XANTHATIN INHIBITS MAST CELL ACTIVATION INDUCED BY PRO-INFLAMMATORY NEUROPEPTIDES


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Mast cells are connective tissue cells involved in the genesis and modulation of inflammatory responses. We have previously shown that xanthatin (xanthanolide sesquiterpene isolated from Xanthium cavanillesii Schouw) inhibits mast cell activation induced by experimental secretagogues. However, the effect of xanthatin on mast cell activation induced by pathophysiological stimuli remains unknown. These stimuli include, among others, the pro-inflammatory neuropeptide substance P and neurotensin, responsible for one of the main pathways of neurogenic inflammation. The present study was designed to examine the effects of xanthatin on mast cell activation induced by pro-inflammatory peptides, such as substance P and neurotensin. Rat peritoneal mast cells were incubated with: 1) PBS (basal); 2) substance P (100 µm); 3) neurotensin (50 µm); 4) xanthatin (8-320 µm)+substance P; 5) xanthatin (8-320 µm)+neurotensin. Concentration-response studies of mast cell serotonin release evoked by pro-inflammatory neuropeptides, evaluation of mast cell viability and morphology by light and electron microscopy, and drug stability analysis by thin layer chromatography were performed. Serotonin release studies, carried out together with morphological studies, showed the effectiveness of xanthatin to stabilize mast cells. The present study provides the first strong evidence in favour of the hypothesis that xanthatin inhibits substance P - and neurotensin-induced serotonin release from peritoneal mast cells. Our findings may provide an insight into the design of novel pharmacological agents which may be used to regulate the mast cell response in neurogenic inflammation.

Key words: xanthanolide – substance P – neurotensin

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