INTRODUCTION

Gallium maltolate, an experimental anticancer compound, has been discovered to have an intriguing additional effect against neuropathic pain, the skin or mucus membranes. In several case studies involving neuropathic pain, topical gallium maltolate demonstrated remarkable efficacy, even when other analgesic agents had been ineffective.

Gallium

The semimetallic element gallium has repeatedly shown anti-inflammatory and anti-inflammation activities in preclinical and clinical studies [1]. These biological activities stem largely from the chemical similarities between Ga3+ and Fe3+ (feric iron), which allow gallium to enter many of the biochemical pathways of ferric iron. Unlike ferrous iron, however, gallium is unable to be reduced to the divalent state under physiologic conditions, and it thus cannot participate in redox reactions. These factors make gallium an irreplaceable, and therefore non-functional, biochemical mimic of ferric iron.

For example, the iron transport protein transferrin can bind to Ga³⁺, which can then be internalized by rapidly multiplying cells that overexpress transferrin receptor—in particular, many types of cancer cells. Such cells require iron to synthesize DNA, because the enzyme ribonucleotide reductase requires feric iron in its active site. Gallium, by acting as a non-functional competitive mimic of feric iron, can act to inhibit DNA synthesis and thus cellular proliferation [1].

The potent anti-inflammatory activity of gallium is due in part to its ability to selectively inhibit the activity of members of the TpH type 1 (pro-inflammatory) cells, and also the secretion of pro-inflammatory cytokines from activated macrophages. Small molecules containing iron tend to be highly pro-inflammatory; it is likely that gallium enters these inflammatory pathways but, due to its lack of redox activity, suppresses inflammation [1].

Gallium Maltolate

Gallium maltolate (GaM) is a coordination complex of gallium and maltolate. The hydroxochromochelate is naturally present in many plants and also occurs in baked foods, where it is a sugar degradation product. Due to its octanol-water partition coefficient of 0.41, it is soluble in both aqueous and lipid phases. GaM allows easy penetration of skin and cell membranes, including the membranes of neurons.

Anti-inflammatory activity has been shown in rat models of rheumatoid arthritis, in which orally administered GaM significantly inhibited ankle swelling, joint pain, bone degradation, and enlargement of the spleen and liver [2]. In human cancer clinical trials, GaM has been well tolerated, with no dose-limiting or other toxicities observed at oral doses of up to 3500 mg/day. GaM is known to be taken up by rapidly multiplying cells that overexpress transferrin receptor [2]. In human cancer clinical trials, GaM, dramatic pain reduction has often been noted, though it has not been clear whether the anti-cancer or anti-inflammatory effect was or primarily related to GaM’s anticancer activities.

CASE STUDIES

Materials: For most of the case studies reported here, a topical cream formulation was prepared that consisted of 0.5% w/w GaM in an emulsion of 50% w/v water and 50% w/v hydrophilic petrolatum. For one case (tongue cancer), a solution of 1% GaM in water was used.

Doses: Patients in these cases received a maximum of a few milligrams of GaM in one or two applications. In some cases, less than 1% of the daily dose of GaM, or about a thousandth of the doses found to cause no serious adverse effects in the clinical trials of oral GalM.

Other Cases

Two other patients with refractory postherpetic neuralgia (a 73-year-old man and a 72-year-old woman) experienced substantial pain relief from the topical GaM cream. Analgesia with severe, refractory trigeminal neuralgia experienced great pain relief within 20 minutes of applying GaM cream. Other individuals have experienced substantial relief of pain and itching following burns, hemangiomas, insect bites, spider bites, psoriasis, surgery, trauma, and complex regional pain syndrome. The author experienced nearly complete elimination of pain following a bee sting, without numbing.

REFERENCES