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Gender Medicine and Frankincense: Novel Findings in Inflammation Research

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Detailed insights into the pathobiochemical mechanisms of the inflammatory process and the molecular actions of anti-inflammatory drugs are determinants for successful intervention with inflammatory diseases. Gender differences regarding susceptibility to inflammatory diseases are well known, for example rheumatoid arthritis and systemic lupus erythematosus more often affect women. In asthma, sex differences are apparent with a male predominance in childhood, whereas after puberty females predominate, due to a drop in males, reflecting a protective function of androgens. However, the biochemical mechanisms underlying these gender disparities are not understood. Leukotrienes, generated by the 5-lipoxygenase (5-LO) pathway, are involved in inflammatory and allergic disorders, and leukotriene receptor antagonists are used in asthma therapy. We found that leukotriene formation is substantially higher in females versus males, accompanied by different 5-LO trafficking, due to male-specific activation of extracellular signal-regulated kinases (ERKs). The differences are directly related to male/female testosterone levels. Our data suggest that gender issues should be considered in the use of anti-leukotrienes as therapeutics to optimize pharmacological therapy, in men and women.

The anti-inflammatory properties of frankincense, the gum resin derived from *Boswellia* species, are well-recognized. Boswellic acids (BAs) are major ingredients of frankincense that were shown to inhibit 5-LO *in vitro,* but recent data question the pharmacological relevance of such interference *in vivo.* We report about the identification of human cathepsin G as pharmacologically relevant target of BAs. In particular, the major naturally occurring β-BA, reaching pharmacological relevant plasma levels (6.5–10 μM) after oral intake of medical frankincense preparations, potently inhibits cathepsin G *in vitro* and *ex vivo*, and exhibits high efficacy in animal models of inflammation, supporting an anti-inflammatory efficacy of frankincense in patients.

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