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Red yeast rice extract reduces interleukin-1 beta secretion from peripheral blood mononuclear cells when treated with cholesterol crystals

P. V. Kavanagh[1], P. T. Walsh[2],M. Lucitt[1]. [1]Pharmacology and Therapeutics, Trinity College Dublin, Dublin, Ireland, [2]Clinical Medicine, Trinity College Dublin, Dublin, Ireland

Introduction: Red yeast rice (RYR) nutraceutical contains monacolin K, a natural occurring statin (1). Here we compare lovastatin and simvastatin effects on interleukin-1 beta (IL-1β) levels to that of extracts from a RYR product sold in health food stores in Ireland.

Method: Standard curves using 0.375-24 μg/mL of lovastatin pre and post hydrolysis with NaOH were constructed using liquid chromatography-mass spectrometry (LC-MS) operated with selected ion monitoring (SIM) and a mass-to-charge ratio (m/z) of 427 to detect the lactone and m/z of 445 to detect the hydroxyl acid forms of lovastatin. RYR, 0.22μm filtered ethanol extractions pre and post hydrolysis were analysed by LC-MS for lactone (inactive) and hydroxyl acid (active) forms and quantified from the standard curves generated above. Human peripheral blood mononuclear cells (PBMCs) treated *in vitro* with lovastatin (100μM), simvastatin (100μM) or RYR extracts (9μg/ml, 18μg/ml) and stimulated with lipopolysaccharide (LPS) (100ng/ml) for 3hrs, followed by cholesterol crystals (CC) (1mg/ml) stimulation overnight. IL-Iβ levels in the supernatants form PBMCs were measured by ELISA. Data shown as mean ± sem, N=3. Statistical analysis carried out using unpaired students t-test with significance taken at $P<0.05$.

Results: Extracts from 9g of RYR (3 capsules) analysed by LCMS detected 1.86-2.43mg /capsule of the lactone. Extract levels of monacolin K lactone form to monacolin K hydroxyl acid form, pre and post hydrolysis was determined, (15:1) pre and (1:2) post hydrolysis. PBMCs treated with lovastatin or simvastatin reduced secreted levels of IL-1β when stimulated with LPS and CC, (0.99 ± 0.05ng/ml) lovastatin, (1.75 ± 0.14ng/ml) simvastatin vs. (2.6 ± 0.47ng/ml) LPS and CC treatment alone. Similarly, i*n vitro* treatment of PBMCs with RYR extracts also resulted in reduced IL-1β secretion when stimulated with LPS and CC (2.6 ± 0.47ng/ml) vs. (1.15 ± 0.09ng/ml) RYR 18μg/ml and (1.49 ± 0.28ng/ml) RYR 9μg/ml. *Values presented are mean ± sem, n=3.*

Conclusions:
As part of our preliminary investigations, we have demonstrated extraction of lactone and hydroxyl acid forms of monacolin K from a RYR commercial available product. LPS and CC induced IL-1β release by PBMCs are reduced when treated with prescription statins, and levels of IL-1β released are reduced to comparable levels when treated with RYR extracts. These data identify a previously unappreciated anti-inflammatory effect of RYR supplements that may have potential benefit in atherosclerosis disease.

References:
1. Zhao SP *et al*. (2004). *Circulation* **110**: 915-920.