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Assessment of anti-atherosclerotic potency of poly herbal nutraceutical (PHN)

Chetan C. Nimgulkar
National Institute of Nutrition, India

Background: There are enormous efforts going on to develop suitable therapeutics for atherosclerosis, a multi etiological disease due to chronic inflammation, hyperlipidaemia and oxidative stress. Clinical and experiential hit nutraceutical and herb *Allium sativum, Zingiber officinale, Curcuma longa, Terminalia arjuna* and *Cyprus rotundus* were integrated in the current study to obtained safe, effective and target specific treatment to prevent atherogenesis, using trans disciplinary exploratory studies.

Methodology: Poly herbal nutraceutical (PHN) was prepared by combination of hydro-alcoholic extracts of WHO and IP monographs complied above selected test materials. All above test materials and PHN were assessed for activities viz., antioxidant activity by free radical scavenging and inhibitory effect LDL oxidation, anti-inflammatory activity in acute paw edema and cotton pellet induced granuloma in C57Bl/6 mice, anti-hyperlipidemic and anti-obesity activity in high fat and cholesterol diet fed C57Bl/6 mice and WNIN Ob/Ob rats, respectively and Anti-atherosclerotic activity in high fat and cholesterol diet fed New-Zealand rabbit.

Results: PHN was found to be 5 to 100 times potent free radical scavenger and equipotent with *Allium sativum* to inhibit the oxidation of LDL than all individual test material extracts. PHN significantly inhibited carrageenan induced paw edema at initial and late phase of acute inflammation in C57Bl/6 mice and cotton pellet induced chronic inflammation maximum by 50% possibly due to reduction in IL1-β (82%), IL-6 (89%), TNF-α (95%) and CRP (70%) as compared with positive control. *In-silico* results suggest that COX-2 enzyme protein was strongly docked by curcumin, dimethoxy curcumin and alliin, whereas polyphenols like gallic acid, ellagic acid, gallo catechin and alliin docked NF-κB protein with an average binding at 8 sites. PHN also reduced plasma cholesterol, triglyceride, LDL, VLDL by 39%, 71%, 45% and 71%, respectively, in a dose dependent manner when compared to positive control. It also inhibited the levels of IL6, IL-1β, TNF-α by 50%, 60%, 65%, respectively, in the same animals. PHN reduced total fat and increased lean body mass in WNIN Ob/Ob rats. T wave amplitude in ECG was normalized from inverted but lipid parameters remained unchanged in WNIN Ob/Ob rat. Rabbits treated with PHN for 3 months had reduced plasma cholesterol, triglyceride, LDL, VLDL by 24%, 74%, 20% and 74%, respectively as compared to positive control. HDL was found to be non-significantly increased. Atherogenic index of PHN and positive control were 23% and 113%, respectively. PHF at 50 mg/Kg significantly reduced plasma cholesterol, triglyceride, LDL and VLDL by 20%, 70%, 14% and 68% respectively. Aortic atheroma formation was barred by PHN as observed in Oil red O histopathological staining and normalized endothelial cells of intimal region of aortic arch and medial architecture was observed in scanning electron microscopy.

Conclusion: PHN is possibly, a potent anti-atherosclerotic formulation as it has anti-hyperlipidemic, anti-inflammatory and anti-obesity potencies may be due to enriched with phytochemicals.

chetanmhrpharma@gmail.com