INTRODUCTION

Modern man is exposed to stressors like highly ambitious and competitive lifestyle, food adulteration, atmospheric pollution, and synthetic drugs. Work-related stress results in health problems\(^1\). Homeostatic mechanism is geared towards counteracting the everyday stressed living. If the stress is extreme, long lasting or unusual, the normal mechanism may not be sufficient. In this case the stress causes a wide set of bodily changes, called the general adaptation syndrome (G.A.S)\(^2\). There is abundant literature on the effects of stress on the physical and mental illness and infections. Body reacts to such a situation by eliciting various autonomic and visceral and endocrinal responses in a variety of situations for example release of hormones like cortisol and adrenaline, disruption of gastric mucosal integrity has also been reported during stress. Both peripheral and central mechanism seems to regulate these changes\(^2\). These lead to increased heart rate, rise in blood pressure, and metabolic rate. All intended to increase the performance and the ability to reduce stress. But beyond threshold these factors can be damaging\(^3\). Stress has been postulated to be involved in the pathogenesis of variety of diseased states, for example disorders like depression, peptic ulcer, diabetes mellitus, cognitive dysfunction, male impotency, hypertension, endocrine disorders and ulcerative colitis. The stress effects are determined by the duration rather
than the intensity of stressful stimuli. Acute stress generally has positive effects, while chronic stress typically provokes immunosuppression\textsuperscript{4–8}. Therefore chronic mild stress is more damaging than acute transient stress\textsuperscript{9}. The immune system is particularly sensitive to stress\textsuperscript{10–12} and the suppression, thus induced, depresses the immune functioning and increases susceptibility to diseases\textsuperscript{13–16}. Reactive oxygen species (ROS) including superoxide anion radical, hydroxyl radical, and hydrogen peroxide, are formed during stress and, can cause oxidative damage of all major groups of biomolecules (DNA, proteins, lipids and small cellular molecules), which in turn leads to cardiovascular and neurodegenerative diseases\textsuperscript{17}. Production of free radicals may be formed by exogenous factors like environmental pollutants, pathogens, radiation, and drugs. These reactive oxygen species (R.O.S) create a homeostatic imbalance which generates oxidative stress and causes cell death and tissue injury. Involvement of R.O.S is implicated in neurodegenerative and other disorders such as alzheimers disease, parkinsons disease, multiple sclerosis, down syndrome, inflammation, viral infection, autoimmune pathology and digestive ulcers. Toxic effect of the free radicals causes oxidative stress and results in pathogenesis of diseases.

Enzymes (superoxide dismutase, catalase and glutathione peroxidase) and non-enzymes defenses (gluthatione, vitamins C are the antioxidant defenses systems\textsuperscript{18,19} Antioxidants are present with protective efficiency. Depending on the balance between R.O.S and the availability
of antioxidants in the microenvironment of the cell, antioxidants can inhibit or delay the initiation or propagation of oxidative chain reaction and thus prevent or repair cell damage caused by reactive oxygen\textsuperscript{20}.

Foods containing phytochemicals such as phenolic compounds have potential protective effects against many diseases\textsuperscript{21}. Antioxidant approach to disease management holds potential as most of the diseases are mediated through reactive oxygen species, also with the rapid advancement of civilization, industrialization, overpopulation, there has been proportional rise in stressors. However, the possible toxicity as well as general consumer rejection lead to decreasing use of the synthetic antioxidants\textsuperscript{21}. Epidemiological researches strongly suggested that foods containing antioxidants and scavengers have potential protective effect against disorders caused by reactive oxygen species\textsuperscript{22}.

There are many formulations available in the modern medicine regime that is effective against mental and physical disorders in stress. Modern medical practitioners prescribe antianxiety drugs, like benzodiazepines, in stress, which are intended for symptomatic relief rather than dealing with the root cause and stress. They have limited role in prevention of the stress disorders because they cause sedation or euphoria and periodic paralysis and may even cause tolerance and physical dependence on prolonged use. Moreover they are not effective against chronic stress. Chronic stress results in depressed immunity, cognition and male sexual dysfunction. Evidence of impaired immune
function has been conclusively shown in both experimental and clinical stressful situations.

In Indian system of medicine, there are a number of herbal drugs and formulations available, to withstand stress without changing any physiological function of the body. These drugs improve physical and mental health, resistance of the body to infections and other external factors, which perturb the homeostasis of human systems. Drugs showing such activities are called as adaptogens. A considerable research on pharmacognosy, chemistry, pharmacology and clinical therapeutics has been carried out and the Ayurvedic database has detailed descriptions of over 700 medicinal plants\textsuperscript{23}.

The present work deals with the evaluation of certain Ayurveda and Siddha drugs for antioxidant and adaptogenic activity. The Ayurveda and Siddha system of medicine includes several plants that are categorized as Rasayanas and are agents that promote health and longevity by enhancing defense against disease, arresting aging, revitalizing the body in debilitatng conditions and increasing the capability of individual to resist the adverse environmental factors\textsuperscript{24}. The Kayakarpam therapy in Siddha acts by imparting absolute immunity to disease. The very meaning of kayakarpam or kayakalpam rasayana as it is termed in Ayurveda or rejuvenation refers to nutrition and its transportation in the body. ‘Rasayana’ drugs act inside the human body
by modulating the neuro-endocrino-immune systems and have been found to be a rich source of antioxidants\textsuperscript{25}. Plenty of study has been undertaken to provide scientific evidence to the ‘Rasayana’ drugs as immunomodulators and adaptogens\textsuperscript{26}. Such a state of improved nutrition leads to a series of secondary attributes like prevention of aging, improved longevity, immunity against diseases, increased vitality and luster of the body.

Siddha is an ancient system of medicine in India. It has its literature in Tamil and is of Dravidian origin. Siddha system of medicine is widely used to treat cough, cold, joint diseases, fever, fungal diseases and diarrhoea. It is also very popular for their use as antioxidants and adaptogenic drugs. Siddha uses metals and minerals in the treatment line. The use of metals and minerals helps to preserve the body from decomposing. According to Siddha literature the materials that do not decompose themselves easily should be used as drugs. The other reason why Siddha system uses minerals is that the south Indian rivers were not perennial and many medicinal plants were not available throughout the year. Siddha system of medicine is one of the oldest medical systems of India. The palm leaf literature could be traced in Tamil dating back 3100 B.C giving a detailed account of the intensive work done by Siddhas of south India. Kayakarpa drugs are potent preparations that might prove to be right alternatives to address some untackled present
day diseases and conditions. They can be good resources to improve general immunity and prevent diseases. In Siddha literature the preparations called Amuri and Muppu are highly acclaimed Kayakarpa preparations. They emphasize more on preventive aspects and preventing the diseases through kalpam and kalpa sadanai. The bestowing of longevity is attained through karpa aviltham. Karpa medicines and karpa yogam (regimens of life). Amuri, Muppu are indicated as primordial preparations used in kayakarpa procedure and are mixed with every other Siddha formulation to improve the efficacy. To carry out the pharmacological screening of these ayurvedic and siddha drugs is the objective of the study

In modern days practice of Siddha system of medicine has declined due to lack of scientific proof. By providing rational proof to the formulations and carrying out various studies with the experimental data’s would help in re-establishing their claim which otherwise would become extinct. By the above work we can provide universal acceptance and usefulness to this system of medicine and give recognition to this ancient system of medicine.
OBJECTIVES

The Primary objective of the study involves evaluation of some selected Ayurvedic drugs and traditional Siddha preparation for their antioxidant and adaptogenic activity (Part A)

The second part of the study involves the detail chemical investigation of the bioactive fraction (Part B)

The specific objectives were:

Part A

➢ To prepare the extract of *Buchanania lanzan*.

➢ To study the preliminary phytochemical investigation on *Buchanania lanzan*.

➢ To carry out the dose determination of extract by acute toxicity studies.

➢ To investigate the antioxidant and adaptogenic activity of the extract and of formulations Muppu and Vidakanachoornam using following animal models.

*In vivo* antioxidant activity will be evaluated by well-established animal models of acute nature.

Carbon tetrachloride induced acute hepatic injury.

The following parameters will be estimated:

➢ AST, ALT, ALP, Total and direct bilirubin (In serum).

➢ SOD and Catalase activities (In liver tissue homogenate).

➢ Histopathological studies.
- Liver weights.

The list of models used for the evaluation of adaptogenic activity used is as follows:

- Forced Swimming Test.
- Swim endurance test in mice.
- Anoxic stress tolerance test in mice.
- Restrain stress induced changes in rats.
- Elevation in plasma corticosterone levels.
- Changes in the weight of different organs.
- Estimation of urinary VMA and Ascorbic acid after swim induced stress.

Hepatoprotective activity will be evaluated by estimation of:

- Serum SGOT
- Serum SGPT
- Serum ALP
- Total bilirubin
- Drug induced potentiation of pentobarbitone sleeping time in mice.

The anti-inflammatory activity will be evaluated by Carraggenan induced rat paw oedema model.
Part B

The isolation of the compounds from the bioactive fractions will be carried out using column chromatography and the characterization of the isolated compounds will be carried out using IR, Mass and NMR spectral analysis.