OMICS International
conferenceseries.com

Nawaf Farhan Alrawili et al., Clin Pharmacol Biopharm 2015, 4:4
http://dx.doi.org/10.4172/2167-065X.C1.014

Pharma Middle East
November 02-04, 2015 Dubai, UAE

Investigation of the anti-inflammatory effects of Rolipram in a rat model of rheumatoid arthritis

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Background & Aim: Rheumatoid Arthritis (RA) is an autoimmune disorder of unknown cause. It is a highly inflammatory polyarthritis disease often leading to joint destruction, deformity and loss of function. There is conflicting data about the effect of PDEIs on pathogenesis of RA. This work aims at investigation of the effect of rolipram as representative of PDEIs on signs, symptoms, histopathology and cytokines of Adjuvant-Induced Arthritis (AIA), a model of RA in rats that exhibit several pathological changes similar to those occurring in RA.

Methods: In the present study, we used rat model of Adjuvant-Induced Arthrits (AIA), a model of RA in rats that exhibit several pathological changes similar to those occurring in RA in human, by sub-plantar administration of Freund's adjuvant into hind paws of rats. Arthritis index, volume of hind paws edema, body weight ,rectal temperature and pain threshold to pressure on hind paws, were measured daily from day 0 until day 30 after adjuvant inoculation. At the end of the study, the animals were sacrificed and the blood was collected for measurement of serum levels of TNF-alpha and IL-10. To assess the secondary immune reaction, specimens of left ankle joint tissues were also examined for histopathology.

Results: Rolipram therapy, either prophylactic or therapeutic, significantly leads to marked suppression of adjuvant arthritis in rats depending on the dose administered. The therapeutic efficacy of rolipram was evidenced by decreased arthritic scores, and hind paw volumes of arthritic rats. Hyperalgesia of adjuvant arthritic rats was significantly reduced in rolipram-treated animals compared to non-treated group. Prophylactic rolipram protocols have dramatic protective effect as evidenced by inhibition of inflammatory cellular infiltrate in synovium of arthritic rats, pannus formation and alleviation of the destruction of the articular cartilage. The present study demonstrated that prophylactic or therapeutic administration of rolipram did not alter significantly the serum level of TNF-α. Regarding IL-10, our study demonstrated a significantly augmenting effect of treating adjuvant arthritic rats with rolipram, from day 16 to day 25 after disease induction in a dose of 3 mg/kg/d given orally. Interestingly, the present work demonstrated that joint inflammation was significantly attenuated by DMSO treatment as evidenced by lower clinical scores and reduced paw swelling.

Conclusion: The results presented in this study shows that rolipram, a PDE 4 inhibitor displayed an anti-inflammatory, anti-arthritic and anti-hyperalgesic actions in adjuvant arthritic rats in a dose-dependant manner. In conclusion, these findings suggest that rolipram may have therapeutic value for various autoimmune diseases such as rheumatoid arthritis.

Biography

Dr. Romany Helmy Thabet has completed his PhD at the age of 30 years from University of Assiut, Egypt. Now He is an assistant professor of Pharmacology, faculty of medicine, NBU, KSA. He has published several international papers in reputed journals. His Co-investigators are Nawaf Farhan Alrawili and Meshal Odhayb Alanazi who are now internship at Prince Sultan Military Medical City (PSMMC) in Riyadh, KSA.

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