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TRICYCLIC ANTIDEPRESSANT AMITRIPTYLINE ATTENUATES Ca^{2+} RESPONSES IN RAT PERITONEAL MACROPHAGES

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Amitriptyline is a tricyclic antidepressant widely used in clinical practice for the treatment of anxiety, depression and chronic pain. These drugs have a multifaceted effect on cellular processes. One of their targets is sigma-1 receptors. Sigma-1 receptors are molecular chaperones located in endoplasmic reticulum membrane; they are characterized by a unique structure and pharmacological profile. Sigma-1 receptors regulate many cellular processes in health and disease, including Ca^{2+} signaling. Using Fura-2AM microfluorimetry, it was shown for the first time that sigma-1 receptor agonist, antidepressant amitriptyline, significantly suppresses both Ca^{2+} mobilization from intracellular Ca^{2+}-stores and subsequent store-dependent Ca^{2+} entry into cells, induced by endoplasmic Ca^{2+}-ATPase inhibitors thapsigargin and cyclopiazonic acid, as well as disulfide-containing immunomodulators glutoxim and molixan, in rat peritoneal macrophages. The results suggest the involvement of sigma-1 receptors in a complex signaling cascade induced by glutoxim or molixan, leading to an increase of intracellular Ca^{2+} concentration in macrophages. The results also indicate the participation of sigma-1 receptors in the regulation of store-dependent Ca^{2+} entry in macrophages.

Keywords: amitriptyline, sigma-1 receptor, peritoneal macrophage, intracellular Ca^{2+} concentration