2.1 Selection of herbs for polyherbal formulation

A plant is a general term for any type of plant, while an herbal plant is a plant that is used for its medicinal, culinary or aromatic properties. An herb is a plant or plant part used for its scent, flavour, or therapeutic properties. In our literature survey, herbal plants have demonstrated promising effects in combating inflammation. A diverse array of natural products, spanning from crude extracts to isolated compounds, exhibit anti-inflammatory properties, making them valuable in managing inflammatory conditions. Botanical drugs offer advantages in terms of expedited and cost-efficient development compared to traditional pharmaceuticals. These botanicals serve as safe, natural, and economically viable alternatives to synthetic drugs. Each plant operates through distinct mechanisms to address inflammation, attributed to the presence of active metabolites such as flavonoids, alkaloids, glycosides, amino acids, essential oils, tannins, and phenolics.

Table 2.1 The plants reported in the treatment of inflammation.

Sr. No	Name of Herb	Plant Part	Chemical Constituents	Reference
1	*Curcuma longa*	Rhizome	Curcumin	[1-3]
2	*Moringa oleifera*	Flower, leaf	Phenolic compounds Illyricum, terpenoids, glycosides, tannins, and saponins	[4,5]
3	*Matricaria recutita*	Extract of flower	α-Bisabolol	[6]
4	*Zingiber officinale*	Rhizome	Gingerols, shogaols, and paradols diarylheptanoids	[7,8]
5	*Phyllanthus emblica*	Plant branch, fruit	Minerals, vitamins, amino acids, fatty acids, glycosides tannins, and flavonoids	[9,10]
6	*Azadirachta indica*	Fruit skin	Azadiradione	[11, 12]
7	*Linum usitatissimum*	Leaves	Flavonoids, tannins, anthocyanins, carotenoids, lignans, and proline, and phenolic compounds	[13]
8	*Ocimum basilicum*	Leaves	Essential oil, estragole	[14]
9	*Sambucus australis*	Leaves and bark	Phenolic compounds (caffeic acid and chlorogenic acid) and tannins	[15]
10	*Berberis vulgaris*	Roots and barks	Ascorbic acid, vitamin K, triterpenoids, phenolic compounds, and alkaloids	[16,17]
11	*Phyllanthus acidus*	Aerial parts	Flavonoids, (kaempferol and quercetin)	[18]
12	*Jasminum lanceolarium*	Stems and roots	Iridoids and lignanoids	[19]

13	*Morus alba* L.	Stem	Oxyresveratrol	[20]
14	*Clinacanthus nutans*	Leaves	Phenolic compounds (gallic acid) and Illyricum (schaftoside, gendarucin A, apigenin)	[21]
15	*Psidium guajava* L.	Leaves	Tannins, polyphenolic compounds, llyricum, el- lagic acid, triterpenoids, guiajaverin, quercetin	[22, 23]
16	*Macrosiphonia longiflora*	Whole plant	Alkaloids, phenolic compounds, terpene and flavanoids (naringin rutin, myricetin, morin, quer- cetin, naringenin, luteolin)	[24]
17	*Sarcocephalus pobeguinii*	Leaves and bark	Saponins, alkaloids, phenolics, Illyricum, terpe- noids, and tannins	[25]
18	*Armillaria mellea*	Whole plant	5-Hydroxymethylfurfural, 2-furoic acid, 4- hydroxybenzoic acid, vanillic acid, syringate, daidzein, genistein	[26]
19	*Chrysanthemum indicum*	Whole plant, flowers	Triterpene (lupeol), flavonoids, glycoside, pheno- lic compounds	[27, 28]
20	*Aegle marmelos*	Dried flowers	Flavonoids	[29]
21	*Ananas comosus*	Leaves	Illyricum, phenols, tannins, carbohydrates, gly- cosides, and proteins	[30]
22	*Nelumbo*	Leaves	Phenolic compounds (catechin, rutin, procyanidin B, and quercetin pentosyl hexosid)	[31]
23	*Dysoxylum hainanense*	Bark	Triterpenoids	[32]
24	*Withania somnifera*	Root powder	Withaferin A (steroid)	[33, 34]
25	*Cistus albidus*	Leaves	Flavonols such as kaempferol and quercetin de- rivative	[35]
26	*Quercus gilva*	Whole plant	Phenolic compounds	[36]
27	*Litsea coreana*	Stems and leaves	Flavonoids	[37]
28	*Sonchus oleraceus*	Whole plant	illyricum triterpenes, iridoids, sterols, coumarins and organic acids	[38-42]
29	*Zephyranthes candida*	Whole plant	Flavans	[43]
30	*Vitis vinifera*	Leaves	Resveratrol, quercetin, catechin, lyrics, flavonols, anthocyanin, gallic acid and epicatechin	[44]
31	*Rosa laevigata*	Fruit	Flavonoids	[45]
32	*Citrus sinensis*	Fruits	Flavonoids	[46]

33	*Rosa indica*	Flowers	Flavonoids	[47]
34	*Gynostemma pentaphyl- lum (Thunb.) Makino*	Leaves and whole-plant	Flavonoids and phenolics	[48]
35	*Punica granatum* L.	Peels, seeds, and leaves	Polyphenols (ellagic acid, gallic acid, and punicalagin) and flavonoids, tannins	[49, 50]
36	*Adhatoda vasica*	Leaves	Alkaloids, Saponins, Tannins	[51]
37	*Xanthium strumarium*	Aerial parts	Caffeic acid and resveratrol	[52]
38	*Schisandra chinensis*	Fruit	Schizandrin	[53]
39	*Byrsonima cydoniifolia*	Fruit	Flavonoid, derivatives and stilbenes, resveratrol	[54]
40	*Dioscorea nipponica*	Rhizomes	Diosgenin Diarylheptanoids Phenolic derivatives	[55, 56]
41	*Laennecia confusa*	Aerial parts	Flavonoids, cyanogenic and cardiotonic glycosides, saponins, sesquiterpene lactones, and triterpenes	[57]
42	*Scutellaria indica*	Whole plant	Flavonoids	[58]
43	*Passiflora foetida.*	Stem bark	Flavonoids	[59]
44	*Calea urticifolia*	Leaves	Phenolic Compounds and Flavonoids	[60]
45	*Houttuynia cordata*	Aerial parts	Alkaloids	[61]
46	*Calotropis procera*	Roots	Phenolic glycoside, Saponins, Tannins, Proteins	[62]
47	*Butea monospera*	Flowers	Flavonoids	[63]
48	*Solanum nigrum* L.	Unripe fruits	Steroidal saponins	[64]
49	*Rosmarinus officinalis*	Leaves	Verbenone, cirsimaritin, salvigenin, carnosol, and carnosic acid	[65]
50	*Lithocarpus pachylepis*	Seeds	Phenolic Compounds	[66]
51	*Ipomoea asarifolia*	Leaves	Phenolic compounds	[67]
52	*Schefflera octophylla*	Root bark	Triterpenoids	[68]
53	*Onopordum Illyricum* L.	Aerial parts	Sesquiterpenes	[69]
54	*Cariniana rubra*	Stem bark	Saponins, triterpenes, sterols and phenolic com- pounds	[70]

55	*Persicaria chinensis*	Aerial parts	Flavonoids and phenolic acid	[71]
56	*Polygonum hydropiper*	Leaves	Flavonoid	[72]
57	*Lychnophora trichocarpha*	Aerial parts	Flavanoids, terpenes and steroid	[73]
58	*Globularia alypum* L. *(GA)*	Leaves	Polyphenols, phenolic acids, fatty acids, glycerol and a phytol	[74]
59	*Vernonia patula (Dryand.) Merr.*	Aerial part	Reducing sugars, saponins, glycosides, lavanoids, and tannins	[75]
60	*Salvia connivens*	Aerial parts	Oleanolic acid, ursolic acid and hydroursolic acid.	[76]
61	*Cerbera manghas*	Leaves	Curcumin, resveratrol, quercetin, kaempferol (KF), and apigenin	[77, 78]
62	*Barringtonia racemosa*	Fruits	Triterpenoid (bartogenic acid)	[79]
63	*Siegesbeckia orientalis* L.	Aerial parts	Phenolic compounds and flavonoids	[80]
64	*Hancornia speciosa Gomes*	Fruits	Chlorogenic acid and rutin	[81]
65	*Terminalia catappa* L.	Stem bark	Phenolic compounds (ellagic acid, catalagin, and gallic acid)	[82]
66	*Bridelia retusa*	Fruits	Phenolic compounds (gallic acid and ellagic acid)	[83]
67	*Lolium multiflorum.*	Aerial part	Phenolic acids (caffeic acid, ferulic acid) and flavonoids (myricetin and kaempferol)	[84]
68	*Calamintha nepeta*	Aerial parts	Terpenoids (camphor, pulegone, trans-caryophyllene, and farnesene) and Essential oils	[85]
69	*Ocimum sanctum*	Leaves, whole plant	Fixed oil, linolenic acid	[86]
70	*Crotalaria pallida*	Seeds	Flavonoids, alkaloids	[87]

From the above list of medicinal plants, the following herbs were chosen for further studies based on their ease of availability, mention in traditional literature, and absence of evidence regarding the presence of their extracts in any marketed herbal formulation.

1) *Calotropis procera*
2) *Rosa indica*
3) *Adhatoda vasica*

2.2 Plant profile

2.2.1 *Calotropis procera*

Calotropis procera is an erect, tall, and highly branched perennial shrub or small tree, typically growing up to 5.4 meters in height. The plant is characterized by its milky latex, which is present throughout its tissues. Calotropis procera is known for its distinctive appearance and is used in traditional medicine for its various therapeutic properties.

2.2.1.1 Geographical distribution and ecology

Calotropis procera (Aiton) W.T (Asclepiadaceae) is a xerophytic perennial shrub or shallow tree that grows in many arid and semi-arid countries. It is native to tropical and subtropical Africa and Asia, common in the Middle East and in Latin America, where the species has high socioeconomic value. It often grows in saline or slightly saline soils with low soil moisture.

Calotropis procera is a drought-resistant and salt-tolerant species that is capable of surviving in a range of soil types including alkaline and saline soil and prefers free draining sandy soils. It grows abundantly in arid and semiarid regions without irrigation, chemical fertilizers, pesticides or other agronomic practices reported its growth as secondary vegetation after the eradication of Acacia trees for fuel purposes. It produces deep roots and root suckers, and rarely grows in shallow soils over unfractured rock. It grows in open habitats and is particularly common in overgrazed pastures and poor soils, where there is little competition with grasses. It is also found along roadsides, watercourses, river flats and coastal dunes, and is often prevalent in disturbed areas. *C. procera* favors the habitats that receive 150–1,000 mm annual rainfall.[88]

2.2.1.2 Common names [89]

- **Arabic:** Dead sea plant, Debaj, Usher, Oshar, Kisher
- **English:** Calotrope, Calotropis, Dead Sea Fruit, Desert Wick, Giant Milkweed, Swallow-Wort, Mudar Fibre, Rubber Bush, Rubber Tree, Sodom Apple
- **French:** Pomme De Sodome, Algodón De Seda, Arbre Á Soie, Coton Soie, Arbre A Soie Du Senegal
- **German:** Wahre Mudarpflanzer, Gomeiner
- **Hindi**: Madar, Akada, Akdo,Aak
- **Italian**: Calotropo

- **Marathi**: Rui, Mandara
- **Punjabi**: Ak
- **Sanskrit**: Arka, Alaka, Ravi
- **Spanish:** Bomba, Algodón Extranjero, Cazuela
- **Tamil:** Vellerukku
- **Telgu**: Jilledu
- **Turkish:** Ipekag
- **Urdu:** Madar, Aak

2.2.1.3 Taxonomic classification [90,91]

- **Kingdom**: Plantae,
- **Subkingdom**: Tracheobionta,
- **Superdivision**: Spermatophyta,
- **Division**: Magnoliophyta,
- **Class**: Magnoliopsida,
- **Subclass**: Asteridae,
- **Order**: Gentianales,
- **Family**: Asclepiadaceae,
- **Genus**: Calotropis,
- **Species**: *Calotropis procera*

2.2.1.4 Morphology [94,95]

The morphological studies revealed the plant is erect, tall, large, much branched and perennial with milky latex throughout. *Calotropis procera* have large bushy shrub, leaves decussate, inflorescence extra axillary umbellate panicale, corolla purple, lobes erect. The leaves are sub-sessile, 6-15 cm by 4.5-8 cm, broadly ovate, ovate-oblong, elliptic or obovate acute, pubescent; when young and glabrous on both sides when mature. (Figure 2.1 A, B)

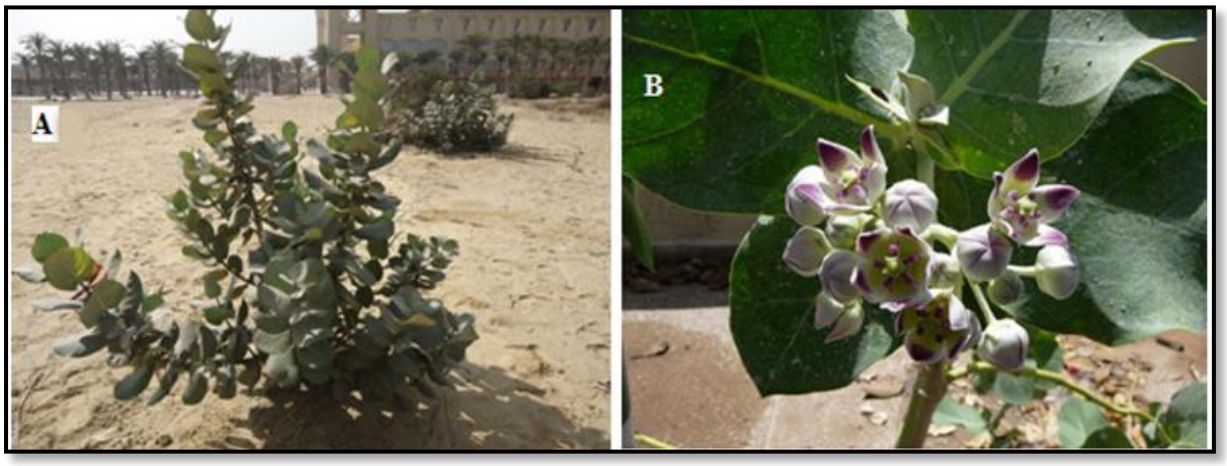

Figure 2.1 A, B Morphology of *Calotropis procera*

2.2.1.5 Description

Calotropis procera is a soft-wooded, evergreen, perennial shrub. It has one or a few stems, few branches, and relatively few leaves, mostly concentrated near the growing tip. The bark is corky, furrowed, and light gray. A copious white sap flows whenever stems or leaves are cut. Giant milkweed has a very deep, stout taproot with few or no near-surface lateral roots. Giant milkweed roots were found to have few branches and reach depths of 1.7 to 3.0 m in Indian sandy desert soils. The opposite leaves are oblong obovate to nearly orbicular, short-pointed to blunt at the apex and have very short petioles below a nearly clasping, heart-shaped base. The leaf blades are light to dark green with nearly white veins. They are 7 to 18 cm long and 5 to 13 cm broad, slightly leathery, and have a fine coat of soft hairs that rub off. The flower clusters are umbelliform cymes that grow at or near the ends of twigs. The flowers are shallowly campanulate with five sepals that are 4 to 5 mm long, fleshy and variable in color from white to pink, often spotted or tinged with purple. The fruits are inflated, obliquely ovoid follicles that split and invert when mature to release flat, brown seeds with a tuft of white hairs at one end. [96,97,98]

2.2.1.6 Chemical constituents

The preliminary phytochemical screening of leaf powder of *Calotropis procera* showed that the leaves contained cardenolides, steroids, tannins, glycosides, phenols, terpenoids, sugars, flavonoids, alkaloids and saponins. [99,100] The leaves also contained bitter compound (mudarine) and many glycosides, calotropin, uscharin, calotoxin and calactin. Procesterol, a new steroidal hydroxy ketone was isolated from the fresh and undried flowers of *C. procera*

Leaf and stem of *Calotropis procera,* gave 0.133% and 0.09% essential oils**.** Leaf oil is dominated by tyranton (54.4%), 1- pentadecene (9.5%) and 1-heptadecene (8.2%). Most abundant compounds in stem oil are Z-13-docosenamide (31.8%), isobutyl nonane (13.7%) and 2,7,10-trimethyldodecane (12.3%). Both leaf and stem volatile oils contain octadecenamide and its saturated form in appreciable amounts. Also characterized by the presence of long chain fatty acids, amides, sulfurate, halogen compounds and carbonyls like ketones. The fresh *C. procera* leaves produced volatile organic compounds that included thioacetic acid, 2,3-dihydro-3,5-dihydroxy-6- mehtyl-4H-pyran-4-one, and 5-hydroxymethyl-2- urancarboxaldehyde [89,100,101].

2.2.1.7 Pharmacological effects

1) Antimicrobial effects

The antimicrobial activity of aqueous and ethanolic extract of roots and leaves of *Calotropis procera* against *Staphylococcus aureus, Streptococcus pyogen, Escherichia coli* and *Pseudomonas aeruginosa* was studied on disc method. Both ethanolic and aqueous extracts of *Calotropis procera* had inhibitory effect on the growth of isolates. The effect exhibited by ethanolic extract of leaves and roots was significantly greater than that of the aqueous extract of leaves and roots. [102]

2) Anthelmintic effects

Different extracts of *Calotropis procera* leaves were evaluated for *in-vitro* anthelmintic activity against Indian earthworms *Pheritima posthuma.* The perusal of the anthelmintic activity data reveals that 70% hydroethanolic extract at the concentration of 12.5 mg/ml showed paralysis and death in 18.58 and 29.05m. respectively. Similarly, *n*-butanol and chloroform extract at the concentration of 12.5 mg/ml showed both paralysis in 21.03 and 48.26 and death in 26.53 and 51.25m. respectively. The effect was positively correlated with concentration. [103]

3) Analgesic effects

A single oral dose of DL ranged from 165 to 830 mg/kg produced a significant dose dependent analgesic effect against acetic acid induced writhings. The effect of DL at a dose of 415 mg/kg was more pronounced as compared to a 100 mg/kg oral dose of aspirin. On the other hand DL (830 mg/kg) produced marginal analgesia in a tail-flick model which was comparable to aspirin. The analgesic effect of DL was delayed by 1 h by naloxone at a dose of 0.5 mg/kg, i.p., which completely blocked the analgesic effect of morphine (10 mg/kg, i.p.). However, the

effect of aspirin was not blocked by naloxone. The 830 mg/kg oral dose of DL did not produce toxic effects in mice and the LD50 was found to be 3 g/kg. A significant analgesic property by the hot plate method was showed which were described previously against mice. It is clearly concluded that *C. procera* shows tremendous analgesic activity which is a boom for medicinal world. [104] The ethanol extract of *C. procera* produced significant reduction of yeast induced increase in body temperature. There was a significant increase in reaction time of the treated mice placed on hot plate confirming analgesic activity of the extract. [104]

4) Anti-inflammatory effects

The methanolic extract of plant *Calotropis procera* roots has been reported to exhibit potent anti-inflammatory activity against carrageenan induced paw oedema and cotton pellet induced granuloma in albino Wistar rats. The different extracts of the roots of *C. procera* and standard anti-inflammatory drugs were administered orally 1 hour before inducing of inflammation. The methanolic extracts (180mg/kg) of roots of *C. Procera* has potential to inhibit sub-acute inflammation by interruption of the arachidonic acid metabolism in both paw oedema as well as cotton pellet model and showed inhibition of inflammation ($p<0.01$ and $p<0.001$) very close to the inhibitory effect of diclofenac sodium (25 mg/kg, ip). [105]

5) Anticancer effects

Anti-tumor studies with extracts of *C. procera* root employing Hep2 cancer cells and their possible mechanism of action was observed, results indicated that the root extracts of the plant inhibited the proliferation of Hep2 cancer cells via apoptotic and cell cycle disruption-based mechanisms. Recently the cardiotonic steroid UNBS1450 (derived from 2 oxovoruscharin) from *C. procera* was shown to additionally exert an anticancer activity. UNBS1450 has been proven to be a potent sodium pump inhibitor, showing anti-proliferative and cell death-inducing activities. This anti-cancer potential of UNBS1450 is achieved by disorganization of the actin cytoskeleton after binding to the sodium pump at the cellular membrane, by inducing autophagy-related cell death, by repressing NF-KB activation as well as by down-regulating c-Myc in cancer cells. [106]

6) Anti-Fertility Effect

The ethanolic extract of the roots of *Calotropis procera* was investigated for its anti-fertility and hormonal activities in albino rats. The study revealed a significant anti-implantation effect, achieving 100% inhibition at a dose level of 250 mg/kg, which corresponds to one-quarter of

the LD50. Additionally, the extract demonstrated potent uterotropic activity, indicating its potential as an anti-fertility agent.

7) Anti-Ulcer Effect

The anti-ulcer properties of *Calotropis procera* were assessed using various in vivo ulcer models. The results indicated that the extract significantly inhibited ulceration induced by aspirin, reserpine, absolute alcohol, and serotonin in rats. It also provided protective effects against aspirin-induced gastric mucosal damage in pyloric-ligated rats and demonstrated notable protection against histamine-induced duodenal ulcers in guinea pigs. These findings underscore the potential of *Calotropis procera* as a therapeutic agent for ulcer-related conditions.

2.2.2 Rosa indica

Rose (*Rosa* species) occupies first position in international flower trade. Its popularity as a garden plant, cut flower and as a source of essential oil makes it very important among the ornamental plants. They have been cultivated for the last 5000 years during ancient civilization of China, Western Asia and Northern Africa. The genus *Rosa* belongs to *Rosaceae* and contains approximately 150 species. From many of the wild species, the large number of cultivated varieties and hybrids were developed. Frequent hybridizations and allopolyploidization have occurred, which make the classification and the search for relationships between species difficult. The *Rosa indica* belongs to the family of Rosaceae. It is known for various pharmacological activities, and the presence of colored pigments and chemical constituents like flavonoids. It is also valued for their culinary, medicinal, cosmetic and aromatic properties.

2.2.2.1Common Names [109]

- **Sanskrit:** Taruni, Shatapatri, Karnika, Charukeshara, Laksha, Gandhadhya
- **Hindi, Marathi, Gujarathi:** Gulab
- **Bengal:** Golap
- **Tamil:** Irasha
- **Telugu:** Gulabi
- **Arabi:** Varde ahmar
- **Farasi:** Gulesurkh
- **English:** Rose

2.2.2.2 Taxonomic classification

- **Kingdom**: Plantae
- **Division**: Magnoliophyta
- **Class**: Magnoliolpsida
- **Order**: Rosales
- **Family**: Rosaceae
- **Genus**: *Rosa*
- **Species**: *indica*

2.2.2.3 Morphology [109]

The plant is shrubby and is 6.15cm to 3 meters in height. Branches bear thorns. Leaves have serrate margins. Flowers have many shades of colors. Fruit – oval and becomes red on ripening.

Figure 2.2 Morphology of *Rosa indica*

2.2.2.4 Chemical Constituents

The important chemical constituents isolated from flower petals by gas chromatography analysis were Phenyl ethanol (43%), Geranyl acetate (15.6%), Geraniol (10.5%), Linalool (6.9%), Benzyl alcohol (3.3%), Benzaldehyde (1.5%), Nerol (5-10%), Citronellyl acetate (0.3%). It also contains tannins, oloigomeric proantrocyanides, saccharine matter, mineral salts, salt of mallic acid & tartaric acid, Pectin (11%), Riboflavin, sugars, purgative glycosides (multiflorin A & B). [110]

2.2.2.5 Traditional uses of Rose [111-117]

Traditionally it is observed that the Plant pacifies vitiated *Vata, Pitta dosha*. It is also useful in inflammation, burning sensation, conjunctivitis, cough, skin disease, cardiac disability, fever, and general weakness. Generally, several rose products are used to make different cosmetic

preparation like creams, lotions and other cosmetic uses. It was also used in toilet preparations, lozenges and toothpaste for its perfumery. Rose water is used in desserts, pastries and cakes. The flower buds are generally used in cardiac troubles as a tonic and aperients. Gulkand made from the petals possesses mild laxative properties and is useful in sore throat and enlarged tonsils.

2.2.2.6 Pharmacological Activities

1) Cardiotonic Activity

It was showed that the therapeutic efficacy of extract of *Rosa centifolia* Linn was found dose dependent and like that of Digoxin. Also, it has Cardiotonic activity. Researcher also states that it may be a safe alternative to Digoxin in the treatment of congestive cardiac failure. Alcoholic extract of *Rosa centifolia* Linn showed similar therapeutic index like cardiac glycosides. [118]

2) Anti-inflammatory and Anti-arthritic Activity

Oral administration of the aqueous extract of Rosa centifolia (Linn.) flower petals suppressed the edematous response after 2 h and this effect continued up to 5 h. The observed effect was comparable with that produced by indomethacin administration. In this study, it was found that aqueous extract of *Rosa Centifolia* (Linn.) flowers possess anti-inflammatory and antiarthritic activity may be because of presence of flavonoids in it. [119,122]

3) Analgesic Activity

It states in this study that the entire test extracts of *Rosa Centifolia* exhibited significant analgesic activity. The methanol extract was found to be the most potent followed by ethyl acetate and benzene extracts respectively. In this preliminary study demonstrated marked analgesic activity of *R. indica* leaf in Swiss albino mice. [120]

4) Antibacterial Activity.

The methanolic extracts of Red rose petals found effective against all the pathogens used (Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus). They gave a zone of inhibitions of 27 mm against Escherichia coli, 26mm against Pseudomonas aeruginosa, and 25 mm against Staphylococcus aureus which was far better than the zone of inhibition given by the standard antibiotic Tetracycline used throughout the study. [121]

2.2.2.7 Uses of Rose water

Rose water which is a by-product of rose is widely used as skin cooling and cleaning agent. In addition to this, dried rose petals are also be used for skin care and the preparation of Gul-e-

Roghan for making hair oils. Different kinds of value-added products are nowadays formulated and marketed by the companies. Some existing rose products in the market are mostly with synthetic colour and flavor like rose lassi (sour milk), rose ice-cream, rose syrup and sweets with rose. These synthetic colors and flavors are sometimes carcinogenic and may cause allergens. For this reason, food and medical industries are increasingly interested in natural sources with high anthocyanin contents for manufacture of supplements with therapeutic and nutritional uses. Rose preparations could be applied in the food industry as a good source of natural pigments such as anthocyanins due to their attractive color and beneficial health effects and antioxidant activities. Therefore, the present study was undertaken for the purpose of extraction and concentration and utilization of rose preparations in different valuable products and by products.[143]

2.2.3 Adhatoda vasica

2.2.3.1 Common names [123]

- **Hindi-** Arusa
- **Kannad-** Adusoge
- **Bengali-**Basak
- **Gujarati-**Aradusi
- **Tamil-** Adhatodai
- **Panjabi-** Bansa
- **Urdu-** Arusa
- **Uriya-** Basongo
- **Garhwal-** Bangra
- **Telugu-** Addasaramu
- **Kashmir-** Bahekar

2.2.3.2 Taxonomic Classification [124]

- **Kingdom -** Plantae
- **Subkingdom -** Tracheobionta
- **Superdivision -** Spermatophyta
- **Division -** Magnoliophyta

- **Class -** Magnoliopsida
- **Subclass -** Asteridae
- **Order -** Scrophulariales
- **Family -** Acanthaceae
- **Genus -** *Adhatoda*
- **Species -***vasica*

2.2.3.3 Morphology

The leaves of *Adhatoda vasica* are light green in colour, characteristic odour, taste is bitter, size is 10-13 cm long. The shape of leaves is ovate-lanceolate, apex is acuminate, margin slightly crenate to entire, base is symmetric, venation is pinnate, and texture is leathery as shown in Figure 2.3

Figure 2.3 Morphology of *Adhatoda vasica* plant

2.2.3.4 Chemical constituents

A. vasica contains phytochemicals such as alkaloids, glycosides, sterols, and phenolic acid. Alkaloids (quinazoline) (vasicine, vasicinone, 7-hydroxyvasicine, vasicinolone, 3-deoxyvasicine, vasicolinone, vasicol, vasicoline) betaine, steroidscarbohydrate and alkanes are the most common constituents. The major pharmacological actions are due to the presence of alkaloidal content specially vasicine (7.5%) in the plant. Besides vasicine, the leaves include alkaloids (Vasicinone, Adhatodine, Vasicinol, Adhvasinone, Anisotine Adhatonine, and Hydroxypeganine), betaine, steroids, alkanes, kaempferol and quercetin. The leaves are high in vitamin C and carotene, making this plant a potential essential oil source. In addition, it

contains amino acids and proteins. Triterpenes and flavonoids are abundant in flowers. Apigenin, astragalin, kaempferol, quercetin, and vitexin are flavonoids. The majority contain potassium, sodium, calcium, and magnesium, while zinc, copper, nickel, cadmium, manganese, and iron are negligible. The seeds contain 25.8% deep yellow oil consisting of glycerides of be-henic 11.2 percent, arachidic 3.1 percent, cerotic 5 percent, lignoceric 10.7 percent, linoleic 12.3 percent, oleic 49.9 percent, and -sitosterol (2:6 %). *A. vasica* contains significant (Ca, K, Na, and Mg) and trace (Zn, Cu, Cr, Ni, Co, Cd, Pb, Mn, and Fe) elements.[125]

2.2.3.5 Pharmacological activities

1) Bronchodilator activity

Vasicinone isolated from the leaves has a bronchodilator action on the normal lungs and powerful bronchodilator action against the histamine-induced bronchoconstriction in guinea pig's lungs and tracheal chain. *l* –Vasicinone was, however, stronger in action than *dl*-form. Vasicine showed bronchodilator activity in both *in vivo* and *in vitro* experimental studies, its activity being comparable to theophylline.[126]

2) Platelet Activity

Vasicine hydrochloride, when administered orally and intramuscularly in repeated doses, was found to significantly increase platelet counts in various animal models, including rats, mice, rabbits, and dogs. This dose-dependent increase in platelet count was accompanied by marked hyperplasia of megakaryocytes in the bone marrow, suggesting enhanced platelet production. These findings indicate that vasicine could be a promising therapeutic agent for managing capillary hemorrhages and correcting drug-induced bone marrow suppression.[127]

3) Antitussive Activity

The antitussive (cough-suppressing) activity of *Adhatoda zeylanica* extract was assessed in both anesthetized and unanaesthetised guinea pigs, as well as in rabbits. The results demonstrated that oral administration of the extract provided cough relief comparable to that of codeine, particularly against coughing induced by irritant aerosols. This suggests that *Adhatoda zeylanica* extract has significant potential as a natural antitussive agent.[128]

4) Antimicrobial activity

The alcoholic extracts of the leaves and root showed antibacterial activity against *Staphylococcus aureus* and *Escherichia coli.* The water extract of the leaves also showed activity against *Staphylococcus aureus.* Aqueous and ethanolic extracts from various parts of

seven plants were screened against three gram – positive and five gram - negative bacteria. Of the twenty – four extracts assayed by agar well diffusion method, ethanolic extract from the shoots of *Adhatoda zeylanica* was the most active, exhibiting greatest inhibitory activity against multi- drug-resistant *E. coli.* [129-132]

5) Hypoglycaemic activity

The non-nitrogenous principle obtained from the leaves as suspension administrated orally (25 mg/kg) to fasting male rabbits lowered the blood sugar of rabbits for a short period of two hours. The average fall over a period of four hours was 7.5 percent which was far less than the fall due to similar dosage of tolbutamide. The ethanolic extract of the leaves exhibited hypoglycaemic activity in rats. The effect of the two unani drugs, Arusa (leaves of *Adhatoda zeylanica*) and Kalongi (seeds of *Nigella sativa*) was studied in induced diabetic rabbits. Both the extracts were compared for hypoglycemic effect with a standard drug glibenclamide. Diabetes was observed in rabbits (fasting blood glucose level ranged from 200–250 mg/100 ml) within 24 hrs after injection of alloxan and divided into four groups i.e. diabetic control (distilled water), diabetic standard (glibenclamide), diabetic test (Arusa) and diabetic test (Kalongi). The test drugs were administered to the treated group, while the vehicle was administered to the animals of control group, orally. Blood glucose was estimated by the end point *o*-toluidine. The study revealed that the aqueous extract of Arusa and Kalongi in the dose of 100 mg/kg and 200 mg/kg, respectively given orally reduced the blood glucose level in induced diabetic rabbits. The significant reduction (P less than 0.05) in blood glucose level started after 3 hrs which continued for 6 hrs in both the groups. [133]

6) Anti-inflammatory activity

The anti-inflammatory effect of carrageenan and formalin was assessed in rat paws using an ethanolic extract of vasaka (200-400 mg/kg/per oral). This study found a strong anti-inflammatory effect. Vasicine is the main active element in alkaloids that has anti-inflammatory properties. The modified hen's egg chorioallantoic membrane test revealed that the methanolic extract has substantial anti-inflammatory activity due to saponins and alkaloids. [140]

7) Anti-cancer activity

The anticancer efficacy of A. vasica leaf extract nanoparticles loaded with Argentum and gold and doped with cerium oxide is substantial. Another study found metal and metal oxide nanoparticles to be anticancer in the same Hela cell line model. So bi-metal doping can improve biological qualities and may be linked to cancer. *A. vasica* alkaloids inhibit the growth of

oxidative stress-driven lung cancer cells in A549 cells. Reduced cell viability, DNA fragmentation, mitochondrial potential disturbance, and cell wound repair activity may be the mechanism. It is mediated by Bcl-2 associated agonists of cell death (BAD) and Fas death receptors. Methanol extract of *Justicia adhatoda* was also an anticancer in MCF-7 cells.[141]

8) Analgesic activity

In acetic acid-induced writhing response, hot plate analgesiometer and warm water tail immersion test, *A. vasica* showed substantial analgesic and anti-inflammatory activity in albino rats. Maharasnadhi quathar is an ayurvedic polyherbal remedy for arthritis. This investigation found that the formulation had powerful anti-inflammatory and analgesic activity dosage dependent. [142]

2.2.3.6 Traditional Uses

The plant is pungent, bitter, acrid, cooling, useful in bronchitis, leprosy, blood impurities, heart troubles, thirst, asthma, fever, vomiting, loss of memory, leucoderma, constipation, jaundice, tumors, and diseases of the mouth. [134] The root is diurectic, useful in bronchitis, asthma, bilious vomiting, sore eyes, fevers, gonorrhoea. The leaves are emmenagogues, useful in gonorrhea. The flowers improve the circulation of the blood. The fruit is useful in bronchitis.[135] The leaves and the roots of this plant are considered a very efficacious remedy for all sorts of coughs, being administered along with ginger.[136] The leaves are also used for rheumatism. The flower, leaves, and root but especially the first, are supposed to possess antispasmodic qualities. The flowers and the fruit are bitter, aromatic and antispasmodic.[137] The fresh flowers are used in ophthalmia.[138] The powdered root is used in Mysore by native doctors in cases of malarial fever. It has expectorant and antispasmodic properties and its use has been recommended in the treatment of cold, cough, asthma and even diphtheria.

2.3 References

1. Kumari A, Dash D, Singh R. Curcumin inhibits lipopolysaccharide (LPS)-induced endotoxemia and airway inflammation through modulation of sequential release of inflammatory mediators (TNF- α and TGF- α 1) in murine model. Inflammopharmacol 2017; 25(3): 329-41.
2. Mohanty C, Sahoo SK. Curcumin and its topical formulations for wound healing applications. Drug Discov Today 2017; 22(10): 1582-92.
3. Ma F, Liu F, Ding L, You M, Yue H, Zhou Y, *et al*. Anti-inflammatory effects of curcumin are associated with down regulating microRNA-155 in LPS-treated macrophages and mice. Pharm Biol 2017; 55(1): 1263-73.
4. Tan WS, Arulselvan P, Karthivashan G, Fakurazi S. *Moringa oleifera* flower extract suppresses the activation of inflammatory mediators in lipopolysaccharide-stimulated RAW 264.7 macrophages via NF-αB pathway. Mediators Inflamm 2015; 2015: 720171.
5. Adedapo AA, Falayi OO, Oyagbemi AA. Evaluation of the analgesic, anti-inflammatory, anti-oxidant, phytochemical and toxicological properties of the methanolic leaf extract of commercially processed *Moringa oleifera* in some laboratory animals. J Basic Clin Physiol Pharmacol 2015; 26(5): 491-9.
6. Dawid-Pac R. Medicinal plants used in treatment of inflammatoryskin diseases. Postepy Deramatol Alergol 2013; 30(3): 170-7.
7. Makchuchit S, Rattarom R, Itharat A. The anti-allergic and anti-inflammatory effects of Benjakul extract (a Thai traditional medicine), its constituent plants and its some pure constituents using *in vitro* experiments. Biomed Pharmacother 2017; 89: 1018-26.
8. Jolad SD, Lantz RC, Chen GJ, Bates RB, Timmermann BN. Commercially processed dry ginger (*Zingiber officinale*): composition and effects on LPS-stimulated PGE2 production. Phytochem 2005;66(13): 1614-35.
9. Sripanidkulchai B, Junlatat J. Bioactivities of alcohol based extracts of *Phyllanthus emblica* branches: Antioxidation, antimelanogenesis and anti-inflammation. J Nat Med 2014; 68(3): 615-22.
10. Yadav SS, Singh MK, Singh PK, Kumar V. Traditional knowledge to clinical trials: A review on therapeutic actions of *Emblica officinalis*.Biomed Pharmacother 2017; 93: 1292-302.

11. Ilango K, Maharajan G, Narasimhan S. Anti-nociceptive and anti-inflammatory activities of *Azadirachta indica* fruit skin extract and its isolated constituent azadiradione. Nat Product Res 2013; 27:1463-7.
12. Tiwari R, Verma AK, Chakraborty S, Dhama K, Singh SV. Neem (*Azadirachta indica*) and its potential for safeguarding health of animals and humans: A review. J Biol Sci 2014a; 14(2): 110-23.
13. Rafieian-Kopaei M, Shakiba A, Sedighi M, Bahmani M. The analgesic and anti-inflammatory activity of *Linum usitatissimum* in Balb/c Mice. J Evid Based Complementary Altern Med 2017; 22(4):892-6.
14. Rodrigues LB, Oliveira Brito Pereira Bezerra Martins A, Cesário FR, Ferreira E, Castro F, de Albuquerque TR, Martins Fernandes MN, *et al*. Anti-inflammatory and antiedematogenic activity of the *Ocimum basilicum* essential oil and its main compound estragole: *In vivo* mouse models. Chem Biol Interact 2016; 257: 14-25.
15. Benevides BJ, Marques FM, Figueira MM, Vargas TS, KondratyukTP, Endringer DC, *et al*. Potential anti-inflammatory, antioxidant and antimicrobial activities of *Sambucus australis*. Pharm Biol 2017; 55(1): 991-7.
16. Rahimi-Madiseh M, Lorigoini Z, Zamani-Gharaghoshi H, Rafieian- Kopaei M. Berberis vulgaris: Specifications and traditional uses. Iran J Basic Med Sci 2017; 20(5): 569-87.
17. Yesilada E, Kupeli E. Berberis crataegina DC. root exhibits potent anti-inflammatory, analgesic and febri-fuge effects in mice and rats. J Ethnopharmacol 2002; 79: 237-48.
18. Hossen MJ, Jeon SH, Kim SC, Kim JH, Jeong D, Sung NY, *et al*. *In vitro* and *in vivo* anti-inflammatory activity of *Phyllanthus acidus* methanolic extract. J Ethnopharmacol 2015; 168: 217-28.
19. Yan WX, Zhang JH, Zhang Y, Meng DL, Yan D. Antiinflammatory activity studies on the stems and roots of *Jasminum lanceolarium* Roxb. J Ethnopharmacol 2015 2; 171: 335-41.
20. Soonthornsit N, Pitaksutheepong C, Hemstapat W, Utaisincharoen P, Pitaksuteepong T. *In vitro* anti-inflammatory activity of *Morus alba* L. stem extract in LPS-stimulated RAW 264.7 Cells. Evid Based Complement Alternat Med 2017; 2017: 3928956.
21. Mai CW, Yap KS, Kho MT, Ismail NH, Yusoff K, Shaari K, *et al*. Mechanisms underlying the antiinflammatory effects of *Clinacanthus nutans Lindau* extracts:

Inhibition of cytokine production and toll-like receptor-4 activation. Front Pharmacol 2016; 7: 7.

22. Sen SS, Sukumaran V, Giri SS, Park SC. Flavonoid fraction of guava leaf extract attenuates lipopolysaccharide-induced inflammatory response via blocking of NF-□B signalling pathway in Labeo rohita macrophages. Fish Shellfish Immunol 2015; 47(1): 85-92
23. Ojewole JA. Antiinflammatory and analgesic effects of *Psidium guajava* Linn. (Myrtaceae) leaf aqueous extract in rats and mice. Methods Find Exp Clin Pharmacol 2006; 28(7): 441-6.
24. Da Silva AO, Damaceno Alves A, Almeida DA, Balogun SO, de Oliveira RG, Aires Aguiar A, *et al*. Evaluation of anti-inflammatory and mechanism of action of extract of *Macrosiphonia longiflora* (Desf.) Müll. Arg. J Ethnopharmacol 2014; 154(2): 319-29.
25. Mfotie Njoya E, Munvera AM, Mkounga P, Nkengfack AE, McGaw LJ. Phytochemical analysis with free radical scavenging, nitric oxide inhibition and antiproliferative activity of *Sarcocephalus pobeguinii* extracts. BMC Complement Altern Med 2017; 17(1): 199.
26. Geng Y, Zhu S, Cheng P, Lu ZM, Xu HY, Shi JS, *et al*. Bioassayguided fractionation of ethyl acetate extract from *Armillaria mellea* attenuates inflammatory response in lipopolysaccharide (LPS) stimulated BV-2 microglia. Phytomed 2017; 26: 55-61.
27. Kang SC, Lim SY, Song YJ. Lupeol is one of active components in the extract of *Chrysanthemum indicum Linne* that inhibits LMP1- induced NF-□B activation. PLoS One 2013; 8(11): e82688.
28. Luyen BT, Tai BH, Thao NP, Cha JY, Lee HY, Lee YM, *et al*. Anti-inflammatory components of *Chrysanthemum indicum* flowers.Bioorg Med Chem Lett 2015; 25(2): 266-9.
29. Kumari KD, Weerakoon TC, Handunnetti SM, Samarasinghe K, Suresh TS. Anti-inflammatory activity of dried flower extracts of *Aegle marmelos* in Wistar rats. J Ethnopharm 2014; 151(3):1202-8.
30. Kargutkar S, Brijesh S. Anti-inflammatory evaluation and characterization of leaf extract of *Ananas comosus*. Inflammopharmacol 2017.

31. Park E, Kim GD, Go MS, Kwon D, Jung IK, Auh JH, Kim JH. Anti-inflammatory effects of Nelumbo leaf extracts and identification of their metabolites. Nutr Res Pract 2017; 11(4): 265-274.
32. Zou YH, Liu WT, Zhang JX, Xiang DC. Triterpenoids from the bark of *Dysoxylum hainanense* and their anti-inflammatory and radical scavenging activity. Fitoterapia 2017; 121: 159-163.
33. Tiwari R, Chakraborty S, Saminathan M, Dhama K, Singh SV. Ashwagandha (*Withania somnifera*): Role in safeguarding health, Immunomodulatory effects, combating infections and therapeutic applications: A review. J Biol Sci 2014; 14: 77-94
34. Kaur N, Niazi J, Bains R. A review on pharmacological profile of *Withania somnifera* (Ashwagandha). Res Rev: J Botanical Sci2013; 2(4): 6-14.
35. Tahiri O, Atmani-Kilani D, Sanchez-Fidalgo S, Aparicio-Soto M, Alarcón-de-la-Lastra C, Barrajón-Catalán E, *et al*. The flavonolenriched *Cistus albidus* chloroform extract possesses *in vivo* anti-inflammatory and anti-nociceptive activity. J Ethnopharmacol 2017; S0378 8741(17)31020-6.
36. Youn SH, Kwon JH, Yin J, Tam LT, Ahn HS, Myung SC, *et al.* Anti-inflammatory and anti-urolithiasis effects of polyphenolic compounds from *Quercus gilva* Blume. Molecules 2017; 22(7): E1121.
37. Jia X, Li P, Wan J, He C. A review on phytochemical and pharmacological properties of *Litsea coreana*. Pharm Biol 2017; 55(1):1368-1374.
38. Li Q, Dong DD, Huang QP1, Li J, Du YY, Li B, *et al*. The anti-inflammatory effect of *Sonchus oleraceus* aqueous extract on lipopolysaccharide stimulated RAW 264.7 cells and mice. Huyan T Pharm Biol 2017; 55(1): 799-809.
39. Liu B, Piao X, Guo L, Liu S, Chai F, Gao L. Ursolic acid protects against ulcerative colitis via anti-inflammatory and antioxidant effects in mice. Mol Med Rep 2016; 13: 4779-85.
40. Hassan EM, Matloub AA, Aboutabl ME, Ibrahim NA, Mohamed SM. Assessment of anti-inflammatory, antinociceptive, immunomodulatory, and antioxidant activities of *Cajanus cajan* L. seeds cultivated in Egypt and its phytochemical composition. Pharm Biol 2016; 54: 1380-91.

41. Hu N, Kong L, Qian A, Meng Q, Li C, Yu X, *et al*. HMGB1 Silencing potentiates the anti-inflammatory effects of sodium ferulate in ox-LDL-stimulated vascular smooth muscle cells. Cell Biochem Biophys 2015; 72: 297-304.
42. Yoo H, Ku SK, Baek YD, Bae JS. Anti-inflammatory effects of rutin on HMGB1-induced inflammatory responses *in vitro* and *in vivo*. Inflamm Res 2014; 63: 197-206.
43. Zhan G, Zhou J, Liu T, Zheng G, Aisa HA, Yao G. Flavans with potential anti-inflammatory activities from *Zephyranthes candida*. Bioorg Med Chem Lett 2016; 26(24): 5967-70.
44. Aouey B, Samet AM, Fetoui H, Simmonds MS, Bouaziz M. Antioxidant, anti-inflammatory, analgesic and antipyretic activities of grapevine leaf extract (*Vitis vinifera*) in mice and identification of its active constituents by LC-MS/MS analyses. Biomed Pharmacother, 2016; 84: 1088-98.
45. Tao X, Sun X, Xu L, Yin L, Han X, Qi Y, Xu Y, *et al*. Total flavonoids from *Rosa laevigata* Michx fruit ameliorates hepatic ischemia/reperfusion injury through inhibition of oxidative stress and inflammation in rats. Nutrients 2016; 8(7). pii: E418
46. Pepe G, Pagano F, Adesso S, Sommella E, Ostacolo C, Manfra M, *et al*. Bioavailable *Citrus sinensis* extract: Polyphenolic composition and biological activity. Molecules 2017; 22(4). pii: E623
47. Battiwala A, Chandragopal SS, Kumar, S (2013) Evaluation of Anti-Inflammatory and Anti-arthritic activity of Rosa centifolia (Linn.) Flowers in experimental rats. International Journal for Pharmaceutical Research Scholars V- 2, I-4,2013 414–26.
48. Xie Z, Huang H, Zhao Y, Shi H, Wang S, Wang TT, *et al*. Chemical composition and anti-proliferative and anti-inflammatory effects of the leaf and whole-plant samples of diploid and tetraploid *Gynostemma pentaphyllum* (Thunb.) Makino. Food Chem 2012;132(1): 125-33.
49. BenSaad LA, Kim KH, Quah CC, Kim WR, Shahimi M. Antiinflammatory potential of ellagic acid, gallic acid and punicalagin A&B isolated from *Punica granatum*. BMC Complement Altern Med 2017; 17(1): 47.
50. Houston DM, Bugert J, Denyer SP, Heard CM. Anti-inflammatory activity of *Punica granatum* L. (Pomegranate) rind extracts applied topically to ex vivo skin. Eur J Pharm Biopharm 2017; 112: 30-7.

51. Chakraborty A, Brantner AH. Study of alkaloids from Adhatoda vasica Nees on their anti-inflammatory activity. Phytother Res. 2001;15(6):532-534.
52. Hossen MJ, Cho JY, Kim D. PDK1 in NF-□B signaling is a target of Xanthium strumarium methanolic extract-mediated anti-inflammatory activities. J Ethnopharmacol 2016; 190: 251-60.
53. Dilshara MG, Jayasooriya RG, Kang CH, Lee S, Park SR, Jeong JW, *et al*. Downregulation of pro-inflammatory mediators by a water extract of *Schisandra chinensis* (Turcz.) Baill fruit in lipopolysaccharide-stimulated RAW 264.7 macrophage cells. Environ Toxicol Pharmacol 2013; 36(2): 256-64.
54. Santos VSD, Nascimento TV, Felipe JL, Boaretto AG, Damasceno- Junior GA, Silva DB, *et al*. Nutraceutical potential of *Byrsonima cydoniifolia* fruits based on chemical composition, antiinflammatory, and antihyperalgesic activities. Food Chem 2017;237: 240-246.
55. Woo KW, Moon E, Kwon OW, Lee SO, Kim SY, Choi SZ, *et al*. Anti-neuroinflammatory diarylheptanoids from the rhizomes of *Dioscorea nipponica*. Bioorg Med Chem Lett 2013; 23(13): 3806-9.
56. Zhou Q, Liu S, Yua D, Zhang N. Therapeutic Effect of total saponins from *Dioscorea nipponica* Makino on gouty arthritis based on the NF-κB signal pathway: An *in vitro* study. Pharmacogn Mag 2016; 12(47): 235-40.
57. Martínez RMG, Richard-Greenblatt M, Juárez ZN, Av-Gay Y, Bach H, Hernández LR. Antimicrobial, anti-inflammatory, antiparasitic, and cytotoxic activities of *Laennecia confusa*. ScientificWorld J 2012; 2012: 263572.
58. Cuong TD, Hung TM, Lee JS, Weon KY, Woo MH, Min BS. Antiinflammatory activity of phenolic compounds from the whole plant of *Scutellaria indica*. Bioorg Med Chem Lett 2015; 25(5):1129-34.
59. Nguyen TY, To DC, Tran MH, Lee JS, Lee JH, Kim JA, *et al*. Anti-inflammatory flavonoids isolated from *Passiflora foetida*. Nat Prod Commun 2015; 10(6): 929-31.
60. Torres-Rodríguez ML, García-Chávez E, Berhow M, de Mejia EG. Anti-inflammatory and anti-oxidant effect of *Calea urticifolia* lyophilized aqueous extract on lipopolysaccharide-stimulated RAW 64.7 macrophages. J Ethnopharmacol 2016; 188: 266-74.

61. Ahn J, Chae HS, Chin YW, Kim J. Alkaloids from aerial parts of *Houttuynia cordata* and their anti-inflammatory activity. Bioorg Med Chem Lett 2017; 27(12): 2807-11.
62. Suresh BAR, Karki SS. Anti-inflammatory activity of various extracts of roots of *Calotropis procera* against different inflammation models. *International Journal of Pharmacy and Pharmaceutical Sciences,* 3(3), 2011, 191-194].
63. Krolikiewicz-Renimel I, Michel T, Destandau E, Reddy M, André P, Elfakir C, *et al*. Protective effect of a *Butea monosperma* (Lam.) Taub. flowers extract against skin inflammation: Antioxidant, anti-inflammatory and matrix metalloproteinases inhibitory activities. J Ethnopharmacol 2013; 148(2): 537-43.
64. Wang Y, Xiang L, Yi X, He X. Potential anti-inflammatory steroidal saponins from the berries of *Solanum nigrum* L. (European Black Nightshade). J Agric Food Chem 2017; 65(21): 4262-72.
65. Kuo CF, Su JD, Chiu CH, Peng CC, Chang CH, Sung TY, *et al*. Anti-inflammatory effects of supercritical carbon dioxide extract and its isolated carnosic acid from *Rosmarinus officinalis* leaves. J Agric Food Chem 2011; 59(8): 3674-85.
66. Xie Y, Ma G, Wei H, Yuan J, Wu H, Zhou X, *et al*. Three new phenolics and other constituents from the seeds of *Lithocarpus pachylepis*. Molecules 2013; 18(9): 10397-403.
67. Furtado AA, Torres-Rêgo M, Lima MC, Bitencourt MA, Estrela AB, Souza da Silva N, *et al*. Aqueous extract from *Ipomoea asarifolia* (Convolvulaceae) leaves and its phenolic compounds have anti-inflammatory activity in murine models of edema, peritonitis and air-pouch inflammation. J Ethnopharmacol 2016; 192: 225-35.
68. Chen Y, Tao S, Zeng F, Xie L, Shen Z. Antinociceptive and anti-inflammatory activities of *Schefflera octophylla* extracts. J Ethnopharmacol 2015; 171: 42-50.
69. Formisano C, Sanna C, Ballero M, Chianese G, Sirignano C, Rigano D, *et al*. Anti-inflammatory sesquiterpene lactones from *Onopordum illyricum* L. (Asteraceae), an Italian medicinal plant. Fitoterapia 2017; 116: 61-5.
70. Santos EN, Lima JC, Noldin VF, Cechinel-Filho V, Rao VS, Lima EF, *et al*. Anti-inflammatory, antinociceptive, and antipyretic effects of methanol extract of *Cariniana rubra* stem bark in animal models. An Acad Bras Cienc 2011; 83(2): 557-66.

71. Hossen MJ, Baek KS, Kim E, Yang WS, Jeong D, Kim JH, *et al*. *In vivo* and *in vitro* anti-inflammatory activities of Persicaria chinensis methanolic extract targeting Src/Syk/NF-□B. J Ethnopharmacol 2015; 159: 9-16.
72. Yang Y, Yu T, Jang HJ, Byeon SE, Song SY, Lee BH, *et al*. *In vitro* and *in vivo* anti-inflammatory activities of *Polygonum hydropiper* methanol extract. J Ethnopharmacol 2012; 139(2): 616-625.
73. De Souza MR, de Paula CA, Pereira de Resende ML, Grabe- Guimarães A, de Souza Filho JD, *et al*. Pharmacological basis for use of *Lychnophora trichocarpha* in gouty arthritis: Antihyperuricemic and anti-inflammatory effects of its extract, fraction and constituents. J Ethnopharmacol 2012; 142(3): 845-850.
74. Ghlissi Z, Sayari N, Kallel R, Bougatef A, Sahnoun Z. Antioxidant, antibacterial, anti-inflammatory and wound healing effects of *Artemisia campestris* aqueous extract in rat. Biomed Pharmacother 2016; 84: 115-22.
75. Hira A, Dey SK, Howlader MS, Ahmed A, Hossain H, Jahan IA. Anti-inflammatory and antioxidant activities of ethanolic extract of aerial parts of *Vernonia patula* (Dryand.) Merr. Asian Pac J Trop Biomed 2013; 3(10): 798-805.
76. González-Chávez MM, Ramos-Velázquez CS, Serrano-Vega R,Pérez-González C, Sánchez-Mendoza E, Pérez-Gutiérrez S. Antiinflammatory activity of standardized dichloromethane extract of *Salvia connivens* on macrophages stimulated by LPS. Pharm Biol 2017; 55(1): 1467-72.77.
77. Jeong HY, Sung GH, Kim JH, Yoon JY, Yang Y, Park JG, *et al*. Syk and Src are major pharmacological targets of a *Cerbera manghas* methanol extract with kaempferol-based anti-inflammatory activity. J Ethnopharmacol 2014 3; 151(2): 960-9.
78. Yi YS, Cho JY, Kim D. *Cerbera manghas* methanol extract exerts anti-inflammatory activity by targeting c-Jun N-terminal kinase in the AP-1 pathway. J Ethnopharmacol 2016; 193: 387-96.
79. Patil KR, Patil CR. Anti-inflammatory activity of bartogenic acid containing fraction of fruits of *Barringtonia racemosa* Roxb. In acute and chronic animal models of inflammation. J Tradit Complement Med 2016; 7(1): 86-93.
80. Nguyen TD, Thuong PT, Hwang IH, Hoang TK, Nguyen MK, Nguyen HA, *et al*. Anti-hyperuricemic, anti-inflammatory and analgesic effects of *Siegesbeckia orientalis* L.

resulting from the fraction with high phenolic content. BMC Complement Altern Med 2017; 17(1): 191.

81. Torres-Rego M, Furtado AA, Bitencourt MA, Lima MC, Andrade RC, Azevedo EP, *et al.* Anti-inflammatory activity of aqueous extract and bioactive compounds identified from the fruits of Hancornia speciosa Gomes (Apocynaceae). BMC Complement Altern Med 2016; 16: 275.
82. Abiodun OO, Rodríguez-Nogales A, Algieri F, Gomez-Caravaca AM, Segura-Carretero A, Utrilla MP, *et al.* Antiinflammatory and immunomodulatory activity of an ethanolic extract from the stem bark of *Terminalia catappa* L. (Combretaceae): *In vitro* and *in vivo* evidences. J Ethnopharmacol 2016; 192: 309-19.
83. Kumar T, Jain V. Antinociceptive and anti-inflammatory activities of *Bridelia retusa* methanolic fruit extract in experimental animals. Scientific World J 2014; 2014: 890151.
84. Choi KC, Son YO, Hwang JM, Kim BT, Chae M, Lee JC. Antioxidant, anti-inflammatory and anti-septic potential of phenolic acids and flavonoid fractions isolated from Lolium multiflorum. Pharm Biol 2017; 55(1): 611-9.
85. Araniti F, Graña E, Reigosa MJ, Sánchez-Moreiras AM, Abenavoli MR. Individual and joint activity of terpenoids, isolated from *Calamintha nepeta* extract, on *Arabidopsis thaliana*. Nat Prod Res 2013; 27(24): 2297-303.
86. Kumar A, Rahal A, Chakraborty S, Tiwari R, Latheef SK, Dhama K. *Ocimum sanctum* (Tulsi): a miracle herb and boon to medical science - A review. Int J Agronomy Plant Prod 2013; 4(7): 1580-9.
87. Hu XR, Chou GX, Zhang CG. Flavonoids, alkaloids from the seeds of *Crotalaria pallida* and their cytotoxicity and anti-inflammatory activities. Phytochem 2017; 143: 64-71.
88. The plant list. A working list of plant species, *Calotropis procera.* http://www.theplantlist.org/tpl/record/kew-2693660
89. Gupta S, Bhawani G, Karishma K, Pooja S. Ehnopharmaological potential of *Calotropis procera*: An overview. *IRJP,* 3(12), 2012, 19-22.
90. Sharma AK, Kharab R, Kaur R. Pharmacognostical aspects of *Calotropis procera* (Ait.) R. Br. *International Journal of Pharma and Bio Sciences*, 2(3), 2011, B480-B488.

91. Orwa C, Mutua A, Kindt R, Jamnadass R, Simons A. Agroforestree Database: a tree reference and selection guide version, 2009, http://www.world agroforestry.org/af/treedb/.
92. El Bsma Adam SEI. Studies on laticiferous plants: Toxic effects in goats on *Calotropis procera* latex given by different routes of administration, Deutsche Tieraerztliche Wochenschrift, 105(11), 1988, 425-427,
93. Jain SC, Sharma R. Antimicrobial activity of *Calotropis procera*, Fitoterapia. 67(3), 1996, 275- 276.
94. Rastogi, R. & Mehrotra, B. (1999). Compendium of Indian medicinal Plant. Central drug research Institute Lucknow, National Institute of Science, New Delhi, Vol. 2, 1st Edn., p. 147.
95. Murti, Y., Yogi, B. & Pathak, D. (2010). Pharmacognostic Standardization of Leaves of *Calotropis procera* (Ait.) R.Br. (Asclepiadaceae). Inter. J. Ayur. Res., 1(1): 14-17.
96. Sharma BM. Root systems of some desert plants in Churu, Rajasthan. *Indian Forester,* 94(3), 1968, 240-246.
97. Parihar G, Sharma A, Ghule S, Sharma P, Deshmukh P, Srivastava DN. Anti-inflammatory effect of *Calotropis procera* root bark extract. *Asian Journal of Pharmacy & Life Science,* 1(1), 2011, 29-44.
98. Grace BS. The biology of Australian weeds 45. *Calotropis procera* (Aiton) W.T.Aiton. *Plant Protection Quarterly,* 21, 2006, 152–160.
99. Begum N, Sharma B, Pandey RS. Evaluation of insecticidal efficacy of *Calotropis procera* and *Annona Squamosa* ethanol extracts against *Musca domestica*. *J Biofertil Biopestici,* 1(1), 2010, 1-6.
100. Shrivastava A, Singh S, Singh S. Phytochemical investigation of different plant parts of *Calotropis procera. International Journal of Scientific and Research Publications,* 3(3), 2013, 1-4.
101. Khan AQ, Malik A. A steroid from *Calotropis procera. Phytochem*, 28(10), 1989, 2859-2861.
102. Ramos MV, Araújo ES, Jucá TL, Monteiro-Moreira AC, Vasconcelos IM, Moreira RA, Viana CA, Beltramini LM, Pereira DA, Moreno FB. New insights into the complex mixture of latex cysteine peptidases in *Calotropis procera*. *Int J Biol Macromol,* 58, 2013, 211-219.

103. Freitas CD, Lopes JL, Beltramini LM, de Oliveira RS, Oliveira JT, Ramos MV. Osmotin from *Calotropis procera* latex: new insights into structure and antifungal properties. *Biochim Biophys Acta,* 8(10), 2011, 2501-2507.
104. Kumar VL, Sangraula H, Dewan S. Preliminary studies on the analgesic activity of latex of *Calotropris procera. Journal of Ethnopharmacology,* 73(1-2), 2000, 307-311.
105. Suresh BAR, Karki SS. Anti-inflammatory activity of various extracts of roots of *Calotropis procera* against different inflammation models. *International Journal of Pharmacy and Pharmaceutical Sciences,* 3(3), 2011, 191-194.
106. Mathur R, Gupta SK, Mathur SR, Velpandian T. Anti-tumor studies with extracts of *Calotropis procera* (Ait.) R.Br. root employing Hep2 cells and their possible mechanism of action. *Indian J Exp Biol* 2009;47(5):343-348.
107. Kamath JV, Rana AC. Preliminary study on anti-fertility activity of *Calotropis procera* roots in female rats. *Fitoterapia* 2002;73(2):111-115.
108. Basu A, Sen T, Pal S, Mascolo N, Capasso F, Nag AK, Studies on the Antiulcer Activity of the Chloroform Fraction of *Calotropis procera* Root Extract. *Phytother Res* 1996;11(2):163-165.
109. Thakare Priya Ashokrao, Deshbhratar Kiran, Suryawanshi M.N. A Brief Review on Therapeutic Effects of – "Ornamental Plant" Rose. International Journal of Ayurveda and Pharma Research. 2017;5(12):46-52.
110. S. G. Agarwal, Aruna Gupta , B. K. Kapahi , Baleshwar , R. K. Thappa & O.P. Suri (2005) Chemical Composition of Rose Water Volatiles, Journal of Essential Oil Research,17:3, 265-267, DOI: 10.1080/10412905.2005.9698897.
111. Mohammad Hossein Boskabady, Mohammad Naser Shafei, Zahra Saberi and Somayeh Amini. Pharmacological Effects of Rosa Damascena. Iran J Basic Med Sci. 2011 Jul-Aug; 14(4): 295–307.
112. Wood G, Bache F. The Dispensatory of the United States of America, 4th ed. Philadelphia: Griggand Elliot; 1839.
113. Sharaf khandy A. Ave-Sina. Law in Medicine. Interpreter. Teheran: Ministry of Guidance publication; 1990. pp. 129–131.
114. Buckle DR, Arch JRS, Boering NE, Foster KA, Taylor JF, Taylor SG, et al. Relaxation effect of potassium channel activators BRL 38227 and Pinacidil on guineapig and

human airway smooth muscle, and blockade of their effects by Glibenclamide and BRL 31660. Pulm Pharmacol. 1993; 6:77–86.

115. Libster M. Delmar's Integrative Herb Guide for Nurses. Albany: Delmar Thamson Learning; 2002. p. 360–370.
116. Zargari A. Medicinal plants. 5th ed. Tehran: Tehran University Press; 1992.
117. Momeni T, Shahrokhi N. Essential oils and their therapeutic actions. Tehran, Iran: Tehran University. Press; 1991.
118. B. Mohammed Ishaq et al. Phytochemical Investigations and Cardiotonic Activity of Rosa Centifolia (Linn.) Flowers. AJCPR, 2014, Vol.2(1): 69-7719.
119. Battiwala A, Chandragopal SS, Kumar, S (2013) Evaluation of Anti-Inflammatory and Anti-arthritic activity of Rosa centifolia (Linn.) Flowers in experimental rats. *International Journal for Pharmaceutical Research Scholars V- 2, I-4,2013 414–26.*
120. Samyak et al (2015) Assessment of in-vivo Analgesic Activity of Rosa indica Linn. Leaf Extracts in Swiss Albino Mice. Indian Journal of Ethno Phyto Pharmaceuticals Oct- Dec.2015, 1 (1), 16-21.
121. Jahir Alam Khan et a. A Study on Antibacterial Properties of Rosa indica against Various Pathogens. Asian J. Plant Sci. Res., 2011, 1 (1):22-30.
122. Lee M-H, Nam TG, Lee I, et al. Skin anti-inflammatory activity of rose petal extract (Rosa gallica) through reduction of MAPK signaling pathway. Food Sci Nutr. 2018; 6:2560–2567. https://doi.org/10.1002/fsn3.870.
123. Md. Tofazzal Hossain Md., Obydul Hoq, Therapeutic use of Adhatoda vasica, Asian J. Med. Biol. Res. 2016, 2 (2), 156-163; doi: 10.3329/ajmbr. v2i2.29005.
124. Shah Unnati, Pharmacognostical and Phytochemical Evaluation of Adhatoda vasica Leaf, International Journal of Research Studies in Biosciences (IJRSB) Volume 2, Issue 11, December 2014, PP 144-148.
125. Amin AH, Mehta DR and Samarth SS. In: Proceedings, First International Pharmacological Meeting. Stockholm, Pergamon Press Ltd., Oxford. 1963; 7: 377.
126. Gupta OP, Sharma ML, Ghatak BL and Atal CK. Pharmacological investigation of vasicine and vasicinone–the alkaloids of Adhatoda vasica, Indian J Med Res, 1977; 66: 680–691.
127. Atal CK, Sharma ML, Khajuria A and Kaul A. Thrombopoietic activity of vasicine hydrochloride. Indian J Exp Bio. 1982; 20: 704–709.

128. Dhuley JN. Antitussive effect of Adhatoda vasica extract on mechanical or chemical stimulation induced coughing in animals. J Ethnopharmacol, 1999; 67: 361–365.
129. George ML, Venkataraman PR and Pandalai KM. Investigations on plant antibiotics. Part II. A search for antibiotic substances in some Indian medicinal plants. J Sci Ind Res 1947; 76 (Suppl): 107–114.
130. Kurup PA. Studies on plant antibiotics. Screening of some medicinal plants. J Sci Ind Res. 1956; 15C: 153–154.
131. Joshi CG and Magar NG. Antibiotic activity of some Indian medicinal plants. J Sci Ind Res. 1952; 11B: 261–263.
132. Thomas E, Shanmugam J and Rafi M. In vitro antibacterial activity of certain medicinal plants of Kerala. Biomedicine. 1999; 19: 185–190.
133. Zainab K, Rehman SZ, Latif TA, Jahan N. Hypoglycemic activity of Barg-e-Arusa and Tukhm-e-Kalonji on alloxaninduced diabetes mellitus. *Hamdard Medicus*. 2008; 51(1): 77-81.
134. Kirtikar KR and Basu BD. *Indian Medicinal Plants*, International Book Distributors, Book seller and Publisher. 2005; Vol-III: p.1899.
135. Jarald EE and Jarald SE. *Textbook of Pharmacognosy and Phytochemistry*, CBS Publishers and Distributors. 2009, p. 29.
136. Chopra RN, Nayar SL and Chopra IC. *Glossary of Indian Medicinal Plants*, National Institute of Science communication (Council of Science and Industrial Research New Delhi). 1999; p. 7.
137. Heinrich M, Barnes J, Gibbons S and Williamson EM. *Fundamentals of Pharmacognosy and Phytochemistry*, Churchill Livingstone, 2008, p.49.
138. Nandkarni KM and Nandkarni AK. *Indian Materia Medica*, Vol-I, Bombay Popular Parkashan. 2000; p.40.
139. Rao, R.R., Jamir, N.S., 1982. Ethnobotanical studies in Nagaland, I. Medicinal plants. Economic Botany 36, 176–181.
140. Chakraborty A, Brantner AH. Study of alkaloids from Adhatoda vasica Nees on their anti-inflammatory activity. Phytother Res. 2001;15(6):532-534.
141. Jain R, Jain SK. Traditional medicinal plants as anticancer agents from Chhattishgarh, India: An overview. International Journal of Phytomedicine. 2010;2(3).

142. Thabrew MI, Dharmasiri MG, Senaratne L. Anti-inflammatory and analgesic activity in the polyherbal formulation Maharasnadhi Quathar. J Ethnopharmacol. 2003;85(2-3):261-267.
143. Poonam Aggarwal and Sukhpreet Kaur, Technology development for the preparation, concentration, and utilization of rose extract in different valuable products and by products with retention of color and flavor, The Pharma Innovation Journal 2017; 6(6): 189-193.