Need to clinically investigate BHUx for atherosclerosis and osteoporosis

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Cardiovascular diseases have been associated with reduced bone mineral density and fracture risk[1]. A major atherogenic molecule is believed to be oxidized phospholipid, which has also been found to inhibit the spontaneous osteogenic differentiation of marrow stromal cells, suggesting a link between atherosclerosis and osteoporosis. These oxidized phospholipids have also been shown to alter the net effects of bone anabolic agents, such as bone morphogenetic protein and parathyroid hormone, as seen in MC3T3-E1 cells[2]. Secondly, a negative association between plasma lipid concentrations and bone mineral density supports the hypothesis of harmful effect of hyperlipidaemia on bone metabolism[3].

Further, osteoporosis and osteoarthritis are major concerns for aging societies worldwide. Epidemiological and genetic studies have shown that it is a polygenic disease and involves both genetic and environmental factors. Interestingly, patients with osteoporosis frequently suffer from vascular calcification, which predicts both cardiovascular morbidity/mortality and osteoporotic fractures. Both atherosclerosis and osteoporosis often appear together, especially in the elderly and post-menopausal women[4].

In the near past, inflammation has been associated with the pathogenesis of atherosclerosis[5] and inflammatory genes are good candidates for the risk of developing atherosclerosis. Further, vascular mineralization and loss in bone density have been significantly correlated by clinical and experimental investigations (genetic, hormonal and biochemical)[6], and indicate common signalling pathways, transcription factors and extracellular matrix interactions for both skeletal and vascular abnormalities. Various common risk factors have been suggested, such as aging, estrogen deficiency, vitamin D and K abnormalities, chronic inflammation and oxidative stress[1]. Pro-inflammatory cytokines, like interleukin-6 and tumour necrosis factor-alpha, C-reactive protein, resistin, an adipokine, and polymorphism of the Toll-like receptor 4 are also implicated in the development of atherosclerosis and osteoporosis[7]. Recent evidence indicates that *LOX* genes are associated with osteoporosis and atherosclerosis[8].

Although soy consumption has been associated with decreased incidence of atherosclerosis and osteoporosis, acting through receptors for estrogens, progesterone, androgen, vitamin D, retinoic acid and also thyroid hormones, it may adversely influence these endocrine functions[9]. Therefore, new herbal formulations are the demand of time.

In this series of searches, we have developed BHUx (a polyherbal formulation patented by DBT and BHU in EU, USA, China and India), which has shown significant antiatherosclerotic property[10]. It enhances the HDL level and also inhibits lipoxygenase 15, which are directly associated with the oxidation of LDL phospholipids, turning it to atherogenic molecule and cyclooxygenase-2, responsible for the release of inflammatory molecules[11]. Recently, we have reported that its precursor formulation, (Sandhika, an ayurvedic medicine already in clinical use for arthritis)[12], enhances Ca nodule formation in osteoblast-like cells, both in the presence and absence of LPS[13].

Thus BHUx has shown therapeutic response for both pathologies in the experimental set-up and this formulation may be worth international patenting. However, it would be futile if BHUx cannot be delivered to the society for its clinical use and for this, collaborative research in project mode with leading laboratories and hospitals is needed. The Ministry of Health and the Ministry of Science and Technology, Government of India, must take up this project for further studies, by breaking the boundaries of ayurvedic and allopathic drugs.

Studies in terms of multi-centric clinical trials, toxicity and side effects, accumulative consequences when given with conventional drugs of these diseases and also pharmaco-genomics are needed. These studies will help doctors in making specific recommendations of BHUx to various patients with these age-related diseases, such as type-2 diabetes, atherosclerosis, cancer and osteoporosis according to the individual's susceptibility for better response.

Without coordinated efforts of scientists and doctors, from leading laboratories of our country, BHUx can never be delivered to the international society and it may remain confined to research papers and project reports, as happens with most of the patents.

If BHUx is developed as functional food or as food supplement, on the above suggested line of further research, it can be safely recommended by doctors of both the systems of medicine and can benefit the suffering humanity. It will also capture the big international herbal export market, where India has only 2% share.

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