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Ahmed Gaafar Ahmed Gaafar, Basim Anwar Shehata Messiha. Ahmed Mohamed Labib Abdelkafy



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ACCEPTED MANUSCRIPT

Nicorandil and theophylline can protect experimental rats against complete Freund's adjuvant-induced rheumatoid arthritis through modulation of JAK/STAT/RANKL signaling pathway

Ahmed Gaafar Ahmed Gaafar^a, Basim Anwar Shehata Messiha^{b*1}, Ahmed Mohamed Labib

Abdelkafy^c

^aPharmacology and Toxicology Department, Faculty of Pharmacy, Port Said University, Egypt

^bPharmacology and Toxicology Department, Faculty of Pharmacy, Beni-Suef University, Egypt

^cPharmacology Department, Faculty of Medicine, Al-Azhar University, Egypt

*The corresponding author: Egypt, Beni-Suef University, Faculty of Pharmacy, Department of Pharmacology and Toxicology. drbasimanwar2006@yahoo.com

Abstract

Signaling pathways are interesting fields of study of pathogenesis and treatment trials. We elucidated the possible protective effects of nicorandil (15 mg/kg/day) and theophylline (20 mg/kg/day) on experimentally-induced RA, focusing on the role of JAK (Janus Kinase) / STAT (Signal Transducer and Activator of Transcription) / RANKL (Receptor Activator of Nuclear factor-Kappa B Ligand) / cytokine signaling pathway. Four sets of experiments were performed. First, effect of test agents on normal animals was evaluated. Second, effect of test agents was evaluated on Complete Freund's Adjuvant (CFA; 0.3 ml, s.c.)-induced RA to investigate anti-arthritic effect. Third, effect of test agents was evaluated on growth hormone (GH; 2 mg/kg/day, s.c.)-induced stimulation of JAK/STAT/RANKL/cytokine signaling pathway to investigate the role of this signaling pathway in their anti-arthritic effect. Fourth, the effect of test agents was

¹ N.B. The indicated corresponding author will handle correspondence at all stages of refereeing and publication, as well as post-publication.

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