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Herbs Having Analgesic Activity

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ABSTRACT

Healthcare maintains a high priority on pain management, and research to develop safer and more potent analgesics is ongoing. Natural goods, especially plants, have recently attracted renewed interest as potential sources of analgesic medications. In this study, various techniques are used to measure pain. The rich source of analgesics found in medicinal plants includes *Moringa oleifera, Aloe barbadensis, Curcuma longa, Eugenia caryophyllata, Adhatoda vasica, Mentha piperita, Ocimum sanctum, Zingiber officinale, Lavandula angustifolia, Epilobium angustifolium, Dialium guineense, Sida acuta, Stylosanthes fruticose, Bougainvilla spectabilis, Ficus glomerata, Polyalithia longifolia, Calotropis gigantea, Tinospora cordifolia, Ageratina glabrata, Mangifera indica, Peperomia pellucida, Jatropha gossypifolia, Leonotis leonurus, Mimosa rubicaulis, Cussonia paniculate, Biebersteinia multifida, Alternanthera sessislis, Mentha arvensis, Oroxylum indicum, Tamarindus indica, Cucurbita maxima, Cucumis sativus, Emblica officinalis, Angiopteris evecta, Parastrephia lephidophylla, Peperomia pellucida, Scoparia dulcis, Ficus racemose, Eremostachys laciniata, Phlogacanthus thyrsiflorus, Kigelia pinnata, Molineria capitulate, Manihot esculenta, Ficus religiosa, Dalbergia sissoo, Grangea maderaspatana, Nothospondias staudtii, Rhodiola rosea, Juniperus communis, Erythrina*

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variegate **etc. The results reported in this review paper represent scientific knowledge that may be applied in the future to isolate potentially active molecules from some of these medicinal plants.**

Keywords- Algesia, Analgesic, Herbal medicine..

I. INTRODUCTION

Algesia (Pain):

Pain is characterized as an acute somatic discomfort, a sign of a bodily injury or disease, and sometimes emotional distress. A vital part of the body's defense mechanisms, pain serves as a quick warning signal that instructs the motor neurons in the central nervous system to prevent physical harm.

There are two main different categories of pain: (a) Acute pain (b) Chronic pain.

(a) ***Acute pain:*** The body warns of current sickness or tissue damage with acute discomfort. It often comes on quickly and sharply and is followed by aching discomfort. It is either temporary pain or pain with recognizable origins.

(b) ***Chronic pain:*** Chronic pain can be described as pain that persists significantly longer than would be the case with a specific injury. Acute pain is usually easier to cure than chronic pain, which can be continuous or intermittent. Additionally, different types of pain can be categorized according to their origin and associated pain-detecting neurons, such as cutaneous, somatic, visceral, and neuropathic pain.[1]

There are many different types of pain, including neuropathic, visceral, inflammatory, and acute. In addition to reflecting the influence of numerous psychological factors including attention, worry, stress, suggestion, or prior experiences, it may also be significantly influenced by genetics. It is not just the outcome of tissue damage. The majority of diseases seen in modern medicine are accompanied by pain, and 25% of Americans, for instance, report having everyday discomfort. The statistics were on pain's side, making it a global public health issue and the main cause of disability worldwide.[2]

Table 1: Characteristics of pain[3]

Receptor pain	From irritation the receptors of integuments, muscles, joints and internal organs
	No changes in the nervous system
	Skin, osteoarticular, muscular, and organ pain
Non-receptor pain	Nerve or central nervous system damage
	Damaged nervous system
	Neuropathic pain – from the nerves, central pain – from the spinal cord

Analgesics**:**

Greek words an- ("without") and algos- ("pain") give us the word analgesic. Analgesics are medications that act to relieve pain without making a person unconscious. On the peripheral and central neural systems, analgesic medications act on it and produce analgesic effects.[1]

Three categories can be used to classify analgesics:

(a) Opioid/narcotic analgesics.
(b) Non-opioid/non-narcotic analgesics.
(c) Adjuvent analgesics.[4]

There are three primary factors that regulate the analgesia system:

- The periaqueductal grey matter (in the midbrain)
- The nucleus raphe magnus (in the medulla)
- The dorsal horns of the spinal cord contain pain-inhibitory neurons that block pain-transmitting neurons that are also found there. [1]

II. METHODS OF TESTING PAIN IN ANIMALS:[5]

Hot plate test:

To reduce nervous pressure, mice are placed individually on plates three to four times during intervals of three to five minutes in this technique. The interval between placing the mice on the plate and when they begin to lick it is referred to as the threshold, and the animal's latency in licking or kicking at various intervals is noted. Each mouse is placed on a plate 4-5 times over the course of five-minute intervals to obtain an average that can be calculated more precisely. Animal tissue damage cutoff time is taken into consideration. In this test, pain control mechanisms are presented. For substances that resemble opioids, the hot plate test is a selective test. An extra-spinal pain model is used in this exam. This test's ability to produce automatic defensive behaviors is its key feature.

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Writhing test:

Acetic acid solution is intraperitoneally injected into mice as part of this test. The number of writhing individuals is determined during 30 minutes following acetic acid injection. If an animal writhes, it should include abdominal muscle contractions followed by the opening of the back feet or stretching of the entire body. The sensitivity of pain receptors to substances like prostaglandins is a prerequisite for abdominal muscle contractions.

Damage to the tissue results in the release of chemicals including prostaglandins, bradykinin, serotonin, substance P, histamine, and PGF2, which express inflammatory pain by increasing capillary permeability. This test can be used to measure the analgesic activity of opioid agonists and non-steroidal anti-inflammatory medications.

Tail flick test:

The mouse has been placed in the restrainer device in the light tail flick such that the animal's tail is outside the chamber. The lamp light is employed in this technique to inflict agony. The animal flicks its tail as a result of heat-induced pain after being exposed to a light beam for a while. In the beginning, animal tolerance is assessed, and the tolerance period is regarded as control latency. The time to get maximum analgesic response is then estimated using the formula below at various intervals up to 120 minutes following medication administration.

$$\textbf{Maximum analgesic response} = \frac{\textbf{Test latency} - \textbf{Control latency}}{\textbf{Cut off time} - \textbf{Control latency}} \times 100$$

Cut off time is the greatest tolerance period for avoiding injury to an animal's tail.

Tail immersion:

To evaluate acute pain, a hot water tail immersion test or short tail immersion is utilised. The mouse is first placed in a restrainer, then after 20 minutes, its tail is submerged in a hot water bath. Acute pain threshold is defined as the amount of time a mouse can tolerate its tail being submerged in water before it pulls it out. Each mouse's mean threshold is determined by immersing its tail in water five times at intervals of seven minutes. After determining the average threshold for each mouse, the percentage of analgesia index is derived using the formula below:

$$\textbf{Analgesia index} = \frac{\textbf{Drug latency} - \textbf{Control latency}}{\textbf{Cut off time} - \textbf{Control latency}} \times 100$$

Formalin test:

In this technique, an animal is placed in a glass container, and the animal's reactions are then observed. Underneath the container, a mirror is placed and tilted at a 45° angle to ensure clear visibility. To conduct the test, 20 µL of 2.5% formalin is injected subcutaneously into the paw's surface. Following that, the lengths of time spent licking or biting the formalin-injected paw during two delay and quick stages are timed. Typically, the acute phase occurs in the first 0–5 minutes, while the chronic phase occurs in the last 5–60 minutes.

III. HERBAL REMEDIS AND ANALGESICS ACTVITY

Since the earliest days of time, people have looked for medicines for their diseases in nature.[6,7] Plants include a large number of biologically active substances that have been utilized for countless years to treat a wide range of human disorders. Today, a variety of traditional medicines are widely accessible and are said to have higher cultural acceptance, better compatibility with the human body, fewer side effects, and greater efficacy. Around 80% of the population receives their primary care from traditional medicine, according to estimates from the World Health Organisation. Since medicinal plants are the "backbone" of traditional medicine, more than 3.3 billion people in less developed nations regularly utilize herbal remedies. [8,9,10,11]

Using medicinal plants as an acceptable source of innovative therapy has become more popular recently due to the various adverse effects of synthetic medications. One of the most significant foes in modern medicine, pain has a high influence on living quality and has significant economic implications. According to estimates, 80% of people worldwide utilize plants as analgesics or antinociceptive medications in traditional therapy. With the vast variety of medicinal plant resources available, research into new analgesic combinations is expanding. This is due to the fact that such information offers assurances for the discovery of novel therapeutic medicines that can prevent, reduce, or relieve pain. Much older than the present medical sciences practiced in developing nations is the folk medical practice of using herbs as analgesics. [2]

IV. HERBS HAVING ANALGESIC ACTIVITY

Due to the potential adverse effects and low efficacy of synthetic and chemical medications, the use of alternative drugs, particularly herbal painkillers, is developing.[5] Different pain tests, such as the writhing test, light tail flick test, tail immersion test, hot-plate test, and formalin test, have been used to study the effects of herbal extracts. [2] There are some of the plants listed in Table-2. which in conventional medicine have analgesic properties. Among the plants whose analgesic properties have been established.

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Table 2: List of plants having analgesic activity

Sl. No.	Plant name	Family	Using part	Type of extraction	Animal used	Methods	Effective dose	Result
1.	*Moringa oleifera* (Drum stick)	Moringaceae	Leaf	Non-polar and polar extracts	Male and female Wistar rats	Formalin test	30-300 mg/kg	Its capability to reduce pain.[12]
			Seed	95% alcohol	Wister male albino rats	Hot plate method & tail Immersion Method	30 mg/kg	Alcoholic extract displayed strong analgesic effects.[13]
2.	*Aloe barbadensis* (Aloe vera)	Asphodelaceae	Leaf	Aqueous extract	Male Wistar rats	Hot plate method	300 mg/kg	It has analgesic efficacy. [14]
3.	*Curcuma longa* (Turmeric)	Zingiberceae	Rhizome	Aqueous & alcoholic extract	Wistar rats	Tail Immersion Method	100, 200 mg/kg	It has an analgesic effect.[15]
4.	*Eugenia caryophyllata* (Clove)	Myrtaceae	Bud	Aqueous and ethanolic extracts	Mice	Hot plate method	50, 100, and 200 mg/kg	It was proven that clove extract in aqueous form, but not in ethanol, has analgesic properties.[16]
5.	*Adhatoda vasica* (Vasaka)	Acanthaceae	Leaves	Methanolic extract	Wistar albino rats	Hot plate method & tail immersion method	200, 400 and 600 mg/kg	It significantly inhibited the pain.[17]
6.	*Mentha piperita* (Pudina)	Lamiaceae	Leaves	Methanolic extract	Wistar albino rats	Hot plate method & tail immersion method	200, 400 and 600 mg/kg	It significantly inhibited the pain. [17]
7.	*Ocimum sanctum* (Tulsi)	Labiatae	Seed	Petroleum ether	Albino rats, albino mice	Tail flick method, tail clip method, and tail immersion method	1.0, 2.0 ml/kg	The analgesic effects are proven.[18]
8.	*Zingiber officinale* (Ginger)	Zingiberaceae	Rhizome	Ethanol extract	Male and female mice, Wistar rats	Hot-plate test method & acetic acid test method	50, 100, 200, 400, 800 mg/kg	It has an analgesic effect.[19]
9.	*Lavandula angustifolia* (Lavender)	Lamiaceae	Leaves	Hydro-alcoholic extract	Male swiss mice	Formalin test and acetic acid-induced writhing test	100, 200 mg/kg	It has analgesic activity.[20]

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10.	*Epilobium angustifolium* (Alpine willowherb)	Onagraceae		Ethanolic tincture	Swiss male mice	Hot plate test and the writhing test	0, 47.5, 95, 190, and 380 mg/kg	The herb shows strong analgesic properties.[21]
11.	*Dialium guineense* (Black velvet tamarind)	Fabaceae	Stem bark	80% methanol	Albino Wistar mice	Tail immersion test and hot plate method	250, 500, 1000 mg/kg	It has analgesic Activity. [22]
12.	*Sida acuta* (Common wireweed)	Malvaceae	Whole plant	Ethanol	Wistar albino rats/ swiss albino mice	Hot plate method & tail immersion method	100, 300 and 500 mg/kg	Analgesic activity was observed. [23]
13.	*Stylosanthes fruticosa*	Papilonaceae	Whole plant	Ethanol	Wistar albino rats/ swiss albino mice	Hot plate method & tail immersion method	100, 300 and 500 mg/kg	Analgesic activity was observed. [23]
14.	*Bougainvilla spectabilis*	Nyctoginaceae	Leaves	Ethanol	Wistar albino rats/ swiss albino mice	Hot plate method & tail immersion method	100, 300 and 500 mg/kg	Analgesic activity was observed. [23]
15.	*Ficus glomerata*	Moraceae	Bark, leaves	Ethanol	Wistar albino rats/ swiss albino mice	Hot plate method & tail immersion method	100, 300 and 500 mg/kg	Analgesic activity was observed. [23]
16.	*Polyalithia longifolia*	Annonaceae	Leaves	Ethanol	Wistar albino rats/ swiss albino mice	Hot plate method & tail immersion method	100, 300 and 500 mg/kg	Analgesic activity was observed. [23]
17.	*Calotropis gigantea*	Asclepiadaceae	Flowers	Alcoholic extract	Swiss mice	Eddy's hot plate method and acetic acid induced writhing	250 and 500 mg/kg	The plant is used as a potential analgesic. [24]
18.	*Tinospora cordifolia* (Guduchi)	Menispermaceae	Stem and aerial parts	Aqueous extract	Albino rats	Hot plate and abdominal writhing method	300 mg/kg	The plant extract showed analgesic activity.[25]
19.	*Ageratina glabrata* (Kunth)	Asteraceae	Leaves	Dichloromethane extract	Female Sprague Dawley rats	Hot plate test	100 and 150 mg/kg	In animal studies, the plant has analgesic properties that are mediated

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								by COX-2 enzyme inhibition. [26]
20.	*Mangifera indica* (Mango)	Anacardiaceae	Leaves	Aqueous extract	Albino rats	Hot plate method and acetic acid induced writhing	200 and 400 mg/kg	Leaves extract in an aqueous form significantly reduces pain.[27]
21.	*Peperomia pellucida*	Piperaceae	Aerial part	Aqueous extract	Rats and mice	Abdominal writhes and hot plate method	200 and 400 mg/kg	The plant showed analgesic activity.[28]
22.	*Jatropha gossypifolia*	Euphorbiaceae	Aerial part	Methanolic & petroleum ether extract	Albino mice	Eddy's hot plate method & tail flick method	100 and 200 mg/kg	It has significant analgesic activity.[29]
23.	*Leonotis leonurus*	Lamiaceae	Leaves	Aqueous extract	Male Wister rat	Acetic acid-induced writhing test	50, 100, 200 mg/kg	It has a significant analgesic effect.[30]
24.	*Mimosa rubicaulis*	Fabaceae	Stem	Ethanol	Swiss albino rat	Hot plate method & tail immersion method	100, 250 mg/kg	It has analgesic activity.[31]
25.	*Cussonia paniculata*	Araliaceae	Stem bark	Aqueous extract	Male Wistar rat	Formalin test	50, 100 and 200 mg/kg	It acts as an analgesic. [32]
26.	*Biebersteinia multifida*	Geraniaceae	Root	Ethanol	Male Albino Wistar rat	Formalin test	50 mg/kg	It has analgesic effects.[33]
27.	*Alternanthera sessislis* (Chanchi shak)	Amaranthaceae	Aerial parts	Methanolic extract	Swiss albino mice	Abdominal writhing test	50, 100, 200 and 400 mg/kg	It is used to alleviate pain.[34]
28.	*Mentha arvensis* (wild mint)	Lamiaceae	Whole plant	Ethanolic extract	Swiss albino mice	Acetic acid induced writhing method	250 and 500 mg/kg	The plant is used as an analgesic. [35]
29.	*Oroxylum indicum* (Indian trumpet tree)	Bignoniaceae	Bark	Ethanol	Swiss albino mice	Hot plate, acetic acid-induced writhing and formalin.	250 and 500 mg/kg	It has analgesic activity.[36]
30.	*Tamarindus indica* (Tamarind)	Fabaceae	Stem bark	Hexane, ethyl acetate, and methanol	Wistar rats	Writhing test	200 mg/kg	It is an indication of potent anti-nociceptive activity.[37]

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			Seeds	Petroleum Ether fraction and Ethyl acetate	Wistar rats	Tail immersion method	50 and 100 mg/kg	Increased latency to tail flick in this method. [37]
			Roots	Aqueous extract	Wistar rats	Hot plate method and acetic acid-induced writhing test	300 and 600 mg/kg	It enhanced pain inhibition. [37]
			Leaves	Ethanolic extract	Swiss albino mice	Tail immersion	400 mg/kg	Enhanced analgesic activity. [37]
31.	*Cucurbita maxima*	Cucurbitaceae	Seeds	Ethanol	Mice	Hot plate method & Tail flick method	50, 100, and 200 mg/kg	It has analgesic properties.[38]
32.	*Cucumis sativus* (Cucumber)	Cucurbitaceae	Seeds	Ethanol	Mice	Hot plate method & Tail flick method	50, 100, and 200 mg/kg	It has analgesic properties.[38]
33.	*Emblica officinalis*	Euphorbiaceae	Leaves	Ethanol and aqueous extracts	Swiss Albino mice	Acetic acid-induced writhing & Tail-immersion test	500 mg/kg	It has a significant analgesic effect.[39]
34.	*Angiopteris evecta* (Giant Fern)	Marattiaceae	Leaves	Methanol	Swiss albino mice	Abdominal writhing test	50, 100, 200 and 400 mg/kg	It is used for alleviating pain.[40]
35.	*Parastrephia lephidophylla*	Asteraceae	Aerial parts	n-hexane, CHCl3 and EtOAc extracts	Rats	Hot plate test	5, 20 mg/kg	It has analgesic activity.[41]
36.	*Peperomia pellucida* (shiny bush or silver bush)	Piperaceae	Whole plant	Ethyl acetate extract	Male Swiss albino mice	Acetic acid-induced Writhing	300 mg/kg	It has analgesic activity.[42]
37.	*Scoparia dulcis* (Sweet Broomweed)	Scrophulariacae	Whole herb	Ethanol	Swiss-albino mice	Hot plate method & acetic acid induced writhing method	100, 200 mg/kg	It has central and peripheral analgesic properties.[43]
38.	*Ficus racemose* (Jagyadumur)	Moraceae	Fruits	Ethanol	Swiss-albino mice	Hot plate method & acetic acid induced writhing method	100, 200 mg/kg	It has central and peripheral analgesic properties.[43]
39.	*Eremostachys laciniata*	Lamiaceae	Rhizomes	n-hexane, dichloromethane and methanol	Swiss Albino mice	Hot-plate test	0.5, 1 and 2.5 mg / kg	Analgesic activity was present.[44]
40.	*Phlogacanthus thyrsiflorus* (Lal basak)	Acanthaceae	Leaves	Ethanol extract	Albino rats	Tail flick method & glacial acetic	500 mg/kg	It has significant central and peripheral

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						acid-induced writhing test		analgesic activities. [45]
41.	*Kigelia pinnata* (Sausage tree)	Bignoniaceae	Flowers	Methanolic extract	Albino Wistar rats	Acetic acid-induced writhing, hot plate method & formalin-induced paw licking	100,200 and 400 mg/kg	It has analgesic activity.[46]
42.	*Molineria capitulata*	Hypoxidaceae	Leaves	Methanolic extract	Swiss Albino mice	Acetic acid-induced Writhing & Formalin-Induced Writhing	200 and 400 mg/kg	This plant showed analgesic activity.[47]
43.	*Manihot esculenta*	Euphorbiaceae	Leaves	Ethanolic extract	Mice	Acetic acid-induced Writhing	12.8, 25.6, 51.3 and 102.6 mg/kg	It has an analgesic effect.[48]
44.	*Ficus religiosa* (Peepal)	Moraceae	Leaves and bark	Ethanolic extract	Swiss albino mice	Acetic acid-induced writing response & Eddy's hot plate method	400 mg/kg	It has both central and peripheral analgesic properties.[49]
45.	*Dalbergia sissoo* (Shisham or Sisam)	Fabaceae	Leaves	Ethanolic extract	Swiss mice and Wistar rats	Acetic acid-induced writing test	100, 300 and 1000 mg/kg	Moderate analgesic activities were present in this plant.[50]
46.	*Grangea maderaspatana*	Asteraceae	Whole plant	Methanol extract	Male Swiss mice	Acetic acid-induced writing test	1 and 3 g/kg	The plant is used as an analgesic. [51]
47.	*Nothospondias staudtii*	Simaroubaceae	Leaves	Water, methanol and chloroform extract	Adult male and female Swiss mice and albino rats	Tail immersion and acetic acid-induced writing	100mg/kg	It has analgesic effect.[52]
48.	*Rhodiola rosea* (golden root or roseroot)	Crassulaceae	Rhizomes	Methanol	Male Wistar rats and male	Tail immersion and acetic acid-	50 and 200 mg/kg	Analgesic activity present.[53]

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					Swiss Albino mice	induced writing		
49.	*Juniperus communis*	Cupressaceae	Leaves	Methanolic extract	Swiss Albino mice	Acetic acid-induced writhing test, formalin-induced pain and tail flick test	100 and 200mg/kg	Analgesic activity present.[54]
50.	*Erythrina variegate* (Mandar)	Papilionaceae	Leaves	Methanolic extract	Swiss albino mice	Acetic acid-induced writhing and tail-flick model	500 mg/kg	It has true analgesic Potential. [55]

V. CONCLUSION

Currently used analgesic medications are either narcotics or non-narcotics with known harmful and adverse effects. Making use of new synthetic chemicals in this area is an expensive venture that could also provide adverse effects issues. On the other hand, numerous medications with a botanical origin have been utilized and are still being used successfully nowadays without any negative side effects. Therefore, studies investigating the clinical effectiveness, safety, and reasonable dosages of extracts and active substances for the treatment of pain should be prioritized in the future. The present paper provides an effective approach for finding more novel chemicals from multiple medicinal plants that may be beneficial in treating pain.

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