

**Title:** Efficacy of oral gallium maltolate in acute and chronic models of rheumatoid arthritis

**Author(s):** Schwendner, Susan W.; Allamneni, Krishna P.; Bendele, Alison; Bucalo, Louis; Sreedharan, Sunil P.

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**Abstract:** Gallium maltolate (GaM) is an oral agent currently in phase I clinical development. The objective of this study was to test the effect of GaM in acute and chronic rodent models. In the adjuvant-induced arthritis (AIA) model, rats received Freund's complete adjuvant in the base of the tail. GaM (0, 100, or 300 mg/kg, po, qd), or dexamethasone (0.1 mg/kg), were administered for 14 days. Significant dose-dependent protection from adjuvant induced ankle swelling (53-88%) joint inflammation (19-46%), bone resorption (43-71%), splenomegaly (36%), and body weight loss were observed with GaM treatment. In a reactivated peptidoglycan-polysaccharide (PGPS) induced arthritis (PIA) model, rats received intra-articular PGPS and 2 biweekly systemic reactivations. Rats were treated with GaM (0, 100, 200 or 300 mg/kg, po, qd) or Cyclosporin A (5-20 mg/kg) until one week after the second reactivation. GaM treatment resulted in a 20-45% inhibition of summed histopathologic scores of arthritic ankles. and had a significant effect on ankle swelling, with significant improvement in periosteal proliferation (18-38%). In conclusion, oral gallium maltolate was effective in improving periarticular inflammation, cartilage destruction, bone damage, and other arthritic complications in acute and chronic rodent models of rheumatoid arthritis.