Cannabinomimetic control of mast cell mediator release: new perspective in chronic inflammation.

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Abstract

The present review aims to elucidate the emerging role played by cannabinomimetic compounds in the control of mast cell activation. Mast cells are immune competent cells strategically localised at the sites directly interfacing with the external environment, which, in case of injury, regulate the immune response by the release of a plethora of both pre-formed and newly-synthesised mediators. However, although the main goal of mast cell activation is to initiate the inflammatory reaction, and thus maintain internal homeostasis, the consequences of dysregulated mast cell activation could be to chronically activate the inflammatory response as occurs in arthritis, inflammatory bowel diseases, atherosclerosis and asthma. Therefore, much effort has been made to develop compounds that act to prevent mast cell degranulation. Cannabinomimetic compounds (i.e. agents able to modulate endocannabinoid function) are considered as an emerging class of regulators of mast cell behaviour. We focus on the evidence for a cannabinomimetic control of both acute and chronic inflammatory disease, recognising a common mast cell origin for problems such as dermatitis, inflammatory gastrointestinal syndrome and granuloma formation. Special emphasis is provided for the recent promising results obtained with palmitoylethanolamide in human studies. In the light of evidence suggesting that the control of mast cell activation at an early time during an inflammatory process may account for its resolution, it is reasonable to propose that cannabinomimetic compounds, including palmitoylethanolamide and its congeners, could represent possible candidates for treating several chronic inflammatory diseases.