Abstract No: BP-04

In silico comparison of hypocholesterolemic effect of orally administered phytochemicals from five different plants on humans

F. B. S. Ameer[1] and W. M. T. D. N. Weerakoon[2*]

[1]Department of Biomedical Sciences, British College of Applied Studies, Sri Lanka
[2]Department of Chemistry, University of Colombo, Sri Lanka
tharindra@chem.cmb.ac.lk

High cholesterol level in the blood is a significant burden that provokes plaque formation in blood vessels which eventually leads to atherosclerotic cardiovascular disease. Currently, statin drugs are widely used to treat hypercholesterolemia. However, long-term statin therapy is known to be associated with adverse effects such as myalgia, rhabdomyolysis, statin-induced myopathy along with other risk factors such as alcohol abuse and hypothyroidism. Due to this reason, plant-based therapies have been tested for decades as a replacement for statin drugs and some of the phytochemicals have been identified to be effective in treating hypercholesterolemia. The utmost goal of this study is to compare major phytochemicals (S-allyl cysteine, Mahanimbine, β-sitosterol, Stigmasterol, Diosgenin and Curcumin) present in five commonly known plants that possess cholesterol-lowering abilities, by using *in silico* approaches. The most effective cholesterol-reducing drug, rosuvastatin has been used as the positive control. Molinspiration software has been used to monitor vital molecular properties and the pkCSM (Small-molecule pharmacokinetics prediction) tool to estimate the toxicity and the pharmacokinetic properties. Lipinski's and Veber's rules were applied to Molinspiration results to discover the oral bioavailability of the phytochemicals. The results of Molinspiration showed that all the phytochemicals have good oral bioactivity as the phytochemicals obeyed Lipinski's and Veber's rule including moderately active and active bioactivity scores for enzyme inhibition in S-allyl cysteine and other phytochemicals respectively. In addition to that, the predictions from the pkCSM tool indicated that Mahanimbine can be associated with hepatotoxicity and mutagenic effects when compared with other phytochemicals and rosuvastatin. However, except S-allyl cysteine from garlic, all the phytochemicals including rosuvastatin drug were identified to be P450 enzyme inhibitors which emphasised that adverse drug-drug interactions can be present with these phytochemicals and rosuvastatin. As the conclusion from *in silico* predictions, S-allyl cysteine was identified as the most effective drug-like agent with minor drawbacks. Anyhow, since all the phytochemicals showed good oral bioactivity, pharmacokinetic properties (except Mahanimbine) with few anomalies and elevated lipophilicity (except S-allyl cysteine which is hydrophilic and Curcumin which has reduced lipophilicity), further *in vivo* and *in vitro* trials under optimised conditions should be undertaken to confirm the effect of the phytochemicals to be used as a cholesterol-lowering drug in hypercholesterolemia patients.

Keywords: Molinspiration, pkCSM, Rosuvastatin, Hypocholesterolemic effect

Acknowledgement
This work was supported by the Oxford Brookes University- United Kingdom and the British College of Applied Studies- Sri Lanka.