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Immunosuppressive effects of alpha beta unsaturated carbonyl based compounds and their most potent curcumin analogue encapsulated PLGA-PEG nanoparticles

Compounds containing α, β-unsaturated carbonyl based moieties such as curcumin and chalcones including their analogues and derivatives possess diverse pharmacological activities. Curcumin has low therapeutic potential due to its physicochemical limitations when administered orally. The present study was aimed to enhance the immunomodulatory activity of curcumin and chalcones through structural modification. A series of α, βunsaturated carbonyl based compounds (curcumin analogues and chalcone derivatives) and their pyrazoline derivatives were investigated for their modulatory effects on chemotactic migration, Mac-1 expression, phagocytic activity and reactive oxygen species production by human whole blood cells and isolated human polymorphonuclear neutrophils. Among all compounds tested, 3,5-bis[4-(diethoxymethyl)benzylidene]-1-methyl-piperidin-4-one (BBP) was the most potent in suppressing the sequential steps of phagocytosis. BBP was further investigated for its immunosuppressive effects on various cellular and humoral immune responses in Balb/c mice. Its effects on immune responses in the mice were determined by measuring phagocytosis, serum levels of ceruloplasmin and lysozyme, MPO plasma level, proliferation of T and B lymphocytes, T lymphocytes subsets (CD4+ and CD8+) and secretion of Th1 and Th2 cytokines as well as serum immunoglobulins (IgG and IgM) and delayed type hypersensitivity reaction (DTHR). BBP significantly and dose dependently reduced the migration of neutrophils, phagocytic activity and serum levels of ceruloplasmin and lysozyme, suppressed lymphocyte proliferation along with the downregulation of effector cells expression and release of Th1/Th2 cytokines. Reduction in DTHR and serum immunoglobulins was also observed. In conclusion, these findings suggest that the novel curcumin analogue, BBP possessed strong immunosuppressive effects.

Keywords: Immunosuppressive, Immunomodulatory

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