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## Effects of phytocannabinoids treatment on insulin sensitivity and glucose impairment in obese and STZ-induced diabetic and obese

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besity-related insulin resistance and Type 2 diabetes accounts for millions of deaths worldwide and to-date, the anti-diabetic drugs currently available on the market are associated with numerous side-effects. Rosiglitazone, a member of the TZD family has been shown to promote weight gain and there is an increased risk of heart diseases in diabetic patients. Therefore, it is crucial to develop new and more effective therapies having fewer side-effects. This study included 2 different rat models, namely a diet-induced obese model where the rats were fed a high carbohydrate diet (HCD) or a high-fat diet (HFD). The second rat model involved HFDfed obese STZ-induced diabetic rats. In both models, rats were fed for 10 weeks on the respective diets after which, treatments were administered orally for a period of 8 weeks. The obese rat model was treated with a cannabis extract at a concentration of 1.25mg/kg body weight (relative to THC content) whereas the STZ-induced obese and diabetic rats were treated with a cannabis concentration of 1.25, 2.5 and 5.0mg/kg body weight or 50mg/kg rat body weight metformin (positive control). Rats' metabolic parameters such as fasting blood glucose, insulin, cholesterol and triacylglycerides levels, intraperitoneal glucose and insulin tolerance, weight and BMI, were monitored. The findings indicated that in the obese model, cannabis-treated rats showed significantly improved fasting blood glucose levels (p<0.01) and beta cell activity (HOMA2%B, p<0.001) relative to their untreated controls. However, insulin sensitivity of tissues (HOMA2%S) was unaffected by the treatment, in both dietary models. Cannabis-treated obese rats showed reduced weight gain which was not observed in the diabetic model. STZ-induced diabetic rats treated with 1.25mg THC/kg cannabis extract displayed improved HOMA2%S (p<0.05) and HOMA2-IR (p<0.0001), relative to the positive control (metformin), but no improvement in HOMA2%B. The efficacy of cannabis treatment in improving glucose tolerance and insulin sensitivity is influenced by the type of diet (HCD or HFD), the metabolic health (obese or obese diabetic). Furthermore, it is important to determine the optimum dosage of cannabis extract, to obtain the most desirable effects depending on the metabolic state of an individual.

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