6.SUMMARY AND CONCLUSION

Ayurveda, the ancient healing system of India, flourished in the Vedic era in India. According to historical facts, the classical texts of Ayurveda, Charaka Samhita and Sushruta Samhita were written around 1000B.C. The Ayurvedic Materia Medica includes 600 medicinal plants along with therapeutics. Herbs like turmeric, fenugreek, ginger, garlic and holy basil are integral part of Ayurvedic formulations. Medicinal herb is considered to be a chemical factory as it contains multitude of chemical compounds like alkaloids, glycosides, saponins, resins, oleoresins, sesquiterpene lactones and oils (essential and fixed). Today there is growing interest in chemical composition of plant based medicines. Several bioactive constituents have been isolated and studied for pharmacological activity. Natural products are more reliable than their synthetic counterparts due to their minimal side effects. In the commercial market, medicinal herbs are used as raw drugs, extracts or tinctures. Isolated active constituents are used for applied research. For the last few decades, phytochemistry (study of plants) has been making rapid progress and herbal products are becoming popular. The prevalence of population suffering from stress related disorders clubbed with hypertension is quite alarming.

In the present study- **(a)** ***Trigonella foenum graecum*** **(seeds) (b)** ***Zingiber officinale*** **(dried rhizome) (c)** ***Panax pseudoginseng*** **(rhizome) (d)** ***Korean ginseng*** **(roots)** have been studied for their anxiolytic and antihypertensive actions. **The Indian variety of ginseng-** ***Panax pseudoginseng*** **has been compared with its Korean counterpart-** ***Korean ginseng*** **in all anxiolytic and antihypertensive studies.**

An extensive literature survey on the above plants suggested that:

a. ***Trigonella foenum graecum*** is well known for its appetite stimulant properties whose effect is mediated through 5-HT receptors. It also has antifatigue effects. Ghosal *et al.,* 1974 has worked on its antihypertensive effects without emphasizing on its 5-HT mechanism. Moreover, it is well known that a rise in endogenous 5-HT levels leads to anxiety and vice versa. This led to a hypothesis that anxiolytic and antihypertensive effects of this plant could possibly be mediated through its 5-HT mechanism.

b. *Zingiber officinale* is well known for its antiemetic effects (Yamahara *et al.*, 1989; Bone *et al.*, 1990) mediated through its 5-HT_3 antagonistic properties. This has prompted us to explore the antihypertensive and anxiolytic effects of this plant through its 5-HT_3 antagonistic effects using Phenylbiguanide- a 5-HT_3 agonist, although literature survey has indicated that the aqueous ginger extract and its phenolic constituents lowers BP through a dual inhibitory effect mediated via stimulation of muscarinic receptors and blockade of Ca++ channels (Ghayur *et al.*, 2005).

c. Ginseng, an adaptogenic is also being used as one of the commonly used over the counter herbal prescription in patients with cardiovascular disease (Pharand *et al.*, 2003). Korean red ginseng can improve the vascular endothelial dysfunction in patients with hypertension possibly through increasing the synthesis of nitric oxide (Sung *et al.*, 2000). Scanty work on *Panax pseudoginseng* has been reported with respect to its antihypertensive and anxiolytic effects. Although these studies have reported different mechanism for their antihypertensive effects, no mechanistic studies involving the 5-HT have been hypothesised.

In search for better alternatives to antihypertensive drugs, the 5-HT class of drugs; the 5-HT_3 receptor antagonists, 5-HT_{1A} agonist and 5-HT_{2B} antagonists are currently being considered for their potential use in hypertension (Tsukomoto *et al.*, 2000; Shingala and Balaraman, 2005). Reports on anxiolytic studies on the above selected plants are very few (Vishwakarma *et al.*, 2002; Hwa-Young Cha *et al.*, 2004). I therefore proposed to study anxiety and antihypertensive properties of the above plant species through its possible 5-HT mechanism.

Specific parts of the plants were extracted using various solvents. The active component(s) were isolated from crude extracts using chromatographic techniques by employing solvents of varying polarity. Anxiolytic activity was studied using various paradigms based on exploratory behaviour in mice like elevated plus maze, open field apparatus and light dark apparatus. Chronic anxiolytic studies were done on elevated T- maze apparatus. The antihypertensive actions of the medicinal plants were studied using invasive and non-invasive blood pressure measurement techniques in rats. Chronic hypertensive studies were carried on DOCA and Fructose-induced hypertensive models. We also made an attempt to

elucidate the mode of action using various agonists and antagonists like *m*-CPP, ondansetron, ketanserin, phenylbiguanide.

The present study shows that that alkaloid and saponin containing ethyl acetate fraction (EAF) and methanolic fraction (MF) of methanol extract of *Trigonella foenum-graecum* seeds possess anxiolytic activity probably by involving the 5-HT_2 receptors. Toluene fraction of pet ether extract of *Zingiber officinale* exerts its anxiolytic effect which is largely attributed to gingerol having 5-HT_3 antagonistic activity and, saponin containing *Panax pseudoginseng* and *Korean ginseng* possess anxiolytic activity which may be contributed by its 5-HT_2 and GABA mediated effect. **An inverse "U" dose response curve [∩] was observed in most of the anxiolytic parameters, a typical feature of a characteristic anxiolytic drug.** A dose producing such an effect was not accompanied by it sedative or neurotoxic actions as observed with benzodiazepines. **Our findings also suggest that fenugreek seeds, ginger rhizome and ginseng roots exert anxiolytic like effects in a specific subset of defensive behaviour, particularly those that have been related to GAD.**

Serotonin plays an important role in development of hypertension. The antihypertensive activity of methanolic extract and its methanolic fraction of *Trigonella foenum graecum* seeds may be partly due to 5-HT_{2B} receptor antagonism; pet ether extract and its toluene fraction of *Zingiber officinale* may be due to 5-HT_{2B} /5-HT_3 receptor antagonism whereas *Panax pseudoginseng* extract and *Korean ginseng* extract may be due to 5-HT_{2B} antagonism and NO production as indicated by a significant ($P< 0.05$) reduction in 5-HT response in DOCA and fructose model in all the four plant species. A significant ($P< 0.05$) reduction in blood pressure with PBG in *Zingiber officinale;* and ACh in *Panax pseudoginseng* extract and *Korean ginseng* in DOCA and fructose model was also observed. *Panax pseudoginseng* was found to have similar anxiolytic and antihypertensive effects when compared with *Korean ginseng.*

Some other studies like reversal of *m*-CPP induced anxiety by fenugreek seeds, significant decrease in the number of head twitches induced by Lithium sulfate by fenugreek and ginseng extracts and a significant ($P<0.05$) increase in clotting time by fenugreek, ginger and ginseng extracts support the 5-HT hypothesis.

In conclusion, our data collectively suggests that *Trigonella foenum graecum, Zingiber officinale, Panax pseudoginseng* and *Korean ginseng* possess antihypertensive and anxiolytic activity. The mechanism of action could be due to the involvement of 5-HT receptors. However further studies like in-*vivo* dialysis or radioligand-binding assays may prove this hypothesis true.

Thus, clinically, formulations with the above plant extracts can be tried in patients suffering from hypertension and anxiety refractory to other conventional drugs, or in cancer patients having excessive drug induced vomiting with hypertension/ anxiety, or in patients having cardiovascular disorder clubbed with diabetes/ anxiety/ 5-HT disorder.