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Anuradha Tamrakar
Department of Biosciences, Barkatullah University Bhopal, Madhya Pradesh, India

Rajendra Singh
Department of Biosciences, Barkatullah University Bhopal, Madhya Pradesh, India

Kapil Kumar Soni
Department of Biosciences, Barkatullah University Bhopal, Madhya Pradesh, India

Corresponding Author:
Kapil Kumar Soni
Department of Biosciences, Barkatullah University Bhopal, Madhya Pradesh, India

A review on anti-inflammatory agents of plant origin

Anuradha Tamrakar, Rajendra Singh and Kapil Kumar Soni

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Abstract
In Traditional System of Medicine (TSM) several edible plants are used for the management of inflammation. Inflammation is one of the immune response processes of the body which shows four types of indications: redness, pain, burning and swelling. Plant possess the ability for synthesizing a number of phytochemicals to defend themselves that are known as secondary metabolites that can be uses for the treatment of inflammation in the body. Medicines used for anti-inflammatory activity are steroidal and non-steroidal in allopathic system of medicines (ASM) which are available in the market frequently used by the patients However; it causes several side effects including blood clotting and increasing risk of heart-attacks. Hence, herbal medicines are safe as compared to allopathic medicines and considered as herbal products. Therefore, there is a need to conduct clinical trials based on the findings of pioneer workers who have compiled the data for the treatment of inflammation using phytochemicals of plant origin by applying advanced techniques and scientific approaches.

Keywords: NSAIDs, inflammation, anti-inflammatory, medicinal plants, phytochemicals, herbal medicines

Introduction
Inflammation is the indicator of immune responses of our body caused due to attacks of foreign particles/antigens and/or allergens and sometimes due to the injury of the tissues of the body. allergy caused due to allergens, cardiovascular disorders, autoimmune disorders and sometimes cancer is the main cause of uncontrolled inflammation in the body that impose a huge amount of economic loss on individuals and on the society, respectively. However, inflammation is a protective and a normal immune response, just giving the information to the body about tissue injury that may be caused by trauma hazards chemicals and/or some of the infectious agents including bacteria, virus, fungi, protozoans and so on. When infectious agents attack on the body it shows acute type of immune responses of inflammation including red spots, swelling, burning and severe pain and itching. In acute inflammation vascular permeability leucocytes emigration and capillary infiltration increases, while in chronic inflammation infiltration of neutrophils, monocytes, macrophages and variety of specialized mononuclear immunocytes including peripheral mononuclear cell (PBMS), lymphocytes including T-cell, B-cell, natural killer (NK) cells and activation of fibroblast endogenesis and fibrosis occur. Moreover, inflammation plays a key indicator role in a number of diseases including asthma, diabetes, arthritis, atherosclerosis, cardiovascular disease, cancer, osteroporosis and parkinson's disease. Menichini *et al.* (2009) [30] have reported biological activity of *Capsicum chinense* plants and isolated some of the phytochemicals. Mueller *et al.* (2010) [34] have reported anti-inflammatory activity of extract isolated from fruits, herbs and spices. Vane and Botting (1987) [55] have shown mechanism of action of anti-inflammatory medicine for controlling the inflammation in the body. However, these medicines are made up of steroids, non-steroids, immunosuppressant agents. Moreover, such type of medications is associated with several harmful chronic effects. If we are using more frequently, while medical practitioner uses these medications by applying minimum effective dose with highest efficacy (potency) and least side effect to the patients. Therefore, Bagad *et al*. (2013) [3] have reported anti-inflammatory activity of *Curcuma longa* Ghasemian *et al*. (2016) [15] have reboot the anti-inflammatory herbal medicines and their pharmacology responses against inflammation. Valsaraj *et al.* (1997) [54] have also reported medicine plant of India for antimicrobial activities.

Mahesh and Sathish (2008) [28] have described efforts of World Health Organization for identification of number of medicinal plants which are being used by the peoples for the treatment of aliments and also listed around approximately 20,000 species of the medicinal plant and their parts are used as a crude material. Panda *et al*. (2009) [36] have also reported number of plants and their parts which are being used by the tribal peoples as herbal medicines for the treatment of chronic and acute inflammatory diseases. In the present review, the efforts have been made just to identify some of the well known locally available medicinally plant which are being used traditionally for anti-inflammatory diseases.

Materials and Methods

The present review is written on the findings of colonist workers on anti-inflammatory agents of plant origin and literature collected from Google Search Machine using database *viz*. Web of Science, Science Direct, Pub-Med and Natural Product Alerts (NAPRALERT). Anti-inflammatory agent are principally secondary metabolites *viz*. flavonoids, alkaloids, terpenoids, saponins, tannins, tri-terpenoids, resins which are derived from medicinal plants and their useful parts *viz*. flowers, leaves, stems, roots, fruits, latex and are isolated from plants using phytochemical analysis (Harborne, 1980 and Handa, 1992) [18, 17] *viz*. Soxhlation, and cold percolation. Secondary metabolites present in the extract of the plant are separated using separation and purification Techniques *viz*. Chromatography including Thin Layer and Partition and Column. For the identification, interpretation and structural elucidation of the bio-active principle present in the purified fraction of the extract spectral analysis technique *viz*. UV, IR, 1HNMR, 13CNMR, Mass Chem-Draw and Chem-Sketch Software were used.

Anti-inflammatory agents of plant origin

Durmowicz and Stenmak (1999) [13] have reported the mechanisms of structural remodelling in chronic pulmonary and hypertension and described that un-like allopathic medicines that contain single bio-active compound targeted for one of the specific pathway, simultaneously, herbal medicines also work. In this context a medicinal plant possess number of active principles that act synergistically on targeted biochemical pathway. Therefore, natural products based ayurvedic medicines are becoming popular as compared to allopathic modern medicines due to its efficacy and no side effects. Dasilva (1999) [10] has reviewed that number of physicians are using medicinal plants in Ayurvedic System of Medicines (ASM) for preventive, promotional and curative applications.

Burke *et al*. (2005) [7] have reported that there are four types of inflammatory indicators *viz*. reddishness, pain, burning and swelling. If the part of the body injured, the blood vessels of the surrounding tissue are dilated and circulation of the blood increases in that area that's why, it causes reddishness.

Tiwari (2008) [50] has described that India is one of the largest developing countries in storing house of ethno-medicinal plants and maintaining their position in the production of crude material directly obtained from plants and indirectly by isolating, separating and purifying biologically active principles from the plants for the formulation of medicines and cosmetics. Similarly, Arif *et al.* (2009) [1] have also reported that now-a-days ethno-medicinal plants have also been a very good source of number of biologically active principles for the treatments of various ailments and are being used frequently for developing potent therapeutic agents.

Pilotto *et al.* (2010) [37] have described principally two types of inflammation *viz*. acute and chronic. Acute inflammation gives responses initially in the body for harmful stimulus while chronic inflammation gives responses slowly in the body. Cyclooxygenase (COX) is one of the well enzyme that plays a key role in all types of inflammatory responses in the body and helps in synthesizing prostaglandins, prostacyclins and thromboxane's, respectively and are involved in platelet aggregation, causing pain and inflammation in the body.

Li *et al*. (2014) [26] have reported that inflammation and stress have been proved to be a critical condition in the pathophysiology of diabetes mellitus. Therefore, for controlling inflammation and stress in the type-2 diabetes have reported anti-inflammatory and anti-stress activities of Berberine (BBR) compound obtained from plants *Coptis chinensis* and *Hydrastis canadensis*.

Soni *et al*. (2014) [48] have isolated a compound quercetin in the ethyl acetate purified fraction of the *Bacopa monnieri* (L.) extracts and have reported the down regulation of mRNA expression in HL-60 cells and also have reported suppression of inflammation in ovalbumin sensitized model of BALB/c mice.

Verma (2016) [56] has described that inflammation is the severe immune response of the living tissues in the body for any type of injury. Ghasemian *et al.* (2016) [15] have reviewed anti-inflammatory activities of some herbs including *Curcuma longa, Zingiber officinalis, Rosamarinus officinalis, Borago officinalis* as complementary medicines that is being used frequently in the treatment of rheumatism, diabetes, and cardio-vascular disorders.

A medicinal plant *Emblica officinalis*, popularly known as Aonla is being used extensively as pickle or dried piece of fruit named "Urgatti" by the peoples for controlling inflammation and stress in the body and is a rich source of Vitamin-C as reported by Tarwadi and Agte (2007) [49]. Dharmananda (2003) [11] and Bhattacharya *et al.* (1999) [5] have isolated compounds Ellagitannins including, Emblicanin A and B, Punigluconin from the plants *Emblica officinalis*. Rehman *et al*. (2007) [39] have also isolated polypheolic compounds *viz*. Phyllanemblinin and Punicafolin and flavonoidal compound *viz*. kaempferol, ellagic acid, gallic acid from *Emblica officinalis*. Asmawi *et al.* (1993) [2] have also reported anti-inflammatory activities of hydroalcoholic extract of *Emblica officinalis* plant leaves.

Leong (2016) [25] has reported that a medicinal plant *Hibiscus rosa-sinensis* of family Malvaceae that is popularly known as "Rose Mallow" and is cultivated in Japan and China and is native flower of Malaysia. Burkil (1993) [8] has reported that the flowers, leaves and roots of *Hibiscus* plant possess medicinal properties and are being used traditionally in Malaysia. Infusion of *Hibiscus rosa-sinensis* flowers is used as expectorant for the treatment of bronchitis. decoction of the root was offered to provide relief from venereal disease, fever and sore eyes. Extract of *Hibiscus rosa-sinensis* leaves isused for the treatment of boils, sores and poultice of its leaves is used to reduce swelling and headaches. According to a report of Salem *et al.* (2014) [42] a wide variety of compounds is found in leaves, flowers and roots of the plant *Hibiscus rosa sinensis* in the form of secondary metabolites *viz*. saponin, tannins, flavonoids, glycosides, terpenoids and so on. Tomar *et al*. (2010) [51] have described that *Hibiscus rosa sinensis* leaves methanolic extract's oral doses (250 and 500mg/kg body weight) reduce inflammation in carrageenan and dextran

induced paw oedema model of Wistar albino rats *Rattus norvegicus*.

A medicinal plant *Cassia fistula* of family Fabaceae that is popularly known as "Golden Shower or Amaltas Falli" is also used in herbal medicine for the treatment of various ailments. Its pulp from ripe pods, leaves, bark, roots and seeds are used for medicinal purposes therefore, it is known as Aarogyavedha in *Ayurveda*. Krishnamurthy (1993) [23] has reported that the bark of the plant *Cassia fistula* is extensively used to isolate tannin. Pole and Sebastian (2012) [38] both have described that the pulp of ripe pods of *Cassia fistula* is purgative and contain number of secondary metabolites which are used in the treatment of inflammation. However, Illavarasan *et al*. (2005) [19] have confirmed that flavonoids are responsible for reducing inflammation in the body.

Montserrat *et al.* (2014) [32] described *Oenothera biennis*, commonly known as evening primrose, a member of the Onagraceae family, as a medicinal plant native to Central America. Montserrat *et al.* (2012) [33] also reported that linoleic acid, linear aliphatic alcohol and a phenolic compound are the active components of evening primrose oil with proven protective roles against pro-inflammatory markers. Montserrat *et al.* (2014) [32] again reported that *Oenothera biennis* oil contains beta-sitosterol and Campesterol which have been shown to inhibit the modulatory effects of nitric oxide, TNF-α, IL-1β and thromboxane B2, leading to suppression of COX-2 gene expression; for these reasons, primrose oil containing hemp seed oil has a greater anti-inflammatory effect than borage oil. Rezapour-Firouzi *et al.* (2013) [40] tested the efficacy of evening primrose oil with hemp seed, which was clinically evaluated in patients with multiple sclerosis (MS). MS patients with chronic inflammatory disease were randomized to hemp seed/evening oil and placebo and found a significant reduction in IFN-γ and IL-17 in the treatment group. The rate of recurrence of the disease also decreases in the treatment group. This study showed the immune-modulatory effects of these oils and their components.

Moringa oleifera of family Moringaceae this is regionally referred to as Munga in Hindi language and is local to India grows within side the tropical and sub-tropical areas of the world. It is a powerful treatment for malnutrition. Rockwood, Anderson and Casamatta, (2013) [41] have pronounced that Moringa is wealthy in nutrients thanks to the presence of a range ofvery important phytochemicals found in its leaves, pods and seeds.

Kasolo *et al.* (2010) [21] have mentioned that each a part of *Moringa oleifera* is a storehouse of essential nutrients. The leaves of *Moringa oleifera* are wealthy in minerals like calcium, potassium, zinc, magnesium, iron and copper. Berkovich *et. al.* (2013) [4] have mentioned range of phytochemicals *viz*. tannins, sterols, terpenoids, flavonoids, saponins, anthraquinones, alkaloids and lowering sugar in *Moringa oleifera* and additionally own anti-cancerous dealers like glucosinolates, isothiocyanates, glycoside compound and glycerol-1-9-ocatadecanoate.

Chandrashekar, Thakur and Prasanna (2010) [9] have mentioned that the aqueous and ethanolic extract of the stem bark of *Moringa oleifera* indicates most 27.27 and 30.30% inhibition with vast discount $p<0.01$ and $p<0.05$ with inside the paw oedema quantity at a dose of three hundred mg/kg frame weight, respectively. The percent of paw oedema became observed to be higher with the alcoholic extract than the aqueous extract.

Ricinus communis of own circle of relatives *Euphorbiaceous* this is regionally called 'Castor plant' and nicely called Arandi in Hindi became mentioned with the aid of using Nadkarni (1927) [35]. The plant is an enormous during tropical areas as decorative plants. The castor oil plant is speedy developing suckering perennial shrub and this plant is not un-usual place and pretty wild with inside the jungles in India and it is far cultivated during India, mainly with inside the Madras, Bengal and Bombay presidencies. The castor oil is acquired from the seed of the plant continues to be broadly used historically as a remedy in the course of being pregnant and parturition. The initial phytochemical take a look at of *Ricinus communis* found out the presence of steroids, saponins, alkaloids, flavonoids and glycosides. Ricinus communis confirmed the presence of alkaloids: ricinine (0.55%) and N-de-methyl-ricinine (0.016%). Illavarasan, Mallika and Venkataraman (2006) [20] have mentioned anti-inflammatory and loose radical scavenging properties of the methanolic extract of *Ricinus communis* root extract in Wistar albino rats *Rattus norvegicus* and feature visible that the methanolic extract exhibited vast anti-inflammatory property in carrageenan-prompted hind paw oedema version of albino rats. The methanolic extract additionally indicates vast loose radical scavenging property with the aid of using inhibiting lipid peroxidation in biochemical assay. They have found that the pharmacological property of *Ricinus communis* can be because of the presence of phytochemicals like flavonoids, alkaloids and tannins with inside the plant extract.

Zingiber officinale of own circle of relatives Zingiberaceae, this is generally called "Adrak" in Hindi language in India is a local plant from Southeast Asia as said through Mahluji *et al.* (2013) [29]. Han *et al*. (2013) [16] have reviewed that Ginger is fed on as a spice and is a famous natural medicinal drug for a long term because of its anti-inflammatory belongings and is being very generally through the peoples in tea as infusion and for reinforcing the flavour of the tea. Most of the peoples make use of Ginger as "Saunth powder" made from Adrak soaked with lime. It is wealthy in diverse chemical constituents, such as phenolic compounds, terpenes, polysaccharides, lipids, natural acid and uncooked fibres. The fitness blessings of ginger are especially attributed to its phenolic compounds, along with Gingerols and Shogaols. Ginger possesses quantity of organic properties *viz*. anti-oxidant, anti-inflammatory, anti-microbial, anticancer, neuro-defensive cardiovascular defensive, breathing defensive, anti-obesity, anti-diabetic, anti-nausea and anti-emetic sports. Ueda, Ippoushi and Takeuchi (2010) [52] have said that once extract of *Zingiber officinale* administered orally, it indicates specific and inconsistent effects, relying on the amount of intake. Moreover, management of squeezed ginger extract to mice one time or two times has expanded the tumour necrosis factor-α (TNF-α) in peritoneal cells and long-time period intake of the extract has accelerated the serum corticosterone stage and has decreased pro-inflammatory markers.

Mahluji *et al.* (2013) [29] have additionally examined efficacy of *Zingiber officinale* with low-grade infection in type-2 diabetic sufferers after two months of remedy and feature visible that serum stage of TNF-α and high-sensitivity C-reactive protein (hs-CRP) had been reduced significantly. Drozdov *et al.* (2012) have said that during sufferers affected by osteoarthritis, Ginger own efficacy in reduction of pain with no side effects. Shimoda *et al.* (2010) [43] investigated an anti-inflammatory impact of *Zingiber officinale*

and organized 40% ethanolic extract from dried purple ginger and evaluated its anti-inflammatory properties in the acute and persistent infectious model of rats. The end result possessed discovered an amazing suppressive impact on acute and persistent infection, and inhibition of macrophage activation appears to be worried on this anti-inflammatory impact.

Soni *et al.* (2017) [47] have said that a purified fraction of *Ocimumtenuiflorum* (L.) inhibits enzymes *viz.* Leukotrienes C-4 Synthase, Leukotriene A-4 Hydrolase, Cyclo-Oxygenase-2 and down regulates mRNA expression in HL-60 cells and decreases lung infection in ova brought about bronchial allergies version in BALB/c mice. They have located that a purified fraction PM-OT suggests full-size anti-inflammatory activities each in-vitro model of HL-60 cells and in-vivo model of BALB/c mice which supported its conventional use with inside the remedy of inflammatory lung disorder and bronchial allergies. Finally, they have got observed that PM-OT inhibits LTC_4-synthase 52%, LTA4-hydrolase 25% and COX-2 99%, respectively. *Boswellia serrata* is a tree usually regarded as "Luban or Salai Guggul or "*Indian Olibanum*" and is local to India, Africa and the Arabian Peninsula. It is usually used withinside the Indian Traditional System of Medicine. *Boswellia serrata* includes chemical compounds that could lower swelling and boom the body's immune response. Extract of *Boswellia serrata's* bark and different components were taken through mouth for the healing purposes. In this context, Kimmatkar *et al.* (2003) [22] have pronounced that the efficacy of *Boswellia serrata* extract in sufferers with osteoarthritis has been substantiated; dramatic remedy with inside the frequency of joint swelling and ache and augmentation in joint flexibility and on moving distance were located on the cease of remedy period.

Etzel (1996) [14] has additionally defined that likewise, a complete reduction in erythrocyte sedimentation rate (ESR), morning stiffness, and NSAID management requirement throughout remedy has passed off in rheumatoid arthritis sufferers inside any other scientific trial. In one of the pilot examine done through Soeken, Miller and Ernst, (2003) [45] on sufferers with persistent poly-arthritis, no full-size lower has been located in patient's manifestations after 12 weeks of remedy with extract of *Boswellia serrata*; simply minor attenuation in NSAIDs requirement has been recorded.

Madisch *et al.* (2008) [27] have pronounced that collagenous colitis is an inflammatory bowel disorder (IBD) and *Boswellia serrata* medicinal plant has been clinically powerful with inside the method of ameliorating this disorder in goal remedy organization in comparison to the placebo organization. Laloo and Hemlatha (2011) [24] have defined that medicinal flora are one of the maximum vital re-assets of medicines. Since, historic instances medicinal flora were used to deal with special illnesses because of their accessibility, availability, inherited practice, monetary feasibility and perceived efficacy.

Soni *et al.* (2021) [46] have pronounced anti-inflammatory properties of the purified fraction of the *Boswellia serrata* for suppressing LTA-four, LTC-four, COX-2 and mRNA expression in HL-60 Cells and for decreasing lung infection in sensitized BALB/c Mice model. They have proven that a purified fraction of *Boswellia serrata* ethanolic extract reduces LTC-four synthase 52%, LTA-four 22% and COX-2 99% with an inhibitory concentration (50%) of 12.5(g/ml in HL-60 cells. They have additionally achieved the bioassay experiments on BALB/c mice model and feature observed that intra-gastric management of the purified fraction of *Boswellia serrata* with 50mg and 100mg in line with kg body weight doses with 2to 3% HPMC reduces 51% (P-Value <0.01%) lung irritation in ovalbumin brought about inflammatory version of BALB/c as determined in lung photographs obtained through In-Vivo Imaging Tomography.

Bhardwaj *et al.* (2020) [6] have reviewed leukotriene antagonistic agents of plant origin and have described the role of secondary metabolites as leukotriene antagonistic agents that may be beneficial for the remedy of inflammatory illnesses such as asthma, allergic reaction, arthritis, rhinitis and so on. Similarly, Meshram *et al.* (2020) [31] have reviewed the function of leukotriene inhibitors of plant origin with inside the control of continual inflammatory illnesses. They have highlighted latest updates at the pharmacology and patents on leukotriene adverse herbal merchandise with inside the control of irritation withinside the respiration illnesses. They have additionally stated that precise leukotriene antagonist's *viz.* Zileuton, Montelukast, Pranlukast and Zafirlukast to be had within side the drug marketplace as allopathic drugs inflicting numerous facet results. Therefore, they have got reviewed and stated range of patents associated with the conventional natural medication which can be primarily based totally at the bio-lively compounds with much less facet results and effective, most secure and preventive drugs for anti-inflammatory sports.

Very recently, Usmani *et al.* (2023) [53] have concluded that in Ayurveda, medicinal plants are used as a remedy for a number of ailments and explained the phytochemical mechanism of action of medicines on targeted organs simply to get the attention of the pharmaceutical industries for making anti-asthmatic natural drugs on low fee with much less facet results to deliver it in to the communities. Singh (2023) [44] has additionally written a review on phytopharmacology for the control of allergic reaction and irritation and have described that number of peoples is suffering from inflammatory disorders and the usage of conventional drug treatments for the control of allergic reaction and irritation.

Conclusion

Plants are one of the major sources of natural medicines. Since, historic times medicinal plants are being used for the treatment of number of ailments because of their conventional knowledge, accessibility, availability, inherited practice, financial feasibility and excellent efficacy. Moreover, a vast majority of tribal peoples is very far from the availability of allopathic medicines and hospitals. Therefore, they are dependent on traditional medicines advised by the Vaidhya, Hakim and tribal practitioners. However because of the numerous aspect outcomes of allopathic drug treatments, phytochemicals which might be essentially secondary metabolites and are bio-lively compounds might also additionally play an critical role with inside the control of irritation with much less aspect outcomes, desirable efficacy and much less steeply-priced natural drug treatments. Thus, the purified fraction of extracts of the plants *Tinospora cordifolia* and *Boerhavia diffusa* can be very beneficial for anti-inflammatory properties.

Future perspective

This review manuscript will assist to the researchers to carry out greater studies on the medicinal plants. Herbal medication

can be one of the best complementary and alternatives of allopathic medication. There are many researches that have been conducted on the medicinal plants for the treatment of number of ailments and there is a need to explore scientific validation of such type of research by conducting clinical trials.

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