

ABSTRACT

Fructose-rich diets and the early nutritional environment have been implicated in the increase in metabolic disorders worldwide. The “two hit” hypothesis has also come under the spotlight as consequences of early nutritional interventions have been shown to appear either spontaneously or after induction by a second intervention leading to worsened disease states. Current research is exploring the potential use of pharmacologically diverse phytochemicals such as ursolic acid (UA) to promote metabolic programming thereby imparting positive health benefits later in life. This study examined the effects of early administration of UA on the subsequent development of complications associated with diet-induced metabolic dysfunction in Sprague Dawley rats.

One hundred and seven suckling, six-day old male and female Sprague Dawley rats randomly received 10 ml/kg of either 0.5% dimethylsulphoxide (control), UA, 50% fructose solution or a mixture of 50% fructose and UA orogastrically for 14 days. They were then weaned onto normal rat chow and plain drinking water on day 21. At adulthood (day 70), half the number of rats in each treatment group either continued on plain drinking water or they received a 20% fructose solution as drinking fluid for eight weeks. Food and fluid intake, body mass gain, fasting blood triglyceride, and oral glucose tolerance were assessed before termination. On termination blood and tissue samples were collected to assess the effect of UA on growth, organ morphometry, adiposity, hepatic lipid storage and surrogate markers of health.

The effects of fructose were found to be dependent on the time of intervention and sex. In males, fructose consumption in adulthood resulted in a 7% increase in body mass and a 35% increase in circulating blood triglycerides which were not observed in females. A single fructose hit and fructose consumption both neonatally and in adulthood caused increased hepatic lipid storage in females by 32% and 67% respectively. In both sexes, fructose intake in adulthood caused decreases in food intake whilst increases in fluid intake were observed in female rats ($P < 0.05$). Fructose consumption had no effect on glucose tolerance, visceral adiposity, organ morphometry and surrogate health markers. Neonatal administration of UA caused a 6% increase in body mass in female rats and prevented excessive fructose-induced hepatic lipid storage in both male and female rats.

Although fructose administration had adverse effects in the liver, especially in female rats, neonatal intervention with UA was found to alter metabolism so as to protect against hepatic lipid accumulation. Therefore, UA is a phytochemical that shows great potential in the control of hepatic lipid metabolism and its metabolic complications.