# EFFECTS OF DIETARY SUPPLEMENTATION WITH PURE NATURAL HONEY ON METABOLISM IN GROWING SPRAGUE-DAWLEY RATS.

# ABSTRACT

The excessive consumption of refined sugars mainly fructose is linked to metabolic dysfunction. The early introduction of refined sugars in the diets of children has resulted in an increased incidence of childhood metabolic dysfunction. There are conflicting reports on the gender susceptibility to developing metabolic dysfunction. Natural honey (NH) has been shown to have health benefits when included in the diet. The neonate is sensitive to dietary manipulations which can have long lasting effects. The short and long term effects of inclusion of NH in the diets of neonates were investigated in rat models. This was with a view to determine whether NH can substitute refined sugars such as cane syrup (GS), without adverse effects, and whether there were any gender differences in response to the dietary modification.

In the long term study, 59 suckling Sprague-Dawley (SD) rats were fed with either NH- or GS-supplemented diets from age 7 (neonate) to 91 (adulthood) days. For the short term study to investigate the effects of NH in neonates, 69 SD pups were gavaged with NH or GS twice daily at 12-hour intervals and allowed to nurse freely in between from age 7 to 20 days. The rats in all groups were weighed daily during the period when they

were gavaged and then twice weekly thereafter to assess body weight gain (BWG) over the study periods. The adult rats were subjected to an oral glucose tolerance test (OGTT) at 13 weeks of age before termination. The rats' growth was determined through their BWG and linear growth was assessed by measurements on the bones (femur and tibia) weight, length and density. Blood was collected for the assessment of clinical biochemistry and plasma markers of general health including the circulating metabolic substrates (glucose, triglycerides (TGs), free fatty acids (FFAs)); hormones (insulin, leptin); liver and renal functions were also obtained. Morphometric measurements (weight, lengths and histology) were also done on the abdominal viscera. Hepatic storage of metabolic substrates (glycogen and lipids) was determined. The analysis of the proximate composition of the NH and GS as well as the diets was performed with the Student's *t*-test. A repeated measures two-way analysis of variance (ANOVA) with Bonferonni's post hoc test was used to analyse the BWG and OGTT, while the other parameters were analysed by one-way ANOVA with Neuman-Keul's post hoc test, and level of significance was set at $p < 0.05$.

The matched diets were found to be isonitrogenous and isocalorific. Following the long term study, the NH fed rats showed tolerance to an oral glucose load. GS increased fasting blood glucose (FBG), TGs ($p < 0.05$), FFAs ($p < 0.0001$), visceral fat weight ($p < 0.0001$), and caused hypercholesterolemia, hyperinsulinemia, hepatomegaly and fatty liver in the males. NH increased intestinal villi growth and preserved the liver integrity in both males and females. Although, the GS-fed female rats did not suffer multiple risks of

metabolic syndrome (MetS), there were high FBG concentration and hypercholesterolemia induced at low dose and metabolic dyslipidemia shown as high TG levels at high dose. These findings were contrary to the notion about the females having a lower susceptibility to developing metabolic syndrome than males.

Some traditional rites include the feeding of honey to infants at birth, and there is evidence of the dietary inclusion of sugars in infant formulations. The need to evaluate the safety of honey consumption vis-à-vis refined sugars in children becomes imperative. Thus, after inducing metabolic syndrome in the rats through 12-week GS feeding, the effects of both diets on neonates were studied. In the neonates, there was no difference in all the parameters measured except the higher circulating non fasting FFAs ($p < 0.0001$) and hepatic storage of lipids ($p < 0.001$) in GS-fed than the NH-fed pups. Metabolic syndrome did not develop within the short term.

NH was thus found to be a healthy source of dietary sugars, improved glycaemic control and metabolic profiles. The study underscored the differential effects of dietary treatments in male and female rodents. This pointed to the advantages of gender based comparative studies in biomedical research. The study confirmed the nutraceutical value of NH, and advocated for its consumption as a healthy substitute to refined sugars. The consumption of refined sugars by infants should be discouraged, and females should also be cautious in excessive sugar intake, as they can also be susceptible to the metabolic adverse health effects of artificial sweeteners.