

**INTERNATIONAL JOURNAL OF ADVANCES IN PHARMACY,  
BIOLOGY AND CHEMISTRY****Review Article****Anti-Inflammatory Activity of Herbal Plants:  
A Review****S. Kumar<sup>1\*</sup>, BS. Bajwa<sup>1</sup>, Singh Kuldeep<sup>1</sup> and AN. Kalia<sup>2</sup>**<sup>1</sup>Lala Lajpat Rai college of Pharmacy, Moga, Punjab, India.<sup>2</sup>ISF college of Pharmacy, Moga, Punjab, India.**ABSTRACT**

Inflammation is a part of the complex biological response of vascular tissues to harmful stimuli, such as pathogens, damaged cells or irritants. It is characterized by redness, swollen joints, joint pain, its stiffness and loss of joint function. Inflammation is currently treated by NSAIDs. Unfortunately these drugs cause increased risk of blood clot resulting in heart attacks and strokes. Therefore, the developments of potent anti-inflammatory drugs from the natural products are now under considerations. Natural products are rich source for discovery of new drugs because of their chemical diversity. A natural product from medicinal plants plays a major role to cure many diseases associated with inflammation. The conventional drug available in the market to treat inflammation produces various side-effects. Due to these side-effects, there is need for the search of newer drugs with less or no side-effects. There are hundreds of phytoconstituents reported to have many pharmacological activities although most of these reports are of academic interest and very few find entry in clinical trials. The present review is directed towards compilation of data on promising phytochemicals from herbal plants that have been tested in inflammatory models using modern scientific system.

**Keywords:** Herbal medicine, NO, NSAIDs, inflammation.**INTRODUCTION**

Inflammation is a normal, protective response to tissue injury caused by physical trauma, noxious chemicals or microbiological agents. There are mainly two types of inflammation which are as follows

**Acute inflammation**

It is associated with increased vascular permeability, capillary infiltration and emigration of leukocytes.

**Chronic inflammation**

It is associated with infiltration of mononuclear immune cells, macrophages, monocytes, neutrophils, fibroblast activation, proliferation (angiogenesis) and fibrosis.

Inflammation is a common clinical conditions and rheumatoid arthritis (RA) is a chronic debilitating autoimmune disorder<sup>1</sup>, that affects about 1% of the population in developed countries<sup>2</sup>. The classic signs of inflammation are local redness, swelling, pain, heat and loss of function<sup>3</sup>. Nitric oxide (NO)

is a gaseous short lived free radical has been implicated as a mediator of inflammation and modulation of biosynthesis or activity of NO results in amelioration of acute inflammation and experimental arthritis model<sup>4,5</sup>. NO is generated via the oxidation of the terminal guanidine nitrogen atom of L-arginine by the enzyme Nitric Oxide Synthase(NOS). Three major isoforms of Nitric Oxide Synthase (NOS) have been identified. Two expressed constitutively, are calcium/calmodulin-dependent and are classified together as constitutive NOS isoforms (cNOS). The third is cytokine-inducible, calcium/calmodulin-independent isoform of NOS (iNOS) is regulated in the gene by a variety of inflammatory mediators<sup>6</sup>. Increased NOS activity or NO release have been demonstrated in both acute and chronic models of inflammation<sup>7</sup>. Further, administration of L-arginine a precursor for NO synthesis increased the paw swelling in adjuvant arthritis<sup>6</sup>. NSAIDs are among the most commonly used drugs worldwide. They are prescribed for orthopaedic conditions such as osteoarthritis, soft-tissue injuries and

fractures etc<sup>8</sup>. NSAIDS e.g Ibuprofen and naproxen etc. are used in the above said conditions. The other class of drugs is glucocorticoids e.g cortisone and prednisone etc. However, besides their high costs, severe adverse reactions and toxicity, including some risk of infections in subsets of patients being treated with biological response modifiers e.g Tumour necrosis factor, alpha blocking agents<sup>9</sup>. The side-effects with currently used drugs are G.I ulceration and bleeding, Renal damage, Hypertension, Hyperglycemia. Besides the above side-effects, the greatest disadvantage in presently available potent synthetic drugs lies in their toxicity and reappearance of symptoms after discontinuation. Therefore, the screening and development of drugs for their anti-inflammatory activity is the need of hour and there are many efforts for finding anti-inflammatory drugs from indigenous medicinal plants<sup>10</sup>.

#### Plants as natural anti-inflammatory agents

Unlike modern allopathic drugs which are single active components that target one specific pathway,

herbal medicines work in a way that depends on an orchestral approach. A plant contains a multitude of different molecules that act synergistically on targeted elements of the complex cellular pathway<sup>(11)</sup>. Medicinal plants have been source of wide variety of biologically active compounds for many centuries and used extensively as crude material or as pure compounds for treating various disease conditions<sup>12</sup>. The use of herbal medicines becoming popular due to toxicity and side-effects of allopathic medicines. Medicinal plants play an important role in the development of potent therapeutic agents. There are over 1.5 million practitioners of traditional medicinal system using medicinal plants in preventive, promotional and curative applications<sup>13</sup>. India with its biggest repository of medicinal plants in the world may maintain an important position in the production of raw materials either directly for crude drugs or as the bioactive compounds in the formulation of pharmaceuticals and cosmetics etc<sup>14</sup>.

**Table 1: Plants having anti-inflammatory potential**

S.No	Plant Name	Family	Plant Part	Type of Extract
1	<i>Achillea millefolium</i>	Asteraceae	Whole Plant	Aqueous, alcohol
2	<i>Aconitum heterophyllum</i>	Valeraneaceae	Root	Ethanol
3	<i>Adhatoda vasica</i> <i>Nees</i>	Acanthaceae	Leaves	Methanol
4	<i>Adansonia digitata</i>	Malvaceae	Fruit	Aqueous
5	<i>Aegle marmelos</i>	Rutaceae	Leaves	Ethylacetate and methanol
6	<i>Aloe vera</i>	Asphodelaceae	Leaves	Pet.ether, Ethanol
7	<i>Azadirachta indica</i>	Meliaceae	Leaves	Hydro-alcohol
8	<i>Annona squamosa</i>	Annonaceae	Seeds	Ethanol
9	<i>Baccharis incarum</i>	Astereae	Whole plant	Ethanol
10	<i>Bacopa Monnieri</i>	Scrophulariaceae	Whole Plant	Ethanol
11	<i>Barleria prionitis</i>	Acanthaceae	Whole plant	Methanol
12	<i>Bonafousia sananho</i>	Apocyanaceae	Whole plant	Ethanol
16	<i>Boussingaultia</i> <i>gracilis</i>	Bassellaceae	Leaves, Stem and Bark	Aqueous
14	<i>Boswellia serrata</i>	Burseraceae	Resin	Methanol
15	<i>Bryophyllum</i> <i>pinnatum</i>	Crassulaceae	Leaves	Methanol
16	<i>Bursera simaruba</i>	Burseraceae	Leaves, Bark	Hexane, Ethanol
17	<i>Caralluma</i> <i>thberculata</i>	Asclepiadaceae	Whole plant	Ethanol
18	<i>Cassia fistula</i>	Caesalpinaceae	Leaves	Methanol
19	<i>Cassia obtusifolia</i>	Leguminosae	Leaves	Methanol
20	<i>Citrus auranticum</i>	Rutaceae	Fruit	Not indicated
21	<i>Commiphora mukul</i>	Burseraceae	Resin	Methanol
22	<i>Cordia ulmifolia</i>	Boraginaceae	Leaves	Pet.ether
23	<i>Curcuma longa</i>	Zingiberaceae	Rhizomes	Ethanol
24	<i>Daphne pontica</i>	Thymelaeaceae	Aerial Parts, Roots	Methanol
25	<i>Elephantophs scaber</i>	Compositae	Leaves	Pet.ether
26	<i>Emblica officinalis</i>	Euphorbiaceae	Fruit	Ethanol and Aqueous
27	<i>Erythrospermum</i> <i>monticoloum</i>	Flacourtiaceae	Leaves	Methanol
28	<i>Garcinia mangostana</i>	Guttiferae	Fruit	Methanol
29	<i>Hammada elegans</i>	Chenopodiaceae	Aerial part	Ethanol
30	<i>Hedera rhombea</i>	Araliaceae	Leaves	Methanol
31	<i>Iberis amara</i>	Brassicaceae	Whole plant	Ethanol
32	<i>Kirkia acuminata</i>	Simaroubaceae	Leaves	Methanol
33	<i>Lantana camera</i>	Verbenaceae	Leaves	Pet.ether

34	<i>Lippia geminata</i>	Verbenaceae	Leaves	Pet.ether, Ethanol
35	<i>Lippia nodiflora</i>	Verbenaceae	Leaves	Pet.ether, Ethanol
36	<i>Lycopodium clavatum</i>	Lycopodiaceae	Aerial Parts	Chloroform extract, the alkaloid fraction
37	<i>Mangifera indica</i>	Anacardiaceae	Bark	Aqueous
38	<i>Marsdenia condurango</i>	Asclepiadaceae	Whole plant	Ethanol
39	<i>Mikania cordata</i>	Compositae	Root	Methanol
40	<i>Moringa olifera</i>	Moringaceae	Root, Flowers,	Methanol, Aqueous
41	<i>Paederia foetida</i>	Rubiaceae	Leaves	Methanol
42	<i>Palisota hirsuta</i>	Commelineaceae	Leaves	Aqueous
43	<i>Petiveria alliacea</i>	Phytolaccaceae	Root	Ethanol
44	<i>Phyllanthus polyphyllus</i>	Euphorbiaceae	Whole plant	Ethanol
45	<i>Piper longum</i>	Piperaceae	Roots	Aqueous
46	<i>Piper ovatum</i>	Piperaceae	Leaves	Hydro alcoholic
47	<i>Pluchea indica</i>	Asteraceae	Root	Methanol
48	<i>Ricinus communis</i>	Euphorbiaceae	Roots, leaves	Methanol, pet ether
49	<i>Rheum australe</i>	Polygonaceae	Root	Pet.ether, Chloroform, Methanol
50	<i>Rubrus ellipticus</i>	Rubiaceae	Leaves	Ethanol
51	<i>Saussurea costus</i>	Asteraceae	Whole Plant	Methanol
52	<i>Sesbania sesban</i>	Leguminosae	Leaves and Bark	Methanol
53	<i>Sida cordifolia</i>	Malvaceae	Whole Plant	Water
54	<i>Sidium guajava</i>	Myrtaceae	Fruit	Methanol
55	<i>Swertia chirata</i>	Gnetaceae	Aerial part	Benzene
56	<i>T. buxifolium</i>	Rosaceae	Leaves, Stem	Methanol
57	<i>T. flavum</i>	Ranunculaceae	Leaves, Stem	Methanol
58	<i>T. micrantha</i>	Myrtaceae	Leaves	Ether, Ethanol
59	<i>Tinospora diversifolia</i>	Menispermaceae	Aerial part	Aqueous
60	<i>Tuberaria lignosa</i>	Cistaceae	Leaves	Hexane
61	<i>Thespesia populnea</i>	Malvaceae	Leaves and Barks	Oil
62	<i>Vinca rosea</i>	Apocynaceae	Leaves	Not indicated
63	<i>Visnea mocanera</i>	Theaceae	Leaves	Ethanol
64	<i>Vitex negundo</i>	Lamiaceae	Leaves	Alcoholic
65	<i>Xeromphis spina</i>	Compositae	Pulp	Ethanol
66	<i>Zanha africana</i>	Sapindaceae	Root bark	Methanol
67	<i>Zingiber officinalae</i>	Zingiberaceae	Rhizome	Ethanol

### 1. *Achillea millefolium* Linn. (Asteraceae)



Fig. 1:

*Achillea millefolium* L. is a perennial herb native to Europe and highly recognized in traditional medicine for its anti-inflammatory properties. The plant has been traditionally used externally for treatment of wounds, burns, swollen and irritated skin. Studies have shown two classes of secondary metabolites, isoprenoids and phenolics, contribute mainly to the anti-inflammatory properties<sup>15</sup>. Aqueous and alcoholic extracts of *A. millefolium* are used in traditional medicine internally in treatment of gastro-intestinal and hepato-biliary disorders and as an antiphlogistic drug. The topical anti-inflammatory activity of sesquiterpenes is

caused by inhibition of arachidonic acid metabolism. The three flavonoids present in the crude extract and enriched in flavonoid fraction are rutin, aspigenin-7-*O*-glucoside and luteolin-7-*O*-glucoside. The crude plant extract and two fractions enriched in the dicaffeoyquinic acids and the flavonoids inhibit human neutrophil elastase as well as the matrix metalloproteinases, which are associated with anti-inflammatory process *in vitro* studies<sup>16</sup>.

### 2. *Aconitum heterophyllum* (Valeraneaceae)



Fig. 2:

*A. heterophyllum* is a plant which is commonly known as 'Ativisha' or 'Patis' in Ayurveda. It is used for the treatment of diseases of nervous

system, digestive system, fever and rheumatism. The ethanolic extract of root of *A.heterophyllum* contains alkaloids, glycosides, flavnoids and sterols. It has been reported that plants with these chemical classes of compounds possess potent anti-inflammatory effects through inhibition of prostaglandin pathways. The cotton pellet-induced granuloma is widely used to assess the transudative and proliferative components of chronic inflammation. The weight of the wet cotton pellets correlates with the amount of granulomatous tissue. The administration of *A.heterophyllum* extract has been observed to inhibit the weight of wet cotton pellet in a dose dependent manner and the higher dose of *A.heterophyllum* exhibited inhibition of inflammation very close to the inhibitory effect of diclofenac sodium. In literature it has been reported that ethanolic root extract of *A.heterophyllum* has potential to inhibit sub-acute inflammation by interruption of the arachidonic acid metabolism<sup>17</sup>.

### 3. *Adhatoda vasica* (Acanthaceae)



**Fig. 3:**

*Adhatoda vasica* L. is an indigenous herb belonging to family Acanthaceae. The plant has been used in the indigenous system of medicine in worldwide as herbal remedy for treating cold, cough, whooping cough, chronic bronchitis, asthma, sedative expectorant, antispasmodic, anthelmintic, rheumatism and rheumatic painful inflammatory swellings. The drug is employed in different forms such as fresh juice, decoction, infusion and powder. It is also given as alcoholic extract and liquid extract or syrup<sup>18</sup>. This plant contains alkaloids, tannins, flavnoids, terpenes, sugars and glycosides<sup>19</sup>. The anti-inflammatory potential of ethanolic extract has been determined by using carrageenan-induced paw edema assay, formalin-induced paw edema assay in albino rats. The ethanolic extract of *Adhatoda vasica* produced dose dependent inhibition of carrageenan and formalin-induced paw edema<sup>20</sup>.

### 4. *Bacopa monnieri* Linn.( Scrophulariaceae)



**Fig. 4:**

The *Bacopa monnieri* is a creeping, glabrous, succulent herb, rooting at nodes and habitat of wetlands and muddy shores<sup>21</sup>. Earlier, it is used as a brain tonic to enhance memory development, learning and concentration<sup>22</sup>. The plant has also been used in India and Pakistan as a cardio tonic, digestive aid and to improve respiratory function in cases of bronchoconstriction<sup>23</sup>. The plant possesses anti-inflammatory activity on carrageenan-induced rat paw edema and it has shown 82% edema inhibition when compared to indomethacin. *Bacopa monnieri* also significantly inhibited 5-lipoxygenase (5-LOX), 15 (LOX) and cyclooxygenase-2 (COX-2) activities<sup>24</sup>. *Bacopa monnieri* possesses significant anti-inflammatory activity that may well be relevant to its effectiveness in the healing of various inflammatory conditions in traditional medicine<sup>25</sup>. The anti-inflammatory activity of *Bacopa monnieri* is due to the triterpenoid and bacoside present in the plant. The ability of the fractions containing triterpenoids and bacosides inhibited the production of pro-inflammatory cytokines such as tumour necrosis factor –alpha and interleukin-6. This was tested using lipopolysaccharide activated peripheral blood mononuclear cells and peritoneal exudates cells *in vitro*. So, *Bacopa monnieri* has the ability to inhibit inflammation through modulation of pro-inflammatory mediator release<sup>26</sup>.

### 5. *Cassia fistula* L. (Caesalpinaceae)



**Fig. 5:**

*Cassia fistula* tree is one of the most widespread in the forests of India. The whole plant possesses medicinal properties useful in the treatment of skin diseases, inflammatory diseases, rheumatism, anorexia and jaundice. The bark extracts of *Cassia fistula* possess significant anti-inflammatory effect in the acute and chronic anti-inflammatory model of inflammation in rats. Reactive oxygen species (ROS) generated endogenously or exogenously are associated with the pathogenesis of various diseases such as atherosclerosis, diabetes, cancer, arthritis and aging process. ROS play an important role in pathogenesis of inflammatory diseases. The main constituents responsible for anti-inflammatory activity of *Cassia fistula* are flavonoids and bio-flavonoids<sup>27</sup>.

#### 6. *Daphne pontica* Linn. (Thymelaeaceae)



Fig. 6:

*Daphne* species are supposed to have anti-cancer activity since the the time of AD 2<sup>nd</sup> century. Flavonoids constituents like daphnodorins were isolated from the roots of *Daphne pontica* which was reported to have antitumour activity. Several *Daphne* species have been used against inflammatory disorders. *Daphne pontica* have been used for the treatment of rheumatic pain and inflammatory ailments. The extracts inhibits the production of PGE<sub>2</sub> and IL-1B<sup>28</sup>.

#### 7. *Emblica officinalis* (Euphorbiaceae)



Fig. 7:

*Emblica officinalis* is a tree growing in subtropical and tropical parts of China, India, Indonesia and Malay peninsula. It has been used for anti-inflammatory and antipyretic activities in these areas. In the recent studies, the anti-inflammatory activity was found in the water fraction of methanol extract of plant leaves. The effects of fraction were tested on the synthesis of mediators of inflammation such as leukotriene B<sub>4</sub>, platelet activating factor (PAF) and thromboxane. The water fraction of methanol extract inhibited migration of human PMN<sub>s</sub> in relatively low concentrations<sup>29</sup>.

#### 8. *Garcinia mangostana* Linn. (Guttiferae)



Fig. 8:

The fruit rinds of *Garcinia mangostana* have been used as a traditional medicine for the treatment of trauma and skin infections. The xanthones,  $\alpha$ - and  $\gamma$ -mangostins are major bioactive compounds found in the fruit hulls of mangosteen. The xanthones exhibits their biological effects by blocking inducible nitric oxide synthase ( $\text{iNOS}$ ) and cyclooxygenase-2 (COX-2). It was reported that two mangostins decrease prostaglandins (PGE<sub>2</sub>) levels through inhibition of COX-2 activity and NO production. It is reported that  $\alpha$ -mangostin shows a more potent inhibition of PGE<sub>2</sub> release than either histamine or serotonin<sup>30</sup>.

#### 9. *Lantana camara* Linn. (Verbenaceae)



Fig. 9:

The aerial parts of many species of *Lantana* are widely used in folk remedies like cancer and tumours. A tea prepared from leaves and flowers were taken against fever, influenza and stomachache. The other uses of plant shows anti-malarial, anti-bacterial and anti-diarrhoeal activities. From the studies it has been reported that aqueous extract of *Lantana camara* leaves is highly effective and safe for the treatment of hemorrhoids. It has been reported that aqueous extract of *Lantana camara* leaves has promising analgesic, anti-inflammatory and anti-hemorrhoidal activities<sup>31</sup>.

#### 10. *Lycopodium clavatum* Linn. (Lycopodiaceae)



**Fig. 10:**

*Lycopodium clavatum* commonly known as club moss has been reported to be used in wound healing effect. According to the study carried out by Orhan *et al*, four extracts prepared with petroleum ether, chloroform, ethyl acetate and methanol as well as the alkaloidal fraction from the aerial parts of *Lycopodium clavatum* using acetic acid-induced increase in capillary permeability assessment in mice revealed that only the chloroform extract and the alkaloid fraction displayed marked anti-inflammatory effect as compared to Indomethacin<sup>32</sup>.

#### 11. *Mangifera indica* Linn. (Anacardiaceae)

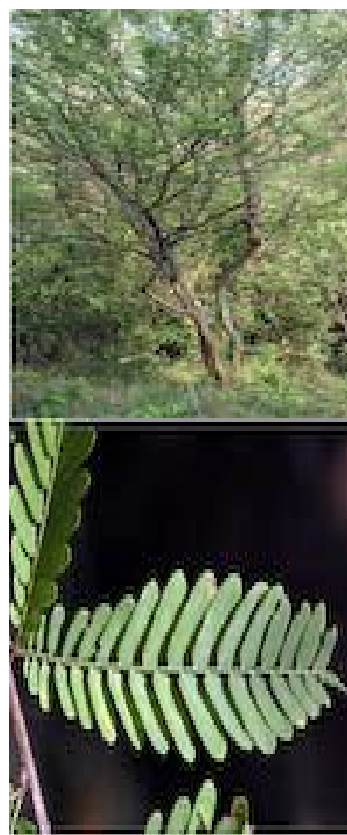


**Fig. 11:**

*Mangifera indica* grows in the tropical and subtropical region and its parts are commonly used

in folk medicine for a wide variety of remedies<sup>(33)</sup>. The plant *Mangifera indica* has been reported for various therapeutic uses in traditional medicines such as, a fluid extract or the infusion of the bark is used in monorrhagia, leucorrhoea, bleeding piles and in case of haemorrhage from the lungs. Idibs of the leaves calcined are used to remove warts of eyelids. Dried powdered leaves are used in diabetes. Dried flowers in decoction or powder are useful in diarrhea, chronic dysentery and gleet<sup>(34)</sup>. The ethyl acetate and ethanol extracts of the roots of *Mangifera indica* has been reported to have considerable anti-inflammatory activity as compared with standard drug Diclofenac sodium<sup>(35)</sup>. The phytochemical analysis revealed the presence of flavonoids. The flavonoids have potent anti-inflammatory activity by inhibiting prostaglandin synthesis<sup>36</sup>.

#### 12. *Phyllanthus polyphyllus* Linn. (Euphorbiaceae)



**Fig. 12:**

It is a small shrub used in anti-inflammatory folk medicine in tropical and subtropical regions in India and Srilanka. Four compounds, one benzenoid and three aryl naphthalide lignans isolated from whole plant showed growth inhibitory effect on production of NO and cytokines (TNF- $\alpha$  and IL-

12). Since TNF- $\alpha$  and IL-12 were known as the main pro-inflammatory cytokines secreted during the early phase of acute and chronic inflammatory diseases, such as asthma, rheumatoid arthritis, septic shock. The use of *Phyllanthus polyphyllus* as anti-inflammatory remedy in traditional medicine may be attributed by these compounds<sup>37</sup>.

### 13. *Ricinus communis* Linn. (Euphorbiaceae)



Fig. 13:

*Ricinus communis* Linn. is found almost everywhere in the tropical and subtropical regions of the world. Anti-inflammatory and free radical scavenging activities of the methanolic extract of *Ricinus communis* root was studied by Ilavarasan *et al* in Wistar albino rats. The methanolic extract exhibited significant anti-inflammatory activity in carrageenan-induced hind paw edema model. The methanolic extract showed significant free radical scavenging activity by inhibiting lipid peroxidation. The observed pharmacological activity may be due to the presence of phytochemicals like flavonoids, alkaloids and tannins in the plant extract<sup>38</sup>.

### 14. *Sesbania sesban* Linn. (Leguminosae)



Fig. 14:

The genus *Sesbania sesban* contains about 50 species, the majority of which are annuals. The

greatest species diversity occurs in Africa with 33 species. Although the annual species have received attention, recent research has focused on perennial species. Of the perennial species, *Sesbania sesban* has shown potential<sup>39</sup>. It is a small perennial tree with woody stems, yellow flowers and linear pods<sup>40</sup>. According to the data from literature the phytochemical investigation of crude saponin extract revealed the presence of various constituents like terpenoidal and steroidal saponins, tannins and flavonoids which had been reported to have anti-inflammatory activity<sup>41</sup>. This was proved by inhibition of carrageenan oedema by crude saponins extract. The crude saponin extract have been able to control the increase in Paw edema in early phase and also in late hours related to inhibition of prostaglandins release. Hence, it can be said that the present anti-inflammatory activity of crude saponin extract might be due to its action on the early and latter phase of inflammation<sup>42</sup>.

### 15. *Sida cordifolia* Linn. (Malvaceae)



Fig. 15:

*Sida cordifolia* is a perennial subshrub of the mallow family Malvaceae. It has naturalized throughout the world and is considered an invasive weed in Africa, Australia, Hawaiian islands, New Guinea and French Polynesia<sup>43</sup>. *Sida cordifolia* is used in folk medicine for the treatment of inflammation of the oral mucosa, blenorrhea, asthmatic bronchitis and nasal congestion<sup>44</sup>. It has been investigated as an anti-inflammatory<sup>45</sup>, for preventing cell proliferation<sup>46</sup> and for encouraging liver growth<sup>47</sup>.

16. *Thespesia populnea* (Malvaceae)

Fig. 16:

The leaves and bark of *Thespesia populnea* are used to produce oil for the treatment of fracture wounds and as an anti-inflammatory poultice applied to ulcers and boils in southern India and Sri Lanka. Ethanolic extract of *Thespesia populnea* shows anti-inflammatory activity in both acute and chronic models. The phytochemical studies indicated that the ethanolic extract of bark contains alkaloids, carbohydrates, proteins, tannins, phenols, flavonoids, gums & mucilage, saponins and terpenes<sup>48</sup>.

**CONCLUSION**

Plants have played a significant role in human health care since the ancient times. Traditional plants exert great role in discovery of new drugs. Majority of human population worldwide is getting affected by inflammation related disorders. It is believed that current analgesia inducing drugs such as opiates and NSAIDs are not useful in all cases, because of their side effects like GIT irritation, liver dysfunction and much more<sup>(49)</sup>. There are number of immuno-suppressing agents have been developed based on their COX-1 inhibition mechanism, but they cause severe side effects on long term administration. So, selective inhibitors of COX-2 were developed to avoid side effects of COX-1 inhibitors. However, one of these inhibitors has been reported to increase the risk of myocardial infarction and atherothrombotic events. Thus, it is likely that COX-2 inhibitors will not be

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suitable for the treatment of chronic inflammatory diseases, such as rheumatoid arthritis<sup>50</sup>. For rheumatoid arthritis currently available drugs are primarily directed towards the control of pain or the inflammation associated with synovitis.

Large number of herbal species has been used traditionally or as folk medicines against inflammatory disorders. Many of them have been studied scientifically and proved to be beneficial anti-inflammatory agents. Despite the divergent bioactivities of the plant medicines against various diseases, active components of most plant extracts have not been elucidated thoroughly, due their complex mixtures. However, the core chemical classes of anti-inflammatory agents from natural sources have been reported to engage a vast range of compounds such as polyphenols, flavonoids, terpenoids, alkaloids, anthraquinones, lignans, polysaccharides, saponins and peptides<sup>51,52</sup>.

From the study done so far, it has been elucidated that flavonoids are major anti-inflammatory agents. Some of them act as phospholipase inhibitors and some have been reported as TNF- $\alpha$  inhibitors in different inflammatory conditions. Biochemical investigations have also shown that flavonoids can inhibit both cyclooxygenase and lipoxygenase pathways of arachidonic metabolism depending upon their chemical structures<sup>53,54</sup>.

Alkaloids in asserted skeletal type based on pyridine ring system have been reported to have striking anti-inflammatory activity, e.g Berberine from *Berberis* is traditional remedy against rheumatism<sup>55</sup>.

Terpenoids significantly inhibit the development of chronic joint swelling. Terpenoids may affect different mechanism relevant to inflammations arising in response to varied etiological factors<sup>56</sup>.

However, still many herbal medicines for inflammation and rheumatism have not undergone through scientific investigations. Hence, it is a need of time that all such herbal medicines should consider for determination of their pharmacological activities, isolation of single entity responsible for anti-inflammatory activity and development of suitable formulation which would be beneficial against inflammatory disorders.

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Plants as natural anti-inflammatory agents Unlike modern allopathic drugs which are single active components that target one specific pathway, herbal medicines work in a way that depends on an orchestral approach. A plant contains a multitude. Studies have shown two classes of secondary metabolites, isoprenoids and phenolics, contribute mainly to the anti-inflammatory properties<sup>15</sup>. Aqueous and alcoholic extracts of *A. millefolium* are used in traditional medicine internally in treatment of gastro-intestinal and hepato-biliary disorders and as an antiphlogistic drug. The topical anti-inflammatory activity of sesquiterpenes is. Fig. 2: *A. heterophyllum* is a plant which is commonly known as 'Ativisha' or 'Patis' in Ayurveda.