**Rationale of the study**

Indukantha Ghritha (IG) is a polyherbal drug preparation, used in ayurveda for many centuries. Preliminary study in this laboratory showed IG to stimulate cell mediate immune responses and also to have a lymphopoietic effect. However the mechanism of action or the probable benefits to cancer patients have not scientifically been documented yet. Hence the present thesis focused on evaluating the immunomodulatory mechanism of Indukantha Ghritha in recurrent respiratory tract infected patients and also in healthy control subjects and an attempt to evaluate its efficacy to counteract immunosuppression and thus could be used as an adjuvant to cancer chemotherapy.

The advantages of natural source medicine are gradually being recognized, the usage of herbal remedies is increasing globally. Use of specific herbs which are very helpful in preventing the progression of the disease also improves the quality of life of the individuals. However, there is relatively little information about the potentially serious consequences and quality of herbal medicine products in the scientific literature. Therefore the extending and expanding use of herbal products demand further attention with a particular focus on their safety and efficacy. Hence the recommended dose regimen, quality and toxicity of IG was investigated.

The immunomodulatory properties and mechanism of action of herbal medicines will provide new insights into immune function and possible avenues of immunotherapy and more widespread use of this centuries old practice of using this medicine. Lag phase for botanical medicine is now rapidly changing for a number of reasons. Problems with drug-resistant microorganisms, side effects of modern drugs, and emerging diseases where no medicines are available, have stimulated renewed interest in plants as a significant source of new medicines. Many herbal preparations alter immune function and have had an amazing array of immunomodulatory effects attributed to them. Hence immunomodulatory role of IG was assessed in terms of modulation of immune parameters such as lymphocyte subsets, lymphocyte and macrophage function, T cell signal proteins, cytokine etc.

Although significant progress has been made in cancer chemotherapy, current drugs are ineffective against many common cancers and are often very toxic. Also at the current time, it is apparent that drug-based therapeutic strategies will predominate
into the 21st century. For these reasons the discovery of new drugs effective against tumors is an important and necessary strategy in improving chemotherapy. Natural products have provided the most important successes in the chemotherapy of cancer. Hence this study also focuses on the anticancer activity of IG in tumor bearing mice.

The major side effect of anticancer drugs, e.g. cyclophosphamide, is the non-specific cytostatic action on normal healthy cells. The extensive death of the immune cells results in leukopenia which severely weakens the immune system of cancer patients and therefore greatly increases the chance of disseminated infections which could be fatal. As a result, drug-free period is always clinically necessary in cancer patients receiving chemotherapy, so as to allow their immune systems to restore function. Hence one of the aims of the thesis was to study the protective effects of Indukantha Ghritha against cyclophosphamide induced toxicity.

It is relevant here to add that evidence of clinical exposure, and thus safety, can often be documented for traditional herbal medicines. Such products can be evaluated in small, well-designed and controlled, clinical studies to test ‘proof of concept’ negating the need for significant investment in preclinical safety prior to having confidence that one has a potential product. Hence the study also assessed the safety and efficacy of IG in healthy control subjects and recurrent respiratory tract infected (RRTI) patients.

**Therefore, the specific objectives of this study were:**

1. To evaluate the immunomodulatory activity of the drug, in toto, in the form given to patients, in patients and experimental animals.
2. To identify the cell populations responsible for the increase in terms of leucocytes and their subpopulations, and also to evaluate the effect on lymphocyte functions, phagocytosis etc.
3. To evaluate its effect on experimentally induced tumors with respect to tumor regression, effects on lymphocyte population numbers and function etc.
4. To assess if IG has the potential to induce leucopoiesis in mice given chemotherapy.
5. To evaluate the efficacy of Indukantha Ghritha in modulating the immune status of the patients with recurrent respiratory infection and healthy subjects.