CHAPTER 9

SUMMARY AND CONCLUSION
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Indukantha Ghritha (rasayana) is a polyherbal preparation made from 17 plants with various biological activities. IG is used in ayurveda for different types of fevers, gastric disorders, cough, respiratory disorders, dyspnoea, as rejuvenation therapy etc. However mechanism of its action is not documented. Hence the thesis focused on the immunomodulatory effects of Indukantha Ghritha (IG) after oral administration in mice and humans. To date, research has mainly focused on identifying the beneficial components of herbs and there has been little study on the possible side-effects of natural products. Time dependant and dose dependant studies were carried out to evaluate the recommended dose regimen, quality and toxicity of the herbal medicine Indukantha Ghritha. Balb/c mice aged 5-6 weeks weighing 20 – 25 gms were used in the present study. IG was given at varying doses from 30 to 1000 mg/kg body weight for 14 consecutive days to determine optimum dose and toxicity for time dependant studies, 250mg/kg body weight was administered for 3,7,14,21 and 28 days. Histological examination of the organs also did not reveal any pathological changes. Histopathological studies also provided supportive evidence for the biochemical analysis. The basic principle in the use of polyherbal preparations in traditional medicine, where the adverse effects of one component will be nullified by the protective effect of the other components, without interfering with their therapeutic properties. Immune parameters evaluated included hematologic parameters, lymphocyte subpopulation enumeration, phagocytic activity of peritoneal macrophages, effects on T-cell signal transduction proteins, Th1/Th2 cytokine profile. The immune response started showing an increase on 3rd day of administration reaching a plateau on the 14th day of administration. Our results also showed increase in the levels of circulating Th1 cytokines IL-2, IFN γ, IL-12 and reduced levels of Th2 cytokine IL-4 along with increase in GM-CSF and MIP-1α.

Indukantha Ghritha was also evaluated for its protective effects against cyclophosphamide induced toxicity and tumor bearing animals. However, the chemotherapy has many toxic and side effects. The life quality of patients who receive chemotherapy treatment is poor because of the side effects of drugs. To improve the clinical application of Indukantha Ghritha, it is very important to know whether they
are able to promote restoration of damaged immune functions. In this study, a cyclophosphamide-treated mouse model was proposed as an approximation for immunomodulation studies in immunocompromised individuals. Mice received cyclophosphamide at a total dose of 250 mg/kg intraperitoneal injections scheduled at day 1 (150 mg/kg) and day 4 (100 mg/kg). The administration of IG restored the immune response in mice to normal levels, suggesting that IG negates the inhibitory action of CTX treated mice. No toxicity of any kind was observed up to a concentration of 1000 mg/kg Body weight.

In addition, study was also performed to evaluate the efficacy of IG when combined with chemotherapy in treating DLA induced solid tumor and EAC ascites in order to substantiate its therapeutic link with regard to their clinical utility. The results from the present investigation had shown that IG effectively induces apoptosis and stimulates immune response in EAC induced ascites tumor model. DLA induced solid tumor was also found to be significantly reduced after IG administration. IG was administered along with CTX in both EAC ascites and DLA solid bearing mice showed significant restoration of values near to basal levels in almost all groups indicating the ability of IG to counteract immunosuppression and thus could be used as an adjuvant to cancer chemotherapy.

The experimental studies were supported by studies in humans. A randomized control clinical trial was carried out in patients with respiratory infections and healthy control subjects. Evaluation of hematological parameters, lymphocyte subset analysis by flow cytometry, levels of circulating immunoglobulins and Th1/Th2 cytokine profile were evaluated before and after administration of IG for 28 in patients with recurrent respiratory tract infection and healthy control subjects. The baseline characteristics of healthy control subjects and demographic, clinical characteristics of the recurrent respiratory tract infected patients group were evaluated. The levels of type 1 cytokines, IFN-γ and IL-2, in patients were significantly lowered when compared with those in healthy control. In contrast, the levels of type 2 cytokines, IL-4 in patients were significantly higher than those in healthy subjects. These results further demonstrated that type 2 cytokine predominance was present in respiratory tract infection. During outpatient follow-up, the patient presented an improvement in
the clinical condition and laboratory findings, including normalization of blood test and remission of symptoms after 28 days of IG treatment. The results imply that respiratory tract infected patients benefit from IG treatment alleviated symptoms associated with recurrent respiratory infection. IG showed significant immune-modulating effects by modifying lymphocyte subpopulations and cytokine secretion. Toxicity was assessed by evaluating the liver and renal function tests.

In conclusion, the present study demonstrated that reversing effects on type 2 cytokines and promoting effects on type 1 cytokines by Indukantha Ghritha (IG) -a classic ayurvedic rasayana drug, will be a promising candidate for treating type 2-biased diseases including tumor, allergic disease and intracellular pathogenic infections.