CHAPTER 12

Ethnopharmacological Strategies for Targeting Pain and Inflammation

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SUMMARY

The ethnopharmacological knowledge propagated over generations in Mediterranean areas. Recent interest in medical ethnobotany and the use of herbs and plants in treating different ailments has rejuvenated interest in herbal medicine, especially those transcendent across generations. By the mid-nineteenth century, plants had provided at least 80% of all medications. To prevent pain and inflammation-related ailments, traditional herbal medicines, NSAIDS and plant bioactive use is a widespread practice. Inflammation is characterized by redness, joint discomfort, stiffness, swollen joints, and reduced joint functionality. Pain is a complex and multifaceted ailment for treatment. Pain and inflammation both may be linked by cyclooxygenase enzyme for the synthesis and release of prostaglandins at the inflammatory site. In the present chapter, an attempt was made to unveil treatment approaches adopted for the management of pain and inflammation with anti-inflammatory and anti-analgesic properties as well as integration with modern medicinal practice. By the mid-nineteenth century, plants had provided at least 80% of all medications.

INTRODUCTION

Natural products for potential drug development promise to play a significant role in drug development initiatives in the future (Newman & Cragg, 2007). Whereas the conventional industrial model of drug discovery involves extensive bio-assay screening and the use of medium and high throughput screening systems for a particular target, ethnopharmacology does the opposite; it brings to the laboratory, compounds that are purported to be effective based on historical use of the medicinal plants.

The ethnopharmacologist investigates the pharmaceutical bases of culturally significant plants. Medicinal products for Traditional Chinese Medicine (TCM), European pharmaceuticals, and many medicinal products from traditional communities are also being researched using this strategy. So, working hypotheses derived from anthropological research are commonly utilized by ethnopharmacologists. They frequently employ working hypotheses developed from anthropological investigations. As a result, ethnopharmacology study is multidisciplinary, encompassing cultural anthropology, ethnobiology, and pharmacy (Etkin & Elisabetsky, 2005).

TRADITIONAL HERBAL MEDICINES

Traditional herbal medicine (TAHM) is one of the oldest natural remedies and the oldest folk treatment still practiced. Traditional medicine is primarily concerned with treating animal and human disorders with botanical remedies. TAHM drugs are developed by extracting parts from whole plants, bark, leaves, flowers, roots, seeds, and aerial portions of a certain herb or plant species. Extracts are prepared in paste form and applied topically to surface lesions such as painful swellings and fractures, decoctions and concoctions, tinctures, bowel movements, and inhalations (Bisi-Johnson et al., 2009). Semi-refined and highly refined preparations, analogous to compound formulations utilized in traditional Chinese medicine are not described (Guo et al., 2012).

Traditional medicines and medical procedures are passed down orally from generation to generation. By the mid-nineteenth century, plants provide at least 80% of all medications. After that, the pharmaceutical industry, and synthetic pharmaceuticals revolutionized, however using natural remedies was always an option. Even today, in Europe pharmacies, 25% of the pharmaceuticals are derived from plants. Indeed, natural product prototypes are being used in several pharmacological groups of medications. Examples of medical plants include atropine, artemisinin, colchicine, aspirin, vincristine, and vinblastine, etc. Most of these plant-derived pharmaceuticals were discovered through traditional treatments and folk knowledge (Gilani, 2005).

Inflammation

Inflammation is a multifaceted functional response and ongoing process that ensues from mechanical traumas, burns, microbial invasions, and other uncomfortable forcing functions Cyclooxygenases synthesize thromboxane's, and the 5-lipoxygenase for arachidonic acid metabolism (Wiart,

How to Cite: Farzeen I, N Zafar, M Shahid, M Yasmeen, H Noor, Afshan & A Ashraf, 2024. Ethnopharmacological strategies for targeting pain and inflammation. In: Zoology: Advancements and Research Trends (Ijaz MU, N Ehsan, M Imran & S Yousaf, eds): FahumSci, Lahore, Pakistan, pp: 88-97. ISBN: 978-627-7745-02-8. https://doi.org/10.61748/Zool.2024/12

2007). Acute inflammation is the first line of defense against danger. Acute inflammation is associated with increased leukocyte migration, capillary damage, and blood flow (Fig 1). Long-term, chronic inflammation is a debilitating immune-mediated illness has both genetic and environmental components. NSAIDs, disease-modifying anti-rheumatic pharmaceuticals, and biological agents are examples of synthetic drugs that can reduce acute and chronic inflammation (Jeoung et al., 2013). Herbal medicines may provide a greater risk-benefit ratio. Herbal plants also include various medicinally essential chemical components. The use of herbal medicine and plant-based medications is increasing due to their inexpensive cost, convenient availability, and minor adverse effects. Nature has endowed humanity with an enormous collection of herbal plants that have been used to treat ailments (Pei, 2001).

According to WHO, more than three-fourths of the world's population uses Traditional Natural Medicine (Uttra et al., 2018). Medicinal plants that possess pharmacological activities have further been categorized into areas that have been identified to contain high levels of components that may help reduce serious diseases. Garrido and colleagues stated that many chemicals found in plants are cytotoxic and antineoplastic, anti-inflammatory, and antibacterial such as acids triterpenes, flavonoids, phytosterols esters, and many others (Karbab et al., 2020).

Pakistan has around 6000 types of wild plants, with 400-600 of them being therapeutically useful. Approximately 84% of Pakistanis practiced traditional treatment (Goodman & Ghafoor, 1992) as well as over 50, 000-60, 000 hakims in rural areas. Exploration of herbal medicines' anti-inflammatory potential has resulted in large extracts and polyherbal formulations used to treat inflammatory illnesses (Uttra et al., 2018).

Pain and its pathology

Pain is a complex and multifaceted ailment, challenging to treat. Pain treatment is so important that it has been designated as a fundamental human right. With chronic pain, almost 1.3 million people are still suffering around the globe. In chronic pain, standard therapies such as non-steroidal anti-inflammatory medications, opioid and non-opioid analgesics, and corticosteroids are ineffective (Bashir & Colvin, 2013).

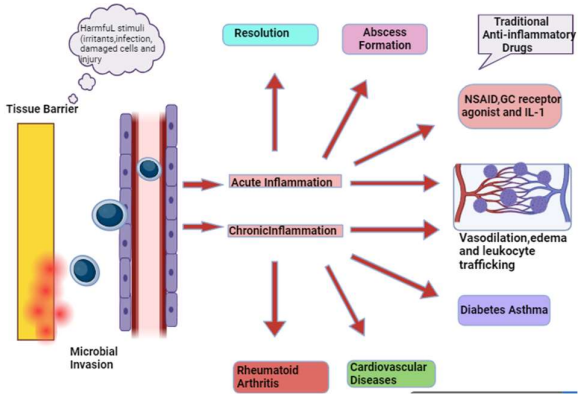

Fig 1. Strategical mechanism of inflammation and pain

For pain, four physiological mechanisms have been identified (Steeds, 2009).

1. Sympathetic nerves make pain through direct action of releasing chemicals at the site of referred pain or by constricting blood vessels supplying the sensory nerve fiber.
2. The brain analyzes wrong information coming from nerve endings in one of the body parts as coming from the nerve branch in the other body part owing to nerve branches.
3. The convergence-projection hypothesis says that skin and muscle nociceptors transmit pain sensation to a single nerve cell in the spinal cord. The brain is thus absolutely unable to judge where stimulation mechanical or otherwise comes from, whether it is gastrointestinal or somatic structures. As this has been illustrated it is clear that somatic and gastrointestinal sensory converge on spinal cord nociceptive neurons.
4. Convergence–facilitation theory postulates that the background firing of pain projection neurons in the spinal cord was amplified in the spinal cord. More specifically, the hyperactivity that leads to facilitation comes from other structures from the site of the myofascial trigger point which is the proposed source of homoeostatic nociceptor input into the dorsal horn and from the region of perceived pain and sensitivity.

Pain is classified into two types: rapid or fast pain and slow pain. Rapid pain is noticed one second or more after a stimulant strike, and its severity gradually increases over several seconds or minutes (Velu et al., 2018). Fast pain is also known as electrical, sharp, tingling, and stinging pain. Fast pain is mostly caused by mechanical or heat painful stimuli, whereas delayed and chronic pain is primarily caused by painful chemical stimuli (Newman & Cragg, 2007). As a result, chronic pain has significant consequences in daily living, such as anxiety, depression, sleep difficulties, and low quality of life (Sreekeesoon & Mahomoodally, 2014). Different stimulants and inflammatory mediators could activate pain receptors (Bahmani et al., 2014)

Conventional therapy has low reliability and tolerance issues with other negative consequences. These disadvantages have resulted in an increasing prevalence of TM, as supported by several researchers. TM application has different issues such as psychosocial aspects, ethnic and cultural traits, access to healthcare resources, and physical and medical issues. One of the most widely used techniques for treating and managing pain is herbal therapy (Yoon & Kim, 2013). Secondary metabolites in plants are primarily responsible for healing a variety of disorders. Secondary metabolites are plant ingredients or natural chemicals that have important pharmacological and toxicological effects on humans. It is reported that 1/10,000 examined chemicals may lead to an effective medicine in nearly ten years (Pirintsos et al., 2022).

Computational drug development has been increasingly important in recent decades, owing to low hazards, time, expenses, and resources as compared to traditional practices. This special area of development of computational methods

was motivated by the growth of computational power and the availability of AI-based methods, as well as globally accessible large datasets (Pirintsos et al., 2022).

STRATEGIES FOR PAIN AND INFLAMMATION

Nonsteroidal anti-inflammatory drugs (NSAIDs)

Nonsteroidal anti-inflammatory drugs (NSAIDs) are prescribed to treat fever, mild-to-moderate discomfort, and musculoskeletal diseases (Babaei et al., 2023). NSAIDs, or non-steroidal anti-inflammatory medicines, are widely utilized in medicines (Huynh et al., 2023). At the moment, aspirin, ibuprofen, naproxen, ketorolac, indomethacin, diclofenac, and celecoxib are the most widely used NSAID formulations (Sobhani et al., 2023). Since NSAIDs do not cause addiction and just relieve pain, their primary uses are in the treatment of rheumatological disorders and general pain reduction. Several major side effects such as renal damage, cardiovascular disease, hypertension, and gastrointestinal issues caused by NSAIDs. NSAIDs work well as anti-inflammatory and analgesic because they can stop prostaglandin synthesis at the cyclooxygenase enzyme level (Crofford, 2013).

The cytokines cause COX-2 to release prostaglandins (PGs), which cause inflammation and discomfort. Therefore, selective COX-2 inhibitors can be used to have an efficient anti-inflammatory impact without having any negative effects on the stomach or kidneys (Ali et al., 2023). In addition to their medicinal qualities, they can be harmful if used excessively or over extended periods. Overdosing on NSAIDs typically causes excessive inhibition of COXs, which lowers prostaglandin synthesis as part of its harmful action (Panchal & Sabina, 2023). Long-term NSAID use exacerbates the toxic state of the stomach because gastric acid and NSAIDs work together to increase the necrosis factor (Page et al., 2010).

NSAIDs cause topical mucosal damage and deplete prostaglandins generated from COX-1, which damages both the upper and lower gastrointestinal tracts (Sostres et al., 2010). Nonsteroidal anti-inflammatory medications (NSAIDs) may cause high blood pressure to become uncontrolled, increasing their risk of morbidity, death, and healthcare expenses (Aljadhey et al., 2012). Recent research indicates that using NSAIDs in the early stages of acute pain can prolong pain and inflammation and postpone its recovery, despite their effectiveness (Sisignano & Geisslinger, 2023).

Narcotic drugs

Narcotics are medications used to alleviate extreme forms of pain (Arome et al., 2014). For a very long time, severe acute and chronic pain has been treated with morphine and other opioid substances. The parent substance of many effective medicinal drugs with either antagonistic or agonistic effects on the opioid receptors is morphine. Three categories exist for narcotic drugs, synthetic derivatives with structures unrelated to morphine, natural opium alkaloid semisynthetic opioid (oxycodone, for example), and both (Arome et al., 2014). Owing to its pharmacological characteristics, opium's alkaloids are used to treat chronic cough, laxity, and cramps (Labanca et al., 2018). Accordingly, papaverine can dilate blood vessels in the heart, morphine, and codeine have analgesic effects, and noscapine suppresses coughing and may have anti-cancer effects.

Primarily, multiple receptors mediate the pharmacological action of opioids. When the terminal ending of the descending pain inhibitory fibers is stimulated, endogenous opioids such as enkaphalin and dynorphin are released. These opioids connect to receptors on the terminal of the ascending pain convey fibers and stop substance P from being released. Some of the side effects of narcotic analgesics include euphoria, tolerance, nausea, vomiting, and sleepiness (Arome et al., 2014).

Corticosteroids

Corticosteroids lowers inflammation levels and are also used as medications to treat conditions like lupus, asthma, arthritis, and allergies (Tiwari et al., 2023). Corticosteroids can be administered orally, topical administration, aerosol for inhalation, intravenously, intramuscularly, and intraarticularly (Kapugi & Cunningham, 2019). Mineralocorticoids and glucocorticoids are two types of corticosteroids (Ramamoorthy & Cidlowski, 2016). Hepatitis, allergic responses, and inflammatory bowel disorders are the usual conditions for which glucocorticoids are recommended. When treating cerebral salt depletion, mineralocorticoids are used in conjunction with other drugs (Arome et al., 2014).

Hydrocortisone secreted by the adrenal cortex, functions as an agonist of the corticosteroid hormone receptor. Synthetic glucocorticoids like dexamethasone are created by adding a fluorine atom to prednisolone (Hindmarsh & Geertsma, 2017). Due to their high lipophilicity, corticosteroids are highly accessible and mostly absorbed into the bloodstream via albumin and corticosteroid-binding globulin (Dubois et al., 2017). Non-genomic action does not require transcriptional mechanisms or protein production, nor control gene expression. Signal transduction pathways are activated by non-genomic activity. It is dependent upon the nonspecific interactions that occur between glucocorticoids and the cell membrane and between glucocorticoids and membrane-bound or cytosolic glucocorticoid receptors (Panettieri et al., 2019).

Immune-selective anti-inflammatory derivatives (ImSAIDs)

A class of peptides with anti-inflammatory characteristics is called Immune Selective Anti-Inflammatory Derivatives, or ImSAIDs. ImSAIDs function by modifying the immune cells that activate and migrate inflammatory cells, which are in charge of escalating the inflammatory response (Bao et al., 2006; Mathison et al., 2003). Potential veterinary medications for managing and lowering inflammation have been linked to ImSAIDs. Immune-selective anti-inflammatory derivatives are not connected to steroid hormones. ImSAIDs cause the immune system's inflammatory response to be amplified by activating and migrating inflammatory cells like neutrophils (Mathison et al., 2003).

HERBAL TREATMENT STRATEGIES FOR PAIN AND INFLAMMATION

The immune system's reaction in the body includes inflammation. Four primary symptoms are associated with inflammation: pain, redness, warmth, and swelling. According to Virshette et al. (2019), the most commonly given medications in the world for treating both acute and chronic pain caused by inflammatory progression are nonsteroidal anti-inflammatory medicines, or NSAIDs. The actions of NSAIDs are all connected to the inhibition of COX in the synthesis of prostaglandin and thromboxane (Pereira-Leite et al., 2017).

Humans have traditionally utilized nonsteroidal anti-inflammatory medicines or NSAIDs. Consequently, prolonged usage of these medications leads to adverse reactions and compromises the proper functioning of human organs, including the digestive and liver systems. Due to adverse effects that include gastrointestinal, renal, cardiovascular, and stomach lesions (Sostres & Lanas, 2016). Many different phytochemical substances with anti-inflammatory properties can be synthesized by plants as secondary metabolites (Verma, 2016). Numerous phytochemicals have been successfully employed to treat a wide range of human illnesses. The World Health Organization has cataloged over 20,000 species to identify every type of medical plant used worldwide (Saleem et al., 2020). Different medicinal plant with anti-inflammatory and antinociceptive potential are enlisted (Table 1).

***Aegle marmelos* (Rutaceae)**

The standard medication, indomethacin, was taken along with the water-based extract of Bilwa root bark. In the carragenan model, the result shown proved that suppression of anti–inflammatory activities. Several experimental investigations proved that the plant possesses anti-diarrheal, anti-microbial, anti-viral, anticancer, chemo preventive, anti-pyretic, ulcer healing, anti-genotoxic, diuretic, anti-fertility and anti-inflammatory properties. A. marmelos is said to possess other chemical constituents that include alkaloids such as aegeline, fragrine, and aegelenine; coumarins containing marmin, marmelide, psoralen, and imperatonin; and terpenoids including cineol and Caryophyllene (Mairuae et al., 2023).

***Cassia fistula* (Caesalpiniaceae)**

The bark extracts of *Cassia fistula* show potent anti-inflammatory effects in both the acute and chronic anti-inflammatory models of inflammation in rats. Reactive oxygen species (ROS) can be endogenous or exogenous, and they are associated with the pathophysiology of several diseases, such as diabetes, cancer, atherosclerosis, arthritis, and aging. The etiology of inflammatory disorders heavily relies on ROS. The principal anti-inflammatory components of *Cassia fistula* are flavonoids and bioflavonoids (Bhakshu et al., 2023).

***Sida cordifolia* (Malvaceae)**

Perennial *Sida cordifolia* belongs to the Malvaceae family of mallows. In folk medicine, *sida cordifolia* root extract is used to cure Balmorhea, asthmatic bronchitis, nasal congestion, and inflammation of the oral mucosa. It has been studied for its anti-inflammatory, anti-proliferative, and liver-growth-promoting properties (Kumar et al., 2024).

***Cuminum cyminum* (Apiaceae)**

Rats with paw edema brought on by carrageenan were used to test *Cuminum cyminum* volatile oil's anti-inflammatory characteristics. In contrast to the control group, the oil, at a dose of 0.1 ml/kg (intraperitoneal route), reduced rat paw edema in a dose-dependent manner (Feng et al., 2016).

***Anacardium occidentale* (Anacardiaceae)**

Anacardium occidentale possesses anti-inflammatory characteristics, and one of the most bioactive components associated with these properties is oleamide, which is found in leaf extract (Awakan et al., 2018).

***Jasminum sambac* (Oleaceae)**

The roots and leaves of *Jasminum sambac L*, which is extensively grown throughout India, have been used for many years as an antidote for inflammation, discomfort, and fever (Sengar et al., 2015).

***Hypericum perforatum* (St. John's Wort)**

It is also known as Millepertuis, John’s Wort (Wirth et al., 2005). It belongs to *Hypericaceae* family (Bilia et al., 2002). It is made from the leaves and flowers of the Hypericum perforatum plant. The two primary pharmacological components with benefits are hyperforin and hypericin (Hodges & Kam, 2002). Additionally, it has been discovered that combining SJW with sertraline, an antidepressant used to treat chronic pain, might result in nausea, vomiting, and anxiety. It shows antibacterial, antidepressant, wound-healing and anticancer (Wirth et al., 2005).

***Zingiber officinale* (Ginger)**

It is also known as African ginger, black ginger, gingerbread, ginger root, zingibers rhizome (Wirth et al., 2005). It is a common plant of the family Zingiberaceae (Francisco et al., 2010). The rhizome is used extensively in medicine (Deng et al., 2022). Ginger has a range of anti-inflammatory (Grzanna et al., 2005), and antioxidant properties. Two of the main bioactive components are shogaols and gingerols (Sang et al., 2020). It is used to treat nausea, vomiting, osteoarthritis, and ulcer healing, and to stop heart attacks and strokes (Dissanayake et al., 2020).

***Curcuma longa* (Turmeric)**

It is a common plant of the family Zingiberaceae family (Saboo et al., 2014). Curcumin is one of the active polyphenolic substances that may be discovered in the rhizome of the turmeric plant (Sahbaie et al., 2014). It is used for treatment of various illnesses such as cancer, coughs, diabetes,

diarrhea, inflammation, and skin disorders (Ayman et al., 2019). It shows anti-inflammatory (Kinney et al., 2015) and antidepressant activities (Aggarwal et al., 2013).

***Tripterygium wilfordii* (Thunder God Vine)**

It belongs to the Celastraceae family (Goldbach-Mansky et al., 2009). It possesses immunosuppressive, and anti-inflammatory qualities (Canter et al., 2006). One of *T. wilfordii's* main bioactive metabolites is the pentacyclic triterpenoid celastrol, which possesses a variety of biological characteristics such as immunosuppressive, anticancer, antioxidant, and anti-obesity activities (Xu et al., 2019). Although the plant is poisonous, its root pulp contains several medicinal chemicals, including steroids, alkaloids, and terpenoids (Brinker et al., 2007). Thunder gods vine a potential new treatment for rheumatoid arthritis (Song et al., 2020).

Tanacetum parthenium (Feverfew)

It belongs to the Asteraceae family (Pareek et al., 2011). Its active agent is the parthenolide within the leaves (Sun-Edelstein & Mauskop, 2009). It has historically been used to treat fever, inflammation, stomachaches, and migraine headaches. It shows biological qualities like antibacterial, anti-inflammatory, and anti-cancer (Pareek et al., 2011).

***Salix* (Willow Bark)**

It belongs to the Salicaceae family (Mahdi, 2010). The health benefits of willow bark, specifically its antiproliferative, analgesic, antipyretic, and anti-inflammatory qualities, have been acknowledged (Tawfeek et al., 2021). It contains phenolic acids including salicylic acid (Warmiński et al., 2021). Bark or leaf extracts from willow trees are used to treat common fever, discomfort, and inflammation (Mahdi, 2010).

***Cinnamomum* (Cinnamon)**

Cinnamomum is also known as Cinnamon bark (Wirth et al., 2005). It is a member of the family Lauraceae. The bark, leaves, blossoms, fruits, and roots of the cinnamon tree are all used in medicine (Shen et al., 2002). Cinnamon aldehyde is the basic compound found in the cinnamon bark. There have been numerous recognized health benefits of cinnamon due to its high antioxidant content. Because of the characteristics of its bioactive components, it has an impact on diabetes as well as neurological, microbiological, and cardiovascular illnesses (Gruenwald et al. 2010).

***Syzgium aromaticum* (Cloves)**

It is also known as Caryophylli (Wirth et al., 2005) and belongs to the Myrtaceae family (Milind & Deepa, 2011). Eugenol is the primary bioactive component of cloves (Cortés-Rojas et al., 2014). One of the essential foliage sources of phenolic chemicals is cloves (Neveu et al., 2010). Cloves are known to possess a wide range of bioactivity properties such as antioxidant, and antimicrobial properties (Idowu et al., 2021). Considerable volumes of volatile oil used in medications are found in cloves which is mostly restricted to the plant's aerial portions (Arshad et al., 2014; Hussain et al., 2017).

***Mentha arvensis* (Japanese Mint)**

It is a member of the Lamiaceae family (Salehi et al., 2018). Mint infusions help relieve pain and reduce swelling. Mint extracts provide anti-inflammatory, antibacterial, antiviral, anticancer, and antioxidant properties (Balakrishnan, 2015). Alkaloids, flavonoids, polyphenols, tannins, cardiac glycosides, and eugenol are the main ingredients of *M. arvensis* (Malik et al., 2012). It has been used as a folk cure for nausea, bronchitis, anorexia, ulcerative and liver ailments (Moreno et al., 2002). Their leaves and stems are primarily used in medicine (Srivastava et al., 2003).

***Brassica juncea* (Mustard)**

Mustard also commonly known as Chinese mustard. It belongs to the cruciferous family (Lin et al., 2011). It has bioactive ingredients like glucosinolates (Kim et al., 2007). The overall phenolic content and antioxidant activity of mustard sprouts are high (Pant et al., 2020). Cultivars of mustard showed significantly improved antioxidant activity (Li et al., 2023). It is utilized for aperitif, digestive, and appetizing purposes (Kumarasamy et al., 2004).

***Panax quinquefolius* (Ginseng)**

Ginseng is the root of the Araliaceae family (Choi et al., 2013). Ginsenosides, or thirty triterpene glycosides, are the bioactive substances found in ginseng. It can help the body regain physiological functions after exposure to stressful or painful stimuli (Kim et al., 2013). Asian ginseng is the most familiar herbal medicine which has been used as a tonic, sedative, anti-fatigue, or anti-gastric ulcer drug, and also has antidiabetic and antitumor activities (Shin et al., 2006). Panax ginseng root is regarded as the most significant component of the plant (Attele et al., 2002).

Integration with modern medicine and healthcare system

Three major categories have been used to categorize diseases, traditional or indigenous medicine, Western medicine and self-limiting and unaffected by any of these methods (Pizzorno & Murray, 2020). Since prehistoric times, humans have used natural products, such as plants, animals, microorganisms, and marine organisms, in medicines to alleviate pain and treat diseases. Every society has used traditional medicine to some extent. Words like "folk medicine" and "indigenous medicine" The terms "African, Asian, or Chinese medicine" are frequently used to characterize current customs. A World Health Organization (WHO) research on traditional medicine states that almost 70% of people in underdeveloped nations, particularly in Africa, rely on medicinal plants to address their medical needs (Karunamoorthi et al., 2013). In African societies, traditional

Table 1. Medicinal Plants with anti-inflammatory and anti-nociceptive bioactives

Plant Name	Plant Parts	Chemical components	Activities	Uses in	References
Aegle marmelos (Rutaceae)	Root bark	Alkolids, cumarins, terpenoids	anti-inflammatory activities	diarrhoea, cancer	Mairuae et al., 2023
Cassia fistula (Caesalpiniaceae)	Bark Extract	flavonoids and bioflavonoids	anti-inflammatory	diabetes, cancer, atherosclerosis, arthritis, aging	Bhakshu et al., 2023
Zingiber officinale (Zingiberaceae)	Root extract	Phenolic and terpene	anti-inflammatory, antioxidant, antiviral	nausea, vomiting, osteoarthritis, and ulcer healing	Shimoda et al., 2010
Sida cordifolia Linn. (Malvaceae)	Root extract	alkaloids, sterols, sugars, glycosides, phenols	anti-inflammatory, anti-proliferative, and liver-growth	blenorrhea, asthmatic bronchitis, nasal congestion	Kumar et al., 2024
Ajuga laxmannii (Lamiaceae)	Leaf and root extract	Chlorogenic acid, coumaric acid, caffeic acid, rutin, apigenin, quercetin	anti-inflammatory properties	Cancer and diabetes	Toiu et al., 2018
Syzygium caryophyllatum (Myrtaceae)	Root leaves extracts	terpenoids, carotenoids, flavonoids, coumarins, saponins,	anti-microbial, antioxidant, antidiabetic, anticancer activities	Cancer, diabetes	Heendeniya et al., 2018
Leonotis ocymifolia (Lamiaceae)	leaf extract	(Z)-β-ocimene, nonanal, β-caryophyllen, α-humulene	anti-infalmmatory	Inflammations and pain	Alemu et al., 2018
Cuminum cyminum (Apiaceae)	Seeds extract	Cuminaldehyde	anti-inflammatory	Inflammations and pain	Yin et al., 2020
Dendropanax morbifera (Araliaceae)	Leaf extract	quercetin, myricetin, rutin, resveratrol, chlorogenic acid, catechin, and ferulic acid	anti-inflammatory	Inflammations, cancer	Noh et al., 2015
Nicotiana tobacum (Solanaceae)	Leaf extract	4-vinylguaiacol, 1,8-cineole, acetaldehyde, alkaloids, anabasine, nicotinic acid, acetophenone, nicotine	antispasmodic, discutient, diuretic, emetic, expectorant, irritant, narcotic,	Cancer, diabetes	Azab et al., 2016
Anacardium occidentale (Anacardiaceae)	leaf extract	Oleamide	anti-inflammatory	Inflammations	Awakan et al., 2018
Linn, *Jasminum sambac* (Oleaceae)	roots and leaves	Alkolids, flavonoids	anti-inflammatory	India, inflammation, discomfort, and fever	Sengar et al., 2015
St. John's Wort (Hypericaceae)	leaves and flowers	Hyperforin and hypericin	antibacterial, antidepressant, wound-healing and anticancer	chronic pain, might result in nausea, vomiting, and anxiety	Bilia et al., 2002; Hodges & Kam, 2002
Ginger (Zingiberaceae)	Rhizome	shogaols and gingerols	anti-inflammatory, antioxidant properties	nausea, vomiting, osteoarthritis, ulcer healing	Francisco et al., 2010; Deng et al., 2022
Turmeric (Zingiberaceae)	Rhizome	polyphenolic substances	anti-inflammatory antidepressant activities	cancer, coughs, diabetes, diarrhea, inflammation and skin disorders	Saboo et al., 2014
Thunder God Vine Celastraceae family	Root pulp	pentacyclic triterpenoid celastrol	Immunosuppressive, and anti-inflammatory qualities	rheumatoid arthritis	Xu et al., 2019; Song et al., 2020
Feverfew Asteraceae family	Leaves	Parthenolide	antibacterial, anti-inflammatory and anti-cancer	fever, inflammation, stomachaches, and migraine headaches	Sun-Edelstein & Mauskop, 2009
Willow Bark (Salicaceae)	Bark or leaf extracts	Salicylic acid	antiproliferative, analgesic, antipyretic, and anti-inflammatory qualities.	common fever, discomfort, and inflammation	Mahdi, 2010; Tawfeek et al., 2021
Cinnamon (Lauraceae)	The bark, leaves blossoms, fruits, and roots of the cinnamon tree	Cinnamon aldehyde	Antioxidant	diabetes as well as neurological, microbiological, and cardiovascular illnesses	Gruenwald et al., 2010
Japanese Mint (Lamiaceae)	leaves and stems	Alkaloids, flavonoids, polyphenols, tannins, cardiac glycosides,	anti-inflammatory, antibacterial, antiviral, anticancer	nausea, bronchitis, anorexia, ulcerative and liver ailments	Balakrishnan, 2015
Mustard (Cruciferous)	Mustard sprouts	glucosinolates.	Antioxidant activity	Appetizing, digestive, and aperitif	Pant et al., 2020
Ginseng (Araliaceae)	Root	Ginsenosides, or thirty triterpene glycosides	tonic, sedative, anti-fatigue, or anti-gastric ulcer drug, antidiabetic and antitumor activities	stressful or painful stimuli	Choi et al., 2013

medicine is commonly employed for chronic diseases, psychological and social disruptions, reproductive system issues. According to the WHO, traditional medicine encompasses knowledge, skills, and practices based on

cultural theories and experiences, used for health maintenance, prevention, diagnosis, and treatment of physical and mental illnesses. It adopts a holistic approach, often involving the use of herbs or rituals, emphasizing the spiritual and natural aspects of treatment. The period of "modern" pharmaceuticals began at the start of the nineteenth century. Young German pharmacist Friedrich Serturner extracted morphine, the first pharmacologically active substance, from the poppy plant in 1805 (Seddon, 2009).

There seems to be a limit to the amount of progress that can be made in the development of novel pharmaceuticals using only contemporary technologies. Since the 1980s, the pharmaceutical industry has sought to use combinatorial chemistry and high-throughput synthesis in the creation of new medications (Akram et al., 2023). Between 1981 and 2002, natural inventions significantly contributed to the creation of innovative pharmaceuticals, particularly in exploration of new chemical compositions. Medicines derived from natural products played a crucial role during this 22-year period. This influence was particularly evident in the field of antihypertensive medications, where approximately 64% of newly synthesized pharmaceuticals were based on natural product structures (Gassmann et al., 2008).

The diffusion of modern Western medicine in most of the developing regions has both advantages and disadvantages. TM constitutes an essential part of Indigenous health care and health management since it was practiced before modern scientific medicine took its root through scientific and methodical advances which have greatly enhanced life span and decline in death rates have been of great importance in the society (Ebrahimnejad, 2009). Subsequently, natural items were reduced to relatively low importance with the innovation of synthetic approaches. However, natural sources have been employed hitherto and are instrumental in the development of new drugs (Newman & Cragg, 2016). Herbs could be useful for the development of some forms of medications, and this applies to antihypertensive, anticancer, and antimigraine medications. It would be impossible to overemphasize the importance of traditional medicine in the development of modern pharmaceuticals. In conventional medicine, one herb or a combination of herbs may contain many phytochemicals such as flavonoids, terpenoids, alkaloids, and several others. In general, these substances act singly or synergistically provide the required pharmacology effect (Yuan et al., 2016).

Modern medicine was introduced to China in the sixteenth century, but it did not develop significantly until the nineteenth century. Prior to this period, Traditional Chinese Medicine (TCM) dominated medical care and continues to play an important role now, undergoing steady improvement. A medical system founded on knowledge obtained via a scientific method is known as scientific medicine, sometimes known as "orthodox medicine" (Enebeli et al., 2021). Like traditional medicine, scientific medicine aims to preserve and improve the physical well-being of society's members.

Today's scientific doctors approach the patient (body) as if it were a separate entity, and they think the body is capable of repairing itself by utilizing potent artificial substances to disrupt its natural balance. This action contrasts with the traditional medical approach, which holds that every ailment must be treated holistically, utilizing natural resources that the body has evolved to utilize and cure (Opoku et al., 2013).

Globally, the WHO recognizes around a hundred traditional medical practices, each deeply rooted in cultural and regional contexts. Examples include herbal medicine in Sweden, acupuncture in China, shiatsu in Japan, magnetic healing in France, Heilpraxis in Germany, and Sowa Rig-pa in Tibet and Bhutan (Kala, 2017). In the Indian subcontinent, traditional systems like Ayurveda, Siddha, and Naturopathy continue to play a significant role in treating various ailments. Many of these traditional healthcare systems are plant-based, and people worldwide rely on them for primary healthcare (Payyappallimana, 2010).

There are several obstacles to overcome when combining traditional and modern medicine since they are practiced, assessed, and managed differently. Certain facets of traditional medicine, which are grounded in moral, spiritual, and other fundamental ideas, cannot be successfully incorporated into contemporary scientific medicine. It will be challenging to merge practices like ritual cleaning, incantation, and divination into contemporary scientific medicine. On the other hand, the health care delivery system can benefit greatly from the integration of both systems. It provides benefits to both parties in return and advances our understanding of general healthcare for the benefit of society as a whole. Additionally, patients will feel secure since doctors will analyze their physical, emotional, and spiritual health needs, and they will quickly determine how to cope with different illnesses (Ross, 2009). This is not meant to disprove current worries about the spiritual requirements of patients receiving medical care in modern times. The integration of diverse healthcare systems presents numerous advantages, particularly in enhancing overall healthcare, especially for underserved rural populations (Marcin et al., 2016). Through this integration, practitioners' skills are enhanced, and information on basic healthcare may be shared more easily. However, challenges arise due to fundamental differences in the underlying philosophies of life, health, and disease across various medical systems. Nomenclature discrepancies, particularly in disease classification, pose a significant hurdle, with healers often using generic terms that encompass both benign and malignant conditions.

To overcome these challenges, there is a pressing need for improved communication, improved terminology definitions, and reliable techniques for assessing therapeutic approaches. However, because modern scientific health care is expensive, people are dependent on traditional medicine, which plays a crucial complementary role in the delivery of healthcare (Asakitikpi, 2019). Scientific medicine, recognized and heavily funded by the state, has become the official medical system, while traditional medicine relies on individual practitioners for sustenance. Research suggests that consumers prefer traditional medicine because of its availability, affordability, and accessibility in addition to its effectiveness.

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