Chapter # 1
INTRODUCTION
Plants have served mankind since ages as they are reservoirs of important medicinal components and help to alleviate chronic diseases. The past was considered the synthetic era due to the commercial production of large varieties of synthetic drugs by pharmaceutical industries. Over time the continuous use of synthetic drugs caused severe side effects, and led to resistance of microbes. Also synthetic drugs are expensive and large populations cannot afford to get benefit from these drugs. During the last decades a global trend with focus on green medicines due to minimum side effects and cost effectiveness is seen. Medicinal plants play an appreciable role in the development of modern herbal medicines as many diseases like cancer, liver diseases and arthritis do not find complete cure in allopathy. The bioactive compounds of medicinal plants are used as chemotherapeutic, anti inflammatory, anti arthritic agents where no satisfactory cure is present in modern medicines.

Many plants have shown their immense potential to fight against dreadful diseases including cancer. Plants produce a wide variety of secondary metabolites with different functions like growth regulation, defense against infections and predations etc. Most important secondary metabolites include polyphenols, alkaloids, saponins, steroids etc. Many of these natural compounds have great medicinal importance due to their interesting biological and pharmacological actions. Polyphenols form one of the most common and widespread groups of compounds in flowering plants and occur in all vegetative organs as well as in flowers and fruits. They are the important secondary metabolites involved in the chemical defence of plants against predators. The plant polyphenols include a wide variety of molecules that contain at least one aromatic ring with one or more hydroxyl groups in addition to other substituents. The biological properties of polyphenols include anticancer, antioxidant, anti inflammatory, enzyme inhibitory, antimicrobial and antidiabetic effects. Recently polyphenols have attracted the scientists with more attention on the research on phenolic acids and flavonoids. Phytochemical studies have gained the attention of plant scientists due to the development of new and sophisticated techniques. These
techniques have a significant role in the search for additional resources of raw materials for pharmaceutical industry. Phytochemicals are chemicals derived from plants and are often used to describe the large number of secondary metabolic compounds found in plants. Bioassay guided fractionation is commonly employed in drug discovery due to its effectiveness to directly link the analyzed extract and targeted compounds using fractionation procedure that is followed with certain biological activity that it possesses. Modern approaches for drug discovery focus on availability of some simple and inexpensive biological assays to evaluate medicinal potential of plant species\textsuperscript{115}. Herbal medicine is also called botanical medicine or phytomedicine. It refers to using a plant’s seeds, berries, roots, leaves, bark, or flowers for medicinal purposes. Herbalism has a long tradition of use outside of conventional medicine. It is becoming more main stream as improvements in analysis and quality control along with advances in clinical research show the value of herbal medicine in the treating and preventing disease. Plants had been used for medicinal purposes long before is recorded in history.

Indigenous cultures used herbs in their healing rituals, while others developed traditional medical systems in which herbal therapies were used. Researchers found that people in different parts of the world tended to use the same or similar plants for the same purposes\textsuperscript{51}. In the early 19th century, when chemical analysis first became available, scientists began to extract and modify the active ingredients from plants. Later, chemists began making their own version of plant compounds and, over time, the use of herbal medicines declined in favour of drugs. Almost one fourth of pharmaceutical drugs are derived from botanicals. Herbal medicine is used to treat many conditions, such as asthma, eczema, premenstrual syndrome, rheumatoid arthritis, migraine, menopausal symptoms, chronic fatigue, irritable bowel syndrome, and cancer\textsuperscript{125}.

Some common herbs and their medicinal uses are discussed below\textsuperscript{25}:

- Alfalfa (\textit{Medicago sativa}) leaves have been used to lower cholesterol and also for kidney and urinary tract ailments.

- Bitter leaf (\textit{Vernonia amygdalina}) is used to treat intestinal ailments such as dysentery.

- Arnica (\textit{Arnica montana}) is used for treating osteoarthritis and as an anti inflammatory agent.
• Kava kava (*Piper methysticum*) is shown to elevate mood, enhance well being and produce a feeling of relaxation. Several studies have found that kava may be useful in the treatment of anxiety, insomnia, and related nervous disorders.

• Celery (*Apium graveolens*) seed is used primarily as a diuretic.

• Asthma weed (*Euphorbia hirta*) has been used traditionally in Asia to treat bronchial asthma and laryngeal spasms. It is also used to treat dengue fever.

• Barberry (*Berberis vulgaris*) has been used to treat scurvy, skin ailments and gastrointestinal ailments.

• *Aloe vera* leaves are widely used to heal wounds, burns and other skin ailments.

• Astragalus (*Astragalus propinquus*) has long been used in traditional Chinese medicine to strengthen the immunity, to treat hepatitis and as an adjunctive therapy in cancer.

• Chili (*Capsicum frutescens*) active ingredient, capsaicine is used in commercially available pain relief ointments in Western medicine. The fibronolytic action of Capsaicine ie its ability to dissolve blood clots has been related to the low incidence of heart attacks.

• Fenugreek (*Trigonella foenum-graecum*) has been used since a long time to treat symptoms of menopause and digestive ailments. More recently it has been used to treat loss of appetite and Diabetes mellitus.

• Garlic (*Allium sativum*) is widely used as an antibiotic and recently for treating cardiovascular diseases.

• Ginger (*Zingiber officinale*) is used to relieve symptoms of nausea.

• Papaya (*Carica papaya*) is used for treating scars and wounds.

• Coffee senna (*Cassia occidentalis*) is used for a variety of roles in traditional medicine, as a broad spectrum antimicrobial agent, for hepatic disorders, intestinal worms and other parasites and also as a stimulant of the immune system.
Valerian (*Valeriana officinalis*) is a popular alternative to commonly prescribed medications for insomnia and has fewer side effects such as morning drowsiness compared to sleeping pills.

Peppermint (*Mentha piperita*) oil is used for a variety of conditions including symptoms of the common cold, nausea and indigestion.

Turmeric (*Curcuma longa*) has long been used in Ayurvedic and traditional Chinese medicine to aid digestion and liver function, regulate menstruation and relieve arthritic pain.

Clove (*Syzygium aromaticum*) is used for stomach upsets, as an expectorant and also to treat toothache.

Ginkgo (*Ginkgo biloba*) has been used in traditional medicine to treat circulatory disorders and enhance memory, dementia (including Alzheimer’s disease) and intermittent claudication (poor circulation in the legs). Laboratory studies reveal that ginkgo improves blood circulation by dilating blood vessels and reducing the stickiness of blood platelets.

Saw palmetto (*Serenoa repens*) is used for the treatment of benign prostatic hyperplasia, a non cancerous enlargement of the prostate gland. A number of studies suggest that it is effective for treating symptoms of frequent urination.

Purple cone flower (*Echinacea purpurea*) is shown to improve and boost the body’s natural immunity. Echinacea is one of the most commonly used herbal products used to prevent or treat colds.

St. John’s wort (*Hypericum perforatum*) is well known for its antidepressant effects and is an effective treatment for mild to moderate depression. It has fewer side effects than other prescription antidepressants.
Three plants *Artocarpus altilis*, *Piper betle* and *Artocarpus heterophyllus* were selected for the research purpose. The brief description of the selected plants is given below:

**Piper betle**

*Piper betle*, commonly called betel plant belongs to the piperaceae family and originated from South and South East Asia. It is valued both as a mild stimulant and for its medicinal properties. The betle plant is an evergreen and perennial creeper with glossy heart shaped leaves and white catkin. The betle plant is one of the highly investigated plants and phytochemical studies reveal that *Piper betle* contains a wide variety of biologically active compounds whose concentration is dependent on the variety of the plant, climate and season. The aroma of betle leaf is due to the presence of essential oils comprising of phenols and terpenes. The various phytochemicals found in the betle plants include estragole, eugenol, chavibetol, chavicol, hydroxychavicol, methyl eugenol, hydroxycatechol, caryophyllene, eugenol methyl ether, cadinene, γ-lactone, allyl catechol, p-cymene, cephradione A, dotriacontanoic acid, tritriacontane, terpinene, eucalyptol, carvacrol, sesquiterpenes, cadinene, caryophyllene, dotriacontanoic acid, hentriacontane, pentatriacontane, stearic acid, n-triacontanol, tritriacontane, piperlonguminine, allylpyrocatechol diacetate, isoeugenol, 1,8-cineol, α-pinene, β-pinene, ursolic acid, ursolic acid 3β-acetate, sitosterol, β-sitosteryl palmitate, γ-sitosterol, stigmasterol etc.

For a very long time the leaves and the stalk of the betle plant have been used to treat various ailments in the traditional Indian system of medicine and also in various folk medicines in South east Asia. Chewing betle leaf is thought to improve the vocalization, prevent bad breath, harden the gum, protect the teeth and sweeten breath. The infusion prepared from the stems and leaves are used in treating constipation, indigestion, bronchitis, asthma, coughs and congestion. The essential oil isolated from the leaves is supposed to be useful in treating respiratory problems and as an antiseptic. Several workers have reported on the various biological activities of *Piper betle* using different *in vitro* and *in vivo* test models. Many of these studies have validated the traditional uses and explored the pharmacological activity of the different parts of the plant. Preclinical experiments have shown that betle
leaf possess immunomodulatory, anti bacterial, anti carcinogenic, anti fungal, anti larval, anti protozoal, anti filarial, anti allergic, antidiabetic, anti inflammatory, hepatoprotective, anti ulcer, anti fertility, cardioprotective, anti hyperlipidaemic, anti platelet, vasorelaxation effects\textsuperscript{121}.

\textit{Artocarpus heterophyllus}

\textit{Artocarpus heterophyllus} is commonly known as the jackfruit tree and belongs to the family Moraceae, originally native to the Western Ghats of India. The fruits are of dietary use and are an important source of minerals, vitamins carbohydrate, protein and fat. The heart wood is a very durable timber and is used for making furniture. The leaves, fruit, bark and roots have diverse medicinal properties and are used in the various traditional and folk systems of medicine to treat a variety of ailments. Preclinical studies have shown that jackfruit possesses antibacterial, anticariogenic, antioxidant, anti inflammatory, antifungal, hypoglycemic and antineoplastic and wound healing. Clinical studies have also shown that the decoction of the leaves possesses hypoglycemic effects in both healthy individuals and non insulin dependent diabetic patients. Phytochemical studies have shown that jackfruit contains useful compounds like sterols, prenylflavones and flavonoids which may have been responsible for the various pharmacological properties. It is reported in Ayurveda to possess antibacterial, anti inflammatory, antidiabetic, antioxidant and immunomodulatory properties. It is an important source of bioactive compounds like isoartocarpin, cyloartocarpin, morin, dihydromorin, cynomacurin, artocarpin, heterophylol, oxydihydroartocarpesin, artocarpetin, norartocarpetin, cycloartinone, betulinic acid, artocarpanone and artocarpesin which are useful to treat wounds, fever, boils, skin diseases, diuretic, constipation, ophthalmic disorders, snake bite and convulsions etc\textsuperscript{200}.

\textit{Artocarpus altilis}

\textit{Breadfruit (Artocarpus altilis)} is a species of flowering tree belonging to the mulberry family, Moraceae. It grows throughout Southeast Asia, most Pacific Ocean islands and widely distributed over the tropical regions of Asia including Thailand. It is mainly grown
for edible fruits and parts of this plant are also utilized as traditional medicine. The roots have been used as a component in folk remedies for cancer and venereal diseases, the stems and roots have been used traditionally for the treatment of hypertension and liver cirrhosis. Preliminary bioactivity study of the crude extract of the roots of *A. altilis* revealed that it possessed antitubercular activity against *Mycobacterium tuberculosis*. Furthermore, a moderate antiplasmodial activity against the parasite *Plasmodium falciparum* was also reported. Bioactivity screening led to the isolation of nine prenylated flavones from the plant. Cycloartocarpin, artoecarpin, and chaplashin were isolated from the dichloromethane extract of the root stems, whereas cycloartobiloxanthone, morusin, cudraflavone B, artoobiloxanthone, cudraflavone C and artonin E and were found in the root barks. The isolated compounds were reported to possess antitubercular and antiplasmodial activities and also moderate cytotoxicity against BC (human breast cancer) and KB (human oral epidermoid carcinoma) cell lines.

Modern medicine now tends to use the active ingredients of plants rather than the whole plants. The phytochemicals may be synthesized, compounded or otherwise transformed to make pharmaceuticals. Examples of such derivatives include Digoxin, from digitalis; capsacine, from chili; and aspirin, which is chemically related to the salicylic acid found in white willow.

The opium poppy continues to be a major industrial source of opiates, including morphine. Few traditional remedies, however, have translated into modern drugs, although there is continuing research into the efficacy and possible adaptation of traditional herbal treatments. There is a great need for the isolation of effective, medicinally important bioactive constituents from natural sources in order to prevent and treat various diseases. Recent interest in polyphenolic compounds and their bioactivities prompted this research work to explore the potential beneficial health properties of many indigenous medicinal plants. The present study demonstrates a modern strategy with combination of local and modern knowledge for evaluation of biological activity of medicinal plant species. The main steps of this strategy includes selection of plant material, extraction and preliminary phytochemical screening of selected plant extracts, bioassay guided fractionation of plant extracts, biological screening of plant extracts by *in vitro* and *in vivo* bioassays, and identification of components of plant extracts by analytical techniques.