CHAPTER - 2

LITERATURE REVIEW

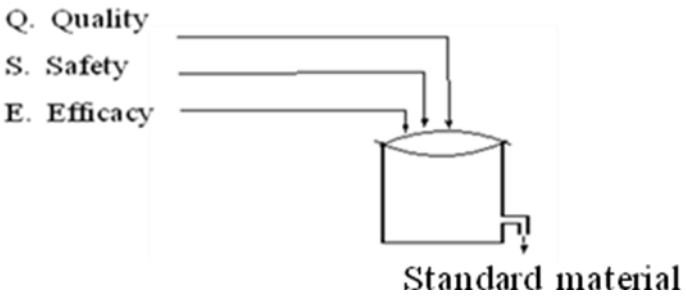
2.1 Pharmacognostical Study

Pharmacognostical study basically deals with the standardization, authentication and study of natural drugs. Much of the research in pharmacognostical study has been done to identify controversial species of plants, authentication of commonly used traditional medicinal plants through morphological, histological, physicochemical and toxicological parameters, prescribed by an authoritative source. The importance of pharmacognosy has been widely felt in recent times. Most of the cases of accidental herbal medicine misuse start with wrong identification of a medicinal plant prescribed. The main goal of pharmacognostical study is to assess the value of raw materials. Strict standardization procedures and pharmacognostical studies of medicinal plants would reduce drastically much of the accidents in wrong prescriptions of traditional herbal medicines.

Any filth found in a raw material is not only repugnant in it, but also is indicative of insanitary and improper conditions of production. Filth such as manure, rodent hairs, rodent fecal, flies and other insects, fragments of feathers, and dirt may be found in raw materials. When such filth is found, it demonstrates conclusively that the pharmaceutical product was produced under insanitary conditions and the type of contamination gives a clue to the nature of the objectionable condition. Compared with synthetic drugs, the criteria and the approach for herbal drugs are much more complex. Phytopharmaceuticals are always mixtures of many constituents and are therefore very variable and difficult to characterize. The active principles in phyto-pharmaceuticals are not

always known. The quality criteria for herbal drugs are based on a clear scientific definition of the raw material. Depending on the type of preparation, sensory properties, physical constants, moisture, ash content, solvent residues and adulterations have to be checked to prove identity and purity. Microbiological contamination and foreign materials such as heavy metals, pesticide residues, aflatoxins and radioactivity also need to be tested for. To prove the constant composition of herbal preparations appropriate analytical methods have to be applied and different concepts have to be used in order to establish relevant criteria for uniformity **[1]**.

Standardization is an essential measurement for ensuring the quality control of the herbal drugs. "Standardization" expression is used to describe all measures which are taken during the manufacturing process and quality control leading to a reproducible quality. It also encompasses the entire field of study from birth of a plant to its clinical application. When the active principles are unknown, marker substances should be established for analytical purposes and standardization. Marker substances are chemically defined constituents of a herbal drug that are important for the quality of the finished product. Ideally, the chemical markers chosen would also be the compounds that are responsible for the botanical effects in the body **[2]**. Standardization simply says to maintain three letters QSE of wide coverage



In order to obtain quality oriented herbal products, care should be taken right from the proper identification of plants, season and area of collection and their extraction and purification process and rationalizing the combination in case of polyherbal drugs **[3]**.

2.2 Adaptogenic Activity

A number of experimental models in animals were designed to evaluate the adaptogenic effects of the drugs. Several theories have been suggested to explain the effects of adaptogenic substances. One theory proposed by Dardymov and Kirkorian argues that adaptogens function primarily due to their antioxidant and free radical scavenging effects. While their theory is partially accurate, it is inadequate to explain the full effects of these medicinals. More recent research postulates that adaptogens work primarily by affecting the Hypothalamic/ Pituitary/Adrenal (HPA) axis and the Sympatho-adrenal System (SAS). The stressor (realisation of danger) sends immediate stimuli to brain, and it, in turn, mobilises all biochemical mechanisms of the body resulting in release of adrenaline and other hormones in the blood which help in the release of glucose and other stored energy supplies. There is rise of blood pressure and pulse rate, more supply of energy to muscles, and the animal is ready for "fight and flight'. Later the adaptation is mainly mediated through anterior pituitary (ACTH) and release of corticoids from adrenal cortex. Various other changes also occur in the body for conservation of 'vital adaptation' energy for the survival of the animal. The failure of adaptation may result into one of the many stress-induced diseases in genetically prone individuals e.g. a chronic tooth infection may result in diabetes in one individual and hypertension in the other. The same stress can cause advance ageing and loss of vitality in the young **[4]**.

Adaptogens modulate our response to stress (physical, environmental, or emotional) and help regulate the interconnected endocrine, immune, and nervous systems. This re-regulation of a disordered or highly stressed system is achieved by metabolic regulators such as cytokines, catecholamines, glucocorticoids, cortisol, serotonin, nitric oxide (NO), cholecystokinin, corticotrophin-releasing factor (CRF), and sex hormones. This broad array of biochemical activators helps explain why adaptogens also have antiinflammatory, antioxidant, anxiolytic, antidepressant, nervine, and amphoteric effects as well. So while most or all adaptogens are antioxidants, having antioxidant properties (Green Tea, Rosemary and Cranberry) is not enough to make a substance an adaptogen. This is true of many amphoteric herbs as well **[5]**. Plants used as adaptogens has been validated by pharmacological studies are summarized below.

Panax ginseng: Korean ginseng tea (KGT), prepared from the roots of *Panax ginseng*, is widely used by Korean people for antistress, antifatigue, and endurance promoting effects. Traditionally it is used in Chinese medicine for older men with deficient kidney, impotence, fatigue, low back pain. Recent human studies using Asian Ginseng showed it reduced improved survival times in patients with gastric cancer, and reduced incidence of metastases **[6]**.

Eleutherococcus senticosis: Eleuthero root is less tonifying than the true Ginsengs (*Panax* spp.) formerly known as Siberian Ginseng. It is neutral energetically and so is appropriate for daily use. Taken regularly it enhances immune function, reduces cortisol levels and inflammatory response, and it promotes improved cognitive and physical performance **[7]**.

Codonopsis pilosula: Dang Shen root also known as "poor man's ginseng" is used in TCM as a mild substitute for *Panax*. It is a spleen tonic and is used for poor appetite, gastric irritation, and/or ulcers, fatigue, and weak limbs. It is also a lung tonic and can be used for shortness of breath with a dry cough and frequent respiratory tract infections **[8]**.

***Glycyrrhiza glabra*:** Licorice is a versatile and commonly used drug in TCM, Unani-Tibb, Ayurveda and European herbal traditions. It is an immune amphoteric and can be useful for autoimmune disorders Scleroderma, Crohn's disease, Arthritis and immune deficiency conditions like cancer, HIV. It strengthens adrenal function and used with ginseng for Addison's disease **[9]**.

Withania somnifera: Ashwagandha root is one of the rejuvenative drug of Ayurveda. It is one of the few calming adaptogens and has traditionally been used for anxiety, insomnia, and nervous exhaustion. It acts as an antispasmodic & antiinflammatory and is very useful for fibromyalgia and osteo-arthritis. **[10]**.

Cordyceps sinensis: Cordyceps fungus is one of the more unusual adaptogens. While the parasitized larvae are still available, most Cordyceps is now grown on soybeans. It is used in TCM for deficient kidney yin and yang caused by chronic disease or extremely rigorous labour/athletic training **[11]**.

Ocimum sanctum: Holy Basil has a long tradition of use in Ayurvedic, Siddha, and the Unani-Tibb systems of medicine. It is considered as rejuvenative drug and traditionally used to improve memory, coughs, colds, digestion, asthma and fatigue. More recent research has shown it reduces excess immune response in allergic asthma and normalized immune function **[12]**.

Emblica officinalis: Amla is a rejuvenative remedy used in Ayurvedic medicine. It has been investigated that Amla is not only a useful antioxidant and

antiinflammatory, but had adaptogenic activity as well. The extract was shown to protect against biological, physical and chemical stressors **[13]**.

Asparagus racemosus: Shatavari is used as a Rasayana. It has long been used as a tonic remedy, especially for women, promoting fertility and reducing menopausal symptoms. Recent research indicates Shatavari enhances immune function, corticosteroid production, and promotes cell regeneration **[14]**.

2.3. Medicinal plants under present investigation

2.3.1 Karonda

Carissa carandas L. (Apocynaceae) is an important minor fruit crop commonly known as Karonda, 'Christ's thorn and has been cultivated in a limited way in the tropical subtropical and mediterranean region **[15]**. In Ayurveda, it is known as Karamarda **[16]**. It is a perennial plant and very easily maintains a hardy shrub. The plant produces abundant whitish pink berry size fruits in the monsoon of tropical climate and is commonly used as a condiment or additive to Indian pickles and spices **[17]**.

Taxonomical classification

Class	Magnoliopsida
Order	Gentianales
Family	Apocynaceae
Genus	*Carissa*
Species	*Carandas*

Vernacular names

Bengali	Karamacha
Hindi	Karaonda, Karaondi, Gotho

Gujrati	Karamada
Sanskrit	Karamla, Karamardaka, Dimdima
Tamil	Kalakkai
Urdu	Karwanah
Marathi	Karabanda

Figure 2.1 *Carissa carandas* (Apocynaceae) plant with fresh fruits

❖ Botanical descriptions

Leaves are simple, opposite, alternate petiolate and pinnate. Inflorescences of the plant is cymose, terminal with bracteoles. Flowers are bisexual, pentamerous, actinomorphic, hypogynous and complete **[18]**.

❖ Geographical distribution

There are about 30 species in genus *Carissa* being native of tropics and subtropics of Africa, Asia, Australia and four species in China **[19]**.

❖ Traditional uses

The plant is very valuable for the Indian system of medicine particularly Ayurveda. It is used for alleviating vata and pitta disorders and commonly used

as a condiment, pickles and spices. Its fruits and seed latex are used for treating rheumatoid arthritis, anorexia, indigestion, colic, hepatomegaly, splenomegaly, piles, cardiac diseases, oedema, amenorrhoea, fever and nervine disorder **[20]**. The roots are useful in stomach disorder, intestinal worms, scabies, diabetic, ulcer and pruitis. It is employed as a bitter stomachic and vermifuge and it is an ingredient in a remedy for itches **[21]**. The fruit exudes much gummy latex when being cooked the rich red juice becomes clear and is used in cold beverages **[17]**. The fruits are one of the richest sources of iron (39.1 mg/100 g) and possess appreciable amount of jelly grade pectin hence a large number of processing factories have been built for making commercial jam / jelly and a product by the name 'Nakal cherry' which closely resembles the canned cherry fruits **[22]**. The sour unripe fruit is reputed for its aphrodisiac, appetizer, antipyretic and astringent properties and is used in the treatment of diarrhoea and intermittent fever **[23]**. The ripe fruit is acidic and cooling; used to treat mouth ulcer, sore throat and skin disorders **[24]**. 12 gm each of fresh leaves, fruits and root bark is grounded and taken once a day with water for eight days for the permanent cure of piles and the formulation of bark is mentioned in Ayurveda in the name of 'Marma gutika' **[16]**. Unripe fruit is Antiscorbutic and astringent. Leaves decoctions of leaves are given in the commitment of remittent fever **[25]**. Two drops of oil of the plant is given with half cup of honey for controlling worms of minors **[26]**.

❖ Phytoconstituents

The chemical investigations of *C. carandas* had led to the isolation of several substances including *β*-sitosterol, lupeol, ursolic acid and a new cardioactive substance; glucosides of odoroside-H **[27]**. Bark, leaves and fruit contain an unnamed alkaloid **[17].** The leaves are reported to have triterpene,

tannins and carissic acid **[28]**. Fruits of this plant have been reported to contain a mixture of volatile principles like 2-phenyl ethanol, linalool, *β*-caryophyllene, isoamyl alcohol and benzyl acetate **[29]** and a novel (Carissol) triterpenic alcohol **[30]**. A mixture of cardenolides, carissone, carindone **[31]** and a new lignan carinol, carinol dimethyl ether diacetate amorphous powder was isolated from e fruit **[32]**. Various fatty acids such ‘as palmitic (66.42%), stearic (9.36%), oleic (2.04%) and linoleic (0.99%) acids were found in the seed **[33]**. Glucose and galactose as well as the amino acids serine, glutamine, alanine, valine, phenylalanine has been reported in the fruit **[34]**.

- **Pharmacological activity**

The alcoholic extract of the roots of *C. carandas* has been reported to possess cardiotonic activity **[35]** and to produce a perceptible decrease in blood pressure in normal anaesthetized cats **[36]**. Fruits have been studied for its analgesic, anti inflammatory and lipase activity **[37]**. Aqueous extract of root have been reported various pharmacological activities like histamine releasing used to assess the intensity of snake poisoning **[38]** anthelmintic, sapsmolytic and cardiotonic **[39]**. Leaf of the plant extract showed antimicrobial activity **[40]**. Ethanolic root extract produce anticonvulsant effects via non-specific mechanisms **[41]**. The aqueous extract of root caused a significant hepatoprotective activity against CCl_4 and paracetamol induced hepatic oxidative stress **[42]**.

2.3.2 Amara

Spondias mangifera Willd. (F. Anacardiaceae) is a fast growing tree allied to mangifera, commonly known as Hog-plum or Bile-tree and Amrata in Ayurveda, widely distributed in the tropics and abundantly in the eastern and in north-east region of India. In India, it is cultivated in Punjab, Maharashtra, Bengal and Assam for the edible fruits **[43]**. All parts of the plant have foeted turpentine like odour when broken or brushed. It is the tree with rich tradition in the ancient health system of Ayurveda and North-East people for the management of rheumatism **[44]**.

Taxonomical classification

Phylum	Spermatophyta
Division	Angiospermae
Class	Dicotyledone
Order	Sapindales
Family	Anacardiaceae
Genus	*Spondias*
Species	*mangifera* (Willd) syn. *Pinnata*

Vernacular names

Bengali	Ambra, Amra
Hindi	Amara, Ambodha
Sanskrit	Amrata, Bhrigiphalla, Kapichuta
English	Bile tree, Hog plum, Traveller's Delight
Nagaland	Heining
Manipuri	Toito, Kuki
Mizo	Taito

Figure 2.2 *Spondias mangifera* (F. Anacardiaceae) flowering twig

❖ **Botanical description**

Leaves are alternate unipinnate (imparipinnate) compounds. Leaflets are opposite, 5-7 pairs, oblique base, entire margin, acuminate apex, leaves are 30-45 cm long and leaflets are 9-13 cm long and 2-9 cm width elepticoblong shape. Leaves are turning yellow before falling; petioles are 0.6-0.8 cm glabrous

surface. Stem is woody living over winter and hard in texture arbores cent, succulent fleshy. Flowers are polygamous, pedicilate, bisexual, small, 3.5 mm long, hypogamous, actinomorphic, complete, cyclic, yellowish green colour and scented **[18]**.

❖ **Geographical distribution**

The plant will grow in warm sub-tropical areas where no frost occurs or only occasional light frost. It is a fast growing, massive tree which under favorable condition reaches a height of 28-34 m and may attain a spread of 15-18 m. At present it is cultivated in 34 countries of the world; 12 in its native range **[45]**.

❖ **Traditional uses**

The green fruit is pickled in brine and it is commonly used in culinary preparations such as curries, condiments, jams, sherbet in countries where the tree grows naturally. The green fruit of the plant is useful in bilious dyspepsia as condiment and pickles. The bark of the tree is rubifacient, being used in Indian indigenous medicine for rubbing on the skin over painful joints. A paste of bark is used as an embrocation for both articular and muscular rheumatism **[43]**. The powdered ripe fruit is used as an antidote for wounds caused by poison arrows and is also reported to have anti-tubercular properties. The fruit is aromatic, astringent, refrigerant, tonic and used for treatment of rheumatic articular and muscular pain. The bark is also aromatic, astringent, refrigerant and given in preventing vomiting, dysentery and diarrhea **[44]**. About 10 g of tender fruit juice mixed with 50 g of sugar candy and 0.6-0.8 g of black pepper powder is popular home remedy for biliousness. A decoction of root bark is stated to be useful in gonorrhea. The root is considered useful in regulating menstruation

[46]. Bark paste with three bulb of garlic given twice a day for three days in stomach pain in majidi area of Hazaribag district **[47]**. The ripe fruit juice is highly acidic richest source of vitamins and has nutraceutical potentiality **[48]**. The fruit and bark of the plant is used in diabetes **[49]**. The fruit and leaves are used for tenderization of meat and made it delicious **[43]**.

❖ Phytoconstituents

Only a few phytochemical have been reported on this plant in the literature. Cycloartanone 24-methylene, daucosterol, lignoceric acid, stigmast-4-en-3-one, *β*-amyrin, oleanolic acid and *β*-sitosterol was isolated from fruits and aerial parts of the plant, and also glycine, cystine, alanine and leucine present in fruits **[50]**.

The other constituents of fruit are galloylgeranin, ascorbic acid, and minerals like calcium, alluminium, iodine, iron, sodium potassium and vitamins like vit-A, riboflavin and niacin. Bark of plant contains lignoseric acid glucosides of *β*-sitosterol and ellagitannins **[51]**.

❖ Pharmacological activity

Indian species of the plant was found to posses CNS depressant activity **[52]**. The root bark powders have reported as antibacterial **[53],** antitumor **[54]**, antispasmodic and antihistamine activities **[55]**. The bark of the plant was found hypoglycemic **[56]**, antioxidant, free radical scavenging activity **[57]**. The methanolic extracts of stem heart wood of plant possess hepatoprotective activity against CCl_4 induced liver damage in rats **[58]**.

2.3.3 Jangali baigun

Solanum torvum SW. (Solanaceae) is a small shrub also known as prickly solanum, shoo-shoo bush and wild egg plant usually 2-4m in height. The edible fruits commonly available in the markets are used as a vegetable and regarded as an essential ingredient in Thai cuisine. The plant is cultivated in the tropics for its sharp-tasting immature fruits **[59]**.

Taxonomical classification

Kingdom	Plantae
Division	Tracheobionta
Class	Magnoliopsida
Subclass	Asteridae
Order	Solanales
Family	Solanaceae
Genus	*Solanum*
Species	*torvum*

Vernacular names

Assamese	Hatibhekuri
Bengali	Titbaigun
Hindi	Jagali baigun
English	Devil's fig
Malayalam	Kattuchunta
Nepal	Burabihi
Tamil	Sundai, Kottukkattari
Telgu	Kandavuste

Figure 2.3 *Solanum torvum* (F. Solanaceae) plant with flower and fruits

❖ Botanical description

The plant is an erect spiny shrub, adult leaves are broadly ovate or orbicular shallowly lobed throughout lobes acute or obtuse, lamina 7.5–16.5 cm long and 4–13 cm wide, apex acute. Adult leaves petioles 0.9–4.3 cm long and prickles absent. Upper leaf surface green, prickles absent, lower leaf surface white, prickles absent or present on midvein only. Inflorescence supra-axillary, branched (paniculate to corymbose) 15–50-flowered. Flowers are pentamerous, pedicelate, hypogynous, complete, prickles absent **[18]**.

❖ Geographical distribution

It is native from Mexico to Peru, Venezuela and in West Indies distributed widely in Thailand, India, and Indonesia except the western desert area, Malaya, China, Philippines and tropical America **[60]**.

❖ Traditional uses

In Tripura and Bengal, fruits are crushed or cooked with dry fish (sidhol) and taken with warm rice to cure rheumatic pain. The leaf paste is applied on wound inflicted by black snack **[26]**. Ash of the whole plant with sesame oil is used for healing wounds **[61]**. A decoction of fruits is given for cough ailments and considered as useful in liver and spleen enlargement and possesses sedative, diuretic and digestive properties **[51]**.

❖ Phytoconstituents

Steroidal glycosides 22-*O*-spirostannol (Torvonin-A & B) is a spirostane saponin isolated from leaves **[62]**. It has number of chemical constituents like neochlorogenin 6-O-*β*-D quinovo-pyranoside, neochlorogenin 6-O-*β*-D-xylopyranosyl-(1→3)-*β*-D-quinovopyranoside, neochlorogenin 6-O-α-L-rhamnopyranosyl-(1→3)-β-D quinovopyranoside **[63],** sola-genin 6-O-*β*-Dquinovopyranoside **[62],** solagenin 6-O-*α*-Lrhamnopyranosyl-(1→3)-*β*-Dquinovopyranoside **[64],** flavonoids like rutin, kaempferol and quercetin. Antiviral isoflavonoid sulfate (Torvonol) and steroidal glycoside (Torvoside) were isolated from the fruits **[65]**.

❖ Pharmacological activity

The aqueous extracts plant was found significant antifungal activity tested against ten important seed borne fungal pathogens of paddy by poisoned food technique **[66]**. The methanolic extract of fruits showed a wide spectrum of antimicrobial activities in human and other animal **[67]**. Torvanol A and torvoside H exhibited antiviral activity (herpes simplex virus type 1) **[63]**. The aqueous and methanol extracts from the leaves of *S. torvum* shows immuno-secretory activity (Enhancement of ovalbumin-specific *Ig*A) **[68]**. A novel

antioxidant protein isolated from the water extract of seeds **[69]**. The aqueous and methanol extracts from the leaves of plant shows cardiovascular and antiplatelet aggregation **[70],** anti-ulcer, analgesic and anti-inflammatory activities **[71]**. Oral administration of methyl caffeate, isolated from fruit showed a dose-dependent anti-hyperglycemic effect in glucose fed hyperglycemic and streptozotocin diabetic rats **[72]**. The aqueous extract of fruit was found nephroprotective activity investigated against Doxorubicin (DOX) induced nephrotoxicity in rats **[73]**.

The present review discusses the significance of selected plants *C. carandas, S. mangifera* and *S. torvum* as a valuable source for medicinally important compounds besides theses edible fruit which is a store house of minerals, vitamins, antioxidants and other nutrients. On the basis of literature survey, it was found that all these three selected plants are traditionally important used in culinary preparations and rich source of terpenoids, steroids, saponins, acids, phenolic and flavonoid compounds reported to possess antioxidant and free radical scavenging activity. The antioxidant constituents present in the fruits play important role in scavenging free radicals and reactive oxygen species which are responsible for number of human disorders. These plants reviewed here have been found to have Antioxidant activity, antibacterial activity, antihypertensive, cardioprotective activity, antidiabetic activity, analgesic and anti-inflammatory activity and erythropoietic activity.

2.4. Aim and objective

Still, no scientific claim has been made on pharmacognostical standardisations, adaptogenic and antioxidant activities of the selected plant fruits of *C. carandas, S. mangifera* and *S. torvum*. Hence, in view of the medicinal importance of these three plant fruits, the present investigation was undertaken for standardization, isolation, characterization and screening for adaptogenic and antioxidant activities. The project work was divided into four parts, as given bellow in detail.

I. Pharmacognostical study of plant material

For the development of authentic parameters for the fruits *C. carandas, S. mangifera S. torvum,* following parameters have been determined.

- Morphological study
- Microscopical study
- Histochemical analysis
- Tests for extraneous material
- Loss on drying
- Ash value
- Extractive value
- Crude fibre contents
- Fluorescence analysis of fruit powder and its extractives
- Preliminary phytochemical screening and qualitative chemical tests
- TLC fingerprint profiling

II. Phytochemical investigation

The viscous mass obtained by extraction procedure was dissolved in the minimum amount of methanol and then absorbed on Silica-gel (60-120 mesh)

for preparation of slurry. The column was packed with silica-gel containing petroleum ether as solvent. The column was eluted with petroleum ether, chloroform and methanol in the order of increasing polarity to isolate compounds. The isolated compounds were characterized by chemical tests, melting points and spectral analysis such as UV, FTIR, ^{13}C NMR, ^{1}H NMR and Mass spectroscopy.

III. Adaptogenic activity

Different parameters of adaptogenic activity have been investigated in *vivo* by using healthy albino mice (20-25 g) of either sex.

- Toxicity studies, for determination of lethal dose and effective dose
- Anoxia stress tolerance test
- Swimming endurance test and post-swimming motor function test
- Immunological related studies (Cyclophosphamide induced immunosuppression test) and estimation of immunological parameters like total RBC count, total WBC count and haemoglobin.

IV. Anti-oxidant activity

Following *in vitro* models have been used for estimation of antioxidant activity.

- Estimation of total phenolic content
- Estimation of total flavonoid content
- DPPH radical scavenging activity
- Nitric oxide radical scavenging activity
- Measurement of reducing power
- Effect of extract on the peroxidation of linoleic acid

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