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A Review on Medicinal Plant Extract Used in Analgesic Activity

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ABSTRACT: This review presents updated information gathered on scientifically proved medicinal plants used for Analgesic activity. This study provides the information on plant name, family, and part used, other activity and chemical constituents. There are a large number of studies which supports the Analgesic effects of traditional herbal medicines. The aim of this review is to highlight the work on Analgesic activity of plant origin. The present paper also involves various plant drugs and their bioactive extract involved in Analgesic Mechanism. The use of traditional medicine is expanding to new horizons and plants still remain as the novel source of structurally important compounds that lead to the development of innovative drugs. The traditional Indian system of medicine, the Ayurvedic, mentions the use of plants in the treatment of various diseased conditions. This article may help investigators to identify medicinal plants responsible for Analgesic activity.

Keywords: Medicinal plants, Analgesic Activity, Mechanisms, Physiology.

I. INTRODUCTION:-

An unpleasant sensory and emotional experience associated with actual or potential tissue damage. Pain is a crucial aspect of the body's defense mechanisms & it is a part of a rapid warning relay instruction the motor neurons of the central nervous system (CNS) to minimize physical harm. [1]

Pain can be classified into two types: a) Acute pain b) Chronic pain

- **Acute pain:** Acute pain is the body's warning of present damage to tissue or disease. It is often fast and sharp followed by aching pain. It is short-term pain or pain with easily identifiable causes.
- **Chronic Pain:** Chronic pain is pain that last much longer than pain normally would with a particular injury. Chronic pain can be constant or intermittent and is generally harder to treat than acute pain. Pain can also be grouped by its source and related pain detecting neurons such as coetaneous pain, somatic pain, visceral pain and neuropathic pain.[2]

Causes of pain:

- Pain is caused by the stimulation of pain receptors which are free nerve ending.
- Nocireceptors are pain receptors that are located outside the spinal column in the dorsal root ganglion and are named based upon their appearance at their sensory ends. These sensory endings look like the branches of small bushes.
- The perception of pain is when these receptors are stimulated and they transmit signal to the central nervous system via sensory neurons in the spinal cord.

Sources of Analgesic Drugs: There are various sources of analgesic drugs; they are classified
In following two types: a) Synthetic Drugs b) Natural sources

- **Synthetic Drugs:** There are various synthetic drugs available in market which gives analgesic activity- I) Sike Paracetamol, Ibuprofen, COX-2 inhibitors, NSAIDs, diclofenac etc. II) Analgesics from Natural Sources: There are various medicinal plants available in nature which shows analgesic activity, these are as follow:
- Opioid Analgesics: Opioid are drugs derived from Opium. Opium is derived from the juice of the opium poppy, Papaver somniferous. Opioid are any medication which bind to opioid receptors in the central nervous system & used as analgesic activity. Opioid are used in medicine as strong analgesics, for relief of severe or chronic pain.[3]

These are classified into following types:

- Endogenous opioid peptides (produced in the body: endorphins, dynorphins, encephalin)
- Opium alkaloids (morphine, codeine, the baine)
- Semi-synthetic opioid (heroin, oxycodone, hydrocodone, dihydrocodeine, hydro morphone, oxy-morphone, nico-morphine)

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- Fully synthetic opioid (pethidine or Demerol, methadone, fentanyl, propoxyphene, pentazocine, buprenorphine, butorphanol, tramadol, etc.) [4-5]

Mechanisms of pain: Tissue damage leads to pain. Surgery causes tissue damage and in general, the more the tissue damage, the greater the pain produced. It is important to remember that even in the unconscious patient under general anesthesia, the spinal cord receives a massive barrage of nerve impulses from the surgical site. These impulses are known as 'afferent impulses' as they travel from the peripheral tissues towards the spinal cord. These afferent nerve transmissions are exacerbated when peripheral nerves are cut.

Peripheral sensitization: After tissue damage that may be caused by surgery, inflammation or lack of blood supply (Ischemia), a 'biological soup of molecules' is produced. The ingredients of the soup include substance P, calcitonin gene-related peptide, histamine, hydrogen ions, bradykinin, nitric oxide, inflammatory cells, and platelets. This is perceived as pain by the patient. The soup, spreading locally, causes areas adjacent to the site of tissue damage to become involved. As a result, the nerve fibers become more sensitive (i.e. their pain threshold is lowered) and spontaneous firing of afferent impulses occurs. The total effect on the patient is an expanding area of pain, an increase in pain and greater sensitivity to a light touch that would normally not be painful (called allodynia). The soup produces 'peripheral sensitization.'

Dorsal horn wind-up and central sensitization:- The repeated afferent impulses to the spinal cord, as a result of the sensitizing soup at the site of tissue damage, cause the dorsal horn neurons within the spinal cord to become hyper excitable. This state of hyper excitability is called central sensitization. The whole concept of spinal cord nerve cells undergoing repeated stimulation and activation has been termed 'wind up'. Once established, central sensitization requires high doses of narcotic to suppress it. It should be remembered that the above sequence of events takes place in the patient during general anesthesia while the patient is unconscious and unaware of the 'molecular sensitizing soup' that is cooking in the peripheral tissues at the site of surgery. But once the anesthetic has worn off, the patient begins to feel the consequences of the soup-mix and wind-up and experiences the pain of the surgical procedure.

Controlling Pain in Laboratory Animals:- The pain felt by a laboratory animal, and therefore the appropriate analgesic regime, will depend on the amount of surgical trauma or tissue damage it has undergone as part of the experimental process, as well as on subsequent environmental influences. The degree of trauma per unit body mass has been suggested as a useful measure to determine the analgesic requirements of the patient. A drug with limited analgesic potency may provide sufficient pain control for ovariohysterectomy in the rat, but would be inadequate for the same procedure in a dog, because the procedure is more invasive and causes greater tissue trauma in this species.

The degree of enforced movement may have an effect on the pain animals experience after surgery. Most experimental animals do not enjoy the total post-operative bed-rest afforded to human patients. Caged animals must generally move in order to access food and water. Humans (and presumably animals) can be pain-free at rest, but may experience severe pain upon movement or locomotion. Many readers may be aware of the discomfort and pain experienced by some human patients when nursing staff initiate enforced activity as part of post-operative physiotherapy. In general, animal husbandry practices and rodent cage design do not take this into account. Food and water is frequently placed overhead in the lid of the cage. This requires the animal to stretch up, or in the case of many cages designed for mice, animals have to stand on both hind feet to reach food pellets or water. [6-10]

Classification of Analgesics: Drugs that are included in analgesics work in diverse ways to diminish or relieve pain. They act mainly on the central and peripheral nervous system. Narcotic drugs such as path dine, synthetic drugs such as ketorolac, the non-steroidal anti-inflammatory drugs (NSAIDs) such as the salicylates (aspirin), and a variety of drugs are included in analgesics. However, there are a few exceptions too. For example, tri-cyclic anti-depressants and anticonvulsants are frequently used to treat neuropathic pain syndromes, but these drugs are not considered in analgesics. Based on the narcosis properties of the analgesic drugs, analgesics can be classified into the following groups.

- **Narcotic:** The narcotic analgesics are the agents that cause sleep or loss of consciousness (narcosis) in conjunction with their analgesic effect. In other words, drugs that directly act on central nervous system (CNS) to relieve pain are termed as narcotic analgesics. In addition, the term narcotic becomes associated

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with the addictive properties of opioid and other CNS depressant agents. The opiates and the derivatives of opiates (i.e. opioid) are the most frequently used narcotic analgesics. For this reason, in United States, these analgesics are also known as opioid analgesics (e.g. morphine, codeine, path dine, etc).

- **Non-narcotic analgesics:-** The non-narcotic analgesics act peripherally on the nervous system to reduce pain. Excluding the analgesic effect, the non-narcotic analgesics usually have two other properties (antipyretic and anti-inflammatory effects). Unlike narcotic analgesics, drugs of this class do not cause physical dependencies and narcosis. However, most of the drugs in this class are gastric irritant. For this reason, physicians generally recommend an antacid or anti-ulcerate when prescribing these drugs. Most often, these drugs are used in the management of mild to moderate pain. Usually, they are available as OTC (over the counter) drugs in most drug stores.
- **Non-steroidal anti-inflammatory drug (NSAID):-** Another class of analgesic drug is the NSAIDs or the non-steroidal anti-inflammatory drugs. Drugs of this class not only show chemical dissimilarities but also vary in their analgesic, antipyretic and anti-inflammatory properties. These drugs work principally by inhibiting the COX1 and COX2 enzymes. However, they do not act on the lipooxygenase enzymes. Aspirin, the most widely used analgesic, is a prototype of this class.

Combinations:-Analgesics are frequently used in combination, such as the paracetamol and codeine preparations found in many non-prescription pain relievers. They can also be found in combination with vasoconstrictor drugs such as pseudoephedrine for sinus-related preparations, or with antihistamine drugs for allergy sufferers. While the use of paracetamol, aspirin, ibuprofen, naproxen, and other NSAIDS concurrently with weak to mid-range opiates (up to about the hydrocodone level) has been said to show beneficial synergistic effects by combating pain at multiple sites of action several combination analgesic products have been shown to have few efficacy benefits when compared to similar doses of their individual components. Moreover, these combination analgesics can often result in significant adverse events, including accidental overdoses, most often due to confusion that arises from the multiple (and often non-acting) components of these combinations.

Alternative medicine: Many people use alternative medicine treatments including drugs for pain relief. There is some evidence that some treatments using alternative medicine can relieve some types of pain more effectively than placebo. The available research concludes that more research would be necessary to better understand the use of alternative medicine.

Psychotropic agents: Other psychotropic analgesic agents include ketamine (an NMDA receptor antagonist), celandine and other α_2-adrenoreceptor agonists, and mexiletine and other local anesthetic analogues.

Mechanism of Analgesic Drugs

The perception of pain is due to activation of nociceptive receptor by the neurotransmitters. Three receptor has been identified for the pain perception, mu, kappa, and delta. They initiate the synthesis of either prostaglandin I or prostaglandin II or sometime both. Analgesic dugs block them either selectively or none selectively to the COX-II receptor. Opioid relieve pain by increasing the threshold at spinal cord level, thus individual may withstand with higher level of pain [11-12].

Analgesic Activity of Medicinal Plant:

S. No.	Plant Name	Family	Part used	Other activities	Chemical constituents
1	Aconitum falconeri Stapf.[13]	Ranunculaceae	Root, stem	Sedative, antirheumatic, analgesic, antitussive, antidiarrhoeal	alkaloids contain bishatisine, bishaconitine, falconitine and mithaconitine.

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2	Aconitum deinorrhizum [14]	Ranunculaceae	Root	rheumatism, rheumatic fever and acuteheadache	0.5% total alkaloids, of which 0.51% is pseudoaconitine.
3	Acorus calamus Linn[15]	Araceae	Rhizome	Nervinetonic,hypotensive, tranquilizer, sedative, analgesic, spasmolytic, anticonvulsant	Volatile oil 96%. Indian calamus oil contains asarone up to 82% and its beta-isome
4	Adiantum lunulatum Burm[16]	Adiantaceae	Rhizome	strangury, atrophy, emaciation or cachexy, muscular pain, emetic in large doses	chlorophyll-degradation, Alkaloids.
5	Aerva lanata (L.) [17]	Amaranthaceae	Leaf, root	diuretic, demulcent, anthelmintic, antidiarrhoeal, anticholerin, bechic	palmitic acid, beta-sitosterol andalpha-amyrin.
6	Aglaia roxburghiana Miq. [18]	Meliaceae	Seeds, Fruits	antipyretic, astringent, antidiarrhoeal, antidysenteric, anti-inflammatory, painful micturition, skin diseases and tumours.	Alkaloids, vinblastine
7	Amomum subulatum Rox[19]	Zingiberaceae	Leaf	Stomachic,antiemetic,antibilious, astringent,alexipharmic, abdominal pains, vomiting, headache and stomatitis.	chalconea flavonoid, petunidin, diglucosidean, dleucocyanidin glucocide; aurone glycoside subulin.
8	Rhodiola rosea L. [20]	(Crassulaceae)	Leaf	Altitude sickness, fatigue, depression,anaemia,gastrointestinal ailments, infections, and nervous system disorders.	Rosavin,rosin, rosarin,flavanoids, rodiolin,tricin, tyrosol.
9	Ficus racemosa Linn. [21]	Moraceae	Leaf, bark	hypoglycaemic activity, anti-inflammatory activity,	Gluacol, beta-sitosterol, lupeolacetate,friedelin, higherhydrocarbons,

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				hepatoprotective	andotherphytosterols.
10	Sesbania grandiflora1 [22]	Fabaceae	Leaf	CNS and analgesic activity	acid sapogenin oleanoicacid,galactose, rhamnoseand glucuronic acid, kaempferol-3,7diglucoside, (+)-leucocyanidin and cyanidin-3-glucoside.
11	Ceropegia juncea Roxb [23]	Bhutumbi	Leaf, seed, stem and bark	anti-nociceptive activity	pyridine alkaloid, cerpegin, triterpene
12	Anthemis nobilis Linn[24]	Asteraceae	Leaf	sedative, anticonvulsant, antispasmodic, antiinflammatory, mild analgesic; used externally for skin disorders, poultice of flowers in sprains and rheumatism.	volatile oil, sesquiterpene lactone,flavonoids,cyanogenicglycoside,bitter glucoside,acetylenicsalicylicderivatives,coumarins,valerianic acid, tannins.
13	Anthocephalus cadamba Miq [25]	Rubiaceae	Fruit	antidiuretic, anthelmintic, hypoglycaemic. —cooling; anticatarrhal, blood purifier, analgesic.	alkaloids, steroids, tannins
14	Aphanamixis polystachya (Wall.)Parker [26]	Meliaceae.	Seed	muscular pains and rheumatism	limonoid, ammorinin, saponin, poriferasterol-3-rhamnoside.
15	Scoparia dulcis L. [27]	Scrophulariacae	Leaf	hypertension, diabetes, inflammation, bronchitis, hemorrhoids and hepatosis and as an analgesic and antipyretic.	scutellarein and 7-O-methylscutellarein, triterpenoids, dulcitol,friedelin,scopadol, betulinic acid, dulcitolic acid, hexacosanol
16	Allium sativum (Garlic) [28]	Liliaceae	Whole plant	immunomodulatory and anti-inflammatory, antithrombotic, lipid-lowering, antitumoral	enzyme alliinase. Alliinase, alliin , allicin

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17	Boswellia Serrata [29]	Burseraceae	Whole plant	sedative, analgesic, anti-inflammatory and anticancer effects	3-keto-methylbeta-boswellic ester, oil, gum-resin
18	Sesbania grandiflora[30]	Fabaceae	flowers	anemia, bronchitis, opthalmia, inflammation, leprosy, gout, rheumatism	acid sapogenin oleanoicacid,galactose, rhamnoseand glucuronic acid, kaempferol-3,7diglucoside, (+)-leucocyanidin and cyanidin-3-glucoside.
29	Kalanchoe Pinnata (Lam.) Pers. [31]	Crassulaceae).	Stem	Anti-hyperglycemic, Antiinflammatory, Analgesic	flavonoids—quercetin, kaempferol, quercetin-3-diarabinosideandkaempferol-3-glucoside, n-hentriacontane, n-tritriacontane,
20	Bishkatali[32]	Polygonaceae	Whole plant	Diuretic, analgesic	Amino acids, vitamins, minerals, tannins, protein.
21	Misridana[33]	Scrophulariaceae	Leaves	Antidiabetic, gastric ulcer	Glucose, hexose, pentose, disaccharides.
22	Ti plant[34]	Agavaceae	Leaves	Antipyretic, lung infection	0.64% (v/w) of essential oil.
23	Athalo Bishkatali [35]	Polygonaceae	Aerial parts	Diuretic, analgesic	Flavonoids, saponins.
24	Bakkan[36]	Verbenaceae	Leaves	Stomachic, diuretic, antiasthmatic	Bakken oil,Bakken crude oil, other crude oil.
25	Ulu[37]	Poaceae	Leaves	Fever	Alkaline
26	Dhandul, Amur[38]	Meliaceae	Leaves	Dysentery, skin diseases	tannins, protein
27	Bhant[39]	Verbanaceae	Aerial parts	Bronchitis, asthma	Flavonoids, saponins, clerodone, sugars
28	Choi[40]	Piperaceae	Stem	Paralysis, schizophrenia	Phinolic compound
29	Raktodrone[41]	Lamiaceae	Aerial part	Tonic, febrifuge	Alkaloids, leonurine, flavonoids, caffeine, tannins, furmeic acid.
30	Lajkari[42]	Polygonaceae	Whole plant	Antiasthmatic, antimigraine, antiallergic	tannins, protein, Alkaloids, Flavonoids
31	Kulaliya[43]	Fabeceae	Whole plant	Eye diseases, stomach trouble	Alkaloids, β-phenylamine idole-3-aceticacid, tyramine.
32	Dolon Champa[44]	Zingiberaceae	Rhizome	Antirheumatic, febrifuge	Alkaloids, Flavonoids, saponins.
33	Brela[45]	Malvaceae	Aerial parts	Tonic, astringent, emollient	Acylsterglycoside,sitoindoside, ephedrine.

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34	Chitki, Panjuli[46]	Euphorbiaceae Aerial parts	Aerial parts	Antidiabetic	Alkaloids, Flavonoids
35	Keu, Kemak[47]	Zingiberaceae	Aerial parts	Osteoarthritis, otitis	Alkaloids, Flavonoids
36	Neem[48]	Meliaceae	Leaves	Rheumatic disorders, antiallergic	Isomeldenin, nimbin, nimbinene, beta-sitosterol, tannin, oil.
37	Sirish, Koroi[49]	Fabaceae	Bark	Toothache, gum diseases	Flavonoids, triteroenoids, saponins, oleanoic acids.
38	Monphal[50]	Rubiaceae	Bark	Bronchitis, asthma	Alkaloids, Flavonoids
39	Aam[51]	Anacardiaceae	Leaves	Antiasthamtic	6-aminopurin-7-yl,
40	Muktajhuri [52]	Euphorbiaceae	Whole, plant	Bronchitis, asthma, arthritis	Acalfeemide, acalphine, acalypus, amides.
41	Tridax procumbent linn [53]	Compositae	Leaves	anti inflammatory and analgesic	n-alkanes, beta-amyrin, beta-amyrone, lupeol, fucosterol and beta-sitosterol.
42	Ziziphus Xylopyrus[54-60]	(family Rhamnaceae	Fruit, powder, Bark, stem	Analgesic and anti-inflammatory	alkaloids, amphibine H and nummularine K, tannin (7.5%)
43	Acacia catechu[61]	Leguminosae	Bark and Stem	Analgesic	Tannins2-20%, catechin 25–30%, flavonoids including quercetin, quercitrin, fisetin; gums,resins,pigments
44	Abutilon indicum[62]	Malvaceae	Leaves	Anti-ulcer, Anti-pyretic, Antioxidant, Analgesic	mucilage, tannins, asparagines, gallic acid, sesquiterpenes. alkaloids, leucoanthocyanins,flavonoids, sterols, triterpenoids, saponins and cardiac glycosidesisalso.
45	Boswellia serrata[63]	Burseraceae	Bark	Antiseptic, analgesic, anti-arthritic activity	3-keto-methylbeta-boswellic ester, isolated from the gum-resin.
46	Bauhinia racemosa[64]	Caesalpiniaceae	Stem, bark	Analgesic and anti-inflammatory	Octacosane, beta-amyrin and betasitosterol.
47	Mangifera indica[65]	Anacardiaceae	Leaves	Analgesic and anti-inflammatory	Sugars,citricacid, ascorbicacid, carotenoids as beta-carotene, m-digallicacid, gallotannin, phloroglucinol,

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					protocatechuicacid, flavonoids
48	Nyctanthes arbor-tristis [66]	Oleaceae	Bark	Analgesic, Used to treat rheumatism and fever	mannitol, beta-amyrin, beta-sitosterol, hentriacontane,benzoic acid,astragalin,nicotiflorin,oleanolicacid,nyctanthicacid, friedelin lupeol.
49	Ocimum sanctum L. [67]	Labiatae	Leaf	Expectorant, analgesic, anticancer, antiemetic, diaphoretic, antidiabetic,	ursolic acid, apigenin, luteolin, apigenin-7-O-glucuronide, luteolin-7-O-glucuronide, orientin molludistin.
50	Piper longum L. [68]	Piperaceae	Fruits, Root	Used as counter irritant and analgesic for muscular pain and inflammation	N-isobutyl-deca-trans-2-trans-4-dienamide.
51	Ricinus communis[69]	Euphorbiaceae	Roots	Analgesic, Antihistamine	ricinoleic acid. Stearic, oleic, linoleic anddihydroxystearicacid.
52	Rubia cordifolia[70]	Rubiaceae	Root	gastrointestinal ailments, infections	purpurin (trihydroxy anthraquinone), munjistin, besides xanthopurpurin, peudopurpurin, freealizarin aswellasits glucoside.
53	Sterculia scaphigera hance[71]	Sterculiaceae	Seeds	Analgesic, antioxidant, antiulcer	Alkaloids, Flavonoids
54	Cleome gynandra L. [72]	Cleomaceae	Whole plant	Anti-oxidant, relieves, joint pain	Flavonoids,centanureidin, kaempferol, quercetin, myricitrin, a- & β-amyrins,lauric, myristic, palmitic.
55	Myrtus communis[73]	Myrtaceae	Leaves	Narcotic analgesic	tannins, flavonoids myricetin, kaempferol, quercetin glycosides; volatile oil containing alpha-pinene, cineole, myrtenol, nerol, geraniol and dipentene.
56	Amaranthus viridis[74]	Amarantha ceae	Whole plant	Analgesic, diuretic and galactagogue	Minerals, sterols, fatty acids, oxalic acid .
57	Elephantopus scaber [75]	Asteraceae	Leaves	Cardiac tonic, treat ulcers and eczema, diuretic, analgesic	germacranolide dilactones. Hydroxylated germacanolides,

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					molephantin molephantinin.
58	Rhodiola rosea L. [76]	Crassulaceae	Rhizome	fatigue, depression, anaemia, gastrointestinal ailments, infections, and nervous system	Tyrosol, flavanoids, rosaridin, tricin, monoterpenes.
59	Vernonia hymenolepis [77]	Asteraceae	Leaves	Analgesic activity	Oleic acid, trans-geranylacetone.

II. DISCUSSION:

Literature review afforded several plants extracts and active constituents with significant analgesic activity.[78] The complex relationship between pain and injury turns the perception of pain in an important research issue. It is increasingly evident that the transmission of pain to the brain is under diverse physiological control. This becomes a difficult challenge in the discovery of forms and compounds capable of inhibiting the pain feeling without causing side effects .Complementary health practices are preserved over the decades by different cultures and are supported by institutions such as World Health Organization (WHO), which encourages many countries to adopt new strategies and public health policies including complementary practices in health model aiming at comprehensive care to individuals. The use of such practices is being gradually expanded in health services due to the biomedical.[79] The crude extracts of the various parts or the whole plants of the medicinal plants and isolated compounds from the medicinal plants showed statistically significant anti-inflammatory activity.[80]

III. CONCLUSION:

From this study, it is clear that the medicinal plants play a vital role against on various diseases. The medicinally important plant species, listed in the present paper appear to be promissory sources of analgesic agents. The future outlook for the development of new Analgesic drugs derived from these medicinal plants is therefore positive and this review can help others to explore herbs to further extent and its use in various other disease and toxicity studies along with clinical trials.

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