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SUMMARY OF RESEARCH RELATING TO TOPICAL GALLIUM MALTOLATE

Gallium maltolate is a coordination complex consisting of gallium, a semi-metallic element, and maltol, a sugar-like compound found naturally in many foods. As an uncharged, pH-neutral molecule that is soluble in both water and lipids, gallium maltolate is non-irritating and well absorbed by the skin.[3]

ANTI-INFLAMMATORY ACTIVITY OF GALLIUM

Numerous *in vitro* and animal studies have demonstrated that gallium can suppress pathological inflammation without being generally immunosuppressive. Gallium appears to be particularly effective at inhibiting abnormal T-cell mediated immunological reactions. Though it suppresses inflammatory T-cell activation and proliferation, gallium does not interfere with normal cytokine-activated killer T-cell activity or with the normal cytokine-mediated growth and repair of endothelial cells (which may actually be enhanced by gallium).[9,11] Gallium has also shown selective activity against pathological pro-inflammatory activity by macrophages.[16,17,18]

Intravenously administered gallium nitrate has shown efficacy in a number of rodent models of T-cell mediated autoimmune disease. Efficacy has been observed in adjuvant-induced arthritis, experimental autoimmune encephalomyelitis (a model for demyelinating diseases such as multiple sclerosis), experimental autoimmune uveitis, systemic lupus erythematosus, and Type 1 diabetes.[1,10,15,22]

Orally administered gallium maltolate demonstrated efficacy in two models of inflammatory arthritis in rats: adjuvant induced arthritis and streptococcus cell wall induced chronic arthritis.[19] In both models, oral gallium maltolate dose-dependently reduced joint inflammation, bone degradation, liver and spleen enlargement, and other measures of inflammation. No toxicity was observed.

Many of these immunomodulating effects are likely related to Ga^{3+} being a close chemical mimic of Fe^{3+}: Ga^{3+} competes with the transport and uptake of Fe^{3+}, but is biochemically non-functional because it lacks Fe^{3+}'s redox activity (its ability to exist in both divalent and trivalent states under physiological conditions).[2] Pro-inflammatory T-helper type 1 (Th-1) cells are much more sensitive to inactivation by iron deprivation (from, e.g., competition with gallium) than are anti-inflammatory, pro-antibody Th-2 cells.[21] The known antiproliferative activity of gallium (due to its interference with Fe^{3+}-dependent ribonucleotide reductase activity, and thus DNA synthesis), in this case on certain lymphocytes, may also contribute to gallium's immunomodulating activity.[2] Antiproliferative activity also makes gallium active against some cancers as well as some pathogenic bacteria and viruses,[2,4,8] further contributing to gallium's efficacy.

Clinical observations — Although no controlled human clinical trials have been performed, hundreds of individuals have used topically administered gallium maltolate (0.5% in an emulsion of water and hydrophilic petrolatum) on a wide variety of skin lesions. Apparent efficacy has been observed in cases of psoriasis, acne vulgaris, acne rosacea, seborrheic dermatitis, eczema, hemorrhoids, herpes simplex lesions, and actinic keratosis.

ANALGESIC ACTIVITY

Gallium maltolate has been administered topically to hundreds of individuals suffering from various types of pain. The first case was a 99-year-old woman who had severe facial (trigeminal) postherpetic neuralgia for four years and who had responded poorly or not at all to a large variety of systemic and locally administered narcotics, anesthetics, analgesics, anti-epileptics, anti-psychotics, and other medications. Topically applied, low-dose gallium maltolate provided nearly complete pain relief that lasted about six to eight hours.[5] Topically administered gallium maltolate has also been found effective in other individuals against postherpetic neuralgia and against pain due to trigeminal neuralgia[6], arthritis, tendinitis, insect bites and stings, spider bites, infections, burns, allergic reactions, plantar fasciitis, complex regional pain syndrome,

cancer, and post-surgical facial pain[12]. The mechanisms for the analgesic activity are not known; they likely relate to gallium's anti-inflammatory activity, plus its possible interference with certain neuropeptides and matrix metalloproteinases (MMPs). Many neuropeptides, and all MMPs, are zinc-dependent, and gallium may act as a zinc mimic in some circumstances.[2] Several MMPs are implicated in the pathogenesis of neuropathic pain,[7,11,13] and substance P, a pain-associated neuropeptide, may be inhibited by high concentrations of zinc.[20] It is also possible that gallium is acting on the NMDA receptor or on one or more presently unknown pain pathways.

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