1. LITERATURE REVIEW.

1.1. *Myristicafragrans*(Nutmeg)

1.1.1. General Information

A *Myristica* genus is spread from India to South-east Asia and North Australia Islands of Pacific. About 3 types found in India, with *Myristica fragrans*, *Myristica beddomeii* and *Myristica malabarica*. *Myristica fragrans* belongs to family Myristicaceae (Parimala et al., 2013). *Myristica fragrans* is usually recognized as, it yields double condiments: mace as well as nutmeg. Nutmeg comprises of seed inside fruit besides mace is red delicate coating on kernel (Pal et al., 2011). Over-allyield of nutmegs is measured to about 10,500 - 12,500 tons per annum beside yearly global wants is about 9,700 tons and industrial predictable production of mace is about 1,500 - 2,500 tons (Abdullah et al., 2010).

Nutmeg is supposed to be an inborn in Banda Islands from East Indonesia, earlier called as ‘Spice Islands’. Within India nutmeg is chiefly cultivated in Southern parts of India mostly in definite places that is Chennai, Karnataka, as well as Kerala is habituated by British in 18th era (Krishnamoorthy et al., 2001). Term ‘Myristica’ was outcome from Greek term ‘Myron’, meaning Sweet liquid cleansed from herb (Latha et al., 2005). It too used equally as constituents from carbonated beverages, curry powder, or assorted in milk or liquor. For a long time, *M. fragrans* has been used as a folklore medicine for treating diarrhea, mouth sores and insomnia (Somani et al., 2008). Since middle ages, Nutmeg has been given such as stomachic, to stimulate appetite, carminative and for intestinal catarrh as well as colic, to control flatulence also holds a status as an agent to stimulate blood flow and abortifacient (Asgarpanah et al., 2012).

1.1.2. Taxanomical Classification (Forrester., 2005)

<table>
<thead>
<tr>
<th>Kingdom          :</th>
<th>Plantae – Plants</th>
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<tbody>
<tr>
<td>Superdivision    :</td>
<td>Spermatophyta</td>
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<tr>
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<tr>
<td>Division         :</td>
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<tr>
<td>Class            :</td>
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</table>
Subclass : Magnoliidae
Order : Magnoliales
Genus : Myristica Gronov. – Nutmeg
Family : Myristicaceae – Nutmeg family
Species : Myristica fragrans Houtt. – Nutmeg

1.1.3. Vernacular Names (API, 1996)

<table>
<thead>
<tr>
<th>Language</th>
<th>Name</th>
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<tbody>
<tr>
<td>Sanskrit</td>
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<td>Urdu</td>
<td>Jauzbuwa, Jaiphal</td>
</tr>
</tbody>
</table>

1.1.4. Traditional Medicinal Uses

Practice of nutmeg as a spice in food preparation and as a medication for common sicknesses such as biliousness, vomiting, and diarrhea is centuries ancient. Seeing historically to 16th period, nutmeg is identified for its motar active possessions that contain anxiogenic and hallucination. Pharmaceutically, nutmeg has been accepted because of its anti-swelling as well as antithrombotic (Olajide et al., 1999), in addition to anti-rheumatic, besides carminative, as well as stimulant (Prabuseenivasan et al., 2006).
1.1.5. **Ayurvedic Properties (API, 1996; Moinuddin et al., 2012)**

- **Guna**: Laghu, Tiksna
- **Rasa**: Katu, Tikta
- **Vipak**: Katu
- **Virya**: Usna
- **Karma**: Dipana, Grahi, Vrsya, Mukhakledanasaka.

1.1.6. **Dose (API, 1996)**

0.5–1.5 gms of Extract in Powder form.

1.1.7. **Pharmacognostic Study**

1.1.7.1. **Macroscopic study (El-Alfy et al., 2009)**

*Myristica fragrans* is a dispersal fragrant ageless tree generally rising to near 5 to 13 m tall, sometimes its 20 m.

1.1.7.1.1. **Leaf:**

Leaves alternative, sharp, dark green 5-14 cm × 2-6.5 cm organized beside divisions stood on leaf stems near 1 cm long, sparkly on superior surface.
1.1.7.1.2. Flora:

Flowers dioeciously, light creamy, smooth, chubby and tumble-shaped. Male floras are about 57 mm lengthy and in clutches of 1-10; female floras is about 1 cm long and in clutches of 1-3 irregularly both genders are found on identical tree.

1.1.7.1.3. Fruit:

Fruits are ample, floppy, milky, smooth, 6 to 8.5 cm stretched along a longitudinal point. Once developed, luscious creamy fruit skin ruptures into two halves illuminating a purple to chocolate, glossy seed walled through a red aril.

1.1.7.1.4. Seeds:

Seeds are largely ovoid elongated about 2.1 to 3.1 cm, steady, overweight, milkyas well as diagonally red to brown strains. While new, aril is cheerful crimson charming hornier, hard too with a yellowish-brunet color once dried.

1.1.7.1.5. Bark:

Bark contains watery pink or red sap.

Photograph No. 2.1: Whole plant, Leaf, Flower and Fruit of Myristica fragrans
1.1.7.1.6. Microscopic Study (API, 1996)

Transverse section of endosperm demonstrate peripheral perisperm of numerous layers of toughly, compressed polyhedral cells with brown fillings, or else inclosing prismatic crystals, internal coating of perisperm of thin-walled parenchyma near 40 µ dense, in folding into tissue of endosperm to produce ruminations having several, bulky oil cells by tanned cell walls, vascular threads, in peripheral section, abundant slight curved vessels, huge celled, endosperm, parenchymatous with irregular tannin idioblasts through thin russet walls, encompassing plentiful modest, smooth and complex starch grains, through around 10 components generally 2-8 discrete grains, up to 20 µ in diameter extant, maximum of cells with crystalline fat and habitually a huge aleurone grain in every cell, holding a rhombic protein crystal up to 12 µ in addition minor aleurone grains with fewer steady crystalloids, embryo, of shriveled besides collapsed parenchyma.

1.1.7.1.7. Ayurvedic Formulations

Jatamamsyarka

1.1.7.1.8. Phytochemistry

1.1.7.1.8.1. Chemical Constituents

Volatile substances, terpenoids, phenolics, lignin compounds, protein, mucilage and starch are commonly known phytochemical compounds in *Myristica fragrans* (Naikodi et al., 2011; Saxena et al., 2012). Phytochemical examination showed occurrence of actual biological composite like alkaloids, steroids, flavonoids, tannins, phenolics, glycosides in essential oil (Saxena and Patil, 2012).

It was also identified main bioactive complexes containing elemicin, camphene, eugenol, isoeuglenol, isoelemicin, methoxyeugenol and elimicin essential oil. Forrest et al. isolated certain diarylpropanoid (bis-C₆–C₃) sorts of chemicals during investigation for psychoactive ingredients present not only in seeds of *Myristica fragrans* but also in fruits as well. Presence of two different structural types,
analogous to β-O-4 and 2, 3-dihydrobenzofuran types of dilignols, has been established (Forrest et al., 1974).

Hada et al. isolated 8 neolignans plus 5 lignans from mace and their chemical as well as molecular making were analyzed by spectroscopic devices (Hada et al., 1974).

Pal et al. characterized Sabinene, α-pinene, β-pinene, terpine-4-ol, limonene, safrole moreover myristicin in essential oil present in Nutmeg collected from Andaman and Nicobar Island (Pal et al., 2011). Ogunwande et al. isolated asinine (49.09%), α-pinene and terpinen-4-ol (6.43%) (13.19%), α-phellandrene (6.72%), from essential oil from seeds (Ogunwande et al., 2003). Hou et al. separated six compounds, licarin-B, dehydro diisoeugenol, malabaricone B, malabaricone C, β-sitosterol, and daucosterol from seed (Hou et al., 2012). Duarte et al. isolated Miristic acid, trimyristin, glycerides, stearic, lauric, linoleic and palmitic acids from nutmeg fixed oil (Duarte et al., 2011). Song et al. extracted Myristica fragrans Houtt in 80% aq. MeOH and solvent fractionated using CHCl_3, EtOAc, n-BuOH and water, successively. n-BuOH fraction gave three phenylpropanoids i.e. meso-dihydroguaiaretic acid, nectandrin B and syringin methyl (Song et al., 2004). Duan et al. characterized two new phenolic compounds i.e. (−)-1-(2,6-dihydroxyphenyl)-9-[4-hydroxy-3-(para-menth-1-en-8-oxy)-phenyl]-1-nonanone besides (7R,8R)-7,8-dihydro-7-(3,4-dihydroxyphenyl)-3′-methoxy-8-methyl-1′-(Epropenyl)-benzofuran on behalf of first stint in fruits (Duan et al., 2009).

1.1.7.1.9. Pharmacological Action
1.1.7.1.9.1. Anticancer Action
Forrest et al. considered consequence of methanolic extract over leukemia T cell line by cell metabolic action with MTT assay besides over apoptosis via staining with annexin V. Appearance of SIRT1 genetic factor was estimated through RT-PCR. Methanolic extract repressed cell multiplying besides tempted apoptosis as identified by staining with annexin V (Forrest et al., 2007).
1.1.7.1.9.2. Effect on Renal Cortical

It was estimated that aq. extract over renal cortical compositions of masculine as well as feminine experimental rats. Plasma reference standard like urea, nitrogen, serum creatinine also alkaline phosphatase from kidney damage jagged over high concentrations, in addition to body weights plus mean relative kidney weights were exaggerated by treatment. These conclusions specify that ingestion of nutmeg might be having some poisonous actions of renal cortical in adult Wistar rats in both sexes at advanced doses and may well disturb kidney metabolic function.

1.1.7.1.9.3. Hepatotoxic Action

Al-Jumaily et al. determine Hepatotoxic Action of Essential oil by (SGPT) and (SALP) besides (SGOT) as factors of liver function examinations in addition to serum total bilirubin (TSB). Arithmetical outcomes disclosed lack of any important variations on body mass besides liver load of mice treated by nutmeg. Still mice treated by nutmeg revealed statistically momentous variation in biochemical signs in function of liver containing noteworthy raise in SAST, SALP, as well as TSB, SALT depending on the dose. (Al-Jumaily et al., 2012).

1.1.7.1.9.4. Antidiabetic, Anti-hyperlipidemic, Hypoglycemic Effects

Arulmozhi et al. scrutinizes upshot of hydro alcoholic extract of fruits over chlorpromazine- persuaded glucose as well as triglyceride boosts. It pointedly abridged higher TG (reduction by 47% at dose of 450 mg, and p < 0.01) as well as lipid (66.7% reduction at 450 mg, p < 0.01), besides presented a drop on hepatic TG exudation later intake of tyloxapol. The outcomes from statistics direct that above extract promotes hyperglycemia plus irregular lipid breakdown in experimental rats. (Arulmozhi et al., 2007).

Somani, measured antidiabetic action of seeds of normal glycemic and alloxan-attracted diabetic rats. Blood glucose stages were assessed by means of glucometer. Also, variations in body mass, organ weight, and serum fatty acid
summary and blood factors assessed. Experimental rats possessing diabetes were managed by extract demonstrated enlargement in physique mass, organ weight, as well as sterol summaries besides composition of hemoglobin compared to diabetic control experimental rats. (Somani et al., 2008)

1.1.7.1.9.5. **Haematological Indices**

Bamidele et al. conducted work to evaluate effects of ethanolic extract on some haematological indices using albino rat as a model. Results showed that ethanolic seed extract of *M. fragrans* at high dose appears to suppress haemopoietic system. There were major decreases in RBC count, packed cell volume, haemoglobin concentration and platelet count. (Bamidele et al., 2011)

1.1.7.1.9.6. **Antibacterial action**

Bhamarapravati has reported antibacterial action of dried aril on gram-negative bacterium i.e. *Helicobacter pylori* by Disc diffusion method. Aqueous extract was also found significantly effective against *Helicobacter pylori* as compared to standard Chung et al. measured antibacterial action of Macelignan by *Streptococcus salivarius, Lactobacillus acidophilus, Streptococcus sobrinus, Streptococcus sanguis*, as well as *Lactobacillus casei*. Macelignan markedly lessen acid forming assets of bacteria (Chung et al., 2006).

1.1.7.1.9.7. **Aphrodisiac effect**

Tajuddin et al. evaluated aphrodisiac consequence of extract (50% ethanolic) by learning overall breeding behaviour, libido and potency. Extract when given orally at dose about 500 mg/kg, created major increase of sensual movement in male wistar rat. It suggestively improved growing Incidence, Intromission Occurrence, and Intromission Potential in addition initiated momentous lessening in Mounting Potential and Post Ejaculatory Intermission (Tajuddin et al., 2003).

1.1.7.1.9.8. **Antimicrobial Action**


**Takikawa et al.** Inspected variance among *Escherichia coli* 0157 as well as non-pathogenic strain of *E. coli* by agar plate method. When antibacterial result of volatile oils was examined on 0157 and non-pathogenic strains of *E. coli*, every 0157 strains verified were more sensitive to P-pinene rather than non-pathogenic strains of *E. coli* (*Takikawa et al.*, 2002).

### 1.1.7.1.9.9. Anxiogenic action

**Sonavane et al.** evaluated anxiogenic action of acetone unsolvable portion of *n*-hexane extract and trimepristin of seeds by open field test whole board test. *N*-hexane, acetone-insoluble part and trimepristin administered i.p. showed anxiogenic action in raised plus-maze paradigm (*Sonavane et al.*, 2002).

### 1.1.7.1.9.10. Anticonvulsant and Behavioral Actions

**Sonavane et al.** investigated anticonvulsant, cataleptic also sedative effects of *n*-hexane fragment of acetone unsolvable part of petroleum extract of seeds. Seizures brought by supreme electroshock, pentylenetetrazol, picrotoxin, besides lithium sulphate-pilocarpine nitrate. Upshot on gross behaviour, motor coordination, haloperidol-induced catalepsy plus pentobarbitone - induced sleep was calculated. Result exhibited anticonvulsant motion alongside MES, PTZ as well as lithium-pilocarpine, but it was unsuccessful to prevent picrotoxin-tempted seizures. It decreased central dopaminergic action never less remained with no outcome on sleep induced by pentobarbitone (*Sonavane et al.*, 2002).

### 1.1.7.1.9.11. Antidiarrhoeal and Antispasmodic action

**Shamkuwar et al.** evaluated aqueous extract for its antidiarrhoeal effect in castor oil made diarrhea in mice and antispasmodic consequence on reductions prompted by acetyl choline, nicotine plus histamine in insulated guinea pig ileum. It produced a significant and dose dependent antidiarrhoeal effect also repressed acetyl choline, nicotine and histamine convinced retrenchments of isolated guinea pig ileum. It can be resolved that extract holds antidiarrhoeal and antispasmodic action possibly will
be owing to its anticholinergic and antihistaminic outcome (Shamkuwar et al., 2013).

1.1.7.1.9.12. Anti-parasitic Action

Pillai et al. investigated essential oil for cytotoxicity on normal cell line as well as anti-parasitic action in contradiction of *Toxoplasma gondii* organism. Founded on capable outcomes, volatile essential oil from nutmeg may be additionally considered as mode of action in contradiction of *Toxoplasma gondii* as well as detaching principal components for managing toxoplasmosis (Pillai et al., 2012).

1.1.7.1.9.13. Improvement of Memory

Parle et al. investigates effect of n-hexane seeds extract on knowledge and remembrance in mice. Extract developed learning plus retaining abilities of young as well as old mice. Nevertheless, discovered remembrance-improving consequence might be recognized due to variation in characteristics. Herb is specified to hold, anti-swelling, or procholinergic action (Parle et al., 2004).

1.1.7.1.9.14. Anthelmintic Action

Dwivedi et al. evaluated crude extracts of seed for Anthelmintic action in experimental adult earthworm’s *Pheritima posthuma*. Result stated in term of period for paralysis as well as period for death. Alcoholic and aqueous extract of *Myristica fragrans* (Nutmeg) show potent Anthelmintic action (Dwivedi et al., 2010).

1.1.7.1.9.15. Antifungal Action

Pooja et al. carried out anti-fungal consequence of hexane, methanolic, chloroform, in addition ethanolic extract attained from Mace. Their *in-vitro* helplessness examination was ended through disc diffusion technique. MIC80 was analyzed by micro broth dilution technique. Methanol as well as n-Hexane extracts are found to be significantly operative against organisms tested. MIC80 observed was lowest
for methanol extract in contradiction of *Candida albicans* as well as *Aspergillus Niger* (Pooja et al., 2012).

1.1.7.1.9.16. **Immunomodulatory and Radio Protective Effects**

Immunomodulatory and radio modifying effects of lignans existent in mace aq. extract of *M. fragrans* in mammalian splenocytes. The macelignans subdued production of splenocytes over reaction to polyclonal T cell mitogen concanavalin A. It endangered splenocytes against intracellular ROS making induced by radiation in dosage dependent way.

1.1.7.1.9.17. **Antioxidant Action**

Kim *et al.* scrutinized Antioxidant ability of nutmeg oil by 2, 2-diphenyl-1-picrylhydrazyl (DPPH) unrestricted radical scavenging test n β-carotene-linoleic acid test. The potential of antioxidant action of nutmeg in DPPH assay counted in following terms: Subsequent order: Eugenol > methoxyeugenol > BHT > isoeugenol > α-tocopherol, whereas in β-carotene-linoleic acid test, antioxidant events of chemicals were in following order: α-tocopherol > BHT > isoeugenol > methoxyeugenol > eugenol (Kim *et al.*, 1999).

Gupta *et al.* appraised Antioxidant activities of acetone, ethanol, methanol, butanol and water extracts of seeds by DPPH scavenging action, Gallic acid equivalents, and total phenolic content. All extracts have shown significant antioxidant and antimicrobial activities against tested microorganisms (Gupta *et al.*, 2013).

The antioxidative effect of open aglycones in difference with essential oil of nutmeg by 2, 2’-diphenyl-1-picrylhydrazyl radical scavenging technique as well as test for ferric decreasing strength. These procedures demonstrated that aglycones portion possesses tougher antioxidant action than free volatiles of the oil.
1.2. Crocus sativus (Kesar)

1.2.1. General Information

About 85 species going to genus *Crocus*, Utmost charming and exciting species is saffron. Name “saffron” is outcome from Arabian term “Zofran”, meaning “yellow” (API, 1996; Maghsoodi et al., 2012). *Crocus sativus L.* is an herbaceous enduring, stemless basil contains of desiccated red stigma along with minor fraction of yellowish flair attached (Srivastava et al., 2010; Kumar et al., 2011). Saffron remained an imperative cultured plant through historical era of Ottoman Empire; however its manufacturing has diminished over time. Total world saffron manufacturing is projected at 220,000 kg, of which about 90% is formed in Khorasan Province, Greece, Spain, Italy and India (Arslan et al., 2007; Jahan et al, 2007). No additional flower has a more esteemed recognized account than saffron crocus. Saffron crocus is chiefly cultured in numerous countries of mild and dry climate (Abdullaev et al., 1990). Cost of saffron is resolute due to presence of chief tributary metabolites: derivatives of Crocin which are responsible for color; taste is due to picrocrocin and safranal accountable for odor. Stigmas from herb are mostly utilized for beneficial purposes. Stigmas of Kesar are utilized widely as coloring along with additive agents in production of food in diverse portions globally. Besides its utilization for preparing nutrition, Kesar stigmas are utilized in management in various illnesses conventionally. Medicinal assets recognized to saffron are widespread (Vijaya et al., 2011). Compounds deliberated pharmacologically dynamic and significant are volatile agents, bitter principles also dye materials.

1.2.2. Taxanomical Classification (Himeno et al., 1987; Nerkar et al., 2011)

Kingdom : Plantae
Division : Magnoliophyta
Class : Liliopsida
Order : Asparagales
Genus : Crocus
Species : *Crocus sativus*
1.2.3. Vernacular Names

Hindi : Kesar, Zaffran
English : Saffron
Sanskrit : Avarakta, Saurab, Mangalya, Agnishikha, Kumkuma
Tam : Kunkumappu
Persian : Zafran, Zipharana
Ben : Jafran
Tel : Kunkum-Purva, Kunkumma-Purru
Bom : Safran, Kessar
Mah : Kecara
Guj : Kesar

1.2.4. Traditional Medicinal Uses (Vijaya et al., 2011)

Charaka used crushed stigmas as unique medications in management of cataracts, night vision impairments as well as poor visualization. Sushruta utilized this to clean the blood also to manage skin outbreaks within. Likewise it is utilized to treat bacterial infections, sepsis, antiflatulent, as well as fungal infections. Kesar is mostly utilized because of healing actions comprehensively in folk medication for several determinations, like erotic action stimulator, antispasmodic, declining stomachache, linctus, plus for decreasing hypertension. In Persian folk medication Kesar is utilized for depression. Similarly utilized in management of insomnia as well as for management of dysentery, measles, cholera, jaundice, and other ailments. Topically in gum formation to manage skin infections resembling acne. In industries Kesar is utilized as staining as well as for manufacture of innumerable fragrances as well as anger sticks. Kesar acts as a stimulant for cardiac as well as central nervous system also easing menstruation.
1.2.5. Ayurvedic Properties

<table>
<thead>
<tr>
<th>Property</th>
<th>Description</th>
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<tbody>
<tr>
<td>Guna</td>
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<td>Ushna</td>
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<tr>
<td>Karma</td>
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</tbody>
</table>

1.2.6. Pharmacognostic Study

1.2.6.1. Macroscopic study (Srivastava et al., 2010; Khare et al., 2004)

- Kesar resembles to grass corm herb having ornate or amethyst flowers with colors.
- Color - Magenta red to rose-colored brunet. Style is yellowish brunet to yellowish color like carrot.
- Odor - Unique as well as aromatic
- Taste- Distinguishable as well as bitter

1.2.6.2. Description

Flower stem arises through a bulb that is long, white, thin duct. Flower them self appears vast, as well as of attractive violet tint. Foliage are deep-rooted, lined, bright green lower, surrounded in a membranous layer, dark emerald green upstairs, infrequently remaining fresh virtually complete wintertime. Stigmas three, huge, virtually an inch extended, trolled at ends, bright auburn. Stigmas of Kesar are parts that have remained salvaged in medication. They have a humorously unpleasant and slightly roasting taste. They include a big part of extractive material, along with small portion of volatile oil.

1.2.6.3. Microscopic Study (Evans, 1996)

Stigma is made up of lengthen, parenchyma cells, thin-walled, including coloring element; at upper end rich cylindrical trichomes about 150 microns in length.
Photograph No. 2.2: Whole plant, Flower, Tuber and Root of *Crocus sativus* Linn

1.2.6.4. Ayurvedic Formulations

Karpuradyarka, Balarka Rasa, Yakuti, Kunkumadya Taila, Mahanarayana Taila, Pusyanuga Curna

1.2.6.5. Phytochemistry

1.2.6.5.1. Chemical Constituents

Phytochemical screening of *Crocus sativus* revealed that saffron contain monoterpenes, carotenoids, picrocrocin, aldehydes, glycosides, and antocyanins, vitamins, amino acids, flavonoids, proteins, minerals and starch. Essential oil includes several terpenes as well as carbonyl complexes (*Esmailian et al.*, 2012). Bitter-taste is created by a monoterpene glycoside pioneer of safranal (C\textsubscript{10}H\textsubscript{14}O) picrocrocin (C\textsubscript{16}H\textsubscript{26}O\textsubscript{7}), key essential oil answerable to fragrance. β-Glucosidase stroke on picrocrocin releases aglycone, 4-hydroxy-2, 6, 6 trimethyl-1-cyclohexene-1-carboxaldehyde, that is distorted to safranal by dehydration through drying procedure for herbalsubstance. Perfume from *Kesar* raises from its essential oils,
mainly composed of terpenes, aldehyde, safranal, being chief volatile constituent in stigmas of Kesar. (Roedel et al., 1991; 2009). Maximum absorbance for safranal is about 330 nm. Dye ingredients cooperatively signified because of crocins, instigated from glycosidic which is water soluble carotenoid, glucosyl esters of crocetin. Crocins liquefy effortlessly in H₂O to afford an orange to red solution. Hence utilized as food dye (ISO/TS, 2003).

Chemical readings on stigmas described that it holds carotenoids like crocetin, its glycosidic compositions are digentiobiosideglucoside, γ-crocetin gentioglucoside, as well as zeaxanthin, β-carotene., lycopene, as well as mangicrocin, carotenoid glycosidic a xanthone, α-carotene, conjugate trans crocetin isomer, 13-cis-crocetin (Srivastava et al., 2010).

Saffron comprises about 150 volatile besides fragrance - yielding mixtures. Likewise Kesar possesses various non-volatile vital elements, several like carotenoids together with zeaxanthin, lycopene etc (LiakopoulouKyriakides et al., 2002). Hadizadeh isolated kaempferol from fresh flower petals as sole component. They use methanol containing 1% concentrated HCl for extraction. Structure of entity was analyzed by chemical as well as spectroscopic methods (Hadizadeh et al., 2003).

1.2.6.5.2. Analytical Methods

Process of saffron superiority categorization presently suggested by International Standardization Organization (ISO/TS2003), is UV-viz spectrophotometry. Regrettably, process is not precise and incapable to adequately scatter amongst natural and miscellaneous saffron, and thus unable to afford a dominance class on worldwide arcade. Innumerable precise systems have been recognized with TLC Fingerprinting, (Sampathu et al., 1984); R-HPLC attached by UV–vis sensor as well as PDA. MS as well as GC (Narasimhanet al., 1992). Technique used in this experiment for eminence resolve of saffron is HPLC by PDA sensor. This analytical process best operative analytical system for examination of slight complexes in compound extracts of herbal products (Alonso et al., 2001).
1.2.6.6. Pharmacological Action

1.2.6.6.1. Antitumor Effect

Abdulla et al. scrutinized antitumor actions for Kesar as well as principal elements, also possible mode of activity. Kesar as well as its carotenoid constituents possess chemoprotective in dispromote human malignant cells as well as experimental animal models, hampering cell development. This may elucidate mode of action for herb to decrease extension of tumor cells in human cells. The study has demonstrated that cancer cells are extra delicate compared to normal cells for the inhibitory action of Kesar. (Abdullaev, 1998). He also examined anti-proliferative properties of extract and its chief element on three colorectal cancer cell lines over MTS test. Information by this study established that extract and its chief component profoundly suppressed development of colorectal cancerous cells and it will not influence to original cells. Explored in vitro as well as in vivo xeno graft development inhibition through crocin extracted from saffron. It was established that crocin reduced cell feasibility in DLA cells, which was dependent on concentration as well as time. Similarly Crocin showed main effect on hematological factors, similar to hemoglobin as well as numbers of lymphocytes. These conclusions confirm the assumption that Crocin has considerable anti-tumor action.

1.2.6.6.2. Antidepressive effect

Kamalipour et al. demonstrated efficiency of stigmas of Kesar in management of minor to moderately depressed in a two month binary sightless, placebo and randomized trial. Outcomes of the said research showed utility of Kesar Extract in treatment of minor and adequate depression. Kamalipour et al. criticisms clinical studies about antidepressant effect of saffron (Kamalipour et al., 2010). They also equated usefulness of alcoholic (50-70%) extract of stigma through fluoxetine in management of minor to moderately depressed. Substantial variances in two sets in relations of observed adverse reactions were absent. Consequences of this experiment postulate efficiency of Crocus sativus in management of minor to moderately depressed conditions.
1.2.6.6.3. Antigastric action

Al-Mofleh et al. exposed suspension of saffron in aqueous medium improved gastric antiulcer action induced through pylorus ligation, indomethacin as well as several necrotizing intermediaries also comprising in rats suspension of saffron in aqueous medium at altered doses revealed reduction in basal gastrointestinal exudation as well as ulcer catalog in experimental animals as well as set treated by indomethacin (Al-Mofleh et al., 2006). He also inspected properties of Kesar extract on stomach acid and digestive enzymes discharge. Basal and stimulated acid and pepsin exudations were measured by means of titration and Anson technique. Saffron extract enflamed basal and inspired gastric liberations. It looks that saffron extract rises via NO augmentation.

1.2.6.6.4. Antioxidant Action

It was evaluated that DPPH radical scavenging action of extract as well as its principal elements specifically Safranal as well as crocin. Extraordinary radical scavenging action Crocin was displayed by safranal. The verified samples revealed high radical scavenging action, possibly due to capability of donating a H-atom to DPPH molecule revealed antioxidant features of 50% methanol extract of stigmas by determining ferric-reducing antioxidant influence and Trolox-equivalent antioxidant ability. It retains decent antioxidant features, greater compared to tomatoes as well as carrots.

1.2.6.6.5. Effect on Blood and related products

Bayrami et al. inspected significance of extract as well as safranal, over inflammatory variations of sensitized guinea pigs. These results revealed a defensive action of extract and its element safranal as whole and discrepancy amount of WBC in blood of sensitized guinea pigs (Bayrami et al., 2012). He also inspected characteristic of petal extract over BP in anaesthetized experimental rats as well as on reactions of isolated vas deferens of rat as well as ileum of guinea-pig brought by electrical field incentive. Aq.as well excerpts of petals compact BP on depending on dose.
1.2.6.6. Obsessive–compulsive disorder (OCD)

The Crocin was capable to neutralize excessive self-preparing induced by mCPP in rats. Non-selective serotonin receptor agonist mCPP is famous to encourage OCD-like activities in rodents and aggravate indications in patients with OCD. Their discoveries advise that active elements may assist in habitual activities as well as backing a purposeful collaboration between Crocin and serotonergic organization.

1.2.6.7. Anti-obesity action

Oral supplementation through, an advanced extract stigma of Kesar, might diminish snacking and boost satiety by its proposed attitude enlightening consequence, and therefore contribute to weight loss. Our fallouts specify that through Satiereal feeding it produces a decrease in snacking also generates a satisfying influence which can subsidize to weight loss. Amalgamation of a suitable diet with l supplementation of Satierea diet may support subjects involved in a program of weight loss in accomplishing their object of the experiment

1.2.6.8. Protective effect

Hosseinzadeh et al. patterned Defensive influence of aq. extract of saffron on oxidative injury induced by renal ischemia-reperfusion in experimental animal used. Cellular redox position antioxidant influence was judged in control besides ischemic groups. This learning therefore recommends that aqueous saffron extract its vigorous principal, crocin, could be suitable mediators for avoidance in renal ischemia reperfusion leads to oxidative harm in Animals(Hosseinzadeh et al., 2005).

Hosseinzadeh et al. perused significance of aq. extract of stigmas as well as crocin on methyl methane sulfonate – tempted DNA impairment in multiple mice tissues by comet test. Aqueous saffron extract and crocin ominously lessened DNA impairment by MMS in dosage reliant method. The records signpost that genoprotective property is present in CSE as well as crocin, as per discovered through comet test, in vivo (Hosseinzadeh et al., 2008).
Boroushaki et al. evaluated defensive significance of safranal for HCBD persuaded toxicity of kidney in rats. Blood urea absorption for HCBD cured group is found to be considerably higher. No momentous alterations were detected in of glucose in urine among HCBD as well as safranal cured individuals. Safranal about of 0.25 as well as 0.5 ml/kg possesses protective influence against HCBD persuaded toxicity of nephrons in rats (Boroushaki et al., 2007).

1.2.6.6.9. In premenstrual syndrome

The double sightless besides placebo controlled experimental study showed that saffron might discharge signs of premenstrual syndrome. Fallouts of this study specify usefulness of extract in management of PMS. Nerveless, an acceptable argumentative consequences summary of Kesar could well ratify use of saffron to additional action for PMS.

1.2.6.6.10. Aphrodisiac effects

Hosseinzadeha et al. assessed effect of extract plus its elements, safranal as well as crocin on erotic performances in regular masculine rats. Mounting frequency, erection incidence, intromission dormancy, intromission occurrence, mount dormancy in addition ejaculation dormancy were aspects appraised through sensual performance study. Crocin and extract increase Mounting incidence, intromission incidence erection occurrence and condensed intromission potential, mount expectancy in addition ejaculation potential factors. Safranal failed to demonstrate aphrodisiac properties. Current experiment discloses an anti-fertility action for aqueous extract of saffron than its component Crocin. (Hosseinzadeha et al., 2008). Karimi et al. resoluted antioxidant potential of Stigma Phenolic and Flavonoid Composites. Free radical destroying and decreasing power of ferric actions were greater for extract from methanol as related to boiled water and alcoholic extracts, but events were minor as compared to antioxidant criteria such for α-tocopherols as well as BHT. Outcomes displayed that saffron stigma hold antioxidant action (Karimi et al., 2010).
1.2.6.6.11. Alzheimer's Disease

Khalili et al. explored influence of active constituent Crocin on irregular Alzheimer's disorder persuaded by streptozocin through intra cerebro ventricular routes in male rats. Fallouts reveal usefulness of crocin in provoking cognitive shortfalls initiated through STZ-icv among rats as well as its prospective in management of neuro degenerative syndromes like Alzheimer's disorder (Khalili et al., 2010). It was resoluted that 50% alcohol extracts of stigma for Alzheimer’s disease by thioflavine T-based fluorescence test also by DNA binding shift examination.

Alzheimer’s disorder is considered pathologically by entry fibrils of amyloid β-peptide. Our verdicts recommend possible use of stigma elements for embarrassment of accumulation plus accumulation of Aβ in brain of the human.

1.2.6.6.12. Skin Care

Vyas et al. surveyed collective complexion outcome of dry ethyl acetate: isopropyl alcohol: Water extract from stigmas which was protected in numerous cosmetic goods. Outcomes of complexion property plainly detected shine and lightening of skin owing to crocin and crocetin present in saffron (Vyas et al., 2010).

1.3. Symplcos Racemosa

1.3.1. General Information

In current scenario, attention on plant investigation has improved globally also a huge frame of indication has composed to display enormous possibility of remedial herbs utilized in several traditional medical systems. (Bora et al., 2011;). Symplcos racemosa belongs to trivial, classic tree, upto 8.5 m tall establish in plains and minor hills all over North as well as East India, climbing in Himalayas tillelevation of 1400 m, Bengal and Chota Nagpur (Sharma et al., 2000). Symplcos is a species of blossoming florae in direction Ericales, holding approximately 250 types inborn to Americas, Asia as well as Australia. Around 68 types are originated in India, of which merely a rare are of economic significance (Rao et al., 2011). In Sanskrit this tree was identified as Lodhra.
meaning "Tilaka" as it was used in creating Tilaka spot on forehead (De Silva et al., 1979).

1.3.2. Taxanomical Classification (Sharma et al., 2000)

Kingdom : Plantae
Division : Magnoliophyta
Class : Magnoliopsida
Order : Ericales
Family : Symplocaceae
Genus : Symplocos
Species : *Symplocos racemosa*

1.3.3. Vernacular Names (Kirthikar et al., 1999)

Sanskrit : Rodhra, Paittki Lodhra, Sabara Lodhra, Tirita.
Assamese : Mugam
Kannada : Lodhra
Kashmiri : Kath
Bengali : Lodha, Lodhra
English : Symplocos bark
Punjabi : Lodhar
Tamil : Vellilathi, Vellilothram
Guajarati : Lodhaz
Hindi : Lodha
Malayalam : Pachotti
Telugu : Lodhuga
Urdu : Lodh, Lodhpathani
Marathi : Lodhra

1.3.4. Synonyms
Lodhra, Shavaraka, Akshibhaishajya, Rodhra, Tirita,Sthoolavalkala, Tilva, Galava

1.3.5. Traditional uses (Kirthikar et al., 1999; API, 1996; Raghunathan et al., 2000)

Bark is astringent, expectorant, anti-inflammatory, febrifuge, hemostatic, stomachic, constipating and supportive. It is beneficial in eye diseases, spongy besides bleeding gums, asthma, bronchitis, dropsy, arthritis, ulcers, tumors, leprosy, skin diseases, acne and pimples, fever, hemorrhages, menorrhagia, dyspepsia, flatulence, leucorrhoea, diarrhea, dysentery, hepatic disorders, chyluria (filarial), elephantiasis, hemorrhoids, baldness, scrofula, ear diseases and gonorrhea.

1.3.6. Ayurvedic Properties (API, 1996)

Rasa : Kashaya
Guna : Laghu, Ruksha
Veerya : Sheeta
Vipaka : Katu
Doshaghnata : Kaphapittashamaka
Rogaghnata : Shotha, Vrana, Netrabhishyanda, Atisara, Jwara etc.
Karma : Shothahara, Kushaghna, Chakshushya, Sara,
Vranaropana etc.

1.3.7. Siddha Properties (Sharma et al., 2000).

Siddha Name : Vellilatthi, Velligloththiram
Suvai (Taste) : Thuvarppu (Astringent)
Veeriyam (Potency) : Thatpam (Cooling)
Vipakam (Transformation) : Inippu (Sweet)
Ceikai (Pharmacological action) : Kuzhirchiundakkki (Refrigerant)
Gunam (Uses) : Used in Ascitis and Bone disorders.

1.3.8. Dose (API, 1996)
3-5 gm of drug used in concentrate form
20-30gm of drug used in for decoction

1.3.9. Pharmacognostic Study
1.3.9.1. Macroscopic study (Sharma et al., 2000; Kirthikar et al., 1999)

1.3.9.1.1. Leaf:
Leaves unpretentious, substitute, curved; petiole about 1.5 cm in length, Plano convex in cross fragment, glabrous; lamina 6.5 - 12.52 x 3.5 - 4.5 cm, ob lanceolate toward thin elliptic, peak barely acuminate, small base, boundary indent as well as somewhat curved, glabrous; canaliculated upstairs midrib; ancillary nerves 6-12 pairs; tertiary nerves obliquely faintly per current (Fig 1).

1.3.9.1.2. Fruit:
Drupe, elliptical or rectangle, calcium 1.5 cm lengthy; seeds 1-2 (Fig 1).
1.3.9.1.3. Bark:

Bark darkish, lenticellate; glow cream (Fig 1).

Photograph No. 2.3: Whole plant, Fruit and Bark of *Symplocos racemosa*

1.3.9.2. Microscopic study (API, 1996)

Transverse section of mature bark displays a varied cork of tinny walled, quadrilateral cells, cork cambium 1-3 coated, subordinate cortex contains parenchymatous cells near outside and curved cells near inside, an amount of stone cells distributed through expanse having vastly thickened walls with distinct pits, prismatic and bunch quartzes of calcium oxalate, and starch grains, frequently modest existing in a quantity of cortical cells. Secondary phloem inclusive containing of medullary rays, sieve essentials, phloem parenchyma, phloem fibers and stone cells.
1.3.9.3. Importance of Lodhra in Ayurveda (API, 1996; Chunekaret al., 2010)

In Ayurvedic texts, Lodhra has been elaborated in detail because of Pitta dosha as well as Kapha dosha Shaman accomplishments i.e. it alleviates vitiated doshas of body. Lodhra cleans wound, arrests bleeding and initiate fast healing process of wound. Due to Rodhaka (arresting) property of plant it is also called as Rodhra. Since thousands of years, Lodhra has been used safely to treat many GI tract disorders. Lodhra bark is pungent, assimilating as well as astringent to bowels. Due to its Grahi (anti-diarrheal) property it is commonly used to treat Atisara (diarrhea). Lodhra has also been used as Sheet Virya (cool potency), Laghu (light quality), Netrahitakara (beneficial for eyes) and Rakta dosha Nashaka.

According to Ayurveda, Lodhra reduces fever and cures spongy gums/bleeding. It is useful to treat skin diseases (such as leprosy), dropsy and liver complaints. It has been recognized as drug of optimal in management of gynecological disorders. Lodhra has been used to cure menorrhagia, leucorrhea (excessive discharge from vagina) and or menstrual disorders. It is similarly beneficial for abortions as well as miscarriages and for ulcers of vagina. These officinal properties have made Lodhra as an authoritative herb to treat various health related disorders of mankind.

1.3.9.4. Ayurvedic Formulations (Rao et al., 2011)

Some important Formulations which contains *Lodhra* as an important ingredient are:

<table>
<thead>
<tr>
<th>Table No. 2.1: Formulations of <em>Lodhra</em></th>
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<tr>
<td><strong>Formulation of Lodhra</strong></td>
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<tr>
<td>Rodharasava (Lodhrasava)</td>
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<tr>
<td>Pushyanuga Churna</td>
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<tr>
<td>Formulation of Lodhra</td>
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<tr>
<td>Bruhat Gangadhara Churna</td>
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Some formulations which contain Lodhra as important ingredients are Pushyanug churna, Drakshadi kvath chuna, Rodhrasava, Somnath ras, Srikhandasava, Kunkumadi taila, Sarivadyasava, Vidangarishta, Laghugangadhara churna, Abhrak bhasma, Asthisandhanaka lepa, Vastyamayantaka ghrita, Bhringaraj taila, Ushirasava, Briha gangadhara, Kutajastak kvath churna, Chandanasava, Tutthadi lepa, Nagarjunanjan, Dashmularishta, Kumaryasava, Prameha mihira taila, Gangadharchurna, Grahanimihir taila, Pippaladyasava, Irimedadi taila, Jatyadi taila, Piyushvalli rasa, Jivantyadi ghrita, Kasisadi ghrita, Khadiradi gutika, Nyagrodhadi churna, Lodhrasava, Vimla vartti.

1.3.9.5. Phytochemistry

1.3.9.5.1. Chemical Constituents

Bark holds flavanol glucosides resembling symposide, leucopelargonidin 3-glucoside, symlocoside, ellagic acid, flavonol glycoside like rhamnetin 3-digalactoside, triterpenoids similar 28-O-bis-β-glucopyranosides, 19α-hydroxyarjunolic acid-3, 28-O-bis-β-glucopyranosides, Oleanolic acid, betulin 19α-hydroxyasiatic acid-3, β-sitosterol and α-amyrin (Nagore et al., 2012; Badonia et al., 2010). Apart from chemical constituents bark mainly contains alkaloids loturine, isoloturine and harmane (Junko et al., 2001). De Silva. Al reported Oleanolic acid, Betulinic acid through Petroleum ether extract and Ellagic acid from methanol extract (De Silva et al., 1979). Ali et al. isolated three new triterpenes 18(19)-dien-28-oic acid and 24-hydroxyolean-12-en-3-one, 28hydroxy-20α-urs-12,18(19)-dien-3β-yl acetate, 3-oxo-urs-20α-12 organized with notorious triterpenoids betulin plus oleanolic acid (Ali et al., 1990). Ahmad et al. secluded phenolic glycoside named benzoylsalireposide sideways five recognized compounds i.e. oleonolic acid, salireposide, β-sitosterol, β-amyrin, and β-sitosterol glycoside. They used methanolic extract for obtaining residue. Complete rest was mined with hexane, and butanol, ethyl acetate, chloroform. Extract of Ethyl acetate was exhibited to CC over a column of silica gel by means of n-hexane with incline of chloroform upto 99-
100\% and followed by methanol (Ahmad et al., 2003). Ahmad et al. analysed two novel phenolic glycosides known as Symconoside A and Symconoside B. Extract from methanol is liquefied in aqueous media and divided successively with $n$-hexane, then ethyl acetate, followed by chloroform, and $n$-butanol. Then fraction from Ethyl acetate was exhibited to VLC above plate-silica using gradient of hexane and chloroform followed by methanol (Ahmad et al., 2005). Abbasi et al. isolated novel ethyl replaced glycoside, 1-ethyl brachiose-3'-acetate beside per four identified composites non aeicosanol, keto chaulmoogric acid, triacontyl palmitate and methyl triacontanoate. They dissolved Methanolic extract in water and segregated with chloroform, ethyl acetate, hexane, and $n$-butanol continually. Butanol soluble segment was exposed to column chromatography over a column with silica gel using chloroform with a gradient of methanol up to 99-100\% (Abbasi et al., 2005). Ahmad et al. isolated one new C-glycoside, symcososide along with one known compound sito-glycoside (Ahmad et al., 2006). Ahmad et al. separated two novel phenolic glycosides of salirepin sequence, symplocuronic acid as well as symhocemoside. They dissolved Methanolic extract in $H_2O$ and separated with CHCl$_3$, ethyl acetate, $n$-hexane, and $n$-butanol successively. N-butanol extract was exposed to column chromatography over silica gel through CHCl$_3$ with gradient of methanol.
Photograph No. 2.4: Important chemical constituents of *Symlocos racemose*

1.3.9.6. Standardization by Sophisticated Instrument

Nagore *et al.* established new HPTLC technique to resolve Loturine in dissimilar bark extracts. They established HPTLC plates pre-coated on aluminum with silica gel in escalating direction into identical twin trough chamber formerly saturated by solvent phase containing of chloroform: acetonitrile: triethylamine. Loturine showed a bluish tint on chromatographic plate over a luminous background. Finding and quantification were achieved by densitometry at 280 nm (*Nagore et al.*, 2012). Nagore *et al.* advanced RP-HPLC process for approximation and measurable determination of Loturine. RSD and Correlation coefficient were calculated and initiate to be satisfactory (*Nagore et al.*, 2012). Nagore *et al.* also established original HPTLC method to resolve gallic acid in dissimilar bark extracts. they established aluminum HPTLC plates coated with silica gel in increasing direction into twin channel glass chamber previously soaked with solvent system consisting of toluene: ethyl acetate: formic acid: methanol. Gallic acid was seemed as dark brownish colored chromatographic regions at Rf value 0.70 (*Nagore et
al., 2012). Kumar et al. established fresh HPTLC technique to resolve harmine in diverse bark extracts. They developing aluminum HPTLC plates coated with silica gel in increasing direction into twin channel glass chamber previously soaked with solvent system consisting toluene: Ethyl Acetate: Methanol (Kumar et al., 2006).

1.3.9.7. 3. Pharmacological Action

1.3.9.7.1. Anti-Acne Effect

Kumar et al. examined anti-acne events of ethanolic extracts of Symlocos racemosa bark through disc dispersion besides broth dilution techniques. Consequences after disc diffusion technique indicated that medicinal plants might prevent growth of Propionibacterium acnes (Kumar et al., 2007).

1.3.9.7.2. Analgesic as well as Anti-inflammatory Action

Sharma et al. projected analgesic action of ethanolic besides aqueous extract of bark via formalin made paw licking and tail flick mockups and anti-inflammatory action by Carrageenan persuaded hind paw edema model. Their effects exposed that Ethanolic extract meaningfully defeat inflammation than aqueous extract (Sharma et al., 2013). Vijayabaskaran et al. likewise examined anti-pyretic action of bark ethanolic extract alongside brewer’s yeast induced pyrexia. After study it was manifest that ethanolic extract have antipyretic action (Vijayabaskaran et al., 2010).

1.3.9.7.3. Antioxidant action

Devmurari confirmed free radical scavenging action of ethanolic extract of leaves and flowering topmost thru assessing equal of lipid peroxidation, superoxide dismutase, glutathione, catalase and protein content. Extract indicated momentous events in all antioxidant tests by decreasing lipid peroxidation, superoxide dismutase and catalase action (Devmurari et al., 2010). Vijayabaskaran et al. observes antioxidant action of ethanolic extract of bark by DPPH, Hydroxyl radical, Nitric oxide and ABTS test method. Their outcomes specified that ethanolic extract displayed effective antioxidant action beside ABTS test method (Vijayabaskaran et
al., 2010). Ravichandran et al. also revealed that standard constituents of *Symlocos racemosa* i.e. salireposide and benzoyl salireposide have effective antioxidant action (Ravichandran et al., 2005).

### 1.3.9.7.4. Anthelmintic Action

*Rao et al.* estimated anthelmintic action of chloroform, petroleum ether and ethanol extract of bark on mature Indian earthworms, *P. posthuma*. Current examination divulges that ethanolic extract was brilliant with effective anthelmintic things as equal to further extract (Rao et al., 2011).

### 1.3.9.7.5. Anti-Angiogenic Action

*Hussain et al.* have reported Anti-Angiogenic action of symlocoside I and symponoside II, glycosides insulated from bark. Its outcomes discovered that both isolated glycosides prevent thymidine phosphorylase action and related angiogenesis (Hussain et al., 2003).

### 1.3.9.7.6. Antibacterial Action

*Devmurari et al.* gauged antibacterial action range of ether as well as ethanolic extract of bark which used three Gram negative microorganisms *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, *E. coli* and three Gram positive microorganisms, *Staphylococcus aureus*, *Bacillus cereus*, *Enterococcus faecalis*, ethanolic extract possess good antibacterial action as associate to petroleum ether (Devmurari et al., 2010). In one of their trials, Devmurari similarly displayed that extract has deprived antibacterial action together with gram negative microorganism such as *Pseudomonasaeruginosa* as well as *E. coli* (Devmurari et al., 2010).

### 1.3.9.7.7. Anticancer Action

*Raval et al.* estimated chloroform, n-butanol also ethyl acetate extracts of bark were arranged along with cytotoxicity action resolute by XTT salt established cytotoxicity analysis against one leukemia besides one cervical malignance cell line. They described that butanol extract have maximum cytotoxicity action alongside HeLa cell
line (Raval et al., 2009). Raval et al. similarly stated n-Butanol extract has cytotoxicity action in contradiction HL 60, HeLa. Extract from Ethyl acetate failed to produce cytotoxic action in contradiction of HL 60. Chloroform extract showed no cytotoxicity against both cell lines (Raval et al., 2009).

1.3.9.7.8. Hepatoprotective action

Wakchaure et al. appraised ethanolic extract of bark on carbon tetrachloride possessed hepatic mutilation in rats. Ethanol extract displayed imperative dosage dependent restoration of enzymes of serum, bilirubin level and levels of antioxidant. As well as progresses in hepatoprotection, morphological, and histopathological deviations. So it is an operative hepatoprotective entity in hepatic injury induced by CCl₄, also has prospective medical claims for handling liver disorder (Wakchaure et al., 2011).

1.3.9.7.9. Female Reproductive Disorders

The ethanolic extract of bark in treating female reproductive disability. Cold limitation pressure was utilized to tempt fluctuations in reproductive disabilities. Since trial experiments, Ethanolic extract of bark at two diverse amounts presented auspicious in curing female reproductive disabilities initiated by cold restraint strain. Ali et al. investigated in vivo outcome of aqueous excerpts of bark on serum FSH level as well as LH levels in young feminine rats below basal environments. Aq. extract by orally administration of drug suggestively motivated serum FSH level and also increase in level of serum LH (Ali et al., 2004). Swarup et al. similarly mention practicality of Symplocos racemosa in uterine sicknesses (Swarup et al., 1998).

1.3.9.7.10. Lipoxygenase and Urease inhibitory action

Lipoxygenase and Urease contributes in improvement of kidney stones, pyelonephritis, or disease states (Swarup et al., 1998). Abbasi et al. evaluated action of 1-ethyl brachiose-3’-acetate beside with four identified composites kethochaulmoogric acid, triacontyl, methyl triacontanoate, and palmitate, nonaeicosanol by In vitro lipoxygenase and urease inhibition test. Upshot specify
that 1-ethyl brachiose-3'-acetate plus triacontyl palmitate presented inhibitory possibility for lipoxygenase as well as urease enzyme (Abbasi et al., 2007). Abbasi et al. secluded Triacontanyl palmitate from n-hexane solvable segment of bark investigated Urease inhibitory action by urease inhibition test. Triacontanyl palmitate repressed urease enzymes in a concentration dependent manner (Abbasi et al., 2007).

1.3.9.7.11. Peptic ulcer disease

Gopal Krishna et al. have described possible anti-ulcerogenic action of Aqueous and ethanolic excerpts of bark. They use Pylorus ligated and Aspirin tempted models for assessment of action. Aqueous and Ethanolic extracts has condensed ulcer index extra significantly in pylorus ligation and aspirin tempted models (Gopal Krishna et al., 2013)

1.3.9.7.12. Phosphodiesterase, Thymidine phosphorylase and Butyrylcholinesterase inhibiting action

Gomes et al. stated that Benzoylsalireposide and salireposide inhibited phosphodiesterase I action (Gomes et al., 2010). They completed phosphodiesterase I inhibitory action of benzoyl salireposide and salireposide. They used enzyme known as phosphodiesterase I derived from venom of snake and nucleotide pyrophosphate phosphodiesterase I from human. Outcome signposts that both secluded composite have phosphodiesterase I inhibitory action. Abbasi et al. similarly revealed that symplocomoside, symponoside, symplososide, and salireposide have Phosphodiesterase and thymidine phosphorylase preventing (Abbasi et al., 2007). Ahmad et al. explored Butyrylcholinesterase Inhibitory action of symcososide insulated from bark.

1.4. Piper betel

1.4.1. General Information

Piper betel L. belonging to the Family Piperaceae is a perennial dioecious climber that climbs up trees or supporting materials with help of its adventitious roots (Haider et al., 2013; Seetha Lakshmia et al., 2010). Deep emerald heart formed leaves are
commonly identified as Betel vine, Paan, the leaves have a solid spicy as well as perfumed aromawhich areextensivelyutilized as a mouth freshener. Maximum possible source of betel plant is Malaysia however nowadays herbs are similarly grown in Asia. In India it is grown up in a zone of about 40,000 ha (Babu et al., 1992). Chibber gave an explanation of morphology and past of vegetative structures of *Piper betle* (Murty et al., 1984; Guha et al., 1991). There are hundred varieties of betel plant in ecosphere of which nearly three fourth found in India. Universally its leaves are expended by more than six hundred million people and it grades second to coffee and tea. Plant is a shade loving perpetual climber with diothecy where difference among male and female plants in asensual state is not easy and gender difference can be made only after flowering (Bajpai et al., 2012). Leaves have been conventionally utilized for mastication in their original raw condition also with various supplementary components like sliced areca nut, slaked lime, pepper mint, clove, aniseed, cardamom, jelly etc. (Pradhan et al., 2013).
1.4.2. Taxanomical Classification (Pradhan et al., 2013)

Kingdom : Plantae
Division : Magnoliphyta
Class : Magnolipsida
Order : Piperales
Family : Piperaceae
Genus : Piper
Species : betle
Binomial name : Piper betle L.

1.4.3. Vernacular Names (Chandra et al., 2012)

English : Betel, Betel pepper, Betel-vine
Malaysia : Sirih kerakap, Sirih, Sirih melayu, Sirih cina.
Sanskrit : Nagavallari, Nagini, Nagavallika, Tambool,
Tamil : Vetrilai
Telugu : Nagballi, Tamalpaku
Javanese : Sirih, Suruh, Bodeh
Thai : Pelu
Jakun : Kerekap, Kenayek
Sakai : Jerak
Hindi : Pan
Gujurati : Nagarbael
Marathi : Nagbael
Bengali : Pan
Arabic : Tambol, Tambool

1.4.4. Traditional Medicinal Uses (Kirtikar et al., 1998)

*Piper betle* leaf was recognized for periods for its healing effects like: to diminish/avoid body odor as well as evil breath, cough stoppage, throat and lung difficulties, and curative, to reduce unsolicited vaginal secretion also to avoid itching caused by fungus
as well as inner/exterior bacteria. In Chinese conventional medication betel leaves have been also utilized for management of numerous ailments also requested to possess detoxication as well as anti-mutation activities.

1.4.5. Ayurvedic Properties (Pradhan et al., 2013)

- **Guna**: Laghu, Ruksha, Tikshan
- **Rasa**: Tikta
- **Vipak**: Katu
- **Virya**: Ushan
- **Prabhav**: Hridya

1.4.6. Pharmacognostic Study

1.4.6.1. Macroscopic study (Tin, 2011; Chaveerach et al., 2006)

*Piper betle* is a dioecious climber with semi timbered stem, rising through slight adventitious roots. Stem firm with pinkish-stripe sideways, bulge widened and rootling.

1.4.6.2. Leaf:

Leaves are bright emerald in color and perfumed. Taste was somewhat nasty and spicy. Form of leaves is somewhat chordate, interchangeably organized; 6-7 veins are ascending at base growing towards tip. Taste is pungent, 12-18 cm extended, 9-11 cm widespread, dim emerald glabrous with complete margin. petiole 1 to 4 cm, oval quadrilateral mostly ellipsoid chordate or indirectly elliptic fully leather like appearance 10 to 17 cm in length also 5 to 8 cm wide acuminate slanting as well as curved base primary or subordinate nerves usually 5 to 9; Secondary nerves reach to very near apex; tertiaries numerous.

1.4.6.3. Flower:

Male flower are thick with two stamens and female elongated, hanging having lone ovary.

1.4.6.4. Fruit:
Fruits are hardly created, plump frequently ruined in plump point, creating nodes similar assembly.

Photograph No. 2.5: Whole plant, Leaf and Stem of *Piper betle*

1.4.7. Microscopic Study (Seetha Lakshmia et al., 2010; Tin et al., 2011)

Transverse section of leaf through midrib shows, in adaxial epidermis with a distinct sheet of rectangular epidermal cells through thick cuticle followed by two layers of larger hypodermal cells, Apostomatic. In abaxial epidermis, rectangular cells or 10 mm contacts of silica bodies occur in a stellate mass with irregular outline.

Upper epidermis cells were extensive quadrilateral 15 um dense, apostomatic minor epidermal cells were fine, and rod formed 10 um dense, stomatiferous. The coat of extensive cracked enclosed hypodermis existing on mutually both side. Stomata were cycolcytic. Mesophyll is composed of palisade soft parenchyma tissue and comprising granular crystals. Palisade parenchyma underneath axial epidermis is 1 layer thick, efficiently organized and upright erect with abundant chloroplasts. Vascular bundles of
adjacent veins were entrenched in mesophyll tissues. Phloem self-possessed of mesh tubes, acquaintance cells and phloem parenchyma.

Xylem is self-possessed of scalar form and spirally solidified vessels, tracheids, strands and phloem parenchyma. Petiole remains hemispherical in form by a low dejection along radial side and 2.6 mm in length. Epidermis Layer is papillate beneath which an extensive region of 7-8 covered collenchyma cells. Ground tissue contains of compacted parenchymatous cells. Distinct 5 to10 spherical or ellipsoid as well as vascular package is present as a loop. Several wide globular lysigenous secretory coating ducts are seen in center of petiole.

1.4.8. Ayurvedic Formulations (Chaurasia et al., 2010)
Lokantha Rasa, Puspadhava Rasal, Brhat sarwajwarahara, lanha, laghu sutaseknara Rasa, Brhat visamaj warantaka Rasa

1.4.9. Phytochemistry

1.4.9.1. Chemical Constituents

1.4.9.1.1. Leaf:
Phytochemical screening of leaves discovered that it contains terpenes, saponins anthraquinones, alkaloids, steroids and tannins, (Shetty et al., 2012; Ghosh et al., 2005). Dwivedi et al. produces 4 aliphatic composites in untainted arrangement i.e. Pentadecyl 6 hydroxytridecanoate, Pentatriacontanol besides 6, 9-heptacosa Methyl hexacos-7-enoate diene from Hexane fraction of leaf stalk. Hexane extract was detached by column chromatography also their configurations were resoluted by spectroscopic as well as chemical processes (Dwivedi et al., 2011). Pin et al. insulated Hydroxychavicol from leaves by aqueous extraction (Pin et al., 2006). Dwivedi et al. secluded Octanoic acid, Methyl undecanote, Dodecanoic acid, Hexadecane, Tridecanoic acid, Tetradecanoic acid, 1-Dodecanol from n-hexane extract of leaf stalk (Dwivedi et al., 2010). Amonkar et al. sequestered two phenolic compounds, Hydroxychavicol as well as Eugenol, sequestered via extract of piper betel (Amonkar et al., 1986). Parmar et al. isolated cepharadione, dotriacontanoic
acid plus tritriacontane from petrol extract). Nalina et al. isolated hydroxychavicol, fatty acids [stearic as well as palmitic], besides hydroxy esters of fatty acids hydroxybenzeneacetic acid from aqueous leaf extract (Nalina et al., 2001).

1.4.9.1.2. Root:

Ghosh et al. made Column chromatography study of roots wherein alcoholic extract capitulated aristololactam A-2 novel phenyl propene, categorized as 4-allyl resorcinol, whereas petroleum-ether extract produced a diketosteroid, viz. stigmast-4-en-3, 6-dione (Ghosh et al., 2005). Saeed et al. quarantined β-sitosteryl palmitate from petrol plus dichloromethane extract of root. In antheor study Saeed et al. separated 3β-acetyl ursolic acid as well as ursonic acid from root (Saeed et al., 1993).

1.4.9.1.3. Stem:

Huang et al. isolated ten compounds from ethyl acetate solvable segments of 70% acetone, which was recognized as Pellitorine, Dehydropipernonaline, Piperine, Piperdardine, Pinoresinol, Piperolein-B, Guineensine and Syringaresinol-O-beta-D-glucopyranoside etc. Compounds were secluded and cleaned by reverse phase silica gel on Sephadex LH-20 column chromatography and preparative chromatography (Huang et al., 2010). Yin et al. isolated nine compounds from petroleum ester and ethyl acetate solvable fractions of 70% acetone extract and their structures were identified as 6β-hydroxystigmast-4-en-3-one, oleanolic acid, 2,3-hydroxyursan-12-en-28-oic acid, beta-sitosterol, beta-daucosterol, (2S)-4'-hydroxy-2,3-dihydroflavonone-7-O-betaD-glucoside, beta-sitosterol-3-O-beta-D-glucoside-6'-Opalmitate, alpha-ethyl glucoside (Yin et al., 2009). (Huang et al., 2010).
1.4.9.2. Pharmaceutical Modification

Chaurasia et al. has been established new technique of assessment of leaves extract by UV Spectrophotometric procedure which can be used for straight and quick measurement of extract. This method can be used for approximation of leaves extract in dissimilar formulation and can be extremely supportive in formulation improvement, chiefly in dissolution studies (Chaurasia et al., 2011). Tee et al. investigated possessions of dehydrated powder of the therapeutic compound, particle size distribution, hydroxychavicol (HC) content, loss on drying, powder content and hygroscopicity. Investigational run as well as optimization work were planned by Box-Behnken technique of Reaction Surface Procedure (Tee et al., 2012). Punuri et al. synthesized gold nanoparticle of ethanolic leaf extract of Piper betle. Efficacious development of AuNPs was established by UV visible spectroscopy, as well as diverse constraints like concentration of leaf extract (2%), gold salt concentration (0.5 mM), as well as period (18 s) have been optimized (Punuri et al., 2012).
1.4.9.3. Pharmacological Action

1.4.9.3.1. Acetylcholinesterase Inhibitory Property

Das et al. evaluated acetylcholinesterase inhibitory property of aqueous leaf extract by using acetylthiocholine iodide as well as 5, 5’ dithiobis-2 nitrobenzoic acid solution. They reported that aqueous extracts have acetylcholinesterase inhibitory property (Das et al., 2011).

1.4.9.3.2. Anthelmintic Action

Sudrik et al. took aqueous leaf extract for evaluating anthelmintic action. Result stated by terms of intermission meant for paralysis and interval till demise of earthworm Eisenia fetida. Aqueous extract showed significant anthelmintic action (Sudrik et al., 2012).

1.4.9.3.3. Anti-adherence Action

Razak et al. prepared aqueous leaf extract and verified designed to their anti-adherence consequence over union of early plaque colonizers. Outcomes gotten from this study exhibited that aqueous extracts produced a decrease in union of early plaque colonizers to preserved glass surface (Razak et al., 2003).

1.4.9.3.4. Anti-genotoxic Action

Dhote et al. examined antigenotoxic result of methanolic leaf extract in Gamma irradiation and Cyclophosphamide treated animals. Bone marrow defense was calculated by recording aberration in metaphase chromosomes. Their results revealed that nilnoxiousness was observed at given dose methanol extract (Dhote et al., 2007).
1.4.9.3.5. Anti-Plasmid Action

In one of the study vitro anti-plasmid action of volatile oil of leaves in *Escherichia coli* Flac K12 strain. Betel oil inhibited replication as equated to typical penicillin (Shukla et al., 2009). Kumar et al. confirmed antiseptic action of ethanolic extract of leaf for three typical microorganisms’ byagar diffusion technique (Kumar et al., 2007). Datta et al. scrutinizes antibacterial action of ethanolic extract of new leaves against *Pseudomonas aeruginosa*, *Proteus vulgaris*, *Klebsiella pneumonia* and *Staphylococcus aureus* by Disc diffusion technique, Minimum inhibitory concentration as well as time-kill kinetics. Extract established important antimicrobial action against all bacterial strains verified (Datta et al., 2011). Antibacterial action of aqueous leaf extract was carried out by Subashkumar et al. against 20 strains like *Acinetobactor, Escherichia coli, Klebsiella pneumonia, Pseudomonas aeruginosa, Vibrio cholera, Staphylococcus aureus, Streptococcus faecalis* etc by disc diffusion technique and well diffusion technique. Result indicated that aqueous extract have maximum bactericidal action only towards *E. coli, Pseudomonas aeruginosa*, and *Staphylococcus aureus* (Subashkumar et al., 2013).

1.4.9.3.6. Cytotoxic Action

Chaurasia et al. subjected aqueous leaf extract to cytotoxic readings over Hep-2 cell line by means of Micro culture tetrazolium test as well as Sulphorhodamine B test. Average CTC$_{50}$ was estimated about 96.25 ug/ml, which verify powerful cytotoxic action (Chaurasia et al., 2010). Patel et al. investigated cytotoxic action of Hydroalcholic leaf extract for tumor take inhibition of transplanted B16F10 melanoma in mice. A substantial intensification in quiet period of tumors detected when extracttreated group was equated with control. Treatment showed roughly cancer inhibitory result on transferred mouse sarcoma, by postponing cell growth and extending average persistence period (Patel et al., 2012).
1.4.9.3.7. Anti-cancer Action

Abrahim et al. investigated anti-cancer action of Water, hexane ethyl acetate, as well as methanol leaf extract by MTT test and antioxidant enzyme (catalase, glutathione peroxidase as well as superoxide dismutase,) examinations over MCF-7 cells. Extract of Ethyl acetate displayed extreme inhibitory outcome against multiplying of MCF-7 cells. Accomplishment of MCF-7 cells treated by herbalexcerpt upsurge actions of catalase as well as superoxide dismutase (Abrahim et al., 2012).

1.4.9.3.8. Antiproliferative Action

checked antiproliferative action of ethanolic leaf extract with MTS test. Ethanols extract revealed auspicious antiproliferative action.

1.4.9.3.9. Antifertility Action

Sharma et al. checked antifertility action of ethanolic petiol extract by fertility test, hematology and serum biochemistry. Outcomes discovered that ethanolic extract initiated decrease in reproductive organ masses, number of litters, flowing extent of estrogen, concentration of glucose in serum, fertility, enzyme action of phosphatase as linked to reference value (Sharma et al., 2007).

1.4.9.3.10. Antifungal Action

Ali et al. examined antifungal action of Hydroxychavicol, secluded from chloroform abstraction of aqueous leaf extract, over 124 species of selected fungi utilizing broth micro dilution method following CLSI rules. Time kill arch studies, post-antifungal effects as well as mutation deterrence levels were resoluted. Hydroxychavicol unveiled inhibitory consequence on fungal strains of scientific importance (Ali et al., 2010).

1.4.9.3.11. Antigenotoxic Action

Deshmukh et al. assessed chemo protective action of methanolic leaf extract through bone marrow of a Swiss albino mice considered to be in vivo model. Bone marrow fortification was examined by counting irregularities over metaphase chromosomes.
Methanolic extract successfully prohibited cyclophosphamide tempted chromosomal deviation (Deshmukh et al., 2012).

1.4.9.3.12. Antimalarial Action

Al-Adhroey et al. investigated antimalarial action of methanol leaf extract against *Plasmodium berghei* through initial and well-known infections. Leaf extract confirmed momentous schizonticidal action in all three antimalarial assessment models i.e. 4-day suppressive, curative and Prophylactic action (AlAdhroey et al., 2011).

1.4.9.3.13. Antimicrobial Action

Caburian et al. checked Antimicrobial action of leaf essential oil by agar diffusion technique utilizing *Staphylococcus aureus*, *Candida albicans*, *Trichophyton mentagrophytes* and *Streptococcus pyogenes* as trial organisms. Study presented that Betel oil is a very operative antimicrobial agent (Caburian et al., 2010). Shameem Pasha et al. determined antimicrobial action of aqueous leaf extract against *Salmonella typhi*, *Salmonella para typhi* A as well as B, *Vibrio cholera*, *E. coli*, and by disc diffusion technique. Outcomes discovered that extract exhibited operative inhibitory action against tested microorganisms when compared to standard Chloramphenicol (Shameem Pasha et al., 2013). Suppakul et al. examined antimicrobial action of betel oil from fresh leaves against *Aeromonas hydrophila*, *Bacillus cereus*, *Escherichia coli*, *Listeria monocytogenes*, *Micrococcus luteus*, *Pseudomonas aeruginosa*, *Salmonella enteric*, *Staphylococcus aureus* etc. using a modified agar well diffusion technique. Minimum inhibitory concentrations determined by agar dilution method. Betel oil displayed antimicrobial action against totally test strains excluding *Ps. Aeruginosa* (Suppakul et al., 2006), performed antimicrobial examinations over separated essential oil from fresh leaves over oral microbes such as *Lactobacillus acidophilus*, *Strep. Mutans*, *Staphylococcus aureus* etc. by disc diffusion technique. Antimicrobial usefulness of leaf oil was resoluted using agar disc diffusion technique. Essential oil was effective in contradiction of nearly all verified pathogenic species with diverse range of inhibition region.
1.4.9.3.14. Antinociceptive Action

Arambewela et al. examines antinociceptive action of hot water as well as cold ethanol extract of leaves by means of three models of nociception. Fallouts exhibited that extracts possesses antinociceptive action along with gauged over hot plate as well as formalin examinations absent in tail-flick examination. Complete antinociceptive consequence of cold ethanolic extract was superior compared to hot water extract (Arambewela et al., 2005).

1.4.9.3.15. Antioxidant Action

Abrahim et al. measured antioxidant events of water; hexane, ethyl acetate, as well as methanol, extract of leaf by DPPH, superoxide anion as well as hydroxyl radical scavenging tests etc. Owing to maximum phenolic content extract from ethyl acetate showed maximum ferric decreasing action as well as radical scavenging actions against DPPH and superoxide anion as well as nitric oxide moieties (Abrahim et al., 2012). Widowati et al. resolved antioxidant action of ethanolic leaf extract by means of in vitro assay of DPPH scavenging action. Ethanol extracts revealed auspicious antioxidant action (Widowati et al., 2011). Suppakul et al. inspected antioxidant action of betel oil from fresh leaves by a β-carotene agar well diffusion system, in which minimum oxidative bleaching inhibitory concentration of betel oil were resolved using an agar dilution process. Betel oil was able to prevent oxidative bleaching of β-carotene which signposted that betel oil have antioxidant action (Suppakul et al., 2006).

Arambewela et al. examines Antioxidant action of cold ethanolic, hot water extract besides essential oil of leaf by DPPH method. their fallouts specified that scavenging possessions of extracts on DPPH moieties reduced in following direction Cold ethanolic extract > Essential oil > Hot water extract (Arambewela et al., 2006). Chitra et al. observed dosage dependent consequence of orally administer aq. leaf extract on lipid peroxidation, membrane – bound ATPases antioxidants, etc. A momentous decrease in thiobarbituric acid substances and momentous rise in
ascorbic acid, membrane – bound ATPases super oxide dismutase, as well as catalase have been detected, which directed that aqueous extract offers improved antioxidant potential (Chitra et al., 2006). Pin et al. examined antioxidant potential of water, ethyl acetate, ethanol as well as hexane leaf extracts by two in vitro tests i.e. assay by xanthine oxidase superoxide scavenging as well as 1, 2-diphenyl-2-picrylhydrazyl free radical scavenging examination. All extracts remained very active in two antioxidant examinations with extract of water observing effective inhibition (Pin et al., 2010).

1.4.9.3.16. Anti-inflammatory Action

Pin et al. evaluated anti-swelling action of water, ethyl acetate, ethanol in addition to hexane leaf extracts by xanthine oxidase, hyaluronidase and lipoxygenase inhibition tests technique. All extracts shown momentous inhibition in XOD and LOX tests (Pin et al., 2010).

1.4.9.3.17. Anti-Ageing Action

Anti-oxidant action of enzyme from erythrocyte also superoxide dismutase, catalase etc. levels etc. in aging mice of aqueous leaf extract. It improved actions of catalase, glutathione peroxidase etc. in group ranging from young to old age, respectively, when interrelated to standard.

1.4.9.3.18. Anti-diabetic action

Hewageegana et al. examined anti-diabetic accomplishment of aq. leaf excerpt by checking fasting blood glucose level and serum creatinine, urea, aspartate transaminase, alanine transaminase levels and nominated hematological parameters. Outcome specified that extract can be used as a probable curative for Type 2 diabetic patient (Hewageegana et al., 2011).

1.4.9.3.19. Larvicidal action
Tennyson verified *Aedes aegypti* larval mortality against Methanolic leaf extract. Outcomes of existing study discovered that *Piper betle* exhibited highest larvicidal action with LC50 and LC90 values of 236.73 and 122.99 ppm after 24 and 48 hours respectively

1.4.9.3.20. Oral Health Maintenance

The discrepancy expression investigation of virulence genes in *Streptococcus mutans* of aqueous leaf excerpt. Findings from this experiment might give gene appearance outline over *Streptococcus mutans* when management with diverse concentration of extracts which revealed anti-caries properties.  

**Fathilah et al.** determined antiplaque action on aqueous extracts of leaf using *Streptococcus* and *Actinomyces* sp., chief microorganisms associated at this initial stage of dental plaque growth. Excerpts demonstrated encouraging anti-adherence signal and dense cell surface hydrophobicity of microorganisms which could have reduced adherence properties and also, reducing their union to surface of tooth through initial period of plaque growth *(Fathilah et al., 2011)*.

**Gururaj et al.** observes outcome of traditional aqueous leaf extract on oral microorganisms *Salmonella typhi*. Results were found to be functioning in contradiction of bacterial populace of mouth cavity *(Gururaj et al., 2007)*.

1.4.9.3.21. Anti-platelet effect

**Chang et al.** verified consequence of Hydroxychavicol on aggregation of platelet, thromboxane B\(_2\) as well as production of reactive oxygen moieties, cyclooxygenase action, *ex vivo* antiplatelet aggression etc. Outcomes suggest that hydroxychavicol possesses prevailing inhibitor for COX-1/COX-2, scavenger of ROS and stops platelet calcium indicating, TXB\(_2\) manufacture as well as accumulation. Hydroxychavicol can possibly act as healing mediator for anticipation also handling
of atherosclerosis also or cardiovascular disorders because of its anti-inflammatory as well as antiplatelet effects, deprived of effects on hemostasis (Chang et al., 2007).

He also scrutinized Modulation of Platelet Accumulation of aqueous leaf extract by Platelet aggregation test, Thromboxane B2 and PGD2 test, Scavenger of hydroxyl radicals etc. found that aqueous leaf extract repressed platelet accumulation via both its anti-oxidative properties and effects on thromboxane B2 as well as prostaglandin-D2 production.

1.4.9.3.22. Anti-leishmanial action

Misra et al. defined anti-eishmanial action of methanolic leaf extract by Cytotoxicity test, DNA concentration study by Propidium iodide staining, Double staining with Annexin V and Propidium iodide, Quantity of nitric oxide manufacturing in infected macrophages, Mitochondrial Membrane Potential Determination, DNA fragmentation test, In situ labeling of DNA fragments by TUNEL test. It was detected that methanolic leaf extract exhibited effective anti-leishmanial action (Misra et al., 2009).

1.4.9.3.23. Attenuative effect

Prabu et al. studies attenuative consequence of aqueous leaf against cadmium tempted oxidative hepatic disability in liver of rats. Extract reduced level of serum hepatic markers, thiobarbituric acid reactive substances and conjugated dienes. They pointedly raised enzymatic anti-oxidants viz., catalase glutathione peroxidase, dismutase, superoxide etc. and non-enzymatic anti-oxidants via decreased glutathione, total sulfhydryls etc. In current study, extremely powerful chelation of extract was scrutinized against Cd tempted toxicity in liver of rats (Prabu et al., 2012).

1.4.9.3.24. Anti-mutagenic effect

Amonkar et al. experienced anti-mutagenic consequence of hydroxychavicol against mutagenicity of N′-nitrosonornicotine, 2 tobaccospecific N-nitrosamines and 4-
(nitrosomethylamino)-1-(3-pyridyl)-1-butanone, in 2 dissimilar test schemes, viz. Ames Salmonella/microsome test and micronucleus test using Swiss male mice. These outcomes designated that hydroxychavicol may have a part to performance in dropping risk of oral cancer in betel quid with tobacco chewers (Amonkar et al., 1989).

1.4.9.3.25. Anti-septic action

Amalia et al. measured anti-septic effectiveness hot water leaf extract by counting bacterial gatherings before as well as later administration of antibacterial solutions. Microbes were collected by means of swab from patient’s palpebral skin, immunized on nutrient agar, and then kept warm at 37°C for 20 hours. This experiment demonstrates that mean colony amounts later application of 20% foliagemixture exhibited a momentous drop of 27-100% linked with those before administration (Amalia et al., 2009).

1.4.9.3.26. Anti-virulence Action

Nalina et al. investigated virulence properties of aqueous leaf extract by Streptococcus mutans ATCC 25175. Consequence displayed that crude extract at a low attentiveness showed reduce outcome towards growth, adhering capability, glucosyl transferase action and cell surface hydrophobicity of Streptococcus mutans (Nalina et al., 2006).

Arambewela et al. evaluated safety profile of extract from cold ethanol and leaf extract by hot water. They monitored overt signs of toxicity, stress, morbility, aversive behaviors or mortality throughout experiment. Result showed that both extract were well tolerated in terms of % weight gain, food and water intake, morbility, aversive behaviors, mortality, blood haematology, serum analysis and organ weight (Arambewela et al., 2003).

1.4.9.3.27. Immunomodulatory Action
Kumar et al. revealed immunomodulatory effectiveness of unfinished methanolic extract and various fractions of *Piper betle* landrace at different dose levels. Unfinished methanol extract as well as n-hexane portion potentiate important improvement of humoral and also cell-mediated immune reactions in mice. Improved numbers of T-cells as well as β-cells were detected (Kumar et al., 2010).

1.4.9.3.28. Toxicological Studies (Wang et al., 2008)

Indian FDA and several other administrations wanted to discourage society from mastication betel quid, but they have not yet been efficacious. *Piper betle* liquid mastication can produce psychoactive plus cholinergic properties besides connected with submucosa fibrosis and leukoplakia. Use of leaves to decrease melisma may initiate leukomelanosis that demonstrates as confetti-like skin lightening. They similarly produce allergic hand exchange dermatitis lead by *P. betle* L. inflorescence.
1.5. OBJECTIVES OF THE STUDY

Design, Development and Standardization of an Herbal Medicinal Product for Male Sensual Disability

- Development of physical parameters of raw material
- Development of chromatographic evaluation of raw material.
- Development of physical parameters of finished product.
- Development of chromatographic evaluation of finished product.
1.6. SCOPE OF RESEARCH

- **Selection of Ayurvedic herbs for formulations** – Ayurvedic herbs selected on the basis of literature review.

- **Standardization of the extracts**
  - Standardization of extracts by means of physical evaluation.
  - Standardization of extracts by Chemical evaluation.
  - Standardization of extracts by Chromatographic evaluation.

- **Development of the formulation**
  - Development of stable formulations (oral dosage forms) using the standardized extracts with the standard manufacturing procedure.

- **Development of the analytical method**
  - Development and validation of HPLC method for analysis of herbal formulation.
  - Selection of buffer solution.
  - Selection of mobile phase.
  - Selection of stationary phase.
  - Optimization of chromatographic conditions.
  - Analysis of herbal formulation
  - Development and validation of HPTLC method for analysis of herbal formulation.
1.7. PLAN OF WORK

➤ **Selection of herbal drugs**

Following herbal drugs are selected based on literature review - *Crocus sativus, Piper betel, Symplocos racemosa* and *Myristica fragrans*.

Combination of herbal drugs based on traditional claims and clinical evidences will be selected for aphrodisiac action.

➤ **Selection of dose**

Appropriate dose of extract for aphrodisiac action will be taken by referring previously reported doses.

➤ **Standardization of extracts**

- Standardization of herbal extracts will be done by means of physical evaluation.
- Standardization of herbal extracts will be done by Chemical evaluation.
- Standardization of herbal extracts will be done by Chromatographic evaluation.
- Standardization of herbal extracts will be done by microbial evaluation.
- Standardization of herbal extracts will be done by heavy metal evaluation.

➤ **Formulation Development**

Improvement of effective and suitable herbal oral solid dosage formulation using standardized crude drug material with standard manufacturing procedure will be carried out (Wet granulation/ Dry granulation).

➤ **Development of suitable analytical method**

Development of quantitative method for quality control of finished dosage form by HPTLC and HPLC will be done.

➤ **Preclinical Examinations**
Preclinical studies of product using laboratory animal model for aphrodisiac action will be performed such as-

- Aphrodisiac action by assessing mounting frequency, mounting latency, intromission frequency, erection index
- Androgenic action in rats
- Sensual behavioral study in active and inactive male rats

➤ **Stability studies of finished dosage form**

Stability studies in a preferred type of package as per standard ICH guidelines will be performed for

- Physical parameters.
- Chemical parameters.
- Microbiological parameters

Stability studies by doing comparison of HPTLC fingerprinting will be done.