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Antiproliferative and apoptosis inducing effects of nano-ZER in atherosclerotic-induced New Zealand White rabbit

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Atherosclerosis is a complex chronic inflammatory, degenerative and accumulative consequence of the arterial wall to injurious stimuli, which is significantly driven by persistence proliferative response. The pathophysiology of the disease implies its nanoscale nature and therefore necessitates new nano-medicine approaches to combat it. The role of nanotechnology in diagnosing cardiovascular disorders is expanding rapidly. While many herbs has shown to be efficacious in reducing and/or preventing early development of atherosclerosis, however, the role of the cyclic sesquiterpene, zerumbone (ZER) nanoparticles in this aspect still not documented. Since the objectives of this investigation is to evaluate the antiproliferative property of nono-ZER, in preventing and reducing macrophages assembly and vascular smooth muscle cells (VSMCs) proliferation in early-developed atherosclerotic lesions in the aortas of New Zealand white rabbits fed a cholesterol-rich diet, via induction of programmed cell death (apoptosis) in the built-up cells (macrophages) as well proliferative cells VSMCs. A total of 30 rabbits were equally assigned in to five groups namely, control (CN), hypercholesterolemic diet (HCD) and nano-ZER preventive groups (NZ-I, NZ-II and NZ-III). Control group rabbits received standard pellet, HCD group enriched with 1% pure cholesterol, nano-ZER treated animals supplemented with different concentration of nano-ZER (0.4% 8 mg/kg, 0.8% 16 mg/kg and 1% 20 mg/kg).

Tissue samples were collected from thoracic aorta and aortic arch at 10 weeks post-feeding with cholesterol-rich diet for immunohistochemistry and TUNEL assay. The following antibodies were used against cellular protein components of macrophages (RAM-11) and smooth muscle actin (HHF-35). Atheromas plaque built up were significantly $P<0.05$ diminished in nano-ZER supplemented groups in diverse manner (dose dependent), were it's more pronounced in 16 mg/kg and 20 mg/kg treated groups. However, most of the nano-ZER treated groups showed marked dropping in plaque development in contrast to cholesterol-rich diet group. Our data indicate that is nano-ZER significantly avert and decreases early plague formation and development-establishment via significant induction of apoptosis eventually reduction in monocytes and/or macrophages migration-aggregation, lessen smooth muscle cells proliferation-migration, and finally retards foam cell formation and plaque progression.

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