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Research Based Affirmation of Medicinal Plants Possessing Analgesic Activity

ASSISTANT PROFESSOR, PAL RUCHI
MAA BHAGWATI COLLEGE OF PHARMACY,LUCKNOW

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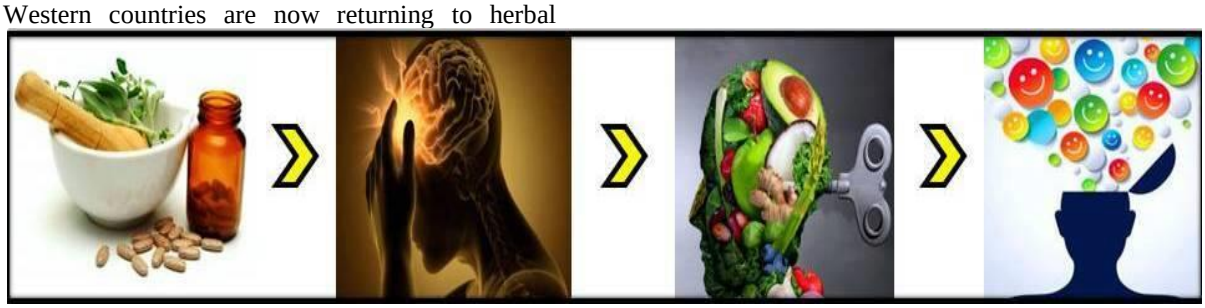
ABSTRACT:
The current communication provides a more comprehensive overview of herbs that have analgesic and anti-inflammatory properties, with a focus on plants found in various parts of the globe. As per the World Health Organization, nearly 80% of the population in underdeveloped nations cannot afford synthetic pharmaceuticals and must rely on traditional medicines, mostly of plant origin, to meet their basic health care requirements. Plants have been used in various disorders such as gastrointestinal disorders, genitourinary problems, pain discomforts, and psychological and respiratory problems since the dawn of time, and people in Western countries are now returning to herbal medicines due to their extensive biological and medicinal activities, higher safety, and lower cost. Many plants have been used in the treatment of pain for centuries, and their anti-inflammatory properties have been scientifically proven. The value of medicinal plants in the management of pain is clearly demonstrated in the current review. This article will benefit both the general public and researchers in their efforts to isolate and characterize the active chemical ingredients responsible for analgesic as well as anti-inflammatory activity.

Keywords: Analgesic, Herbal plants, Folk Medicine.



I. INTRODUCTION:

Natural compounds produced from plants have played an important role in medicine development and will continue to do so. Herbs are gaining in popularity and re-establishing themselves as medicines all over the world. In comparison to synthetic components, which are considered harmful to humans, herbal components currently represent protection. Although herbs have been admired for their medicinal properties for decades, synthetic drugs of the modern era have overshadowed their importance. Human beings are switching to natural components in search of protection and security, while chemical components are being questioned [1].

As per the World Health Organization, about 80% of current medicines are derived from herbs used in herbal medicine. The majority of them are chemical analogs created as proto-type items. In the coming days, the vital use of medicinal plants in therapeutics will proceed. The increasing awareness and use of biologically active items derived from plants in the pharmaceutical industry, and also raising public costs in the regular maintenance of a person's health or well, has indeed been regarded [2].

Plants were the source of remedy and prophylaxis in ancient times. Even so, the decreasing effectiveness of synthetic drugs, as well as the growing number of contraindications to their use, has reintroduced the use of conventional medicine [2, 3].

On the basis of our interest in analgesic drugs, a screening program of some Iranian medicinal plants for analgesic activity has been started. This evaluation was based on the traditional

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use in Iranian medicine and elsewhere, according to other similar selections of plants for research. Natural products are believed to be an important source of new chemical substance with potential therapeutic applicability. Several plant species are traditionally used as analgesics [4].

PATHOGENESIS OF ANALGESIC:

Arachidonic acid is derived from phospholipids (lipids of a membrane). Metabolism of arachidonic acid is done by prostaglandin synthases (PGA_2), which, through its cyclooxygenase (COX) and endoperoxides actions, outcomes in the process and production of PGG_2 to PGH_2. Prostacyclins (PGI_2), PGD_2, PGE_2, PGF_2, and TXA_2 are derived from PGH_2 by prostaglandin synthases.

PGE_2 is chiefly present in the Brain, Kidney, Vascular smooth muscle, and Platelets. PGE_2 is proceeding as a vasodilator by reacting on vascular smooth muscle to cause blood vessel dilation. This result is increased blood circulation. This includes high blood pressure and headache pain [5, 6, 7, 8].

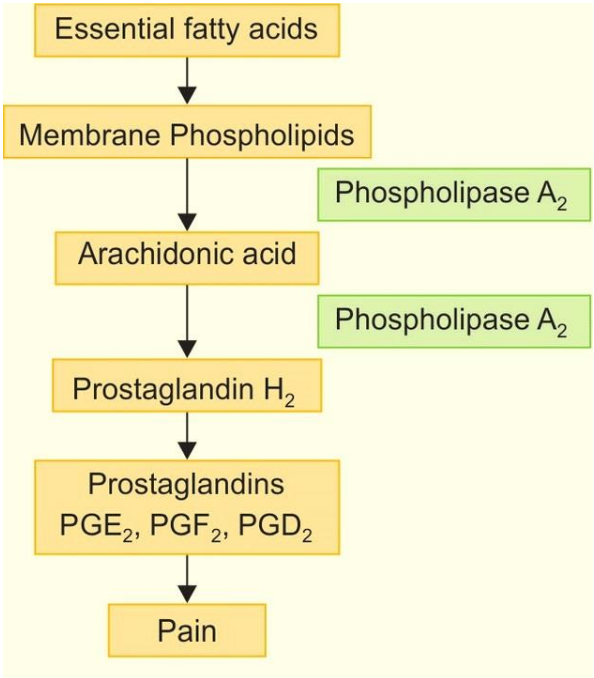

Fig. 1 - Pathogenesis of Analgesic [5, 6, 7, 8].

1) Devil's Claw (*Harpogophytum procumbens DeCandolle, Pealiaceae*) :

Harpogophytum procumbens DeCandolle (Pealiaceae) has brilliant pinkish-red blooms with many tiny hooks. It's also known as 'Devil's claw,' 'Windhoek's root,' wood spider,' hook plant,' and 'grapple plant' in the area. It is regarded as a useful anti-inflammatory and analgesic medicine in Europe and abroad for the treatment of low back pain. Doctors in Europe use Devil's claw extract injections to treat illnesses like joint pain, arthritis, low back pain, and knee discomfort. The principal folkloric applications and relevant sources on Devil's claw's therapeutic benefits are presented in a tabular format for convenient reference [9].

Fever, diabetic, and blood sickness are some of the ethno - medicinal usage of H. procumbens; however there are few recorded historical records. Extracts from the secondary tubers of H. procumbens have been shown to be useful in the treatment of degenerative rheumatoid arthritis, osteoarthritis, tendonitis, renal inflammation, dyspepsia, and lack of appetite in recent scientific investigations. [10].The swelling of arthritic joints in rats with chemically arthritis was reduced significantly by H. procumbens. H. procumbens was shown to have a powerful anti-inflammatory or anti-rheumatic chemical, and further experiments were conducted. The results were encouraging, but the entire plant extract performed better [11].

The ability of H. procumbens to inhibit the synthesis of inflammatory mediators like PGE2 is thought to explain its efficacy in lowering pain and inflammation associated with rheumatoid arthritis and osteoarthritis [12].

The antagonistic activity of an ethanol extract of H. procumbens tubers and its primary major compounds, harpagide, harpagoside, 8-p-coumaroylharpagide, and acteoside, on COX-2expression, was found [13]. In rats, the aqueous secondary tuber extract of H. procumbens (50–800 mg/kg) provided strong analgesic effects against nociceptive pain stimuli elicited thermally (hot-plate) and chemically (acetic acid) [14].

Mice were given 400mg/kg aqueous extract of H. procumbens single dose, which dramatically decreased the number of writhing responses [15]. In the formalin test in mice, H. procumbens extract produced substantial antinociceptive activities [16].

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2) Winter Melon (*Benincasa hispida, Cucurbitaceae*) :

Winter melon, winter gourd, white pumpkin, ash gourd, ash guard, and wax gourd are all names for Benincasa hispida (Benincasa cerifera). The cucurbitaceae family includes gourd melon, white gourd, tallow gourd, and Chinese watermelon [17]. Volatile oils, flavonoids, glycosides, saccharides, proteins, minerals, ß-sitosterin, carotenes, vitamins, and uronic acid were the main contents of Benincasa hispida fruits [18, 19].

The anti-inflammatory effects of Benincasa hispida aqueous extract were discovered during early research. In a rat model, petroleum ether and methanolic extract of Benincasa hispida fruit at 300 mg/kg inhibited carrageenan-induced paw edema, histamine-induced paw edema, and cotton pellet-induced granuloma in a dose-dependent and substantial manner [20].

In rats, the methanolic extract of Benincasa hispida at doses of 250 and 500 mg/kg substantially ($P<0.05$) improved the antinociceptive efficacy (as measured by an analgesiometer that applies force at a steady pace on the rat paw) in a dosage-dependent way. Similarly, the extract substantially (P0.05) reduced Brewer'syeast-induced pyrexia in rats at dosages of 250 and 500 mg/kg [21].

3) Nata Karanja (*Caesalpinia bonducella, Caesalpiniaceae*) :

Seeds of Caesalpinia bonduc have been used in traditional medicine for a long time. It's a large straggling, thorny shrub with hooks and straight, firm yellow prickles on the branches. The leaves have a complex structure. Flowers are pale yellow and grow in supra-axillary racemes at the top of the plant. Nata Karanja (Caesalpinia bonducella), a prickly shrub widespread across India's hotter regions belongs to the Caesalpiniaceae family [22].

Based on the findings of this investigation, it can be determined that the oil of C. bonducella seeds has potential anti-acute and anti-chronic effects in a dose-dependent approach (anti-inflammatory, antipyretic, and analgesic activity) As a result, our research provides a fundamental perspective on C. bonducella and its health advantages. The edema paw volume was significantly decreased after using the oil. There was a dose-related suppression of hind paw edema between 2 and 4 hours. The reference medicine phenylbutazone (100 mg/kg, orally) had a strong inhibitory effect equivalent to the C. bonducella seed oil examined [23].

Induced writhing in rats by acetic acid When compared to aspirin, 100 mg/kg (66.5%) and control groups, the oil of C. bonducella seeds at dosages of 100, 200, and 400 mg/kg demonstrated substantial (p 0.05) suppression of the control writhes at rates of 16.7%, 27.9%, and 48.6%, accordingly. When compared to the control on a hot plate response time in rats, the oil of C. bonducella seeds demonstrated substantial (p 0.01) analgesic efficacy at all dosages tested. Furthermore, when oil was combined with conventional medicine (morphine 5 mg/kg) at different dosages (100, 200, 400 mg/kg), the analgesic activity (response time) was potentiated to 21.37, 23.68, and 27.53 minutes, accordingly, compared to 19.17 minutes with morphine (5 mg/kg). [23, 24].

4) Wild Jujube (*Zizyphus lotus, Rhamnaceae*) :

The majority of plant-based medications that have become essential in contemporary medicine have a folkloric basis and are used in traditional medical systems. Zizyphus spp. fruit trees are examples of multifunctional plants with a lot of promise for ethnomedicinal usage all around the world. Seven cyclopeptide alkaloids [25, 26] and four dammarane saponins were identified from Z. lotus root barks in phytochemical research. The anti-inflammatory and analgesic effects of several root bark extracts are described in this study [27].

When compared to NSAIDs (aspirin (ASA) and piroxicam), the aqueous and methanolic extracts of Z. lotus root barks had a substantial anti-inflammatory impact in the acute phase of the inflammation process. When mice were given acetic acid to cause writhing, aqueous extract of root barks (50, 100, and 200 mg/kg) was found to have a substantial analgesic effect when compared to the control group. In addition, the effects of methanolic, ethyl acetate, and chloroformic extracts of Z. lotus root barks were studied. The methanolic extract exhibited much higher analgesic effectiveness than chloroform and ethyl acetate extracts, according to the findings [28].

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5) Jerusalem Sage (*Phlomis umbrosa Turcz, Labiatae*) :

Phlomis umbrosa Turcz (Caosu) is a medicinal grass (Labiatae) that grows to be between 40 and 100 cm tall. Antinociceptive and anti-inflammatory properties have been identified in several plants related to P. umbrosa. The iridoid glycosides extract of Lamiophlomis rotata (400 mg/kg, i.v.) and the ethanol extracts of Phlomis younghusbandii (200 mg/kg, i.p.) reduced the number of writhings in mice caused by acetic acid and inhibited the inflammatory production caused by certain reagents (pb<0.01). [29].

The aqueous extract of P. umbrosa exhibited strong antinociceptive and anti-inflammatory effects, and indirectly confirmed the local folklore practitioners' traditional usage of P. umbrosa in certain inflammatory and pain illnesses. The Aqueous extract of P. umbrosa (25, 50, and 100 mg/kg) inhibited the writhing activity elicited by intraperitoneal administration of 0.7 percent acetic acid in animals, according to the findings. Our findings suggested that AEP might increase the animal's reaction speed while also acting as an analgesic against the hot plate [29, 30].

6) Gular *(Ficus racemosa Linn, Moraceae)* :

Ficus racemosa Linn. (Moraceae) is a well-known plant species in India that has long been utilized in Ayurvedic medicine, India's traditional medical system, to treat a variety of ailments and problems [31]. It is generally known as 'Jagyadumur' (Bengali), 'Gular' (Hindi), and 'Udumbara' (Sanskrit) [32].

The analgesic efficacy of an ethanolic extract of barks and fruits has been documented [33]. The focus of this study was to assess the analgesic efficacy of F. racemosa fruits and S. dulcis entire herb in mice utilizing two different pain models [34].

When compared to the reference medication diclofenac sodium, the crude extracts of both plants exhibited considerable analgesic effect, although F. racemosa was shown to have better analgesic activity than S. dulcis against acetic acid produced pain in mice at two dosage levels, 100 and 200 mg/kg [35].

In the examined mice, the crude extracts of both plants had considerable (p0.001) analgesic efficacy at oral doses of 100 and 200 mg/kg. In the hot plate test, S. dulcis had a longer latency time than F. racemosa, but in the acetic acid-induced writhing test, F. racemosa had a lower number of writhes than S. dulcis at two dosage levels that were statistically significant (p0.001) when compared to the control [32, 36].

Up to 5000 mg/kg, the extract did not cause death. Ethanol extract at the maximum dose (500 mg/kg) showed comparatively significant (p 0.05) activity in the tail-flick method, significant inhibition of writhes in the writhing test, more significant (p 0.05) response at 90, 120, and 180 minutes in the hot plate method, and comparatively significant (p 0.01) down regulation of paw volume in carrageenan and egg albumin induced paw edema method to that of standard diclofenac [35].

7) Resam (*Dicranopteris linearis, Gleicheniaceae*) :

An aqueous extract of *Dicranopteris linearis* leaves was tested in experimental animals to see if it has antinociceptive, anti-inflammatory, and antipyretic qualities. The abdominal constriction, hot plate, and formalin tests were used to assess antinociceptive effect. The carrageenan-induced paw edoema and brewer's yeast-induced pyrexia tests were used to determine the anti-inflammatory and antipyretic properties, respectively. The extract was shown to exhibit considerable (P 0.05) concentration-independent antinociceptive, anti-inflammatory, and anti-pyretic action at all dosages tested. Finally, the aqueous extract of D. linearis displays antinociceptive, anti-inflammatory, and antipyretic action, corroborating prior assertions of its traditional use by the Malays to cure a number of diseases, including sickness. [37, 38].

8) Beedi Leaf Tree (*Bauhinia racemosa, Caesalpiniaceae*) :

Bauhinia racemosa Lam is a tiny, crooked, thick tree with hanging limbs that can flourish in the harshest climates. This variety may be found all throughout India. The mature leaves of *B. racemosa* are used to make Beedi (Indian cigarettes), whereas the young leaves are utilized by Tamilians as greens (side dish) (Tamil Nadu, India). *B. racemosa* is a sweetish, astringent plant that is used to cure headaches, fevers, skin ailments, blood illnesses, dysentery, and diarrhea. A decoction of the bark is suggested as a good ulcer wash [39, 40].

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The anti-inflammatory, analgesic, and antipyretic effects of 50, 100, and 200 mg/kg body weight of methanol extract extracted from Bauhinia racemosa stem bark, also known as MEBR, were examined in this study. In carrageenan, dextran, and mediators (histamine and serotonin)-induced paw edema and cotton pellet-induced granuloma, the effects of MEBR on the acute and chronic stages of inflammation were investigated. In acetic acid-induced writhing and hotplate tests, MEBR's analgesic efficacy was assessed. Yeast-induced hyperpyrexia in rats was used to test MEBR's antipyretic efficacy. MEBR's anti-edema impact was compared to 10 mg/kg indomethacin taken orally. After 3 h of treatment with MEBR in carrageenan, dextran, histamine, and serotonin-induced paw edema, a maximal inhibition of 44.9, 43.2, 44.8, and 45.9% (P 0.001) was seen in the acute phase of inflammation in carrageenan, dextran, histamine, and serotonin-induced paw edema, accordingly [41, 42].

9) Gokharu *(T. terrestris L, Zygophyllaceae)* :

T. terrestris L. (*Zygophyllaceae*) is an annual creeping herb widely growing in Iran. It is also distributed in Japan, Korea, and the western part of Asia, southern Europe, and Africa [43]. *T. terrestris* is extremely rich in substances having potential biological significance, including: saponins, flavonoids, alkaloids, and other nutrients. The quantities and presence of these important metabolites depend on the various parts of the plant used. The fruit and root of *Tribulus terrestris* (Caltrop fruit) contains pharmacologically important metabolites, such as phytosteroids, flavonoids, alkaloids, and glycosides [44, 45, 46].

Tribulus terrestris has been used in traditional medicine for relieving rheumatic pain and as an analgesic plant for a long time. In this investigation the analgesic effect of methanolic extract of this plant on male albino mice was evaluated by formalin and tail flick test. Extraction of the fruits of the plant was done by two different methods (suxheletion and percolation) with methanol 80%. The percolated extract was injected intraperitoneally in mice at 50, 100, 200, 400, and 800 mg/kg. The results showed that a dose of 100 mg/kg of percolated extract had the highest significant analgesic effect compared to the control group (P <0.01) in formalin and tail flick test. There is no significant difference in the analgesic effect of suxheleted and percolated extract [47, 48].

The analgesic effects of the extract were lower than morphine, 2.5 mg/kg in both tests, and higher than ASA 300 mg/kg in chronic phase of pain in formalin test (P <0.05). Pretreatment of animal with naloxone did not change the analgesia induced by the plant extract in both tests, therefore the involvement of opioid receptor in the analgesic effect of this plant was excluded. The results of ulcerogenic studies indicate that the gastric ulcerogenecity of plant extract is lower than the indomethacin in the rat's stomach. It can therefore be concluded that *T. terrestris* extract has a suitable analgesic effect and further studies are required to produce a more effective product of this plant to substitute for conventional analgesic drugs [47, 48, 49, 50].

10) Bharangi (*Clerodendron serratum, Verbenaceae*) :

In the Ayurveda system of medicine, C. serratum (Linn.) Moon (Verbenaceae) is known as Bharangi. Clerodendron is a significant Verbenaceae genus with a large number of species known to be found in India. Flavonoids, diterpenoid, and sterols have already been discovered from the Clerodendron genus [51, 52].

The anti-nociceptive, anti-inflammatory, and antipyretic effects of the ethanol roots extract of C. serratum at doses of (50, 100, 200 mg/kg.) roots were tested in animal models [53, 54].

11) Ashwagandha (*Withania somnifera, Solanaceae*) :

It belongs to the *Solanaceae* family. Withania somnifera is an esteemed herb in Ayurvedic medication, and as such was utilized and developed for quite a long time in India (Uttar Pradesh, Madhya Pradesh, Gujarat, Rajasthan, and Punjab).). W. somnifera have 1.5-m high shrub with ovate leaves and yellowish-green blossoms. The Roots of W. somnifera are 20-30 cm long and 6-12 mm. It has a trademark scent, taste severe and horse-like smell [1, 55].

W. somnifera has analgesic, anti-inflammatory, and antipyretic [56, 57]. The powder of ashwagandha roots was discovered to have a significant inhibition effect on, as well as other inflammatory markers including interleukin (IL - 6), and tumor necrosis factor (TNF-α). The extract of roots contains biologically active chemical constituents are Alkaloids (Withanine, withananine,

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withasomnine, somninine, somniferine, nicotine, isopelletierine, tropeltigloate, anaferine, and somniferinine), Flavonoids (Quercetin, kaempferol), Steroidal Lactones (Withaferin-A, withanone, withanolides), and Steroids (stigmasterol, β - sitosterol, cholesterol, diosgenin, stigmastadien, sitoindosides), and Nitrogen containing Somnitol somnisol, and withanol [55. 59].

It contains are alkaloids, flavonoids, saponins, sugars, and proteins. The seeds powder of A. aspera gives calmness from solidness and headache. The leaves and seeds of Achyranthes aspera show pain-relieving activity [58, 59].

When active components of W. somnifera Withaferin A were compared to the conventional medicine Indomethacin in mice using the Acetic acid-induced writhing method, they revealed analgesic potency at a dose of 30 mg/kg body mass [60].

12) Latjira (*Achyranthes aspera, Amaranthaceae)* :

It belongs to the *Amaranthaceae* family. It is a yearly, stiff herb, about 0.3 to 0.9m high, and is a typical plant found in badlands, all through roadside and rural fields. It is known by various names in India like Latjira and Chirchira in Hindi, Apamargah, Chirchitaa, and Shikhari in Sanskrit, Chirchitaa in Unani, Pricklychaff flower plant in English, Nayuruvi in Tamil, Uttaraene in Telugu, Kutri in Punjabi, and Kadalad in Malayalam [61, 62].

It contains are alkaloids, flavonoids, saponins, sugars, and proteins. The seeds powder of A. aspera gives calmness from solidness and headache. The leaves and seeds of Achyranthes aspera show pain-relieving activity. Latjira has been recommended to be a possible lead for another kind of anti-inflammatory agent having a double inhibitory action on phospholipase a (corticosteroid) and cyclooxygenase (COX-1, COX-2) which is responsible for pain and inflammation [63].

Ethanolic extract of leaf of A. aspera (400 mg/kg) has produced an analgesic effect at 30, 60, 90 and 120min using Tail flick response and Hot plate methods [64].

II. CONCLUSION:

Herbology is the study of finding healthier and better ways to relieve pain. Several persons seem to recognize the value of pain management for these analgesic plants, which include some of the most well-known and well-liked medicines. Analgesic herbs are used to treat headaches, toothaches, tight muscles, back pain, and nephropathy, among other things. This review paves the path for further investigation into the bioactive components found in these plants, as well as their identification and extraction**.**

Conflict of Interest:

We declare that we have no conflict of interest.

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