Evaluation of the glycemic effect of *Ceratonia siliqua* pods (Carob) on a streptozotocin-nicotinamide induced diabetic rat model

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ABSTRACT

Background. *Ceratonia siliqua* pods (carob) have been nominated to control the high blood glucose of diabetics. In Yemen, however, its antihyperglycemic activity has not been yet assessed. Thus, this study evaluated the *in vitro* inhibitory effect of the methanolic extract of carob pods against α-amylase and α-glucosidase and the *in vivo* glycemic effect of such extract in streptozotocin-nicotinamide induced diabetic rats.

Methods. 2,2-diphenyl-1-picrylhydrazyl (DPPH) and Ferric reducing antioxidant power assay (FRAP) were applied to evaluate the antioxidant activity of carob. *In vitro* cytotoxicity of carob was conducted on human hepatocytes (WRL68) and rat pancreatic β-cells (RIN-5F). Acute oral toxicity of carob was conducted on a total of 18 male and 18 female *Sprague-Dawley* (SD) rats, which were subdivided into three groups ($n = 6$), namely: high and low dose carob-treated (CS5000 and CS2000, respectively) as well as the normal control (NC) receiving a single oral dose of 5,000 mg kg^{-1} carob, 2,000 mg kg^{-1} carob and 5 mL kg^{-1} distilled water for 14 days, respectively. Alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase, total bilirubin, creatinine and urea were assessed. Livers and kidneys were harvested for histopathology. *In vitro* inhibitory effect against α-amylase and α-glucosidase was evaluated. *In vivo* glycemic activity was conducted on 24 male SD rats which were previously intraperitoneally injected with 55 mg kg^{-1} streptozotocin (STZ) followed by 210 mg kg^{-1} nicotinamide to induce type 2 diabetes mellitus. An extra non-injected group ($n = 6$) was added as a normal control (NC). The injected-rats were divided into four groups ($n = 6$), namely: diabetic control (D0), 5 mg kg^{-1} glibenclamide-treated diabetic (GD), 500 mg kg^{-1} carob-treated diabetic (CS500) and 1,000 mg kg^{-1} carob-treated diabetic (CS1000). All groups received a single oral daily dose of their treatment for 4 weeks. Body weight, fasting blood glucose (FBG), oral glucose tolerance test, biochemistry, insulin and hemostatic model assessment were assessed. Pancreases was harvested for histopathology.

Results. Carob demonstrated a FRAP value of 3191.67 ± 54.34 μmoL Fe^{++} and IC_{50} of DPPH of 11.23 ± 0.47 μg mL^{-1}. *In vitro,* carob was non-toxic on hepatocytes and

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