Immunosuppresive Activity of Spirogermanium (SG) on T-Cell Activation and Inflammatory Cytokine Secretion In Vitro

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Division of Clinical Pharmacology, Clinical Research Center, UMDNJ -Robert Wood Johnson Medical School, New Brunswick, New Jersey; and *GeoMed, Inc., Menlo Park, California Spirogermanium (SG) is a novel germanium-containing azasprine compound reported to have antitumor, antiarthritic, and immunomodulatory activity, in this study we were interested in determining the immunosuppressive potentials of SG. We isolated peripheral blood mononuclear cells (PBMC) from healthy human volunteers, induced lymphocyte proliferation with phytohemagglutinin, and incubated them with SG in vitro from concentrations of 0.0006 µg per ml to 10 µg per ml in vitro. After an incubation period of 72 h, cell viability was determined using trypan blue dye exclusion method, a cell proliferation assay was done using BrdU incorporation assay, and interleukin-2 (IL-2), gamma interferon (01γ-IF) and tumor necrosis factor alpha (TNF-01α) cytokine enzyme-linked immunosorbent assays (ELISA) were done on cell culture supernatants. SG was shown to effectively inhibit T-lymphocyte proliferation in vitro by around 100% at concentrations 0.0012-0.15 µg per ml at which cell viability was found to be above 95%. IL-2 and 01γ-IF secretions were strongly inhibited at concentrations of SG above 0.0012 μg per ml, TNF-a secretion was strongly inhibited at concentrations above 0.0098 µg per ml. Our results demonstrate that SG is a potent inhibitor of mitogen induced T cell proliferation and the secretion of inflammatory cytokines IL-2, 01γ-IF, and TNF-01α at noncytotoxic concentrations. SG may have potential beneficial effects in T cell mediated-disorders such as psoriasis, rheumatoid arthritis, inflammatory bowel disease, multiple sclerosis and transplantation rejection.