

[2005] [THU0198] ORAL GALLIUM MALTOLATE IS EFFICACIOUS IN ACUTE AND CHRONIC MODELS OF RHEUMATOID ARTHRITIS

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Background: Gallium, administered intravenously as a salt or a chelate, has demonstrated therapeutic activity in cancer, hypercalcemia and bone disease. Gallium maltolate is an orally active complex currently in phase I clinical development.

Objectives: The objective of the current study was to evaluate the antiarthritic potential of gallium maltolate to improve periarticular inflammation, cartilage destruction, bone damage, and other arthritic complications in acute and chronic rodent rheumatoid arthritis models.

Results: Gallium maltolate was first evaluated in an acute model of developing adjuvant-induced arthritis. Rats (n=4-7 per group) were injected s.c. in the tail base with Freund's complete adjuvant/lipoidal amine, then treated daily with gallium maltolate (100 or 300 mg/kg, p.o.) or dexamethasone (0.1 mg/kg). Serum gallium levels obtained were dose-dependent, with no clinical signs of dose toxicity. Gallium maltolate treatment resulted in significant dose-dependent protection from adjuvant induced ankle swelling, joint inflammation, bone resorption, splenomegaly and body weight loss.

Gallium maltolate was then evaluated in a chronic model of reactivated peptidoglycan-polysaccharide (PGPS)-induced arthritis. Rats (n=12 per group) received an initial intra-articular injection of PGPS and two biweekly systemic reactivations. Concurrently, rats were treated with daily oral doses of gallium maltolate (100, 200, or 300 mg/kg) or cyclosporin A (5-20 mg/kg). At one week following the second reactivation, the rats were euthanized and ankles scored for joint histopathology. Gallium maltolate was safe and effective in this model as demonstrated by a 20-45% inhibition of summed histopathologic scores of arthritic ankles. Evaluation of ankle caliper measurements during multiple reactivation of inflammatory disease indicated that gallium maltolate was therapeutically effective with significant dose-dependent reduction of ankle swelling. There was also significant improvement in periosteal proliferation and summed joint histopathology scores of the arthritic ankles.

Conclusion: Oral administration of gallium maltolate was efficacious, improving periarticular inflammation, cartilage destruction, bone damage, and other arthritic complications in acute and chronic rodent models of rheumatoid arthritis.

Rheumatoid arthritis Etiology and pathogenesis/Animal models

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