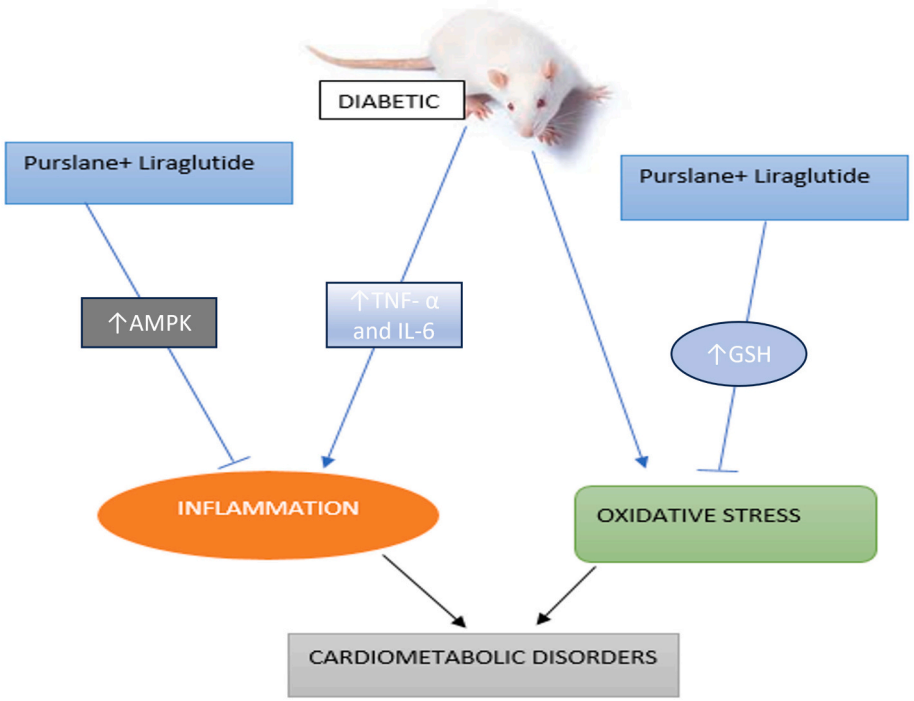

Fig. 7. Graphical abstract showing the effect of ethanolic extract of *Portulaca oleracea* (EPO) in streptozotocin (STZ)-induced cardiometabolic diseases of male Wistar rats.

Diabetes from our study decreased plasma and adipose glutathione when compared with the control and EPO conversely increased it. This effect of EPO is comparable to Liraglutide, which produces an elevated GSH in the diabetes rats (Fig. 6A and B). Oxidative stress increases the development and progression of diabetes due to impaired antioxidant defense enzymes such as glutathione (GSH) (Al-Jaghthmi and Zeid, 2020).

5. Conclusion

The results from this study indicate that a strong correlation exists between diabetes, visceral adiposity and cardiovascular diseases and EPO possesses a liraglutide-like functions which helps to improve glucometabolic derangement associated with STZ- induction. It is suggested therefore, that EPO is a safe nutritional constituent of wide medical importance and further investigation to fully establish additional mechanisms involved in the ameliorating effect of EPO on cardiovascular disorders be studied.

Source of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

CRediT authorship contribution statement

Adewumi O. Oyabambi: Writing – review & editing, Writing – original draft, Visualization, Supervision, Conceptualization. **Blessing B. Aindero:** Writing – review & editing, Writing – original draft, Visualization, Project administration, Methodology, Formal analysis, Conceptualization. **Adeoba M. Awolola:** Writing – review & editing, Writing – original draft, Visualization, Methodology. **Aisha Y. Adebayo:** Writing – review & editing, Writing – original draft, Project administration, Methodology. **Ifeoluwa B. Iluromi:** Writing – review & editing, Writing – original draft, Project administration, Methodology. **Kehinde S. Olorunniyi:** Writing – review & editing, Writing – original draft, Project administration, Methodology.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

Acknowledgment

The authors acknowledged the technical support of HOPE Cardiometabolic Research Team and Mr. Adebowale of Bridge Biotech is also appreciated for the laboratory analysis.

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