Ameliorative potential of Raphanus sativus cv. *Sango* sprout juice in obese rats maintained with high fat diet or switched to regular diet

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Obesity is a worldwide epidemic characterized not only by excessive fat deposition but also by systemic low grade of inflammation and high oxidative stress. Despite much progress has been achieved in recent years, current pharmacological approaches for long-term therapy offer modest benefits for most patients.

The present study evaluated the ameliorative effect of Raphanus sativus *Sango* sprout juice (SSJ), a Brassica extraordinarily rich in anthocyanins (AC) and isothiocyanates (ITCs), in a non-genetic model of obesity (high fat diet-HFD induced). Rats were fed with HFD or regular diet (RD); after 10-weeks, the HFD animals were assigned to four experimental units and the interventional period was 28 days long: 1) HFD-RD, the diet switched from HFD to RD and received the vehicle only; 2) HFD+SSJ and 3) HFD-RD+SSJ, treated with 75 mg/kg b.w. of SSJ; 4) HFD and 5) RD vehicle only, controls.

Our model of obesity showed hyperlipidaemia as well as a marked increase of body and liver weight. The transition from HFD to RD, as expected, led to a significant loss of excess weight (-9.83 g; $p<0.01$) accompanied by a total cholesterol (TC) fall (-12%; $p<0.01$). SSJ provoked a decrement of TC in HFD animals, comparable to that observed in HFD-RD group and a body weight (BW) loss (-5.14 g; $p<0.01$) associated with a reduction of daily food intake (-2 g; $p<0.01$). When SSJ was associated with RD, all marks were significantly improved compared with HFD control group, and notably, BW loss was significantly higher (-23.29 g; $p<0.05$). Obese animals showed an impairment of antioxidant hepatic machinery. Catalase, NAD(P)H:quinone reductase, oxidised glutathione reductase, superoxide dismutase and glutathione peroxidase were significantly down-regulated (ranging from 20% to 28% loss; $p<0.01$). HFD increased the lipid peroxidation *status* measured as malonildialdehyde (MDA) levels (up to 21%; $p<0.01$), and depleted the cellular store of glutathione (GSH) (17% loss; $p<0.01$). The suspension of HFD in favour of RD, resulted in a complete recovery of hepatic enzymatic capability with the exception of NAD(P)H:quinone reductase. The improvement obtained with SSJ involved all tested enzymes, while combining SSJ with RD, NAD(P)H:quinone reductase and glutathione peroxidase significantly ($p<0.01$) exceed the values recorded for HFD-RD group. In HFD-RD+SSJ, MDA levels fell markedly (up to 36% loss, $p<0.01$); moreover, they appeared significantly ($p<0.01$) lower than those obtained in HFD-RD group. The shift from HFD to RD determined an increase of GSH content (up to 19%; $p<0.05$). The association of SSJ intervention further improved ($p<0.01$) the achievement gained with the conversion of the diet.

HFD impaired UDPGT (~30% loss; $p<0.01$). Either SSJ treatment or the transition to a RD resulted in a significant up regulation of UDPGT (43% and 32% respectively compared with HFD; $p<0.01$). SSJ administration improved the effect recorded for HFD-RD with an increase by a further 43% $p<0.01$. HFD determined an up-regulation in almost each cytochrome P450 isoforms tested, CYP2E1, CYP1A2 and CYP3A1/2 were the most affected; the substitution from HFD to RD did not substantially affect CYPs, while, SSJ alone, or when administrated with RD regimen, resulted in a down-regulation to baseline values.

Pulled together, these data suggest that SSJ could be a promising antioxidant and anti-obesity agent, opening up to applications for the management of obesity correlated diseases.