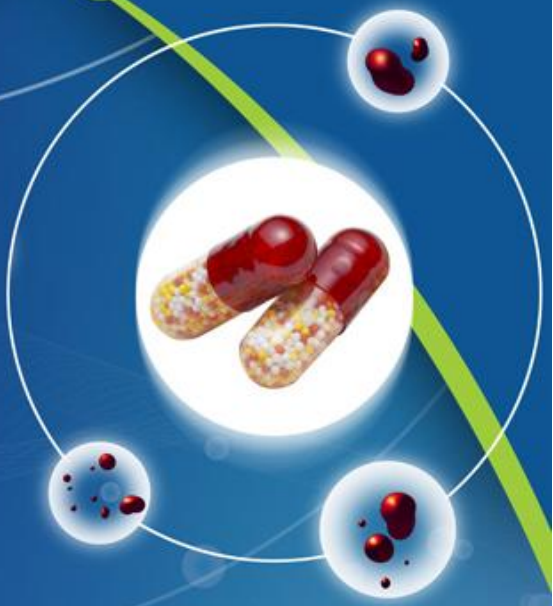
ISSN : 2320 4850

BI MONTHLY

Asian Journal of Pharmaceutical Research And Development

(An International Peer Reviewed Journal of Pharmaceutical Research and Development)



AJPRD

Volume - 02 Issue - 03 MAY-JUN 2014

website: www.ajprd.com
editor@ajprd.com

Asian Journal of Pharmaceutical Research and Development
(An International Peer-Reviewed Journal of Pharmaceutical Research and Development)
www.ajprd.com
ISSN 2320-4850

Review Article

A REVIEW ON ANTI-INFLAMMATORY AND ANALGESIC ACTIVITY OF HERBAL ORIGIN

Sai Kiran A Dara*, Sateesh Belamkar

Department of Quality Assurance, SVKM's NMIMS, School of Pharmacy and Technology, **Shirpur-425405 Maharashtra, India.**

***Received:* March 2014** ***Revised and Accepted:* June 2014**

ABSTRACT

Plants and their products have been used for health and medical purposes form the very ancient times. Most of the world's population in the developing countries still depends on herbal medicines and products to meet its health demands and needs. Herbal medicines are generally used to provide first-line and basic health care, to the people of remote areas and people of poor regions. People having accesses to modern medicines still rely on herbal medicine mostly and such use is being increasingly in the recent years. Medicinal plants are important sources for pharmaceutical development and manufacturing. Medicinal plants and herbal medicines cater significant percentage of the pharmaceutical market. This review article focuses on the need of development of medicines from herbal origin concentrating on the development of more anti-inflammatory and analgesics agents. The products from herbal origin cause negligible of no side effects leading to the betterment of the quality of life of people.

Kew Words: *Analgesic, Anti-inflammatory, Herbal Medicines, Pain, Pharmaceutical Market.*

INTRODUCTION

Herbal medication still forms one of the major part of healthcare system even today. Products from herbal origin seem to have lesser side effects compared to the chemical system of medicine like allopathic system. Inflammation is a normal, protective response to tissue injury caused due to injury or insult to the body[1]. It is a well-accepted fact that pain, whether acute or chronic, peripheral or central, starts from inflammation and the inflammatory response[2].The evaluation of herbal drugs is primarily based upon phytochemical, pharmacological like approaches including various instrumental techniques such as microscopy, extraction, chromatography and others. Drugs which are most commonly being used for the management of inflammation and pain are non-steroidal anti-inflammatory drugs (NSAIDS) or corticosteroids. These drugs generally possess more or less side effects which may be toxic like hypersensitivity, renal failure, haemorrhage, liver dysfunction etc.[3] Comparatively many medicinal plants have been used for ages with almost negligible to no side effects. It therefore becomes essential to explore the plant kingdom to develop more effective herbal products with lesser or no side effects. Plant kingdom is a vast natural resource and can serve as a source of various useful compounds which may lead to the development to novel drugs[4].

The research on plants with ethno-medical value can lead to exploration of new areas.

*Corresponding author.
Sai Kiran Dara
SVKM's NMIMS,
School of Pharmacy and Technology Management,
Near Bank of Tapi River, Agra-Mumbai Road
Babulde, Shirpur- 425405, Dist. **Dhule, Maharashtra**
India, *Tel.: +91-9004066078
E-mail address: darasaikiran@gmail.com

Anti-inflammatory and analgesic agents are a specific area of research. Isolation and purification of certain plant constituents play a major role in developing various herbal formations. Purified natural constituents of plants can serve as templates for the new generation of medicinally important products. This review article focuses on inflammation and pain along with the review of herbals Plumbago zyelanicum and Mentha piperita for aforesaid activities.

Inflamation

The word "inflammation", derived from the Latin word "inflammare", (to set on fire). It involves a cascade of biological process involving several chemical mediators which are secreted by vascular tissue of the body, when it comes in contact with the harmful stimuli like irritants, pathogens etc. It is a protective feedback mechanism that helps in healing of tissues. Sometimes, inflammation leads to events that are quite serious such as occurrence of rheumatoid arthritis, hay fever which may be life threatening[5].

The anti-inflammatory properties of several phyto-constituents origin, containing substances like flavonoids and their derivatives, phytoestrogens, phytosterol, ascorbic acid, tocopherol curcumin etc. can inhibit the molecular targets of pro-inflammatory mediators in inflammatory responses[6].

In brief, inflammations are generally of two types' acute inflammation and chronic inflammation. Inflammatory reactions involve different mechanisms and occur in different phase like acute phase involving temporary local vasodilation with increased capillary permeability, delayed, sub-acute phase which causes infiltration of leukocytes and phagocytic cells and chronic proliferative phase involving tissue damage and fibrosis[7]. Acute inflammation is spontaneous response of the body to risk factors like insult or injury of any type. This is non-specific, first line of defence of the body against danger[8]. The major characteristics of acute inflammation include accumulation of fluid and plasma at the site of infection, activation of platelets and polymorpho-nuclear neutrophils causing inflammation[9].

When the inflammation triggering factors are not decreased or eliminated, acute inflammation leads to chronic inflammation. Chronic inflammation occurs for a longer a longer period of time and is characterised with the presence of macrophages, lymphocytes, tissue damage and necrosis. The macrophages produce a large number of bio-active products which ultimately causes tissue damage and fibrosis which is the characteristic feature of chronic inflammation [10, 11].

There are vast number of inflammatory conditions which trigger various human diseases. Few of them are allergy in which inflammatory cytokines cause autoimmune reactions along with inflammation, gastritis is due to alcohol abuse, Helicobacter pylori infection and gastric acid reflux causes inflammation in mucous membrane of stomach, asthma a respiratory disorder due to allergy leading to smooth muscle hyperplasia, excess mucus secretion and inflammation, Colitis is due to bacterial infections, ulcer formation ultimately inflammation in colon, leprosy is a chronic disorder caused by *Mycobacterium leprae* characterized by formation of inflammatory rashes and nodules on the body surface, tuberculosis is also a common infection of lungs caused by *Mycobacterium tuberculosis* characterized by fever, cough, inflammation, difficulty in breathing etc. Other inflammatory conditions include pneumonia, oesophagitis, pancreatitis, thyroiditis, arthritis etc. to name few [12,13,14,15].

Pain

Pain is an unpleasant sensory and emotional experience in response to tissue damage, threat of tissue damage or perceived tissue damage. Experience and interpretation of pain is subjective and influenced by previous experience and an individual's physical and mental condition at the time. These nociceptors are sensitive to the effects of potentially damaging mechanical, thermal and chemical stimuli. When cells are damaged they release a variety of chemical mediators, which can activate or sensitize nociceptors to other chemicals. This explains acute pain.

Chronic pain is more difficult to explain, especially if it goes on beyond the initial tissue damage. Chronic pain is thought to be associated with changes to the normal physiological pain pathway[16].

The pain reaction is transmitted over the reflex arc by sensory fibers in the dorsal horn of the spinal cord and by synapsing motor neurons in the anterior horn. Due to harmful stimulus anatomic pattern of sensory and motor neurons move quickly, nerve impulses alerting the individual to move away from such stimuli are simultaneously sent along efferent nerve fibers from the brain. Bradykinin, histamine, prostaglandins are major mediators of pain. Various kinds of pain include[17, 18, 19, 20].

Somatic pain: It is caused by the activation of pain receptors of the external body and the skeletal system, due to a number of factors like inflammation, trauma, excessive work, vigorous movements etc. Visceral pain: There is damage to the internal organs and is most general type of pain, results by the activation of pain receptors in the below the cervical area, abdominal regions and pelvic areas.

Somatic and visceral pain can together be classified under nociceptive pain.

Neuropathic pain: It is associated with damage and malfunction of the spinal cord resulting in stinging, shooting, tingling and pricking like sensations.

Psychogenic pain: Pain due to psychological problems is labelled as psychogenic pain. Patients with chronic pain generally have certain degree psychological disturbances. Psychological distress may not be the only triggering factor for pain but may contribute for pain[21].

Pain can be broadly classified as

Acute pain: It results from tissue damage or injury, and usually heals early and the cause of pain will generally be eliminated. It is a short term pain and can easily be identified.

Chronic pain: It is associated with long term pain lasting for more than three months. Its treatment is a great challenge for the physicians as it has the impact on the quality of life.

Nowadays the number of patients that are using herbal remedies and complementary and alternative medicine for treatment of pain is growing rapidly. Over the last 20 years, Americans have sought a more "natural" or "holistic" approach to treatment of medical problems in general and pain in particular[22].

Work done till now

Herbals in the treatment of inflammation and pain have been extensively used and there is still a wide scope in the development in this area as the plant kingdom is vast and it still needs to be discovered. Some of the herbal products used for their activity are given in following table

S. No.	Botanical Nomenclature	Family	Activity*	Active Chemical Constituent	Extract type	Part
1	Plumbago zyelanicum	Plumbaginaceae	Both	Plumbagin, plumbagic acid, flavonoids, beta-sitosterol.	Methanol	Roots 23
2	Mentha piperita	Labiatae	Both	menthol, menthone, 1,8-cineole	Methanol	Leaves 24
3	Amaranthus Viridis (Green amaranth)	Amaranthaceae	A	steroids, alkaloids, glycolsides, flavanoids, phenolic compounds	Methanol	Whole plant 25,27
4	Annona squamosa	Annonaceae	Both	Acetogenines,	Ethanol	Seeds 26

				Cyclopeptides		
5	Commiphora africana	Burseraceae	Both	Flavonoids, tannin, anthraquinone, cardiac glycosides, triterpenoids, saponins, alkaloids	Hydro-Ethanolic	Stem-bark 34
6	Ricinus communis	Euphorbiaceae	I	Steroids, saponins, alkaloids, flavonoids, glycosides.	Methanol, pet ether	Roots, leaves 28, 29
7	Swertia chirata	Gnetaceae	Both	Secoiridoid bitters, alkaloids, xanthones and triterpenoids	Ethanol	Root 30
8	Sesbania sesban (Hadga)	Leguminosae	I	Protein, sterol, saponin, flavonoid, Glycoside	Petroleum ether	Bark 31
9	Emblica officinalis	Euphorbiaceae	I	phenolic compounds	methanol	Leaves and fruit 32
10	Zingiber officinalae	Zingiberaceae	Both	sequiterpene, gingerol and inoleoresin	Ethanol	Rhizome 33

*A= Analgesic; I=Anti- inflammatory; Both= A&I

1. Plumbago zeylanicum

Plumbago zeylanicum is commonly known as 'Chitrak'. It is a perennial and is one of the endangered medicinal plant. The roots of the plant were used traditionally as germicidal, abortifacient i.e., causes miscarriage and in treatment of liver related disorders, pain, inflammation and cancer. It is a potential medicinal plant with multitude uses and hence it is of great interest to evaluate the various activities of the plant and pain and inflammatory activity in particular. It has been characterised as an appetizer, anti-anorexic, anti-haemorrhoidal, pain reliever, anti-inflammatory agent etc. It is available in different ammounts in the herbal formulations like Dabaur Chitrak, Haritaki, Divya Chandraprabhavathi etc.[23, 35]

2. Mentha piperita

Mentha piperita is widely used as a flavouring agent and is commonly known as peppermint, candy mint, pudina etc. It is also used throughout the world for its medicinal value. It is one of the most economical aromatic plant. It has been proven helpful in symptomatic relief of common cold and various digestive and bowel related problems like nausea and

dyspepsia. It has also got very good analgesic and anti-inflammatory properties. Though is proven as medically safe in general but has certain side effects like it is contra indicated in patients with gallbladder diseases and severe liver dysfunction problems. It should be cautiously taken in patients with GI reflux. It may also cause apnoea in infants if inhaled directly[36]. The ayurvedic formulations like Pudin Hara from Dabaur are commercially available.

3. Amaranthus viridis

Amaranthus viridis commonly known as green amaranth. It has been used in traditional system of India to alleviate labour pain and fever. It has a high concentration of antioxidant components along with ant diabetic activity in experimental induced diabetes [16]. It is also used as a cardio protective agent along with anti-inflammatory properties[37].

4. Annona squamosa

Annona squamosa is commonly known as custard apple in English sitaphal in Hindi. It is a small well branched ever green tree is cultivated throughout India for its fruits, various parts of Annona squamosa Linn. Are used for their medicinal value in the treatment of many disorders. Annonaine, an alkaloid is a constituent of leaf and bark. A bark decoction is used to stop diarrhea, while the root is used in the treatment of dysentery. A decoction of the leaves is used as a cold remedy and to clarify urine. Annona squamosa Linn. family Annonaceae, is said to show varied medicinal effects, including insecticide, antiovulatory and abortifacient.The fruits of Annona are Haematinic, cooling, sedative, stimulant, expectorant, maturant, tonic. They are useful in anemia, burning sensation. The seeds are abortifacient and insecticidal and are useful in destroying lice in the hair. Leaves are used to overcome hysteria and fainting spells. Fruit is used in making of ice creams & milk beverages.

5. Combiflora Africana

The common names of *Combiflora africana* include African myrrh, corkwood, poison-grub commiphora in English and angka,gafal in Arabic. Commiphora africana is a small tree, sometimes reaching 10 m but usually not more than 5 m high. The tree is deciduous, coming into leaf at or before the beginning of the wet season, and losing its leaves at the beginning of the dry season. Roots of young plants are juicy with a mildly sweet taste and can be chewed. The gum is also eaten; the bark is brewed to make a red tea. Fruits are chewed or pounded and used against toothache and diseases of the gum[38].

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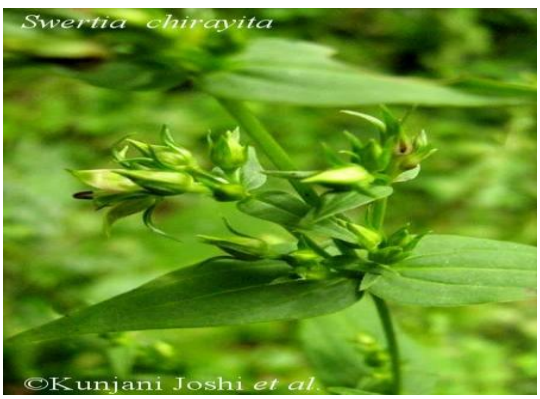
6. Ricinus communis

Ricinus communis, family – Euphorbiaceae, is also known as Castor oil plant in English; in Hindi: arand, erand, andi, rend. Castor oil is widely used as a catharatic, and also for lubrication and illumination. There is extensive applications in industry, particularly in USA. Bulk of the commercial oil is generally processed in a number of ways and then used for different purposes. The treated oil finds use in products like paints, enamels and varnishes, oiled fabrics, linoleum, patent leather, fly-paper, typewriting and printing inks, greases and special lubricants, polishes, waxes, cutting, dielectric and condenser oils, softening agent for gelatin in rayon sizing, nitrocellulose-baking finishes, hydraulic brake fluids, urethane foams and rubber substitutes, cosmetics, pharmaceuticals and insecticidal formulations. Castor oil is a mild and most efficient purgative. The plant is reported to possess antioxidant, anti-implantation, antiinflammatory, antidiabetic, central analgesic, antitumour, larvicidal & adult emergence inhibition, antinociceptive and antiasthmatic activity[39].

7. Swertia chirata

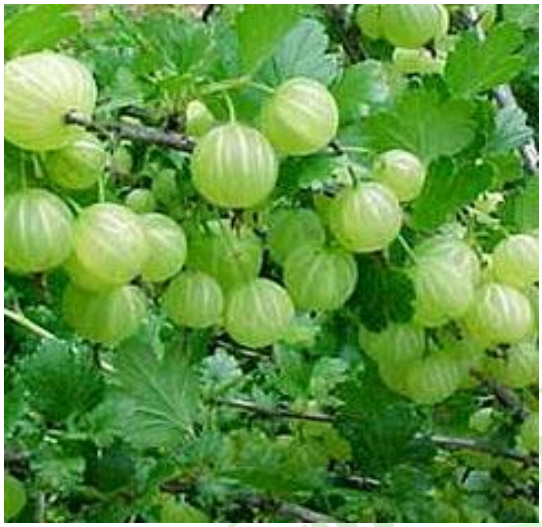


Swertia chirata is a medicinal plant indigenous to temperate Himalaya. Its Indian name is Chirayata. The plant is an erect annual. The drug (chiretta) is obtained from the dried plant.The varios activities repoted of this plant are antihelmintic, antileishmaniak, anticholinergic, anticonvulsant, antiedemic, anti-inflammatory, antimalarial, antipyretic, antitubercular, astringent, CNS depressant, emollient, hepatoprotective, hypnotic, antidiabetic, laxative, tonic and much more. Thus there is still a wide scope for exploring different aspects of S. chirayita. Discrepancies remain about the habit of the plant[30].

8. Sesbania sesban

Sesbania sesban (L.) Merrill is the most productive multipurpose tree widely distributed in tropics and subtropics. The genus Sesbania Scop. (Leguminosae) contains about 50 species, which are widely distributed. The greatest species diversity occurs in Africa. Phytochemical investigations in the seeds led to the isolation of oleanolic acid, stigmastane-5.24(28)-diene- 3β-O-β-D-galactopyranoside and galactomannan. The extracts had a high content of phenols, flavonoids and anthocyanins. Saponin is responsible for the molluscicidal activity of the plant. The leaf extract showed the presence of all these except phenol and fixed oil. The plant shows Anti-inflammatory effect, Antioxidant effect, Anti-microbial effect it is a traditional medicine, it is also has ethnoveterinary use[40].

9. Emblica officinalis



Emblica officinalis (EO) enjoys a hallowed position in Ayurveda- an Indian indigenous system of medicine. It belongs to family Euphorbiaceae. It is also named as Amla, Phyllanthus Emblica or Indian gooseberry. EO primarily contains tannins, alkaloids, phenolic compounds, amino acids and carbohydrates. It has its beneficial role in cancer, diabetis, liver treatment, heart trouble, ulcer, anemia and various other diseases. Similarly, it has application as antioxidant, immunomodulatory, antipyretic, analgesic, cytoprotective, antitussive and gastroprotective. Additionally, it is useful in memory enhancing, ophthalmic disorders and lowering cholesterol level. It is also helpful in neutralizing snake venom and as an antimicrobial. It is often used in the form of Triphla which is an herbal formulation containing fruits of EO, Terminalia chebula and Terminalia belerica in equal proportions. The medicinal activities of E. officinalis include antioxidant activity, immunomodulatory activity, antipyretic activity, analgesic activity, hepatoprotective activity, cytoprotective activity, antitussive activity, gastoprotective activity, antimicrobial activity, anti-inflammatory activity, radioprotective activity, chemopreventive activity, antiatherogenic activity, antitumor activity, apoptotic activity, antiulcer activity, hypolipidemic activity, adaptogenic property, antimutagenic activity, hypocholesterolemic activity etc.[41]

10. Zingiber officinalae

Ginger consists of the fresh or dried roots of *Zingiber officinale*. *Zingiber officinalis* Roscoe, commonly known as ginger belongs to family Zingiberaceae. It is cultivated commercially in India, China, South East Asia, West Indies, Mexico and other parts of the world. It is consumed worldwide as a spice and flavouring agent and is attributed to have many medicinal properties. *Zingiber officinalis* Roscoe, commonly known as ginger belongs to family Zingiberaceae is cultivated commercially in India, China, South East Asia, West Indies, Mexico and other parts of the world. It is consumed worldwide as a spice and flavoring agent and is attributed to have many medicinal properties. Ginger has beneficial effects in osteoarthritis, it has anti-tumour activity. The pungency of ginger is due to gingerol, an oily liquid consisting of homologous phenols. Ginger bears an enormous number of pharmacological activities among those, Neuro-protective activity and activity against colon cancer have facilitated the extent of further research for finding out less toxic and more potent drugs for the better treatment of those diseases.[42]

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