A169 **GAMBOGIC ACID AND CELASTROL ARE TWO POWERFUL ANTI-INFLAMMATORY DRUGS IN ARTHRITIS**

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Background Rheumatoid arthritis (RA) is a chronic inflammatory disease where the excessive secretion of pro-inflammatory cytokines plays an important role. The authors have previously reported an increase in circulating interleukin 1 β (IL-1 β) levels in very recent onset arthritis and in the synovial fluid of established RA patients. This observation may be explained by the continuous activation of caspase-1 that the authors observed both in early polyarthritis and in established RA patients. Therefore, pathways that regulate IL-1 β , such as caspase-1 and nuclear factor- κ B (NF- κ B) activation, might play a relevant role in arthritis onset and drugs that target these pathways could potentially constitute promising therapeutic agents in RA. The authors have thus used a THP1 macrophage-like cell line to screen among several Food and Drug Administration approved drugs those which downregulate IL-1 β and caspase-1 activation. Gambogic acid and celastrol were two of the most promising therapeutic candidates obtained by this screening.

Objectives The study main goal was to investigate whether gambogic acid and celastrol administration is able to attenuate inflammation in a rat model of antigen-induced arthritis (wistar AIA rat).

Materials and methods Drugs and vehicle control were administered to arthritic wistar AIA rats after 4 days of disease induction for a period of 15 days. The inflammatory score, paw diameter and body weight were evaluated during the time of treatment. Rats were killed after 19 days of disease evolution and paw samples were collected for histology observation of erosions, pannus formation and cellular infiltration.

Results The authors found that both gambogic acid and celastrol significantly suppressed inflammation in the joints in comparison with arthritic rats treated with vehicle only. Moreover, the rats treated with these drugs did not show differences in body weight or other evident side effects. The histology results revealed that gambogic acid and celastrol treated rats showed a normal joint structure with a complete abrogation of the inflammatory infiltrate.

Conclusions This results suggest that both drugs have significant anti-inflammatory properties, in agreement with their reported ability to suppress NF- κ B activation. Gambogic acid and celastrol might therefore constitute putative anti-inflammatory drugs with therapeutic efficacy in the treatment of inflammatory diseases, such as RA.