260

Molecular docking study of cassia seed compounds to identify amylase and lipase inhibitors for weight management

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Background: The epidemic of obesity has become a major challenge to health globally. Current pharmacological treatments for obesity are limited by their efficacy and side effects. Cassia seed (CS) is an herb commonly used for weight management in China. However, the bioactive compounds in CS with anti-obesity properties have not been identified and the relevant mechanisms of action are not clear.

Aim: To identify promising active compounds in CS as amylase and lipase inhibitors for weight management with molecular modelling and docking studies.

Methods: Autodock Vina [1] was the molecular docking software used in this study. The selected ligands were orlistat (a drug designed to treat obesity) and 27 compounds reported to be present in CS. Seven amylases and lipases were used as protein targets. Every ligand was docked against each target and the binding affinity of the pair was calculated by Autodock Vina. The binding affinity indicates the strength of interaction between the ligand and target.

Results: The preliminary molecular docking study has shown that CS compounds emodin, alaternin, rubrofusarin gentiobioside and ononitol are comparable, in terms of binding affinity and efficiency, to orlistat. Predicted binding affinity values suggest that rubrofusarin exhibits similar affinity to lipase compared to orlistat; while emodin has substantially (> 20%) higher affinity, indicative of the latter's potential to act as an inhibitor with greater efficacy than orlistat.

Conclusion: The results suggest that some chemical compounds in CS may interact with amylase and lipase via a similar mechanism to orlistat. Further studies, with Biovia Discovery Studio [2], are recommended to identify ligand-receptor interactions at the binding sites to confirm if there is any inhibitory action.

References

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261

Metabolic detection of energy deficit by Crat in AgRP neurons links hunger with reward

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Obese individuals show increased activation of brain reward regions (mesolimbic and mesocortical dopamine projections from the ventral tegmental area [VTA]), and fasting increases the desire to eat in obese more than lean humans. It remains unclear how the brain receives, senses and integrates metabolic information that reinforce food value and motivate feeding behaviours. For example, *does inappropriate sensing of metabolic need drive greater activation of brain pathways underlying motivation and reward*? Agouti-related peptide (AgRP) neurons in the arcuate nucleus of the hypothalamus are one key neuronal population that link homeostatic detection of hunger with dopamine pathways in the brain that control motivation and reward. To assess the role of metabolic sensing in AgRP neurons and the effects on reward and motivation, we studied mice lacking carnitine acetyltransferase (Crat) in AgRP neurons. Previous studies show that Crat in AgRP neurons plays a crucial role during the metabolic shift from fasting to refeeding and thus we hypothesised that it might couple the detection of metabolic state with food reward value and motivated behaviours.

We show that Crat in AgRP neurons is important for sensing of the caloric value of sweet solutions since fasting increases sucrose consumption during states of fasting in WT more than in KO mice. Moreover, during fasting WT mice will still consume sucrose spiked with quinine (unpleasant tastant) in order to consume calories as required, whereas KO mice do not. Intriguingly KO mice continually consume more saccharin despite changes in metabolic state due to fasting. Current studies using operant conditioning to examine motivation to work for caloric versus non-caloric sweet solutions are underway. These studies highlight that Crat in AgRP neurons is crucial for the caloric assessment of sugar solutions and may link the detection of energy deficit with increased food reward and motivation.

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262

Gastric band tubing causing caecal volvulus

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Introduction: Obesity is a major public health issue, with increasing prevalence in western societies. Since 1993, Laparoscopic Adjustable Gastric Band (LAGB) is gradually being replaced in many institutions by other surgical techniques for weight loss, due to high inherent complications.The authors present a rare case of caecal volvulus caused by LAGB inserted 11 years prior. Methods: A 65 year old lady presented with a one day history of abdominal pain. Her past medical history included a LAGB placed 11 years prior, which achieved 11 kg weight loss, 3.8 kg/m^2 body mass index (BMI) reduction, 9.17% weight loss, and 23.04% excess weight loss during this time. For several months prior, she also described of intermittent abdominal bloating and colicky abdominal pain. Her abdomen was mildly distended, and tender in the periumbilical and lower quadrants with no peritonism. Her inflammatory markers were normal. Computed Tomography scan demonstrated a cecal volvulus with displacement of cecum towards the upper abdomen with dilatation of up to 10 cm, with twisting of the ascending colon and terminal ileum inferior to the cecum from the LABG tubing. Major Findings: Laparotomy demonstrated a cecal volvulus associated with the LAGB tubing, which had wrapped and twisted around the cecal mesentery. Macroscopically, the cecum appeared chronically dilated, with no acute compromise to the bowel wall. A limited right hemi-colectomy, and removal of gastric band and port was performed. Histopathology demonstrated benign reactive changes.