A Clinical Assessment of Changes in Cell Mediated Immune Response Induced by Geriforte (An Ayurvedic Herbal Rejuvenative Drug)

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INTRODUCTION
"Geriforte" a geriatric tonic, widely used in this country has been recently reported to induce a state of non-specific increased resistance (SNIR) in animals during stress and was found to prevent various deleterious effects like gastric ulcers, adrenal hyperplasia etc. caused by stress (Singh et al., 1978). This drug was also found to prevent urethane induced lung-adenomas in mice and to cause a marked increase in total lymphocyte count, which by increasing the immune response of the animals might have been responsible for prevention of carcinogenesis (Singh et al., 1980). Besides, it also has anti-viral activity against live-vaccinia virus which, may be again because of its immunostimulant effects (Singh et al., 1981). Considering the above facts, it was thought fit to evaluate its immuno-modulator activity in human subjects through this study.

MATERIAL AND METHOD
The study was conducted in male subjects of 40-65 years age group. Their immune status was assessed by DNCB skin sensitization technique modified by Bleumink et al., (1974).

Initial skin sensitization with 0.2 ml., 1000 µg. 2, 4-dinitro chlorobenzene (DNCB) was done on the flexor surface of the forearm. The area was covered with a gauze piece after the liquid had evaporated. Signs and symptoms like redness, itching etc. were observed after removal of the gauze piece after 48 hrs. initially. Cases which took up the sensitization as evidenced by a local reaction at 48 hrs. after initial application of DNCB were selected for this study. Technical errors like improper dilutions and bacterial contamination were avoided. Care was taken in proper evaluation of the signs and symptoms. The challenge was done after 14 days with 0.1 ml. (100 µg) of DNCB and those subjects who scored (0 or 1) on first challenge dose formed the sample (30 subjects). Signs and symptoms were scored as follows:

- 0 – No reaction,
- + –Erythema,
- 2+ – Erythema and induration,
- 3+ – Erythema, induration and vesiculation,
- 4+ – All above + ulceration.

Out of 30 subjects selected for this study, 20 subjects served as the experimental group and received treatment with Geriforte 2 tablets b.i.d. continuously for next 4 weeks and the other 10 subjects who served as controls received a placebo of multi-vitamin tablets with identical red coloured coating as that of Geriforte tablets with a dose of 2 tabs. x b.i.d. for 4 weeks. The immune status of both the groups was reassessed after the 2nd and 3rd challenges with DNCB done on the 14th and 28th day drug treatment respectively.
RESULTS
Results are summarised in Table I. The subjects who received Geriforte treatment for 4 weeks scored significantly ($p<0.01$) as compared to control group. However, no such increase of scoring was found after 2 weeks of treatment.

<table>
<thead>
<tr>
<th>Group</th>
<th>Age group</th>
<th>Pre-therapy 1st challenge</th>
<th>Post-therapy</th>
<th>Second challenge (2 weeks)</th>
<th>Third challenge (4 weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (n = 10)</td>
<td>44-60</td>
<td>0.8 ± 0.01</td>
<td></td>
<td>1.6 ± 0.01</td>
<td>1.6 ± 0.02</td>
</tr>
<tr>
<td>Geriforte (n = 20)</td>
<td>40-65</td>
<td>0.9 ± 0.013</td>
<td></td>
<td>1.4 ± 0.02</td>
<td>2.8 ± 0.02*</td>
</tr>
</tbody>
</table>

*p<.01, n=number of subjects.

DISCUSSION
Geriforte, an Ayurvedic restorative tonic consisting of several herbal drugs is being used in this country for problems of ageing and allied diseases (Setty and Ambas, 1978). 'Panex ginseng' a single plant drug is being used for similar conditions in European continent (Papov, 1975). Recently Singh, et al., 1978 attributed antistress "Adaptogenic" properties to this drug and later suggested its use in several stress-induced diseases (Singh, et al., 1981). The reason for its being useful in a variety of disease processes appear to be due to the presence of plants like Celastrus paniculata and Withania somnifera which possess anti-stress properties (Singh, et al., 1974; Singh, et al., 1982). Besides this the presence of tumour preventing and antiviral activity in this drug (Singh, et al., 1980, 1981) may be due to its immunomodulator effect. Furthermore, continuous treatment with this drug markedly increased the number of lymphocytes in the blood of mice (Singh, et al., 1980). The present study was undertaken to assess the effect of this drug on the immune response in man.

Direct application to the skin of chemically reactive compounds results in systemic sensitization to various metabolites of the sensitizing compound. In case of DNCB probably dinitrophenyl protein complexes are formed with various skin proteins. It takes 7-10 days before contact sensitivity can develop and persists for a year. The ability of an individual to develop contact sensitivity is a measure of cellular immunity to a new antigen to which the object has never been exposed previously. Thus the establishment of a state of cutaneous anergy in various disease states may be confirmed and extended by testing with DNCB. The DNCB sensitization is a type IV allergic reaction (delayed hypersensitivity or cell mediated immunity). Antigen specific receptors develop on T lymphocytes and subsequent administration leads to local reaction or tissue allergic reaction. Our results show that 4 weeks treatment with "Geriforte" significantly ($p<0.001$) enhances this reaction depicting enhanced cell mediated immunity in human subjects. Thus prolonged use of this drug may be useful in enhancing the body resistance against diseases which occur due to lower cell mediated immunity particularly in aged individuals where decline in normal immune functions occur and are primarily due to changes in the T cell compound of the immune system because of thymus involution (Kay and Makinodon, 1976).

Recently stimulation of host defence mechanism has become a major goal of pharmacotherapeutic research. Immuno-potentiating compounds exert their effects in different ways. On the one hand, they may enhance non-specific effector mechanisms operative in resistance of infectious agents and to neoplastic cells. On the other hand, they may non-specifically increase specific immune response elicited by the recognition of antigenic determinants. Of course, both the mechanisms are operative in the resistance to infectious agents and to neoplastic cells. These may be mediated by the pharmacological activation of common target cells, that is macrophages and other accessory cells such as polymorphonuclear leucocytes (Gisler, et al., 1979). Geriforte may be acting through either one or both mechanisms.
It is known that psychological factors such as housing, fighting and stress may modify the susceptibility of animals to viral and parasitic infections as well as neoplasia. Stress induced immuno-depression is also known (Lattime and Strausser, 1977; Folch and Walksman, 1974), and thus the antistress properties of Geriforte may itself play a major role in enhancing the immune response. However, this is a preliminary communication in which the immune response has been assessed by DNCB challenge test. Further studies both in vivo and in vitro are required to elucidate the detailed immunological profile of Geriforte.

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REFERENCES