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Protective effects of scopoletin against caerulein induced acute pancreatitis and pancreatitis associated lung injury

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Background: Acute Pancreatitis (AP) is a potentially fatal inflammatory condition of the pancreas. The pathophysiology of AP is not yet completely understood and therefore its clinical outcome is unpredictable. To develop an effective treatment strategy for AP, requires a better understanding of the biological interactions between signalling molecules. Phytochemicals from various plants are always an important source in the discovery of new therapeutic agents. Our study utilizes scopoletin; a coumarin compound and pharmacologically active agent that posses' excellent anti-inflammatory activities. In this study we explore the underlying anti-inflammatory activity of scopoletin, mediated via regulating CSE/H2S pathway and mast cell stabilization.

Methodology: In our proposed study we use the widely accepted caerulein induced acute pancreatitis model. Acute Pancreatitis was induced via intraperitoneal (*i.p,*) injection of caerulein (50µg/kg), hourly over 6h-period. In the scopoletin treatment group, SC was administered therapeutically one hour (*i.p,* 10mg/kg) after the first caerulein injection. Mice were sacrificed one hour after the final caerulein injection. Blood samples were collected to determine serum amylase levels. The pancreas and lungs were removed for pathological examination and to measure myeloperoxidase activity, cytokine production, NF-κB activation and H2S synthesizing enzyme cystathionine-gamma-lyase (CSE) activity. Furthermore, we examined the effect of SC on mast cell activation, as well.

Results: Therapeutic administration of SC attenuated the severity of pancreatitis and associated lung injury as shown by histology, reduced MPO activity and serum amylase activity. Scopoletin suppressed CSE activity, release of pro-inflammatory cytokines *viz*. interleukin - 1β, tumor necrosis factor α, and Nuclear Factor-Kappa B activation in lungs and pancreas. Interestingly, SC treatment ameliorated mast cell activation as shown by reduced MCP-1, IL-33 and PPT- A expression in pancreas and lungs. Our results suggest that SC exhibits an anti-inflammatory effect in caerulein-induced pancreatitis and associated lung injury via regulating CSE /H2S pathway and mast cell activation.

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