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THE ANTI-INFLAMMATORY EFFECTS OF FABACEAE AND ALLIACEAE PLANTS: A REVIEW

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Abstract:

In the last few decades there has been an exponential growth in the field of herbal medicine and is gaining popularity among the globally developing and developed countries. Currently there has been an increased interest to identify plants and explore their therapeutic potential. The plants show pharmacological potency and have low or no side effects for use in preventive medicine and health care. Also they represent a potential source of new compounds with different pharmacological activity. Ayurveda, the oldest medicinal system in the world, finds active and therapeutically useful compounds from plants. Considering the growing interest in the field of plant drugs, assessing different pharmacological activities, two plant families Fabaceae and Amaryllidaceae, are available as vegetables all over the country. The therapeutic potential of these families reported activities are inhibition of invasion of carcinoma, cardiovascular protection, lowering of cholesterol and blood pressure, anti-platelet activities, and thromboxane formation with their numerous chemical values and rich phytochemicals. In addition the biological activities include antibacterial, antithrombotic, antioxidant, immunomodulatory, antidiabetic, hepatoprotective, hypolipidemic modulation of drug metabolism etc. In this study we have discussed about the therapeutic potential and chemical constituents and their antiinflammatory activity. Several researchers have provided a mechanism of action for many of their therapeutic effects in this area.

Keywords: *therapeutic, immunomodulatory, hepatoprotective, cardiovascular, hypolipidemic, pharmacological*.

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INTRODUCTION:

This review has discussed on cyclooxygenase (cox) inhibitory activity with plants by examining historical medicinal plants. Plant species with historical uses, which could indicate inhibition of the COX enzymes were included in the present study because these plants are used as vegetables since ages and cyclooxygenases are primary enzymes that use oxygen and free radicals to produce innumerable metabolites that may serve as local hormones.

The cyclooxygenase enzyme has two isoforms, COX-1 and COX-2 [1]. The constitutively expressed COX-1 is present in cells under physiological conditions and produces protective substances for all organs. COX-1 is responsible for the production of prostanoids that maintain mucosal blood flow, promote mucous secretion, inhibit neutrophil adherence and maintain renal blood flow [45].

Prostaglandins (PGs) also function as mediators of the inflammatory response to induce pain, fever and other symptoms [2].The COX enzymes convert Arachidonic acid to prostaglandins. Prostaglandins are involved in the complex process of inflammation and are also responsible for the sensation of pain. Inhibition of the prostaglandin synthesis shall therefore result in pain relief and reduce the inflammation in inflamed tissue. Inhibitors on both forms have side effects, COX-1 inhibitors especially on the gastro-intestinal tract, and COX-2 on the heart, with fatal cases, which have led to restriction on use and withdrawal from the market of some COX-2 inhibitors. A number of studies have shown that plants possess inhibitory activity against the COX enzymes [3-7]. Such plants may therefore be an option in treatment of pain and inflammatory ailments.

Non-steroidal anti-inflammatory drugs (NSAIDs) are a large, chemically diverse group of drugs that act by inhibiting the activity of COX [8]. This explains both their effectiveness (in the inhibition of COX-2) and their side effects manifest in gastrointestinal bleeding, perforation and renal damage (in the inhibition of COX- 1). Aspirin, indomethacin and ibuprofen have been found to be more potent inhibitors of COX-1 than COX-2 in several model test systems. The relative potencies of aspirin and indomethacin vary slightly between models [9].

Among the most widely used medications for analgesia and inflammation are the non-steroidal anti-inflammatory drugs (NSAIDS) and their worldwide use demonstrated their efficacy in reducing pain and inflammation [10]. The NSAIDs consist of traditional non-selective NSAIDs which inhibit both COX-1 and COX-2 and selective COX-2 inhibitors [46]. Although they are effective at relieving pain and inflammation, both types of NSAIDs are associated with serious adverse events specially when used chronically [11]. The traditional NSAIDs are associated with an increased risk of gastrointestinal ulcers, including gastrointestinal hemorrhage, perforation and obstruction [12]. The selective COX-2 inhibitors have an improved gastrointestinal tolerability profile, however, serious cardiovascular effects emerged from clinical studies in recent years [13]. Thus, many researchers have dedicated their efforts to search for safer drugs as well as natural products with less adverse effects.

For the present study we had selected two medicinal plant families *Fabaceae* and *Alliaceae*, and their Anti-Inflammatory effects.

I.Fabaceae:

Pisum sativum

The green pea or garden pea (*Pisum sativum*) belongs to family "*Fabaceae*". The seed of it is commonly small, spherical in shape (Fig. 1A). Each pod contains several peas. It is an annual plant; the pea weight is between 0.1-0.36gms. In leafy types, leaves consist of one or more pairs of opposite leaflets borne on petioles together with several pairs. Garden pea, has long been important in diet due to its content of fiber, protein, starch, trace elements, and many phytochemical substances [14].

Fig. 1: A)*: Pisum sativum,* B)*: Arachis hypogea,* C)*: Tamarindus indica*

The Anti inflammatory activity was studied in Pea fruits and Roots [15]. This study investigates the preventive effects of two pea (Pisum sativum) seed albumin extracts, either in the presence (pea seed extract [PSE]) or absence (albumin fraction from PSE [AF-PSE]) of soluble polysaccharides, in the dextran sodium sulfate (DSS) induced colitis in mice. PSE and AF-PSE ameliorated DSS-induced damage to mice, their effects being due, at least partially, to the presence of active BBI(Bowman-Birk inhibitor) Utrilla *et al*., 2015 [16].

The methanolic extracts of all three peas (Desi chick pea, Kabuli chick pea and Garden pea) were tested *in vitro* for inhibition of PGE2 synthesis catalyzed by COX-2 using purified human recombinant enzyme, inhibited arachidonic acid (AA) induced platelet aggregation. The best potential to inhibit in vitro COX-2 activity showed garden pea (Pisum sativum) the synthesis of PGE2 reduced by 92% in comparison with untreated control wells [17].

Anti-inflammatory properties of peptides from yellow field pea proteins (Pisum sativum L.) were investigated in LPS/IFN-γ-activated RAW 264.7 NO(−) macrophages [18]. In Legumes family the inedible plant parts have a complex chemical composition, with potential biological activities, which are rich in polyphenols, such as flavonoids, isoflavonoids and phenolic acids. The results obtained from pea show the phenolic, invitro antioxidant and anti-inflammatory activity as bioactive agents of legumes, are used as dietary supplements in pharmaceutical and food industry [19].

2. Arachis hypogaea:

The peanut or groundnut belongs to family *"Fabaceae"*. It is annual herbaceous plant growing 30-50cm tall. The leaves are opposite, pinnate with four leaflets (two opposite pairs, no terminal leaflet) (Fig. 1B). The pea flowers are typical in shape and 2-4cm in size.

Resveratrol one of the chief components in these ground nuts exhibits its anti-inflammatory activity via different pathways that are mostly centered on COX-1 and COX-2. In addition to inhibition of COX-1 and COX-2 expression, through upstream suppression of the activity of NF-kB and I-kB kinase, resveratrol reduced the production of prostaglandin E_2 (PGE_2) and the formation of ROS in Lipopolysaccharide (LPS)-activated microglial cells. Candelario-Jalil *et al., 2005 [20]* reported that this activity of resveratrol is based on the inhibition of the expression of microsomal PGE_2 synthase-1 (mPGES-1) and not COX-2 in rat microglia. MPGES-1 is directly involved in the synthesis of proinflammatory PGE_2.

3. Tamarindus indica

Tamarindus indica belongs to *Fabaceae* and is long lived tree; shrub grows to a height of 12-18 metres. The leaves are arranged in pinnately lobed and are bright green in color (Fig. 1C). It needs dry climate, grows and extends from Africa to Senegal west, Sudan and Ethiopia in east, Mozambique and Madagascar in south, India [21,22].

Every part of *T.indica* plant (root, body, fruit, leaves) not only has rich nutritional value and broad usage area in medicine but also has industrial and economic importance. Tamarind can be the most acidic and sweet fruit according to its growing season. The fruit is an indehiscent pod that is sub cylindrical and slightly curved. Tamarinds fruit mainly from May through June.

The effects of methanolic extract of *Tamarindus indica* seeds on anti -inflammatory activity is studied in vivo using rat as an animal model at the doses of different concentrations utilizing carrageenan induced paw edema in rat. The methanolic extract of Tamarindus exhibited significant anti-inflammatory activities [23].

Aqueous, ethanol and chloroform extracts from *T.indica* were evaluated for anti-inflammatory properties in mice (ear oedema induced by arachidonic acid) and rats (subplantar oedema induced by carrageenan) after topical or i.p. administration respectively. Rimbau *et al.*, showed that the *T.indica* exhibits anti-inflammatory activity [24].

The bark of *T.indica* is used in the treatment of pain traditionally, as it has anti inflammatory activity and this is proved scientifically using suitable animal screening models, by hot plate test and acetic acid induced writhing test at the dose of 50 mg/kg, i.p. Petroleum ether extract showed significant increase in reaction time as compared with other extracts [25].The *T. indica* seeds show the Antiinflammatory activity due to the presence of protein and starch, sulfur amino acids and phenolic antioxidants such as proanthocyanidins and epicatechin [26,27].

Akor *et al.*,[28] conducted, study on acute toxicity, the anti-inflammatory activities of the aqueous extract of *Tamarindus indica* (AQETI) leaves *invivo* studies. The results demonstrate that the AQETI leaves contain some pharmacologically active substances, was moderately toxic and possessed significant anti-inflammatory effect [28].

The anti- inflammatory activity was checked by the methods through Hot plate and AAIWT in carrageenan induced rat paw oedema model, AETIRE at different concentrations (100 & 200mg/kg) caused significant dose dependent inhibition of oedema with maximum inhibition in the Carrageenan induced rat paw oedema by the Aqueous

extract. Therefore the AE of *T. indica* root was more effective in showing analgesic and anti-inflammatory activity when compared to the standard drug in each model[29].

Carrageenan induced rat paw edema model was used to evaluate the anti-inflammatory potential. All the three extracts i.e. aqueous, ethyl acetate and methanolic extract of *Tamarindus indica* seeds at 500 mg/kg showed significant anti-inflammatory activity in the second phase of inflammation. For comparison purpose, we used indomethacin (10 mg/kg) as a reference drug. The results showed that methanolic extract exhibited more promising anti-inflammatory activity compared to aqueous and ethyl acetate extracts [30].

Cotton pellet induced granuloma and carrageenan induced paw edema models in rats were used to study anti-inflammatory activity of *T.indica* seed extract of petroleum ether fraction and ethyl acetate fraction. Analgesic activity was studied in mice using tail immersion and hot plate models. Both petroleum ether fraction and ethyl acetate fraction significantly ($P<0.01$) inhibited carrageenan induced paw edema and granuloma formation in cotton pellet induced granuloma model, and increased latency to flick tail in tail immersion method. The ethyl acetate fraction was found to be more effective than petroleum ether fraction [31].

The evaluation of the in vitro anti - inflammatory activity of methanolic extracts of *T.indica* leaf was done by incubating the extracts at different concentrations with egg albumin in controlled experimental conditions and subjected to determination of absorbance and viscosity. Emifenac, a widely used anti-inflammatory drug was used as a reference. The results showed a concentration dependent inhibition of protein (albumin) denaturation by *T. indica* extracts, expressed a higher activity [32].

The methanolic extract of *Tamarindus indica* (TI) seeds were studied on anti-inflammatory activity in vivo using rat as an animal model at the different doses. The activities were tested by using carrageenan induced paw edema in rat. These results showed that the methanolic extract of *Tamarindus indica* (TI) seed exhibited significant anti-inflammatory activities [33].

II. *Amaryllidaceae or Alliaceae:*

In the family *Amaryllidaceae*, Plants of the genus *Allium* are known for their production of organosulfur compounds, which possess interesting biological and pharmacological properties. When extracted and isolated, these compounds exhibit a broad spectrum of beneficial effects against microbial infections as well as cardioprotective, anticancerigenic, and anti-inflammatory activity [34].

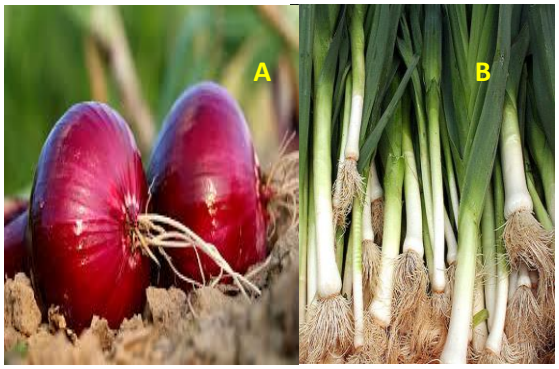

Fig. 2: A): *Allium cepa,* B): *Allium ampeloprasum*

The *Allium cepa* belongs to "*Alliaceae*" It is a biennial garden plant, having a scape, which appears 2 - 4 feet high, being naked, smooth, straight, stout, swollen at the base, and fistulous, bearing at the top a round umbel of greenish-white flowers (Fig. 2A). The leaves are round and fistulous, of a shining green color, acute, and shorter than the stem. Edible parts are Flowers, Leaves, Root, and Seed.

Common names in India and World: Tamil : Chinna vengayam or Sambar vengayam; English : Small onion, Shallots, Multiplier onion; Telugu: Ullipaya, Yerra gaddalu; Hindi:Pyaz Marathi, Marwari and Punjabi : Kanda or Gandana or Pyaaz ; Malayalam : Cheriya ulli or Chuvanna ulli, Bengali : Gundhun; Kashmiri : Praan; Nepali : Chyapi; French : Echalote, oignon patate, Cambodia : Khtum krahaam; Laos : Hoom bwàx; Thailand : Hom, hom-daeng, hom-lek ; Vietnam : Hanh ta, hanh tam, hanh nen [35].

Onion bulbs consist of water, carbohydrate, fibre, protein, fat, vitamins (C, E) and minerals. This plant is a rich source of several phytonutrients with interesting pharmacological properties such as thiosulphinate, volatile sulfur compounds and more polar compounds of phenolic or steroidal origin like flavonoids [36]. Onion shows anti-inflammatory activity, because of the presence of flavanoid quercetin [37]. Ajoene is a natural product isolated from Allium shows anti-inflammatory properties [38]. Fistular onion stalk extract useful for the attenuation of atherosclerosis and the mechanism includes the regulation of the local inflammatory response [39].

The active anti-inflammatory constituents of onion are the flavonoids (quercetin and kaempferol). The flavonoids act as anti-inflammatory agents because they inhibit the action of protein kinase, phospholipase A2, cyclooxygenase, and lipoxygenase, as well as the release of mediators of inflammation (e.g. histamine) from leukocytes [40]. The turmeric and onion mixture is used as home remedy for acute inflammation. The antiinflammatory effect of this mixture was evaluated on acute inflammatory condition induced by 12-O-tetradecanoyl-phorbol-13-Acetate (TPA) in mouse ear. The changes in ear redness, edema, production of pro-inflammatory cytokines (TNF-α, IL-1β, IL-6 and IFN-γ), anti-inflammatory cytokine (IL-10), lipid peroxidation assay and nitric oxide assay were evaluated as indicators of acute inflammation. The results suggest that turmeric and onion extract mixture is topically effective anti-inflammatory agent useful to treat the acute skin inflammatory conditions [41].

The possible anti-inflammatory effects of fresh onion juice in experimental Sprague-Dawley rats were done by the methods Hot plate and formalin tests. The anti-inflammatory effect of fresh onion juice was assessed by applying carrageenan sub plantar injection to Sprague-Dawley rats. In inflammation assessment, fresh onion juice was able to decrease the hind paw thickness significantly in comparison with control group. It can be concluded that fresh juice of onion is capable of inhibiting inflammation [42]. The antiinflammatory activity of silver nanoparticles of *Allium cepa* were tested and confirmed against human blood cells. The leaf of Allium cepa has good antiinflammatory activity. It has reduced the inflammation [43].

Allium ampeloprasum:

Allium ampeloprasum is the member of *Alliaceae* and the genus *Allium*. It is wild and commonly known as wild leek or Broad leaf wild leek (Fig. 2B). It is distributed from Southern Europe to Western Asia, and cultivated in many parts and become naturalized in many countries. This *A.ampeloprasum* is bulbous perennial plant, one of the daily edible green vegetables for Brazilian people. It is widely cultivated and used as food in Brazil. This plant is used, not only as food, but also as medicine. The bulbs have been reputedly used in the traditional Brazilian medicine for treating inflammatory symptoms [44].

The new steroidal saponin was isolated from the bulbs of *Allium ampeloprasum* by the spectroscopic analyses and comparison of known compounds, its structure was established as (3β,5α,6β,25R)-6-[(β-d-glucopyranosyl)oxy]-spirostan-3-yl O-β-d-glucopyranosyl-(1→2)-O-[β-D-glucopyranosyl-(1→3)]-β-d-galactopyranoside. The study indicated that the steroidal saponin showed in vitro assays and in vivo models and demonstrated anti inflammatory activity [44].

CONCLUSION:

In the past few decades there has been an exponential growth in the field of herbal medicine and is gaining popularity both among the globally developing and developed countries. These plants show the pharmacological potency and have low or no side effects for use in preventive medicine and the health care. They represent a potential source of new compounds with different pharmacological activity. The therapeutic potential of these *families* has some reported activities, like they inhibit invasion of carcinoma, provide cardiovascular protection, lower cholesterol and blood pressure, anti-platelet activities, and thromboxane formation etc. They have numerous chemical values and are rich in phytochemicals. Several researchers have provided a mechanism of action for many of their therapeutic effects in this area. The above study gives the knowledge of plants having the anti-inflammatory activity and help to improve future experimental and clinical research plans on plant and animal models.

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