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Regulation of carbohydrate metabolism by indole-3-carbinol and its metabolite 3,3′-diindolylmethane in high-fat diet-induced C57BL/6J mice

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Abstract Indole glucosinolates, present in cruciferous vegetables have been investigated for their putative pharmacological properties. The current study was designed to analyse whether the treatment of the indole glucosinolates—indole-3-carbinol (I3C) and its metabolite 3,3′-diindolylmethane (DIM) could alter the carbohydrate metabolism in high-fat diet (HFD)-induced C57BL/6J mice. The plasma glucose, insulin, haemoglobin (Hb), glycosylated haemoglobin (HbA1c), glycogen and the activities of glycolytic enzyme (hexokinase), hepatic shunt enzyme (glucose-6-phosphate dehydrogenase), gluconeogenic enzymes (glucose-6-phosphatase and fructose-1,6-bisphosphatase) were analysed in liver and kidney of the treated and HFD mice. Histopathological examination of liver and pancreases were also carried out. The HFD mice show increased glucose, insulin and HbA1c and decreased Hb and glycogen levels. The elevated activity of glucose-6-phosphatase and fructose-1,6-bisphosphatase and subsequent decline in the activity of glucokinase and glucose-6-phosphate dehydrogenase were seen in HFD mice. Among treatment groups, the mice administered with I3C and DIM, DIM shows decreased glucose, insulin and HbA1c and increased Hb and glycogen content in liver when compared to I3C, which was comparable with the standard drug metformin. The similar result was also obtained in case of carbohydrate metabolism enzymes; treatment with DIM positively regulates carbohydrate metabolic enzymes by inducing the activity of glucokinase and glucose-6-phosphate dehydrogenase and suppressing the activity of glucose-6-phosphatase and fructose-1,6-bisphosphatase when compared to I3C, which were also supported by our histopathological observations.

Keywords Gluconeogenesis · Insulin resistant · Antihyperglycemic effect · Treatment · Hexokinase · Glycogen

Introduction

The incidence of diabetes in India will increase by 95 % in 2025 and the sufferers will be young age individuals [1]. The high-calorie diets that predispose to the development of the type 2 diabetes (T2DM) was the major concern in this era because the epidemiological observations provide an evidence that the development of insulin resistance and T2DM was positively related to fat consumption and negatively related to carbohydrate consumption [2]. The C57BL/6J mouse has become an important model for understanding the interplay between lipid and carbohydrate metabolism that underlie T2DM as it mimics the human T2DM with major pathological evidence of insulin resistance. Treatment of T2DM necessitates some effective oral antihyperglycemic drugs of naturally derived nutritive phytochemicals due to the side effects of existing drugs.

The carbohydrate metabolic enzymes include hexokinase, insulin-dependant predominant enzyme in glycolytic pathway which is partially responsible for the glucose homoeostasis where it increases the glycolysis and glucose utilization for energy production [3]. Glucose-6-phosphate dehydrogenase (G6PD) is the key in maintaining redox potential and cell survival via production of NADPH and pentose

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