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(REVIEW ARTICLE)

Phytochemical approaches in pain management: Exploring the therapeutic potential of *Tectona grandis* and other natural compounds

Diksha dilliwar, Tilotma Sahu * and Anjali Sahu

Rungta Institute of Pharmaceutical Sciences Bhilai. India.

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Abstract

The phenomenon of pain is complex in nature and multimodal, being a significant contributory factor affecting human health, quality of life, and psychological well-being. Pain can generally be categorized under three types that are nociceptive, neuropathic, and inflammatory pains, each arising from different specific mechanisms and etiologies, and thus effectively managed through this understanding, into various therapeutic procedures, such as pharmacological drugs, physical interventions, and psychologically oriented treatments. There is growing interest in natural alternatives to conventional pain therapies, especially phytochemicals, because of their potential efficacy and fewer side effects. Phytochemical constituent of clove, ginger, and turmeric have been traditionally used for their analgesic and anti-inflammatory effects, and in recent times, they find more usage in the marketed preparations claiming natural pain relief. These compounds thus offer a high level of therapeutic benefits as they alter and reduce the inflammation induced by pain pathways through several biochemical mechanisms. Another plant extensively sought and presently attracting much attention for its medicinal properties is *Tectona grandis* or teak. It contains bioactive compounds, particularly tectoquinone, which has shown promising analgesic and anti-inflammatory effects. Tectoquinone works through the following mechanisms, including inhibition of pain receptors and reduction of inflammatory mediators; therefore, it has the potential as a candidate in future therapies of pain. The growing interest in tectoquinone has led to the development of some commercial products that incorporate this compound in the form of relief against pain. These products, however, give more evidence on the market demands of natural solutions in pain management. In fact, current researches, patents, and associated studies emphasize that the scope of tectoquinone remains to be one of the key additions in the pharmacotherapeutic agent meant for application against pain. With that, it's on this realization that this review unites the varieties of types of pain, forms of mechanisms happening, discussion over the applicability of phytochemicals on the treatment, and a general review of *Tectona grandis* and one of its extracts known as tectoquinone.

Keywords: Pain; Phytochemical constituent; Analgesic; Anti-inflammatory; *Tectona grandis*; Tectoquinone

1. Introduction

When there is no physical disturbance, pain is defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage"(1). It is important to take into account the psychological, social, and spiritual dimensions of pain in addition to its physical manifestation. According to research, a multifaceted approach to pain is necessary because each person's response to their pain experience is unique, as are the ways in which pain is assessed, physically manifested, psychological, social, and spiritual difficulties .The quality of life (QoL) of about 70% of cancer patients is significantly impacted by pain (2). One of the most common clinical symptoms is pain, which is the body's main warning indication of injury or illness. According to data from the World Health Organization (WHO), more than 520 million people globally suffer from pain in one form or another, with a noteworthy 75% reporting moderate-to-severe discomfort. Pain is defined by the International Association for the

* Corresponding author: Tilotma Sahu

Study of Pain (IASP) as an unpleasant emotional and sensory experience connected to real or possible tissue damage (3).

Pain Management: In medicine and healthcare, pain management refers to the treatment of pain in all of its manifestations, from acute and straightforward to chronic and difficult. In the regular course of their work, the majority of doctors and other health care providers manage some level of pain. For more complicated cases, they also seek further assistance from a medical specialty dedicated to treating pain, known as pain medicine (4).

Based on how long a condition has been present, pain can be divided into acute and chronic categories. The term "acute pain" describes quick, fleeting discomfort that typically lasts for a few minutes, hours, or even days. Trauma, surgery, infections, and other temporary irritations including fractures, sprains, toothaches, and so forth are typically the causes. Acute pain is characterized by intense pain that often passes quickly. Recurrent pain that lasts for a long time—typically weeks, months, or even years—is referred to as chronic pain. The most common causes of chronic pain include chronic diseases, injuries, or inflammatory reactions, including arthritis, muscular strains, neuropathy, etc. Low levels of pain are the hallmark of chronic pain, which can last for a long time and significantly affect a patient's quality of life (5,6,7).

2. Types of pain

Based on how long a condition has been present, pain can be divided into acute and chronic categories:

- **Acute pain:** A variety of thermal and mechanical stimuli, as well as endogenous and ambient chemical irritants, are detected and interpreted by the nervous system. The clinical entities of acute and chronic pain are distinct. Acute pain is self-limited, has a beneficial biologic function, is triggered by a particular disease or injury, and is linked to skeletal muscle spasm and sympathetic nervous system activation. Components of the pain transmission route in the peripheral and central nervous systems show significant plasticity in identifying a chronic injury, intensifying pain signals and causing hypersensitivity. Plasticity may be advantageous when it supports defensive reflexes, but if the alterations continue, chronic pain may ensue(5).

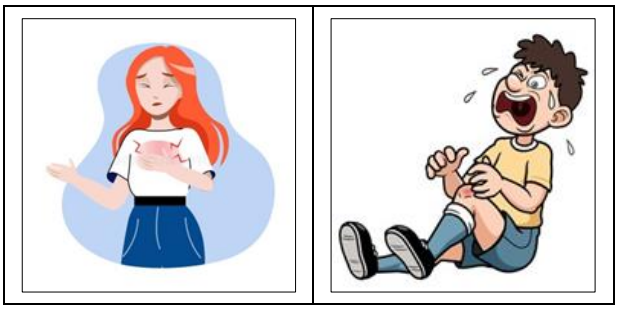

Figure 1 Image of Acute pain

- **Chronic Pain:** A prevalent issue in infancy and adolescence is chronic pain, which is defined as pain that lasts longer than three months or that is continuous or recurrent(6).According to the definition, chronic primary pain is "pain in one or more anatomic regions that persists or recurs for more than three months and is associated with significant functional disability (interference with daily activities and participation in social roles) or significant emotional distress that cannot be better explained by another chronic pain condition." Chronic secondary pain refers to pain that is linked to another illness, such as chronic musculoskeletal pain, chronic headache and orofacial pain, chronic neuropathic pain, chronic cancer pain, chronic postsurgical and posttraumatic pain, and chronic visceral pain (7).

Figure 2 Image of Chronic Pain

3. Etiology of pain

Define the sources of pain which the experts claim as "etiology" which can arise due to many biological, psychological, and clinical factors. Pain can be viewed as an unpleasant feeling. It is not just a simple sensation but rather a combination of sensations and emotions resulting from the activation of defensive behavior in the body due to damaging factors such as injury inflammation or neural damage. When some harmful stimulus occurs, this constructive action on the body results in a pain expression.

3.1. Different sources or causes of pain are divided into multiple groups, such as:

Neuropathic pain after a peripheral nerve injury occurs as a result of a sequence of complex pathological process changes at the level of the spinal cord and the sub-cortical nuclei. Ion channels, receptors, and proteins are all present which increases the abnormal activity and excitability of the nerve. One of the reasons for this is the firing, more importantly, the dysfunctional voltage-gated sodium channels' influence. Furthermore, there is a release of neurotransmitters after an injury that fortifies pain pathways and enhances the level of pain. As a result, one of the important neurotransmitters, when over released, initiates receptor activation while also changing synapses and increasing pain levels.

- **Nociceptive pain:** Nociceptive pain is caused by tissue damage, which is then detected by nociceptors. Patients can clearly describe it, and it is usually well-localized. Examples include pericardial inflammation in pericarditis, tissue ischemia in Raynaud's phenomenon, and pain from inflammation of joint tissues in active rheumatoid arthritis (RA) (11). Nociceptive pain in RA is localized, as evidenced by discomfort felt when actively inflammatory joints are palpated. Peripherally focused therapies including nonsteroidal anti-inflammatory medications, injections, and surgery generally work well for nociceptive pain. Opioids may also be useful for treating acute nociceptive pain. (12)
- **Nociplastic pain:** A dysregulation of the central nervous system's pain processing pathways may be the cause of nociplastic pain, defined as pain with altered nociceptive processing (such as hypersensitivity) (13). In essence, this word is synonymous with more traditional terms like centralized pain or central sensitization. The term "nociplastic pain" is broad and likely encompasses a number of CNS pathways that lead to either reduced inhibition of pain, enhanced processing of pain signals, or both (14). Commonly known as chronic overlapping pain conditions (COPCs), prototypical nociplastic pain conditions include both localized, such as chronic temporomandibular pain disorders (TMDs), chronic primary bladder pain syndrome, irritable bowel syndrome (IBS), tension headaches, and chronic migraine headaches, and widespread, such as fibromyalgia (FM) (15).
- **Inflammatory Pain:** Inflammation in tissues can also cause pain. When tissue is damaged or infected, pro-inflammatory mediators like prostaglandins and cytokines are produced, which increase the sensitivity of

nociceptors and thus enhance pain perception. This type of pain is often linked with common diseases like autoimmune diseases, infections, and rheumatoid arthritis (16).

- **Psychogenic Pain:** This is also due to psychological factors, including mental illness or distress such as anxiety or depression. Psychological variables affect the perception and intensity of pain, which can make treatment and management difficult (17).

4. Mechanism of action for pain relief

This is what the brain feels as a culmination of a series of complex events that begin whenever tissues are injured or when dangerous stimuli are sensed. It includes physiological mechanisms that enable the body to recognize, communicate, and decipher pain signals, having a very important defensive function. The above is a comprehensive description of the mechanism of pain

- **Pain Perception (Nociception) stimuli:** When nociceptors, which are specialized nerve endings located in almost all body tissues, including skin, muscles, joints, and organs, receive noxious stimulating stimuli, pain sets in. Stimuli to nociceptors include:
  - Mechanical: Stimulation by direct compression, extension, or stretching of tissue slicing (18).
  - Thermal: Extreme temperatures.
  - Chemical: Inflammatory mediators- prostaglandins, bradykinin, and histamine (18). This process is called transduction, in which nociceptors convert mechanical, thermal, or chemical insults into electrical impulses when activated by adverse stimuli. The electrical signal is transmitted to the brain and spinal cord after passing through the nerve fibers (19).
- **Pain Transmission:** Through Electrical Signal Pains from the nociceptors are transmitted electrically to the spinal cord through the nerve fibers. Once it sees a threatening signal, the transmission of pain is controlled by two categories of nerve fibers mainly:Pain signals along with sharp, acute feelings are conducted through myelinated, fast conducting A-delta fibers. Their job is to develop such sudden, intense pains(20). C fibers: These slow-conducting, unmyelinated fibers transmit aching, throbbing, or dull pain. Once the primary damage has been sustained, they will continue to perceive pain.These pain messages go through the peripheral nerves to enter the dorsal horn of the spinal cord where the first synapse is made (21).
- **Processing and Modulation of the Spinal Cord:** Processing and regulating pain signals is a crucial function of the dorsal horn of the spinal cord. Neurotransmitters such as substance P, a peptide involved in pain transmission, and glutamate, an excitatory neurotransmitter, are released in this region, allowing pain signals to be transferred to higher brain regions.

Pain here can be interfered with the effects from descending circuits initiated from the brain. Neurotransmitter serotonin and endorphins release by raphe nuclei and the periaqueductal grey matter (PAG) prevent the feeling by inhibiting a pain signal. (22).

- **Ascending Pain Pathways:** Pain impulses are carried through ascending pathways from the spinal cord to the brain, with the most prominent one being the spinothalamic tract. After passing through the spinal cord, the impulses are received by the thalamus, which acts as a relay station and further transmits the pain information to other parts of the brain (23).
- **Perception and Response to Pain:** Finally, the brain perceives pain as a combination of emotional and sensory events. The limbic system and prefrontal brain combine the emotional and psychological responses to create a complete pain experience, while the somatosensory cortex determines the location and intensity of the pain. This can result in reactions such as heightened stress responses, increased heart rate, or disengagement from the aversive stimulus (24).
- **Central Sensitization and Chronic Pain:** Pain may become more enhanced in some instances. The central nervous system is sensitized when it becomes overly active, an issue referred to as central sensitization. Examples of such diseases include chronic pain and hyperalgesia in which pain develops even after the original injury heals or in reaction to stimuli that would not provoke pain (25).

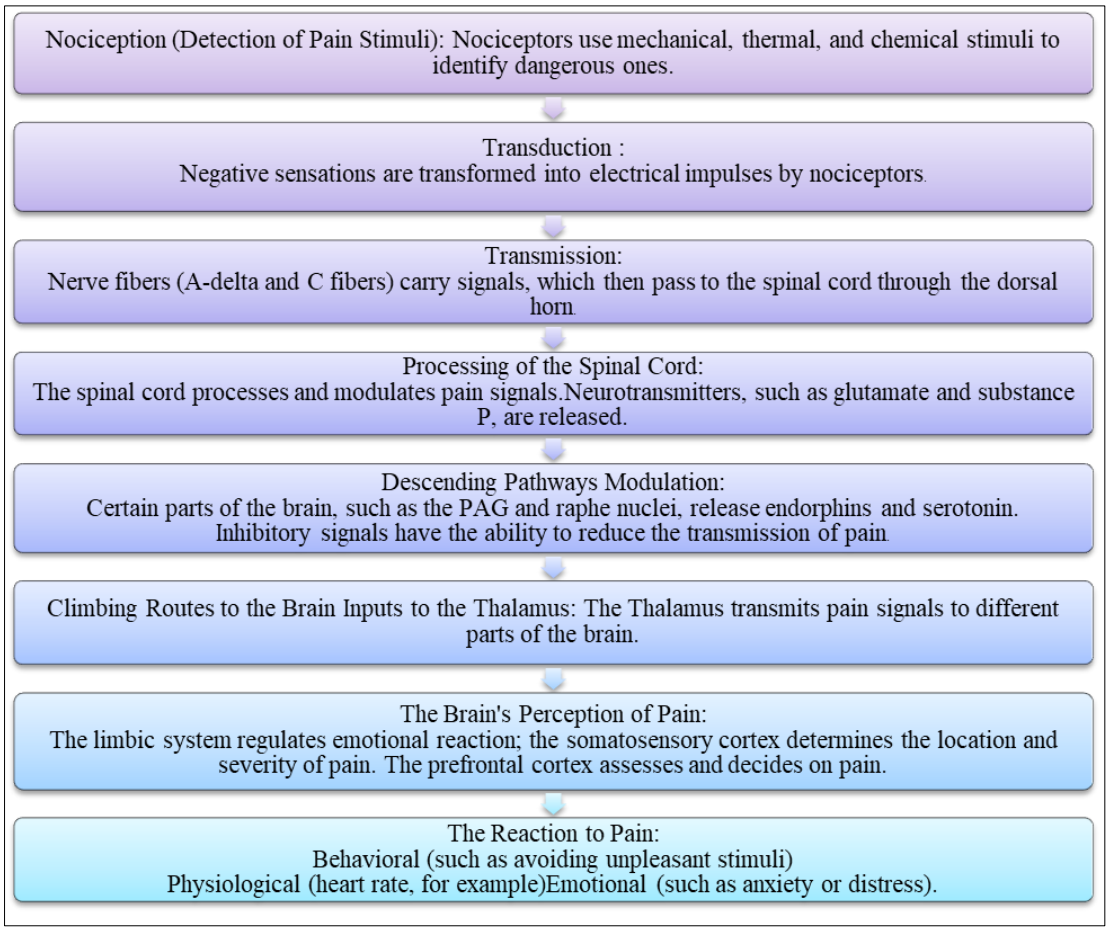

Figure 3 Flow Chart for Mechanism of pain

5. Treatments for pain relief

The approaches to pain control are various and the best therapy depends on the type of pain, its intensity, and the patient's general condition.

Allopathy or Conventional medicine: The basic principle of allopathic treatment is to counteract an ailment with medicine, surgery, or any other form of interference. Some common techniques in pain management under the allopathic approach include the following:

Pharmacological Interventions:

- **Analgesics:** For mid-level to mod pain, many of the most common drugs which are prescribed consist of acetaminophen or NSAIDs.
- **Opioids:** Strong pain can also be treated through prescription opioids in the form of morphine, codeine, and oxycodone but long-term intake is limited in such cases.
- **Antidepressants and Anticonvulsants:** Drugs like amitriptyline, gabapentin or pregabalin are used as treatments for such disorders as well as neuropathic or nerve pain.
- **Topical Agents:** To reduce localized pain, apply creams, patches, or ointments that contain lidocaine or capsaicin (26).

Figure 4 Image of Conventional Medicine

- **Physical Theory:** Physical therapy which includes stretches, exercises, modalities such as heat, ice, or ultrasound to increase the range of movement and reduce the pain, more so for the musculoskeletal and joint-related type of pain is also part of the allopathic treatment besides medicine. Anticonvulsant or antidepressant drugs like gabapentin is used for treating chronic or difficult pain, usually from nerve damage (27). Following conservative therapy, the surgical interventions of hip replacement, spine surgery, or nerve blocks may be indicated. Interventional treatments, like steroid injections in a joint or epidural injections, are also very commonly used to provide pain relief and decrease inflammation in the diseases, for example, arthritis. Allopathy focuses on dealing with the causation and pain management, and these are most of the times delivered in the combination of treatment protocols (27).
- **Homeopathy:** Homeopathy is a holistic medical approach that uses extremely diluted medications to heal patients, following the tenet that "like cures like." The goal of homeopathic treatments is to promote the body's natural healing processes.

5.1. Typical Homeopathic Pain Relief Techniques:

- ***Arnica montana*:** Frequently used to treat pain brought on by bruising, muscle strain, or trauma.
- ***Hypericum perforatum*:** Good for burning or shooting pains in the nerves.
- **Rhustox:** Used to treat stiffness, restlessness, and inflammation-related pain. For severe, stitching pain that gets worse with movement, bryonia alba is advised.
- ***Apis mellifica*:** Reduces swelling-related pain, especially after bug bites or allergic responses (28).

Figure 5 Image of Homeopathic tablet

Benefits: When given by a qualified professional, homeopathic therapies are individualized, non-invasive, and generally regarded as safe. When traditional treatments for chronic pain disorders don't work or have negative side effects, many patients turn to homeopathy.

Ayurveda: Ayurveda, the ancient Indian system of medicine, practitioners believe that pain can be treated using a multidimensional approach which includes the use of dietary practices, herbal medicine, lifestyle changes, and various therapies that work towards restoring balance in the body and mind. The core principle of Ayurveda is based on the three doshas Kapha, Pitta, and Vata working in a stable state. Dasohas imbalance is more likely to cause pain or diseases.

The objective of the therapeutic approach is to restore the harmonic balance, decrease inflammation and improve healing (29).

Figure 6 Image of Herb

Ayurveda employs different herbal remedies to manage pain in the body. For example, turmeric (*Curcuma longa*) is often applied to arthritic conditions and muscle tightness because of its anti-inflammatory properties. An herb known as ashwagandha (*Withania somnifera*) has the ability to relieve stress and inflammation related pain. Ginger is most commonly used for the treatment of pain related to inflammation as well as joints. In the treatment of osteoarthritis, an herb called boswellia or Indian frankincense has been found to be useful in pain relief. To treat chronic pain or musculoskeletal disorders, there is a common use of panchakarma detoxification therapy that consists of massage and oil treatments to remove excess waste and purify the tissues (30).

5.2. Various therapy for pain control

Physical Therapy and Rehabilitation: This is an indispensable part of comprehensive pain management planning for musculoskeletal, neurological, and chronic pain disorders. Aims of physiotherapy or rehabilitation are gaining strength, restoring flexibility, improving general mobility so that function could be regained with a reduction of pain and recurrences. (31)

- **Exercise therapy:** Exercise therapy includes various techniques, such as alleviating pain and increasing range of motion. The strengthening activities may include back and core exercises to manage chronic low back pain that focus on strengthening the muscles around joints or affected areas, reduce pain, promote stability, and prevent further damage. For stiffness, tightness, and muscular spasms caused by joint issues, stretching improves flexibility, eases discomfort, and reduces muscle tension. Walking, swimming, and cycling are low-impact aerobic conditioning exercises that enhance circulation, general fitness, and the production of endorphins, which naturally reduce pain. While trigger point therapy is used to treat muscular knots that cause tension and localized pain, manual therapy techniques such as joint mobility, manipulation, and soft tissue massage assist in relieving pain and muscle tightness (32). It has been proven to improve flexibility while easing discomfort caused by stiffness and tightness along with muscular spasms due to joint issues. Low-impact aerobic conditioning in the form of walking, swimming, and cycling enhances circulation and general fitness by producing endorphins, the body's own natural pain-relieving chemicals. While trigger point therapy is used to treat muscular knots that cause tension and localized pain, manual therapy techniques such as joint mobility, manipulation, and soft tissue massage assist in relieving pain and muscle tightness (32).
- **Thermal and electrotherapy**: Thermal and electrotherapy is often used for pain relief as well as aiding in tissue healing. Cold therapy is effective on acute injuries that reduce swelling, numbing pain, whereas heat therapy is useful on chronic pain and stiffness of muscles and also the circulation of blood. Low voltage electrical currents in TENS that is transcutaneous electrical nerve stimulation, is often utilized to treat the diseases such as arthritis and back pain. Ultrasound therapy makes use of sound waves to relieve spasms in the muscles, reduce inflammation, and promote healing of deep tissues. These therapies have been shown to be effective for both acute and chronic pain management (33).
- **Neuromodulation:** Neuromodulation is an approach to treat pain and other medical disorders in which nerve activity is modified via electrical or chemical stimulation. The mechanism of this treatment is achieved by convincing the neural system that it needs to change how it perceives pain signals or controls physiological

functions (34). The most common of these is the use of TMS or transcranial magnetic stimulation to stimulate the brain, and the blocking of pain signals through electrical impulses to the spinal cord, such as SCS. Another is deep brain stimulation or DBS for depression and mobility difficulties or PNS targeting a particular set of nerves for chronic pain. When traditional treatments like drugs fail or are associated with significant side effects, neuromodulation is commonly used (35).

- **Psychotherapy**: Is a therapeutic approach that assists people in managing emotional problems, mental health concerns, and life with other therapies, such as medicine, and can be conducted alone or in groups (36).

5.3. Few phytopharmaceuticals used for pain relief

The use of plant-based substances in therapy, or phytopharmaceuticals, offers an alternative method for treating pain. Herbal remedies that contain medicinal herbs and secondary metabolites such as flavonoids, alkaloids, and saponins have become viable substitutes because they can reduce pain, regulate the immune system, and protect cartilage.

- **Ginger:** Although ginger, or Zingiber officinale, has lovely blooms, herbalists have been using its tuberous rhizome as a spice and medicinal for the past 2,500 years, primarily in China and India. Most tropical nations are home to the plant.

Figure 7 Image of Ginger

Due to its anti-oxidant function, it can be used to treat cold and bacterial infections, muscle pain and swelling, arthritis, migraines, digestive and appetite issues, motion sickness prevention, postoperative nausea and vomiting, and hyperemesis gravidarum (37). The active ingredients in ginger include gingerols, particularly 6-gingerol (Figure 2). Though its exact mechanism of action is unknown, ginger's anti-emetic effects are thought to be brought on by either directly stimulating the gastrointestinal tract or by blocking serotonin in the gut or central nervous system (38). By preventing the metabolism of arachidonic acid, it has anti-inflammatory properties.

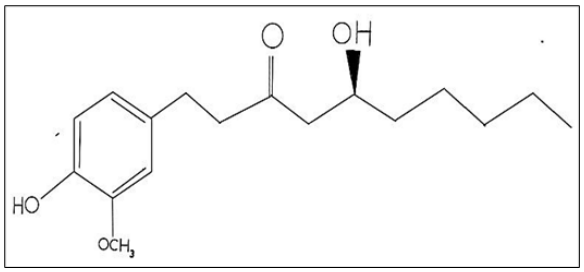

Figure 8 Structure of 6-gingerol

- **Turmeric:** Curcumin is an active polyphenolic chemical found in the rhizome of the turmeric plant, also known as *Curcuma longa* (Figure 3).

Figure 9 Image of Turmeric

It has long been utilized as an analgesic, antioxidant, antibacterial, and anti-inflammatory for wound healing (39). Interleukin (IL)-1 beta, IL-6, IL-12, interleukin (IFN) gamma, tumor necrosis factor (TNF)-alpha, and related AP-1, NF-kappa B, and JAK-STAT signaling pathways are among the inflammatory cytokines that curcumin can control. It has been used to treat autoimmune conditions such multiple sclerosis, inflammatory bowel disease, and rheumatoid arthritis because of its anti-inflammatory properties (40). Regarding medication interactions, it was discovered that giving breast cancer patients turmeric supplements during paclitaxel treatment improved their quality of life and pain ratings (41). Curcumin is an active polyphenolic chemical found in the rhizome of the turmeric plant, also known as *Curcuma longa* (Figure 4).

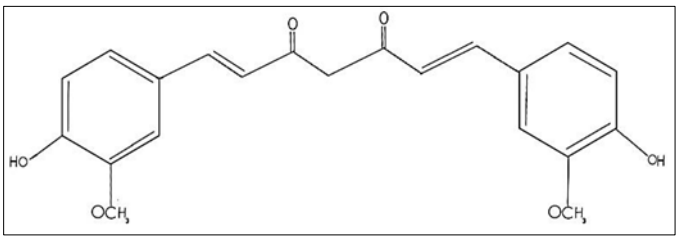

Figure 10 Structure of Curcumin

Clove: Native to Southeast Asia, clove (Syzygium aromaticum) is a popular spice and medicinal herb that is frequently used for its analgesic and anti-inflammatory qualities. Eugenol, clove's main active ingredient, is what gives it its analgesic properties (42).

Figure 11 Image of Clove

Eugenol is very useful for treating toothaches, muscular soreness, and other localized discomforts because it has been demonstrated to function by blocking pain receptors and lowering inflammation. Because it can numb the area and lessen discomfort from infections or dental operations, clove oil is frequently applied topically for pain relief and is also utilized in dental care (43). Numerous studies have shown that eugenol's overall efficacy in pain management is

influenced by its antioxidant and antibacterial qualities in addition to its analgesic benefits. Its calming qualities also make it helpful for reducing pain from ailments like muscle spasms and arthritis (44).

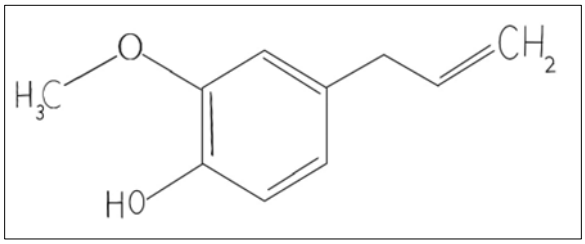

Figure 12 Structure of Eugenol

6. *Tectona grandis*

Originating in Burma and Central and South India, teak (*Tectona grandis*) is also found naturally in Thailand, Laos, and Myanmar. Since the beginning of time, plants have been used as essential medical resources. Natural product research aims to identify the medical benefits of plants by investigating current scientific understanding, customary use, and the identification of possible therapeutic compounds. Programs for lead optimization, which aim to create safe and efficient medications, employ phytochemicals as templates. A quarter of pharmaceuticals in affluent nations are derived from plants or their derivatives. Teak gained momentum because of its physical and aesthetic characteristics, pleasant appearance, superior and most admired timber quality, and durability in furniture manufacture and construction materials (45). The Lamiaceae family includes the tropical hardwood tree species teak (*Tectona grandis*). The mixed hardwood forests are home to this big deciduous tree. The tiny, fragrant white flowers of *Tectona grandis* are clustered in strong clusters, or panicles, at the tips of branches. Traditional Dai medicine has made extensive use of *Tectona grandis*. It is primarily found in tropical and subtropical regions of northern Thailand, India, Laos, and southwest China. It is a huge deciduous tree that can grow to a height of 40–50 m. Its brown or gray bark and strongly fluted trunk can reach a diameter of 2–2.5 m. According to earlier phytochemical studies, T. grandis was abundant in phenolic, steroids, phenylpropanoids, fatty esters, and other chemicals in addition to flavonoids and quinones but also included fatty esters, steroids, phenolic, and phenylpropanoids, among other substances (46). A variety of tree parts, such as the roots, bark, and leaves, have been used to treat pain. The analgesic properties of teak have also been validated by contemporary scientific studies. Research has demonstrated that in animal models, extracts from various teak tree sections can considerably lessen pain. Both acute and chronic pain have been reported to be effectively reduced by these extracts. It is thought that the presence of several phytochemical substances, such as alkaloids, terpenoids, and flavonoids, is what gives teak its analgesic properties (47).

Figure 13 *Tectona grandis*

7. Plant profile

Table 1 Plant Profile of *Tectona grandis*

Kingdom	**Plantae (*Tectona grandis*)**
Division	Magnoliophyta
Class	Magnoliopsida
Order	Lamiales
Family	Verbenaceae
Genus	*Tectona*
Species	*Tectona grandis*

8. Traditional use

Additionally, teak is regarded as a key component of some traditional medications. The numerous extracts from different portions of the fish have anthelmintic, expectorant, and anti-inflammatory qualities. It has long been used as an astringent, a remedy for helmintiasis, diabetes, leprosy, biliousness, bronchitis, and hyperacidity. A plaster made from wood powder has been used in traditional medicine to treat painful headaches and swellings. Swellings are also treated with them (48).

Ayurveda claims that teak wood is cooling, acrid, laxative, sedative for gravid uterus, and effective for treating dysentery, leucoderma, and piles. It has expectorant and anthelmintic qualities and quenches thirst. In folklore, T. grandis Linn. leaf extract is frequently used to cure a variety of wounds, particularly burn wounds (49).

Laxative, cooling, acrid, and sedative to the uterus during pregnancy; works well for piles, leukoderma, and dysentery. Wood-derived oil is the best for headaches, biliousness, and burning sensations, particularly when the pain is restricted to the liver. They are beneficial for urine retention and anuria.They treat bronchitis, urine discharge, and biliousness and are caustic, bitter, and dry. The oil made from the blooms is said to help treat scabies and promote hair growth in the Unani medicinal system. Because teak extracts have antibacterial and anti-inflammatory properties, they are used to treat skin conditions like rashes, eczema, and itching (50).

9. Distribution and description

It is sporadically found in the states of Madhya Pradesh, Maharashtra, Tamilnadu, Karnataka, and Kerala in Peninsular India below the latitude of 24°N. The species can be found in Myanmar all the way up to latitude 25°N. It naturally occurs in the watershed areas of the Mae Khong, Salween, and Chao Phya rivers in Thailand up to 17.5°N and between 97° and 101°E (51).

It is a large deciduous tree, 10-20 m tall; branchletsare 4-angled, densely clothed with yellowish grey tomentum. Leaves are opposite, ovate-elliptic toovate, 30-50 x 15-20 cm, cuneate at base. Flowers are small, whitish andbisexual. They appear in large panicles containing upto a few thousand flower buds,which open only few at a time during flowering period of 2-4 weeks(52).

Calyx in flower is2.5-3 cm long, in fruit enlarged to 2-2.5 cm or more, bladdery, enclosing the fruit. Fruit is a drupe with 4 chambers; round, hard and woody, enclosed in an inflated, bladder-like covering; pale green at first, then brown at maturity. Each fruit contains 0 to 4 seeds. Seeds are oblong, brown, enclosed in bony endocarp (53).

10. Phytochemical constituent

Natural chemicals found in the plant that may impart color, flavor, or resistance to pathogens are called phytochemical constituents. Examples include alkaloids, flavonoids, terpenoids, and phenolic acids. Many of them exhibit antibacterial, anti-inflammatory, and antioxidant properties that have been reported to be health benefits (54).

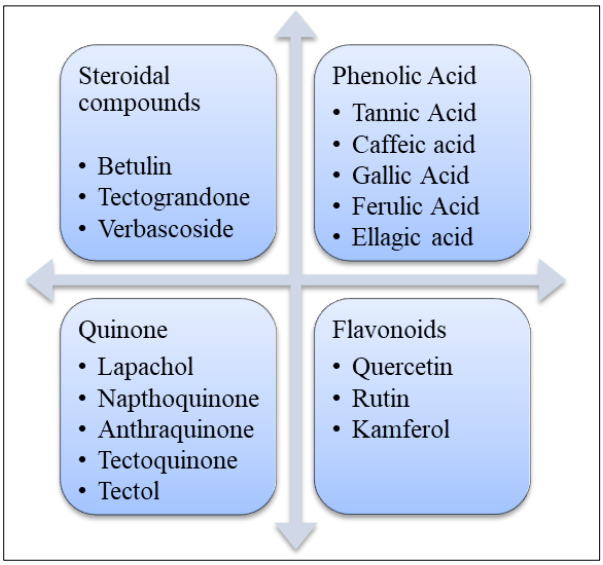

Figure 14 Different type of Phytochemical Constituent Present on *Tectona grandis*

Tectoquinone: Tectoquinone is one of the many bioactive phytochemicals with medicinal and therapeutic potential for strong analgesic effects, among others. The chemical formula for tectoquinone, a kind of naphthoquinone, is C15H10O3. It bears two quinone functional groups at positions 1 and 4 in the naphthalene ring structure. The structures of the compounds cause many of its pharmacological actions.

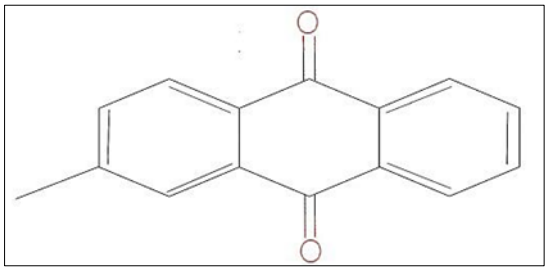

Figure 15 Structure of Tectoquinone

The anti-inflammatory and antioxidant activities of tectoquinone constitute the primary mechanisms behind its analgesic properties (51). Through its influence on inflammatory pathways, tectoquinone exerts its immense influence on the sense of pain. In most diseases-including chronic pain syndromes, muscle injuries, and arthritis-inflammation is the primary cause of pain. Tectoquinone works as an inhibitor that prevents the formation of mediators like prostaglandins and pro-inflammatory cytokines, crucial in the manifestation of pain. Tectoquinone works to decrease inflammatory pain and other discomforts as it reduces levels of these chemical mediators (55).

Tectoquinone is also an antioxidant and thus its analgesic effects are enhanced through the prevention of cellular damage and tissue injury through scavenging ROS and the subsequent reduction in oxidative stress. Antioxidant activity is also important in cases where oxidative stress causes inflammation and pain (56).

Further, through the modulation of neurotransmitters involved in pain transmission, tectoquinone may exert its effects on the CNS. It may exert a dual effect through central action that inhibits pain signals and peripheral action that decreases inflammation. This is evidenced by its ability to modify the pathways used by the CNS to transmit pain (57).

11. Tectoquinone's mode of action in the treatment of chronic pain

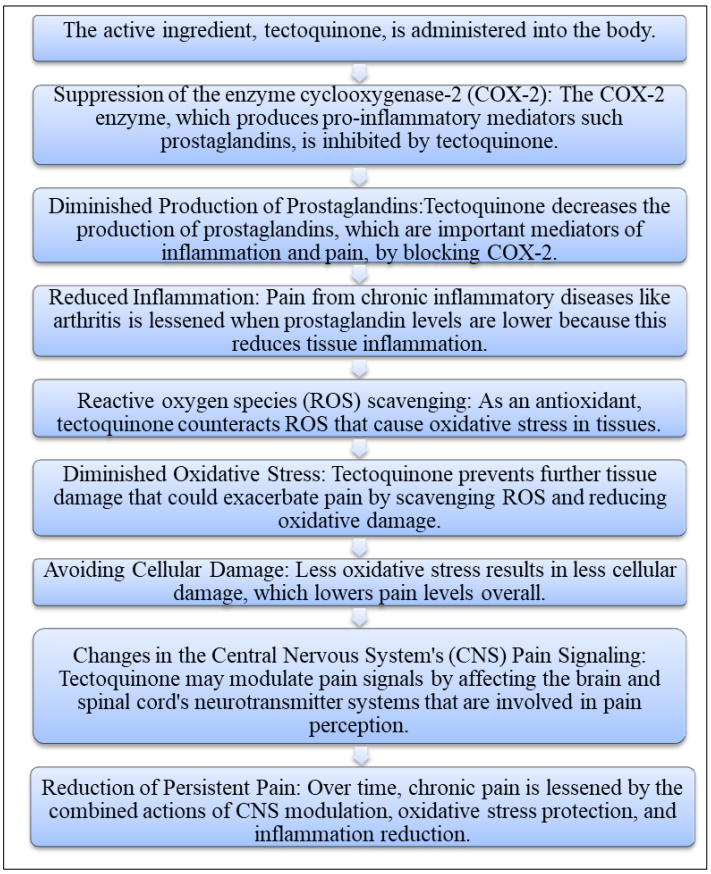

Figure 16 Mode of Action of Tectoquinone in the treatment of chronic pain

12. Few phytopharmaceutical based markted products for pain relief:

Table 2 Route of Administration, Product, and Phytochemical Constituent

S.no	Route of adimistration	Phytochemical constituent	Products
1	Topical	*Arnica Montana*	Numerous creams, gels, ointments
		Capsaicin	Creams, patches, sprays
		Menthol and Camphor	Creams, balms, lotions, liniments
		Essential Oil Blends	Roll-ons, sprays, massage oils
2	Oral Supplements	Turmeric (Curcumin)	Capsules, tablets, powders
		Ginger	Capsules, tablets, extracts, teas
		Boswellia (Indian Frankincense)	Capsules, extracts
		Willow Bark Extract	Capsules, tablets

13. Patentson *Tectona grandis*

Table 3 Patent on *Tectona grandis*

S no.	Patent Number	Title	Description	Applicant	Filling Date
1	CN106728433A	Pharmaceutical composition for preventing and treating insomnia	Discloses a Composition containing *Tectona grandis* among other herbal ingredients aimed at treating insomnia.	Jinan Haoyu Qingtian Medical Technology Company Limited	May 31, 2017
2	CN106728431A	Medicine composition for treating knee joint synovitis	Describes a pharmaceutical composition incorporating *Tectona grandis* for the treatment of knee joint synovitis.	Jinan Haoyu Qingtian Medical Technology Company Limited	May 31, 2017
3	CN106668346A	Pharmaceutical composition capable of preventing and treating thyroid gland diseases	Details a composition comprising *Tectona grandis* for the prevention and treatment of thyroid diseases.	Jinan Haoyu Qingtian Medical Technology Company Limited	May 17, 2017
4	CN106668337A	Pharmaceutical composition for treating optic atrophy	Describes a formulation including *Tectona grandis* intended for the treatment of optic atrophy.	Jinan Haoyu Qingtian Medical Technology Company Limited	May 17, 2017
5	CN106668336A	Pharmaceutical composition for treating otitis media	Discloses a composition containing *Tectona grandis* for the treatment of otitis media.	Jinan Haoyu Qingtian Medical Technology Company Limited	May 17, 2017
6	CN106540004A	Pharmaceutical composition used for treating diabetic retinopathy	Details a formulation incorporating *Tectona grandis* aimed at treating diabetic retinopathy.	Jinan Haoyu Qingtian Medical Technology Company Limited	March 29, 2017
7	CN106138463A	Pharmaceutical composition for treating advanced bladder cancer	Describes a composition containing *Tectona grandis* for the treatment of advanced bladder cancer.	Jinan Haoyu Qingtian Medical Technology Company Limited	November 23, 2016

8	CN106138462A	Medicinal composition for treating advanced colorectal cancer	Discloses a pharmaceutical composition including *Tectona grandis* for treating advanced colorectal cancer.	Jinan Haoyu Qingtian Medical Technology Company Limited	November 23, 2016

14. Conclusion

Pain is a very complex and diversified phenomenon that, to be successfully managed, demands an in-depth understanding of all its forms, causes, and mechanisms. Because many therapy options have been developed to reduce pain, including some traditional medicines, the quest for more natural and efficient alternatives led to the pursuit of phytochemicals. *Tectona grandis* is now promising to become a source of bioactive chemicals, especially tectoquinone, showing a great prospect in pain alleviation. Tectoquinone's medicinal use demonstrates the potential of using biochemical pathways for the alleviation of pain in the human body. The growth of marketed products that contain tectoquinone and related chemicals points toward an increasing requirement for natural sources of pain management. Current research and patents related to the drug also demonstrate the potential of tectoquinone as a useful addition to the pharmacological toolbox for pain management.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed

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