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This study was designed in order to investigate the effect of Myrmecodia platytyrea (MyP) extract as an anti-hypercholesterolemic agent. The acute toxicological test was done by administration of single dose and followed by 14 days observation on the rat. The subchronic toxicological test was done by administration of 28 days repeated dose. Both tests showed that MyP water extract was not toxic. The bioassay-guided isolation revealed that the MyP water extract containing 2-(2-methylbutylryl) phloroglucinol glucoside which reduced 3-hydroxy-3-methylglurutaroyl-CoA reductase (HMGR) activity (p<0.05) with inhibition concentration 50 (IC50) of 75 µg/ml. Besides that, polysaccharide showed effective concentration 50 (IC50) of 50.5 µg/ml for bile acid binding. Meanwhile, rutin actively decreased pancreatic lipase activity with IC50 of 130 µg/ml. Moreover, in vivo study results showed that treatment of MyP water extract can significantly reduce (p<0.05) low-density lipoprotein (LDL) compared to normal control group. The extract significantly increased (p<0.05) high-density lipoproteins (HDL) concentration compared to negative control group. In addition, MyP water extract increased faecal cholesterol and faecal bile compared to normal control group. Lipid peroxidation was significantly decreased (p<0.05) in MyP water extract treatment group. The extract also decreased the formation of the fatty streak at the aorta and significantly decreased (p<0.05) the thickness of foam cell in high cholesterol diet (HCD) induced rat. Then, cell culture study using WRL-68 cell showed MyP water extract significantly increased (p<0.05) apo lipoprotein A-I (Apo A-I), scavenger receptor – B1 (SR-B1) and lecithin: cholesterol acyltransferase (LCAT). The extract can significantly reduce (p<0.05) lipid droplet formation. Furthermore, MyP water extract also significantly increased (p<0.05) the superoxide dismutase (SOD) and catalase (CAT) enzymes. In the molecular study, polymerase chain reaction (PCR) array was performed on the 84 genes that specifically involved with lipoprotein signalling and cholesterol metabolism. The result showed that the treatment of MyP water extract can increase the gene expression related to reverse cholesterol transport (RCT) process. The treatment of MyP water extract did not up-regulate the gene expression of CYP7A1 which is important in the transformation process of bile acid from cholesterol. Therefore, it was suggested that MyP water extract only acted on the bile acid itself and not through up-regulation of bile acid transformation related genes. It was suggested that the bioactive compound’s synergistic effects which are present in MyP water extract also acted as antioxidant and anti-inflammatory. It was concluded that MyP water extract might play an important role in the prevention of hypercholesterolemia related diseases.

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Title : STUDY ON MYRMECODIA PLATYTYREA ANTOINII TUBER AND ITS POTENTIAL BENEFITS IN PREVENTING HYPERCHOLESTEROLEMIA RELATED DISEASES
Supervisor : ASSOC. PROF. DR. IBTISAM ABDUL WAHAB (MS)
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This project aimed to design nanoparticles-in-beads made of alginate, chitosan and their derivatives as oral insulin carrier. In the first part of the study, the calcium alginate beads were prepared using the vibratory nozzle extrusion microencapsulation technique through concurrent core and coat formation with chlorpheniramine maleate as a model drug. These beads were coated with chitosan/chitosan-oleic acid conjugate of which the latter was synthesized via covalent reaction. The formability of beads was optimized through varying alginate solution concentration, alginate/chitosan solution flow rate and nozzle vibrational frequency. The size, shape, morphology, swelling, erosion, water uptake, drug content, drug release and matrix molecular profiles of beads were characterized. Spherical discrete coated beads were produced through critical interplay of nozzle vibrational frequency and polymeric solution flow rate. The conjugate-coated beads had their swelling and water uptake tendency negated through the introduction of tripolyphosphate ions as a coagulizing agent to attract the conjugate to the alginate core interface for coagulation to take place. The drug release propensity of tripolyphosphate-coated, chitosan-oleic acid conjugate-coated beads was unexpectedly higher than the uncoated beads. This was attributed to reduced drug-alginate interaction as a result of alginate coacervating with chitosan-oleic acid conjugate and loss of calcium alginate crosslinkage to tripolyphosphate species. In the second part of the study, nanoparticles of simple calcium alginate, calcium alginate-stearic acid, and calcium alginate-C18 conjugate were prepared by nanospray drying technique. Alginote-C18 conjugate was chemically synthesized with the aim of introducing a hydrophobic segment to the polymer chain for drug release modulation. The nanoparticles size, zeta potential, surface morphology, drug content, drug encapsulation efficiency, drug release, matrix molecular characteristics, mucus penetration, HT-29 cell cytotoxicity and intracellular trafficking profiles were evaluated. Where applicable, the nanoparticles were loaded into calcium alginate beads and had their in vivo blood glucose lowering and insulin bioavailability profiles determined. The calcium alginate-C18 conjugate nanoparticles were characterized by non-toxicity, reduced size and zeta potential thus enhanced mucin penetration and intracellular trafficking, with minimal insulin readsoption tendency as a result of active COOH/COO- sites of alginate being occupied by C18 conjugate. Loading of such nanoparticles into tripolyphosphate-crosslinked, chitosan-oleic acid conjugate-coated beads had their drug release reduced in the simulated gastric phase with the majority of insulin being transported transmucosally in the form of nanoparticles at the intestinal region. The combination of nanoparticles and coated beads increased the blood glucose lowering extent of rats synergistically, and insulin bioavailability instead of nanoparticles alone.

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Title : NANOPARTICLES-IN-BEADS MADE OF ALGINATE AND CHITOSAN DERIVATIVES AS ORAL INSULIN CARRIER
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