047

Antibacterial Agent, Triclosan (TCS), Alters the Production of Pro-Inflammatory Cytokine Interleukin 1 beta from Human Immune Cells: The Role of Mitogen-Activated Protein Kinases

Triclosan (TCS) is an antimicrobial compound widely used in personal hygiene products such as mouthwash and toothpaste; as a result, TCS has been found in human blood, breast milk, and urine. Interleukin-1 beta (IL-1β) is an important pro-inflammatory cytokine produced by lymphocytes, monocytes, and other cells. IL-1β regulates cell growth, tissue repair, and immune function, increased levels in the absence of appropriate stimuli (injury or infection) can lead to chronic inflammation which is been associated with many diseases, including rheumatoid arthritis and certain cancers. Previous studies have shown that TCS stimulated secretion of IL-1β by immune cells and that this TCS-induced increase was dependent on mitogen-activated protein kinases (MAPKs). The current study examines whether this increase in secretion is due to release of already existing stores of IL-1β or if TCS is able to stimulate cellular production (both secreted and intracellular levels) of IL-1β. Additionally the study addresses the role of MAPKs in any TCS-induced increases in production. Human peripheral blood mononuclear cells (PBMCs) were exposed to TCS at concentrations of 0-5 μM. The cellular production of IL-1β was measured at 10 minutes, 30 minutes, 6 hours, and 24 hours. Secreted levels were measured in supernatants from exposed cells using enzyme-linked immunosorbent assay (ELISA) and intracellular levels were measured by Western Blot. Results indicate the production of IL-1β was increased by exposure to one or more concentration of TCS at each length of exposure. The greatest increase in IL-1β production was seen at 6 h, where all TCS exposures caused substantial increases in IL-1 β production. The role of MAPKs (p38 and ERK1/2) in this TCS-induced stimulation of IL-1β production was examined by pretreating PBMCs with a selective inhibitor of p38 (SB202190) and a selective inhibitor (PD98059) of the immediate upstream activator of ERK1/2, MEK, for 1h followed by a 6 h exposure to 5, 2.5, and 1 μM TCS. IL-1β production was measured as described above. The results showed that both p38 and ERK 1/2 were needed for TCS to induce increased IL-1β production by immune cells. Using RT-PCR, it was shown that the increase in IL-1β production stimulated by TCS was accompanied by increased mRNA for the protein. These results of these studies verified that TCS increases immune cell production of IL-1β and that this increased production is dependent on MAPK pathways. The ability of TCS to increase production indicates that rather than activating a self-limiting process of depleting cells of already existing stores of IL-1β, TCS is able to stimulate a process that has the capacity to provide sustained production of IL-1β and thus may lead to chronic inflammation and its pathological consequences.