

CURCUMIN INHIBITS THE INCREASE OF GLUTAMATE, HYDROXYL RADICALS AND PGE₂ IN THE HYPOTHALAMUS AND REDUCES FEVER DURING LPS-INDUCED SYSTEMIC INFLAMMATION IN RABBITS

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Evidence has acculated to suggest that systemic administration of lipopolysaccharide (LPS), in addition to elevating tumor necrosis factor- α (TNF- α), interleukin-1 β (IL-1 β), and interleukin-6 (IL-6) as well as fever, induces overproduction of glutamate, hydroxyl radicals and prostaglandin E₂ (PGE₂) in the rabbit's hypothalamus. Current study was attempted to assess whether Curcumin exerts its antipyresis by reducing circulating pro-inflammatory cytokines and hypothalamic glutamate, hydroxyl radicals and PGE₂ in rabbits. The microdialysis probes were stereotaxically and chronically implanted into the preoptic anterior hypothalamus of rabbit brain for determination of glutamate, hydroxyl radicals, and PGE₂ in situ. It was found that systemic administration of LPS (2 μ g/kg) induced increased levels of both core temperature and hypothalamic levels of both glutamate and hydroxyl radicals accompanied by increased plasma levels of TNF- α , IL-1 β , and IL-6. The rise in both the core temperature and hypothalamic glutamate and hydroxyl radicals could also be induced by direct injection of TNF- α , IL-1 β , or IL-6 into the lateral ventricle of rabbit brain. Pretreatment with Curcumin (5-40 mg/kg, i.p.) one hour before an i.v. dose of LPS significantly reduced the LPS-induced overproduction of circulating TNF- α , IL-1 β , and IL-6, and brain glutamate, PGE₂, and hydroxyl radicals. Both the febrile response and overproduction of both glutamate and hydroxyl radicals in the hypothalamus caused by central administration of TNF- α , IL-1 β , or IL-6 could be suppressed by curcumin. These results indicate that systemic injection of Curcumin may exert its antipyresis by inhibiting the glutamate-hydroxyl radicals-PGE₂ pathways in the hypothalamus and circulating TNF- α , IL-1 β , and IL-6 accumulation during LPS-fever.