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Kappaphycus alvarezii REGULATES CHOLESTEROL DEGRADATION IN HYPERTENSIVE INDUCED SPRAGUE-DAWLEY RATS

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AUTHOR'S DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Teknologi MARA. It is original and is the results of my own work unless otherwise indicated or acknowledged as referenced work. This thesis has not been submitted to any other academic institution or non-academic institution for any degree or qualification.

I, hereby, acknowledge that I have been supplied with the Academic Rules and Regulations for Postgraduate, Universiti Teknologi MARA, regulating the conduct of my study and research.

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ABSTRACT

Kappaphycus alvarezii (*K. alvarezii, K.a*), is a local red seaweed that was claimed to improve health by lowering the risk of CVD. This study explored the presence of phytosterol and the effect of *K.alvarezii* as a potential cholesterol hepatic metabolism regulator in inducing hypercholesterolaemic and hypertensive rats. The presence of phytosterol was identified on the methanolic extract of *K.alvarezii* using gas chromatography-mass spectrum. Five types of phytosterols namely cholesta-4,6-dien-3-ol, (3β), cholest-5-en-3-ol, (3β), ergosta-5,7-dien-3-ol, (3β), cholest-5-ene, 3-methoxy-, (3β) and stigmast-5-en-3-ol, (3β) were identified from the analysis. The *in-vivo* study was proceeded to investigate the potential of *K. alvarezii* on the combination of two cardiovascular risk factors: hypertension (HTN) and hypercholesterolaemia (HC). Seven-week-old 30 male Sprague-Dawley rats were randomly divided into five groups; Normal, HTN-HC, HTN-HC+Captopril-Simvastatin, HTN-HC+5%*K.alvarezii* (w/w) and HTN-HC+10%K.a (w/w). Induction of HTN-HC was done by feeding rats on a high sodium fat diet (HSFD) containing 1.5% cholesterol+7% sodium chloride for 6 weeks. HTN-HC rats were supplemented with *K. alvarezii* powder blended in base diet (5 % (w/w) or 10% (w/w) per food intake) or captopril-simvastatin for 28 days. The study found that HSFD was successfully induced HTN-HC in the rats. HTN-HC rats were found to increase in body weight, systolic-diastolic blood pressure, glucose, plasma total cholesterol, triglycerides, low-density lipoprotein, lower high-density lipoprotein and elevates aspartate transaminase, alanine transaminase compared to other groups ($p<0.05$). Histopathological examination of the liver, kidney and heart found the presence of steatosis, glomerular injury and arterial hyalinisation, and myocardial injury in HTN-HC group. Relative to HTN-HC rats, *K. alvarezii*-supplemented and drug combination-treated rats reduced body weight, normalised blood pressure, plasma lipids and enzymatic activity in the liver. Interestingly, it attenuated the presence of steatosis in the liver, preventing renal and myocardial injury. Increased antioxidant activities were observed in 2,2-Diphenyl-2-Picrylhydrazyl (DPPH) Assay and ferric reducing assay power and reduced the catalase and lipid peroxidation were observed in the liver of *K. alvarezii*-supplemented rat compared to all groups ($p<0.05$). *K. alvarezii* modulated the hepatic cholesterol synthesis by down regulated the mRNA expression of HMG CoA R, SREBP-2, and ACAT-2 and increased expression of CYP7A1 in the liver. Therefore, the collected result indicates the supplementation of *K. alvarezii* reduced cardiovascular risk by improving blood pressure and lipid profile thru regulating cholesterol metabolism. The presence of phytosterol and antioxidant properties in *K.alvarezii* may be the reason behind this effect.

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