

## Gastroprotective Effects of Mokko Lactone Against Indomethacin-Induced Gastric Ulcer: Emphasis on its Antioxidant, Anti-inflammatory and Anti-apoptotic Activities

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### ABSTRACT

Gastric ulcer is a common gastrointestinal disease with a 5-10% global prevalence. It results from the disturbed balance between protective and destructive factors affecting the gastric lining. Indomethacin was shown to possess great ulcerogenic potential, therefore, it is used to induce gastric ulcers in experimental models. Mokko lactone is a promising guaianolide sesquiterpene lactone with reported antioxidant, anti-inflammatory, and anti-apoptotic properties. Therefore, this study aimed to inspect the defensive effects of mokko lactone against gastric injury induced by indomethacin in rats. The ingestion of a single dose of indomethacin (50 mg/kg) provoked gastric injury manifested as abnormal histological features of the gastric mucosa, which are reflected by the scoring of the gastric injury. Indomethacin-induced gastric injury can be explained through multiple mechanisms including the induction of oxidative stress as proven by increased malondialdehyde (MDA) levels, decreased reduced glutathione concentration (GSH), and decreased the cell defense enzymes, superoxide dismutase (SOD) and catalase, activities. It also increased the gastric tissue expression of the inflammatory proteins, cyclooxygenase-2 (COX-2) and interleukin-6 (IL-6). Moreover, indomethacin decreased the gastroprotective mucin and prostaglandin E2 (PGE2) levels, and increased apoptosis through increased gastric expression of caspase-3. It also induced the degradation of the extracellular matrix by increasing matrix metalloproteinase-9 (MMP-9). Interestingly, the pretreatment with mokko lactone (5 and 10 mg/kg) showed promising gastroprotective activities comparable to those conferred by the potent antiulcerogenic, omeprazole. Pretreatment with mokko lactone restored the normal histological characteristics of the gastric mucosa and decreased the ulcer score; it induced antioxidant effects by reducing the levels of MDA, increased GSH, and induced the SOD and catalase activities; decreased the expression of COX-2 and IL-6; increased gastric mucin and PGE2 content; decreased caspase-3 and MMP-9 tissue expression. In conclusion, mokko lactone induced substantial protective action against gastric damage prompted by indomethacin.

**Keywords:** Indomethacin; Mokko Lactone; Gastric ulcer, guaianolide sesquiterpene

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