

Gallium uses

In animal models - and in humans to some extent - Ga has been shown to have efficacy in the treatment of arthritis, type 1 diabetes, experimental autoimmune encephalomyelitis, pulmonary inflammation, cardiac allograft rejection, autoimmune uveitis, endotoxic shock, and systemic lupus erythematosus. Clinical trials have demonstrated efficacy of Ga in Paget's disease of bone. Other clinical trials underway include studies of Ga for sarcoidosis and rheumatoid arthritis.

Based upon its pharmacological properties, Ga may be found to have benefits not only in other autoimmune diseases, such as multiple sclerosis, but also in graft-versus-host disease, leprosy, and acquired immunodeficiency syndrome (AIDS). Ga has been found to have strong anti-HIV properties.

Ga is also known to have immunosuppressive capability, and it has strong beneficial effects generally on inflammation and edema. Unlike steroids, it does not injure the immune system. Injectable GN solutions, approved in the United States for the treatment of hypercalcemia of malignancy, have been known for more than 2 decades to have immunosuppressive properties. At therapeutic doses, Ga has few adverse effects, although high-dose IV infusions may result in severe anemia and severe nephrotoxicity, particularly in patients who are not adequately hydrated. To prevent these side effects, GN is suggested to always be given highly diluted and given with large amounts of water.

Ga has been used to treat other bacterial infections. For example, delivered subcutaneously it produced 100% survival in the lethal *P. aeruginosa*-infected thermally injured mouse model. Ga works in part by decreasing bacterial Fe uptake and by interfering with Fe signaling by the transcriptional regulator *pvdS*. Ga inhibited

Pseudomonas aeruginosa growth and biofilm formation and killed planktonic and biofilm bacteria in vitro. Ga was also shown effective in 2 murine lung infection models. Ga is being investigated to determine its efficacy in suppressing *Rhodococcus equi*, the cause of foal pneumonia. The antibacterial effects of Ga appear extremely broad, since they terminate the growth of all iron dependent bacteria, fungi and parasites. Since Ga does not kill bacteria outright, they do not become resistant to it.

Iron-dependent pathogenic microorganisms treatable with Ga comprise: *Streptococcus*, *Staphylococcus*, *Yersinia*, *Salmonella*, *Chlamydia*, *Coxiella*, *Ehrlichia*, *Francisella*, *Legionella*, *Pasteurella*, *Brucella*, *Proteus*, *Hilicobacter*, *Klebsiella*, *Enterobacterium*, *Escherichia*, *Tropheryma*, *Acinetobacter*, *Aeromonas*, *Alcaligenes*, *Campylobacter*, *Capnocytophaga*, *Bacillus*, *Clostridium*, *Corynebacterium*, *Erysipelothrix*, *Listeria*, *Mycobacterium*, *Pseudomonas*, *Streptococcus mutans*, *Streptococcus sanguis*, *Streptococcus gordonii*, *Atopobium parvulum*, *Porphyromonas gingivalis*, *Eubacterium sulci*, *Staphylococcus aureus*, *Streptococcus pneumoniae*, β -hemolytic streptococci, *Corynebacterium minutissimum*, *Microsporum audouinii*, *Microsporum canis*, *Microsporum gypseum*, *Sporothrix schenckii*, *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Pityriasis versicolor*, *Exophiala werneckii*, *Trichosporon beigeli*, *Malassezia furfur*, *Fusarium* spp. and *Aspergillus* spp.; including the microorganisms that are known to have become resistant to first-line antibiotics. Such resistant microorganisms include *Escherichia coli* O157 (a causative organism for gastroenteritis, haemorrhagic colitis or urinary and genital tract infections), vancomycin-resistant *Enterococcus faecalis* (a causative organism for endocarditis, urinary tract infections, and wound infections), methicillin-resistant *Staphylococcus aureus* (MRSA; a causative organism for various skin infections, eye infection, wound, oral and other infections), *Salmonella* LO typhi (the causative organism for typhoid fever), and fungi, such as *Candida albicans*, *Coccidioides immitis*, *Histoplasma capsulatum*, *Blastomyces dermatitidis*, *Aspergillus fumigatus*, *Epidermophyton* spp., ,

Zygomycetes spp., *Rhizopus* spp. and *Mucor* spp.

Miscellaneous applications of mild, soluble Ga compounds may be utilized in many different applications. For example, Ga compounds may be applied topically or directly to a body area, including an open wound and an internal organ or tissue exposed to an outer environment during surgery in addition to an external area that needs to be protected from or is afflicted with various infections caused by pathogenic organisms.

GN solutions of up to 42% have been used to treat some skin infections, although there may be discomfort. Such infections include acne, cellulites, folliculitis, boils, carbuncles, erysipelas, impetigo, erythrasma, paronychia, staphylococcal scalded skin syndrome, candidiasis (e.g., oral thrush), and ring worm, tinea versicolor and methicillin-resistant *Staphylococcus aureus* (MRSA). Eye infections, such as blepharitis, hordeola and conjunctivitis, must be treated with a < 1% solution and not stronger solutions to prevent eye pain. Causative organisms for skin infections include species of *Staphylococcus*, such as *S. aureus* and *S. epidermidis*; Group A streptococci, such as *Streptococcus pyogenes* and *Pseudomonas aeruginosa*. Typical yeasts or fungi that cause skin infections include *Candida albicans*, species of genus *Microsporon*, such as *M. auduini* and *M. canis*; species of *Trichophyton*, such as *T. metagrophyte* and *T. tonsurans*. Causative organisms for eye infections include *Staphylococcus aureus*, *Streptococcus pyogenes*, *Haemophilus influenzae*, *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Propionibacterium*, *Nocardia*.spp, *Bacteroides* spp and *Fusarium* spp. Nasal infections caused by *Streptococcus pneumoniae* may lead to ear infection, sinusitis, bronchitis, and pneumonia. Heavy metals, such as zinc, nickel and cadmium, have been shown to cause persistent to permanent anosmia when directly applied to the olfactory organ, and caution is advised when applying Ga, a heavy metal, to the nose. The infections caused by these organisms have become more and more common because of the development of drug-resistant microorganisms, such as MRSA, as well as due to the

increased number of immune-compromised individuals due to HIV infection or AIDS, organ transplants and treatments for autoimmune diseases.

Thus, the applications of Ga compounds for human uses as well as veterinarian uses appear highly beneficial especially in view of their low toxicity, absence of side effects and very low risks for generating resistant micro-organisms. Even nanobacteria appear treatable with Ga, resulting in removal of pathological calcium from kidneys, uterus, arteries and eyes.

Probiotic (beneficial) intestinal microorganisms including species of the genera Lactobacillus, Lactococcus and Bifidobacterium are not affected by Ga because they are not iron-dependent. In practice Ga appears harmless to beneficial intestinal bacteria in humans and horses and most likely other species, and oral GN has been used to treat navicular disease in tens of thousands of horses since 1996 without producing colic or other side effects, and it appears harmless in the treatment of human and equine arthritis.

Oral GN solutions must be <1% to prevent mouth discomfort and pain. Severe overdose of Ga may result in displacement of other minerals in tissues and blood, with toxic or even fatal consequences. Modest overdose of GN may cause dizziness, nausea, anorexia, allergy-like symptoms, abdominal cramps, vomiting, itching, bone marrow depression leading to anemia, bloody diarrhea, and blood damage with subsequent renal damage, weakness, convulsions, gastrointestinal tract injury and collapse.

Severe overdose of nitrates may lead to weakness, depression, headache, and mental impairment. GN must not be given with drugs that have kidney injuring potential such as aminoglycosides and amphotericin B, other drugs that lower blood pressure (BP) (since the nitrate in GN may lower BP), and drugs such as Viagra and Cialis and other drugs that are not to be taken with nitrates.