Fig. 4 — The total antioxidant activity (FRAP) in normal control and experimental groups. The values represent the mean±SE for six rats per group.

Cakatay and Kayali[22] reported that in diabetic animals the total antioxidant capacity (FRAP) levels is significantly decreased when compared to non-diabetic control groups. Similar observations were found in this study, where a significant increase in plasma (FRAP) of normal control and pure compounds treated diabetic rats when compared with untreated diabetic rats (Fig. 4). Treatment with SGSS and Reb-A (20 and 30 mg/kg) significantly (P <0.05) enhance the antioxidant potential in treated diabetic rats when compared with the untreated diabetic control group.

The biochemical parameters (total cholesterol, bilirubin, alkaline phosphatase, urea, creatinine and uric acid) indicate that administration with SGSS and Reb-A (20 and 30 mg/kg) provide protective effect by improving the condition of diabetes mellitus in alloxan treated rats and uphold the stable condition in normal rats.

Chronic hyperglycaemia promotes lipid peroxidation of low-density lipoprotein (LDL) resulting in free radical generation through a superoxide-dependent pathway. In diabetes, there is a decrease in endogenous insulin release which inactivates the production of lipoprotein lipase enzymes resulting in hypertriglyceridemia.

In diabetic dyslipidemia, there are an increased concentration in plasma triglyceride and LDL cholesterol particles which enhance the free fatty-acid release from insulin-resistant fat cells[23]. However, administration of methanolic root extract of *S. rebaudiana* significantly reduces the level of total cholesterol (TC), triglyceride (TG), low density lipoprotein (LDL) and very low density lipoprotein (VLDL) by 53.5, 37.4, 82.3, and 45.6% respectively when compared with diabetic control group[24].

The liver is the largest organ that helps in maintaining the concentration of normal blood glucose in fasting and postprandial states. Liver dysfunction due to insulin resistance leads to glycogenolysis (increased production of hepatic glucose). Lack of proper storage of triglycerides and lipolysis in the liver (insulin-sensitive tissue) elevates the hepatic enzyme alkaline phosphatase (ALP) and bilirubin in the bloodstream.

In diabetes, the blood vessels (glomeruli) in the kidneys get damaged which affects the glomerular filtration rate (GFR) with the decreased synthesis of protein and increased tissue proteolysis with raised blood urea, creatinine and uric acid levels (Table 2). Administration with effective and safe hypoglycemic compounds (SGSSand Reb-A) at a dose of (20 and 30 mg/kg b.wt.) restores all the disturbed parameters in alloxan treated rats to the normal level.

Conclusion

In conclusion, the results suggest that two reference standards steviol glycosides system suitability (containing a mixture of nine steviol glycosides) and rebaudioside A has significant antioxidative, antihyperglycemic and antihyperlipidemic properties. These pure compounds in small doses (20 and 30 mg/kg b.w.) are potentially effective in decreasing oxidative damage by enhancing antioxidant levels and maintaining glucose homeostasis in diabetic rats. Thus, these compounds could be used as a potential drug or as a food additive (natural sweetener) in regulating the complications of diabetes and improving stress-related pathological conditions. Toxicological evaluation including clinical trials is required to better understand the mechanism of action at the molecular level and to settle issues associated with safety concerns. Therefore, further studies are necessary to cover a wide spectrum of applications of the bioactive compounds (steviol glycosides) of the herb *S. rebaudiana* before recommending the patients with type 2 diabetes.

Conflict of interest

The authors have declared no conflict of interest.

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