



Review on Analgesic and An Anti-Inflammatory Properties of Polyherbal Drugs

Keshav Deepak Ghadigaonkar¹, Vivek Bhaskar Garje², Saiil Bhaskar Ghodvinde³, Kavita Harishchandra Guhe⁴, Ashwini Rampyare Gupta⁵, Prof. Swati Haridas Pawar⁶

^{1,2,3,4,5} Student, Ideal Institute of Pharmacy, Posheri, Wada, Maharashtra.

⁶ Associate Professor, Ideal Institute of Pharmacy, Posheri, Wada, Maharashtra.

DOI: <https://doi.org/10.55248/gengpi.5.0324.0918>

ABSTRACT

Polyherbal drugs, composed of a synergistic blend of plant-based components, have garnered increasing attention for their potential therapeutic applications in managing pain and inflammation. This review delves into the multifaceted landscape of polyherbal formulations, exploring their analgesic and anti-inflammatory properties. The amalgamation of diverse botanical compounds within these drugs offers a holistic approach to addressing conditions associated with pain and inflammation. The abstract examines the existing body of research, shedding light on the efficacy, safety considerations, and challenges associated with polyherbal interventions. As the boundaries between traditional knowledge and modern science blur, this review navigates through the intricate interplay of polyherbal drugs in the realm of pain and inflammation, underscoring their potential impact on future healthcare practices. And this review also help to know about the detailed information about anti inflammation and analgesic properties and get to know about process , mechanism behind the inflammation. Information of cardial signs and causes of inflammation is also there for more information. Using this review various novel drugs and technique are found and help to improve in medication.

Keywords: Analgesic, Anti-Inflammatory, Herbs, Natures, Ayurveda, Relive, Charaka Samhita, Diseases, Indian Medicine, And Healthy Life.

1. Introduction

Since from ancient time we used a herbal medicines because of less side effect, less adverse effect ,less effect etc.. India has a rich history of traditional system of medicine based upon six systems, out of which Ayurveda stands to be the most ancient, most widely accepted, practiced and flourished indigenous system of medicine. The other allied systems of medicine in India are Unani, Siddha, Homeopathy, Yoga and Naturopathy. history. Archaeological evidence indicates that the use of medicinal plants dates back to the Paleolithic age, approximately 60,000 years ago. Written evidence of herbal remedies dates back over 5,000 years to the Sumerians, who. ince From Ancient Period Of Time, People Are Aware Of The Use Of Plants For The treatment.

1.1 Inflammation, Pain and Fever

Inflammation is a biological miracle and part of the complex reply of vascular tissues to various damaging stimuli/inputs for e.g., pathogens, damaged cells/tissues, or irritants [1]. Inflammation is a composite and active defensive phenomenon of the body to remove the harmful stimuli and to recruit the healing process by stimulating several body processes. This process generally starts with the defense of the body against injurious pathogens or micro-organisms. In biological response, inflammation is not identical to an infection, even inflammation is caused by infection.

Without this protective process, our body would struggle to heal wounds and fight infections effectively. When inflammation happens, it can cause damage to tissues by releasing certain chemicals. This leads to widened blood vessels, increased permeability, fluid buildup, and activation of pain nerves, resulting in the usual signs like heat, redness, swelling, and pain. Similarly, chronic inflammation can contribute to various ongoing issues like hay fever, rheumatoid arthritis, and atherosclerosis.

Inflammation is confidential as any acute or chronic inflammation based on time and severity. Acute inflammation characterizes the initial first response of the body to damaging inputs stimuli and is accomplished by more movement of plasma and leukocytes from the blood into the location of the injury. A cataract of biochemical involved in this rejoinder and circulates and matures the several inflammatory cascades, connecting the local vascular & immune systems along with various cells into the site of injury. Prolonged inflammation which is also known as chronic inflammation outcomes to a progressive modification in the cell's types present into the site of inflammation and is categorized by concurrent destruction and healing of the tissue from the inflammatory cascade.

1.2 Types of inflammation

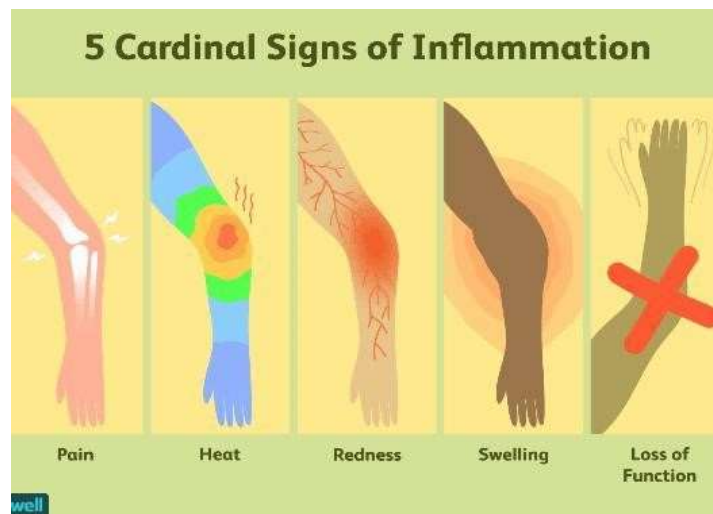
Inflammation can be classified into two categories :

A) Acute inflammation

B) Chronic inflammation

A) Acute inflammation: Acute inflammation usually viewed as therapeutic inflammation is the preliminary response of the immune system in contradiction of exterior pathogens and injury of tissue. It is a rapid self-limiting process that lasts for short period and helps the body ward off infections. This response is mediated by eicosanoids and vasoactive amines which raise the movement of plasma and leukocytes at the site of injury. Acute inflammation generally takes place within minutes or at most hours after tissue injury. The classical seals of acute inflammation are blushing, heat, pain, Edema, and loss of function It's a short period process and mainly considered by the exudation of fluids and plasma proteins and the passage of leukocytes such as neutrophils on a high level into the injured area. This reply of acute inflammation is helpful to the host defense mechanism result in the killing of microbes such as bacteria, viruses, es, and parasites while still allowing wound maintenances [32].

B) Chronic inflammation: Injury by these cells Further, chronic inflammation can also lead to a number of other Chronic inflammation is a type of long duration inflammation (workweeks or months) where inflammation, tissue, or nerve injury then attempt at repair co-exist in changing mixtures. It is of a more protracted duration and histological considered by the existence of lymphocytes and macrophages, which consequences in fibrosis and tissue necrosis. The development from acute inflammatory response to chronic inflammatory response as in many most commonly up human diseases are broadly watched due to excess of pro-inflammatory mediators. In chronic inflammation, inflammatory response and tissue damage is mainly induced by several inflammatory mediators generated through up-regulation of inducible pro-inflammatory genes, such as cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (INOS). During the inflammatory process, both the inducible pro-inflammatory genes produce large amounts of the proinflammatory mediators like nitric oxide and prostaglandins, respectively. In chronic inflammation diverse pro inflammatory cytokines and some growth factors are bent, results in enrolment of sophisticated order immune cells such as leukocytes, lymphocytes and fibroblasts[30].



Cardinal signs of Inflammation

1.3 Cardinal signs of inflammation

There are various signs of inflammation as per the following.

1. **Redness:** redness is also known as rubor. Acutely different inflamed tissues are appearing like red for example skin affected by sunburn, also cellulitis due to bacterial infection, or another acute conjunctivitis. This is due to the dilation of blood vessels within the damaged area[30].
2. **Heat:** Heat is also called color. An increase in the body temperature in the part of the skin generally occurs.it is due to the increased in the blood flow resulting in vascular dilation and the delivery of warm blood to the particular area or region systemic fever which result from some of the different chemical mediators of inflammation also contributes to the surrounding temperature[32].
3. **Swelling:** Swelling is also known as a tumour. The tumour results from Edema, accumulation of fluid in the extravascular space as part of the fluid exudates, and to a much lesser extent from the physical mass of the different inflammatory cells migrating into the various region of the body.[32].

4. Pain: it is also called dolor. Pain is one of the known features of acute inflammation. It results partly from the stretching and in the particular form of the pus under pressure in the abscess cavity. Some of the chemical mediators include bradykinin, various types of prostaglandins, and serotonin are known to induce pain and inflammation[30].
5. Loss of function: A well-known consequence of the inflammation was added by the Virchow to the list of features drawn up by Celsus. Movement of the various inflamed regions is consciously and reflex inhibited by pain while severe swelling may physically immobilize the tissue.[32]

1.4 Causes of inflammation:

Generally, inflammation the process is initiated by a variety of various physical reactions which are triggered by the immune system in response to the physical injury or infection. There are several different other factors that may initiate the inflammation process are discussed below[32].

- A) Hypersensitivity reaction: The various hypersensitivity reactions may take place when an altered state of immunologic responsiveness leads to improper or unnecessary immune reactions which damage the different sites of tissues.
- B) Microbial infections: Microbial infection is one of the most common causes of the inflammation process. Micro-organisms including fungi, viruses, bacteria, protozoa, and other parasites. These organisms lead to the death of a particular cell by the intracellular multiplication and either leads explosion of the cell. On the other hand, bacterial micro-organisms release different specific toxins either exotoxins or endotoxins.
- C) Physical agents: Various physical agents or physical reactions such as trauma, ionizing radiation, or UV, excessive cooling or burns which maybe leads to tissue damage that means they initiate the inflammation process. Corrosive or toxic chemicals are also effective in inflammation for example various acids, oxidizing agents, alkalis extra. This corrosive chemical leads to tissue damage that leads directly to inflammation.
- D) Tissue necrosis: Death of tissue due to the lack of oxygen or the nutrients supply leads inadequate blood flow to the body is a potent inflammatory stimulus.

1.5 Process of Inflammation:

Inflammation is a generally localized defensive response of the body to various allergic or chemical irritation, infections and injury. When a microorganism infection is established within the body, the aim of the system is to manage or eradicate it. There may be several "triggers", which will spur the system into action. The cardinal signs of inflammation resulted by blood vessels dilation leading to an enhanced flow of blood and from augmented intracellular spaces results in the movement of various substances such as leukocytes, fluids and protein into the site of injury. This is very important to understand the role of various chemical mediators of inflammation. These mediators' products are those generally released as plasma proteins, or that originate from different cells types like mast cells, neutrophils platelets, and monocytes/macrophages. These mediators, called proinflammatory factors, are activated by things like allergies, chemicals, infections, or injuries. They decide how severe inflammation is based on how long tissues or nerves are injured. Inflammation has various effects on the body, and it even plays a role in regulating the central nervous system (CNS). Inflammation in the brain is triggered by factors like adhesion molecules on white blood cells and blood vessels. These molecules help immune cells stick to vessel walls, leading to symptoms like swelling, heat, redness, and pain. Released mediators then bind to cell receptors, increasing blood vessel permeability, causing muscle contraction, guiding immune cells, inducing pain, and promoting enzymatic activity or oxidative damage. Examples of these mediators include prostaglandins, leukotrienes, nitric oxide, cytokines, and vasoactive amines like serotonin and histamine. Some cytokines, like IL-3, 4, 5, 6, 10, and 13, can actually be helpful as anti-inflammatory agents within cells.[30]. Pain is defined as an unpleasant sensory and emotional phenomenon related to actual or potential cell or tissue damage[2]. This phenomenon common to various biological responses such as stubbing a toe, burning/heating etc. pain happens because the brain responds to chemical and electrical changes in the body caused by damage, disease, or injury. It starts when pain receptors or the part of the brain responsible for physical feelings (somatosensory system) gets activated. Chronic pain is linked to ongoing tissue damage, and after inflammation, the input from certain nerve fibers creates a sensitive state in the brain, leading to increased pain sensitivity (hyperalgesia), unusual responses to touch (allodynia), and spontaneous pain.[28]. Most of the pain feelings resolve promptly once the painful stimulus/input is removed or body activated the healing process, although sometimes pain continues despite the removal of harmful stimuli or inputs and apparent healing of the body. Besides these sometimes pain feelings initiate in the absence of any noticeable stimulus/inputs, damage or pathological conditions. Pain is the most common reason for physician consultation, world-wide[3]. It is a major symptom in various pathological and medical conditions and can significantly affected the general functioning and quality of life of general population. The simplest example of pain classification by reason simply differentiates "somatogenic" pain from psychogenic pain.

Somatogenic pain is divided into "nociceptive" and "neuropathic".[4]. Various analgesic agents such as non-steroidal anti-inflammatory drugs (NSAID), opioids, cannabinoids and neuro steroids have been used to treat acute and chronic pain[5,6]. In addition, recently, antidepressant and antiepileptic have shown strong analgesic effect in neuropathic pain in animal and human. NSAIDs are documented to reduce acute and chronic pain due to inhibition of cyclo-oxygenase (COX) enzymes[7]. Certain drugs like indomethacin, ketorolac, and rofecoxib that block COX enzymes can help reduce both regular and nerve-related pain in animals and humans. For chronic pain, opioids, which work on specific receptors in the brain, are often the preferred choice. Morphine, a type of opioid, has been shown to lessen pain in both animals and people with diabetes[8,9]. Recently, it is noted that cannabinoids are more effective analgesic than opioids and NSAIDs in chronic pain[10,11]. Tetrahydro cannabinoid (THC) cannabinoid receptor agonists, are reported to reduce chronic pain in diabetic animals[16,17]. Moreover, Δ -THC produce analgesic effect by inter acting with endogenous opioids because, naloxone, an

opioid receptor antagonist, abolish the analgesic effect of cannabinoid[18].Furthermore, Cannabinoids and opioids produce synergistic effect and provide adequate pain reliefs in PDN[19]. In addition, recently, neurosteroids are reported to reduce neuropathic pain[20,21]. Progesterone, pregnenolone, dihydroxyepiandrosterone and testosterone administration have been reported to reduce neuropathic pain in diabetic animals[21,22,23]. However, repeated administration of Δ THC, opioids, NSAIDs, and neurosteroids in diabetic animals produce antinociceptive tolerance[18,24,25]. Although there are many pain-relief medications available, their side effects and limited effectiveness in chronic and nerve-related pain situations restrict their practical use[26]. Society faces a challenge in meeting the needs of effective pain therapy while minimizing side effects. This has led to a demand for new types of pain-relief drugs that work differently. Herbal medicines, used since ancient times, are gaining popularity worldwide due to their natural origin and fewer side effects, even in our technologically advanced era. Plant-based remedies, widely used in developing countries, are now becoming a part of healthcare in developed nations, known as complementary and alternative medicine. Plants have been a valuable source of natural products for human health for a long time. Recently, there's a growing interest in natural therapies, and more people are turning to medicinal herbs to improve their quality of life and overall well-being.

For centuries, people have used medicinal plants to treat human and animal ailments. It's crucial to thoroughly study the side effects of these herbal medicines and establish a solid link between certain markers and plants to ensure their effectiveness and quality. Recently, there's been a growing interest in exploring the health benefits of plant-based medicines due to their natural origin, cost-effectiveness, and fewer side effects. These medicinal properties are often unique to specific plant parts like bark, leaves, flowers, roots, fruits, or seeds. In India, many Ayurvedic practitioners use various indigenous plants to treat inflammation and pain. While these traditional uses have a strong foundation, there's a need to scientifically investigate and understand their effectiveness in modern terms.

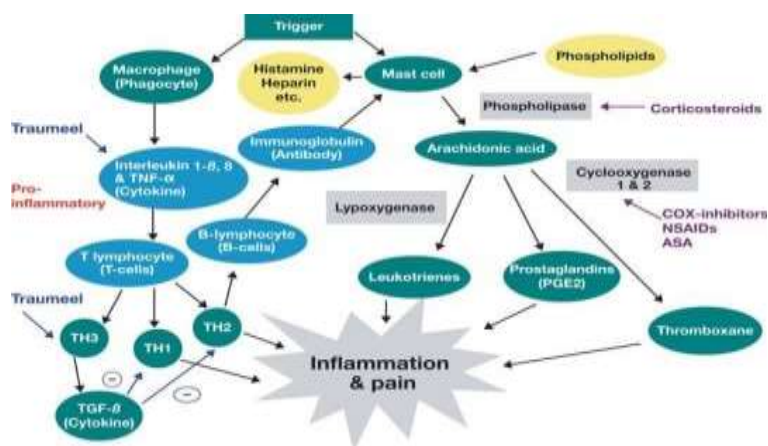
A) Nociceptive Pain : Nociceptive pain is what happens when our normal sensory system gets activated by something harmful or painful. This process involves various steps like transmission, modulation, perception, and transduction. This type of pain is mainly triggered by stimulating nerve fibers in our body that respond to stimuli of harmful intensity, called nociceptors. These stimuli can be classified as "mechanical" (like crushing or tearing), "thermal" (cold or heat), or "chemical" (such as chili powder in the eyes or iodine in a cut).[28]. Nociceptive pain is managed by receptors on A-delta and C-fibers located in skin, muscles, connective tissue, bones, and organs. It can be either somatic or visceral. Somatic pain is well-localized and can feel like throbbing, aching, or sharp pain. Visceral pain originates in organs, is hard to pinpoint, and is described as squeezing, aching, colicky, and deep. When tissues are injured, nociceptors, small nerve fibers with A-delta and C-fibers, get activated and respond to harmful stimuli in joints, skin, muscles, and some organs. These fibers have specific receptors that detect noxious stimuli, whether chemical, thermal, or mechanical.[31].

B) Neuropathic Pain: Nociceptive and neuropathic pain have different causes and need different treatments. Neuropathic pain is considered the most severe and is described as "electric," "burning," "shooting," and "tingling." It results from damage or changes in the central and peripheral nervous systems, causing abnormal sensations like increased pain response (hyperalgesia), pain from non-painful stimuli (allodynia), and unpleasant sensations (dysesthesia).The mechanisms behind neuropathic pain involve both central and peripheral factors. Peripheral sensitization, a lower threshold for nerve endings, often happens due to inflammation. Central sensitization, an increase in spinal neuron excitability, results from prolonged exposure to pain signals. Together, these create heightened sensitivity after surgery (spinal windup), reducing pain thresholds at and around the injury site.Pain is felt when specific nerve cells (nociceptors) send signals to the brain through spinal neurons. Descending pathways from the brainstem can either enhance or reduce pain signals at the spinal level. After nerve injury, inflammation, or ischemia, heightened sensitivity occurs, causing allodynia and hyperalgesia through central sensitization.[31].

1.6 Mechanism of Inflammation

Inflammation involves various pathways triggered by stress on cell membranes. This stress leads to the breakdown of membrane phospholipids into arachidonic acid. This acid then becomes a substrate for enzymes like lipoxygenase (LOX) and cyclooxygenase (COX), producing by-products such as leukotrienes (LTC₄, LTB₄) and prostaglandins (PGE₂, PGH₂). These substances act as chemical signals, starting and amplifying the inflammatory response.

During inflammation, certain proteins called cytokines, like interleukin-1 (IL-1) and tumor necrosis factor- α (TNF- α), play a vital role. These cytokines are key players in responding to bacterial triggers. They're released by various cells, including fat cells, macrophages, and When there's a lot of LTB₄ around, it encourages immune cells (specifically polymorphonuclear leukocytes or neutrophils) to stick together and release substances like superoxide. LTB₄ also makes these immune cells better at sticking to blood vessel walls, moving through these walls, and signals them to produce more pro-inflammatory substances.



When there's a lot of LTB₄ around, it encourages immune cells (specifically polymorphonuclear leukocytes or neutrophils) to stick together and release substances like superoxide. LTB₄ also makes these immune cells better at sticking to blood vessel walls, moving through these walls, and signals them to produce more pro-inflammatory substances. monocytes, working together with growth factors and other cytokines to promote inflammation. Prostaglandins (PGI₂ and PGE₂) help increase blood flow and vessel permeability, aiding in the release of nitric oxide. This causes blood vessel dilation and helps substances like bradykinin and histamine stick to vessel walls. On the other hand, leukotriene B₄ (LTB₄) acts as a powerful signal for immune cells, guiding them to the site of inflammation and promoting their activity. In higher concentrations, LTB₄ influences immune cell behavior, including adhesion to blood vessel walls, migration through vessel walls, and the release of pro-inflammatory substances.[32].

2) Review of Literature

A) **Name of Authors :** Jaya Patel , Nikunjana A. Patel and Tarun Lal.

Year of publishing :

Article Received on: 31.12.2022

Revised on: 24.03.2023, Accepted on: 20.05.2023

Topic of article : Formulation and Evaluation of an Anti-Inflammatory Topical Polyherbal Gel.

Article source : Journal Of Natural Remedies.

Which state that Inflammation is currently treated with NSAIDs. In which these drugs increase the risk of blood clots, heart attacks, And strokes. Therefore, the development of potent antiinflammatory drugs from natural products is currently being Investigated. And the natural products made from medicinal plants play an important role in curing many diseases associated With inflammation. Conventional anti-inflammatory drug available in the market has various side effects. Because of these side effects there is a need to look for noval drugs with fewer or no side effects. The objective of the present study was to develop polyherbal gel containing hydroalcoholic extract of *Berberis aristata* root, *Rubia cordifolia* root and *Boswellia Serrata* gum by using Carbopol 934 and Propylene glycol. And the 32 factorial design was constructed using concentration of Polymer (carbopol 934) and penetration enhancer (Propylene glycol) as independent variables while Viscosity (m.Pas), % in vitro release of Berberine, Rubiadin and AKBA as dependent variables, total 9 possible experimental runs formulate And evaluate. The optimized gel was selected by design of expert employing the overlay plot with desirability approach. Optimized gel showed 39568 m.Pas viscosity, drug content of Berberine 0.48 mg, Rubiadin 0.42 mg and AKBA 0.51 mg. In Vivo and histopathology study was revealed that prepared gel showed good anti-inflammatory activity.

B) **Name of Authors:** Tak Maya Gurung, Atis Kaundinnayanna, Kalpana Parajuli.

Year of publishing : Article Received on 10 Jan 2019,

Revised on 31 Jan. 2018, Accepted on 19 Feb. 2019.

Topic of article : Evaluation Of Antioxidant, Anti-inflammatory And Analgesic Activities Of Traditional Polyherbal Combination Used In Western Nepal.

Article source : World Journal of Pharmacy and Pharmaceutical Sciences.

By the above The present study was aimed for scientific evaluation of Traditional polyherbal combination that has been practicing by the local Traditional practitioner of western Nepal using different parts of five Different medicinal plants which are *Terminalia chebula*, *Terminalia Bellerica*, *Ziziphos mauritiana*, *Mimosa rubicaulis* and *Bergenia ciliate* Primarily for the acceleration of bone fracture repair and the arthritis disease. Methods: The Polyherbal formulation using five different medicinal plants was Formulated and extracted using water and ethanol respectively. In that Preliminary phytochemical analysis was performed. And the antioxidant Activity was evaluated using DPPH assay method. Similarly, for anti Inflammatory activity, carrageenan

induced paw edema test and for Analgesic activity hot plate test and tail immersion test were performed. Results: The Phytochemical analysis revealed the presence of flavonoids, alkaloids, tannins, saponins, Phenols, terpenoids and carbohydrates. The aqueous extract showed high phenol content i.e. 259.96±2.21 mg GAE/g dry weight of extract also the higher antioxidant activity with IC50 Value 4.64 µg/ml followed by the ethanolic extract with IC50 value 4.93 µg/ml and was Comparable with the standard ascorbic acid IC50 value 4.16 µg/ml. Carrageenan induced paw Edema test showed significant inhibition of paw edema at a dose 200 mg/kg when compared To the control. Similarly, the maximum possible analgesic effect of extract was found as 76.61% and 74.82% at a dose 200 mg/kg by hot plate method and tail immersion method Respectively. Conclusion: The traditional use of the combination has been supported Scientifically and tested properly . The study may be helpful for the discovery of new anti-inflammatory and Analgesic drugs.

C) **Name of Authors :** Acharya Balkrishna, Ravikant Ranjan, Sachin S. Sakat, Vinay Kumar Sharma.

Year of publishing : May 2019.

Topic of article : Evaluation of Polyherbal Ayurvedic Formulation 'Peedantak Vati' for Antiinflammatory and Analgesic Properties.

Article source : Journal of Ethnopharmacology.

Which state that Ethnopharmacological relevance Peedantak Vati (PV) is a polyherbal ayurvedic formulation, which is regularly prescribed by the ayurvedic practitioner for the inflammatory disorders and joints pain in India. It is composed of 23 different herbs and minerals which is described in ayurvedic text for their anti-inflammatory and analgesic properties. Aim of the study To investigate anti-inflammatory and anti-nociceptive potential of 'Peedantak Vati' using in vitro and in vivo methods. Materials and methods In-vitro anti-inflammatory activity of PV was studied by estimating the nitric oxide (NO) and LPS-induced pro-inflammatory cytokines IL-6 and TNF- α , using murine macrophage RAW264.7 and human monocyte THP-1 cell lines. PV's anti-inflammatory potential was studied in vivo using carrageenan-induced rat paw edema model. Similarly, anti-nociceptive property of PV was evaluated using hot plate, tail flick, formalin and writhing tests on CD-1 mice. Phytochemical profiling of hydro-alcoholic extract of PV was done using HPLC and HPTLC techniques to identify different marker compounds. These identified marker compounds were confirmed using LC-MS/MS analysis. And finally Results In vitro results strongly suggest that, PV significantly ($p < 0.001$) inhibited NO release and LPSstimulated pro-inflammatory cytokines IL-6 and TNF- α , in murine RAW264.7 and human THP1 cells. Further, PV demonstrated significant ($p < 0.05$) anti-inflammatory activity at different time points after carrageenan injection with maximum effect at 2 h (40.4±5.2% at 400 mg/kg). Similarly, PV significantly ($p < 0.05$) decreased nociceptive pain, studied using hot plate, tail flick, formalin and writhing tests. Moreover, HPLC and HPTLC methods were developed for the standardization of PV. Five marker phytochemicals viz. rutin, caffeic acid, colchicine, withaferin A and curcumin were identified and quantified by HPLC and HPTLC methods. The presence of these phytoconstituents was confirmed by LC-MS/MS analysis. Conclusion The findings of the study strongly suggest that, the polyherbal ayurvedic formulation 'Peedantak Vati' possesses remarkable anti-inflammatory and analgesic property, providing potent alternative for currently available allopathic medicines such as non steroidal anti-inflammatory drugs (NSAIDs).

D) **Name of Authors :** Suresh Kumar Dev, Rajnish Srivastava, Pratim Kumar Choudhury, Maya Sharma.

Year of publishing :

Received on : 9 September 2018.

Received in : revised form 6 December 2018.

Accepted on : 17 December 2018.

Topic of article : Antimicrobial, anti-inflammatory and wound healing activity of polyherbal Formulation.

Article source : Biomedicine & Pharmacotherapy.

According to Ayurveda, individual herbs are insufficient to achieve a desired therapeutic effect. Then When it is Optimized as multiple herbs composition in a particular ratio it will give a therapeutic effect in a better way with Reduced toxicity. Because of that in order to develop such an intervention, the present study was intended to develop a poly-Herbal drug from methanolic extracts of Plumbago zeylanica Linn, Datura stramonium Linn and Argemone mexicana Linn. The study which also aimed to evaluate the impact of polyherbalism on antimicrobial and antioxidant effect And after the ratio of individual plant extracts was optimized accordingly to treat the wound. The polyherbal Drug was put on preclinical trial to access the anti-inflammatory and wound healing activity as 2% and 5% Polyherbal carbopol-940 gels. The antimicrobial activity was assessed by agar well diffusion and broth dilution Method while wound healing activity was evaluated by excision and incision wound models. And topical anti-inflammatory activity was assessed by carrageenan induced paw oedema. The findings of the study revealed the Synergistic antimicrobial potential of Polyherbal drug against gram-positive and negative strains. And the polyherbal Carbopol- 940 gels (2% and 5%w/w) promoted the wound healing and anti-inflammatory effect. The high rate of Wound contraction (< 0.0001), early epithelialization period (< 0.0001) and increased wound breaking Strength (< 0.0001) were observed in 2% and 5% polyherbal gel treated group when compared to the normal Control and negative control group. The antimicrobial and anti-inflammatory effect of Polyherbal drug and promoted the wound healing process through accelerated remodelling of damaged tissue.

E) **Name of Authors :** Ying Chen, Hong Lv, Yu-Ping Du, Jian Wu.

Year of publishing : April 2015.

Topic of article : Polyherbal Gel as an Alternative Herbal Treatment for Arthritis: Physical and In Vivo Characterization.

Article source : Journal of Biomaterials and Tissue Engineering.

Which state that Rheumatoid arthritis (RA) is an autoimmune and progressive systemic inflammatory disease for which non steroidal anti inflammatory drugs (NSAIDs) are used to manage the chronic pain and inflammation. But almost all the NSAIDs are found to be short half-life and shows gastrointestinal side effects. For that To overcome these problems as a safer and more effective alternative the polyherbal gel were prepared for the topical use for prolonged relief from pain and local inflammation in arthritis without any side effect. This polyherbal gels were prepared using ethanolic extract of *Withania somnifera* (seeds) and *Curcuma longa* (rhizomes) in the Aloe vera leave gel base in two different doses. The prepared gels were subjected to physical evaluation (color, appearance, pH, texture, viscosity etc.), in vivo primary skin irritation test, in vivo analgesic and in vivo anti-inflammatory activities against Freund's complete adjuvant induced arthritis in rats. And the prepared polyherbal gels showed good physical properties (like texture, appearance etc.) with pH 6.8 and 6.9; and viscosity of 14.1 and 17.9 cps. The polyherbal gels were found to be non-irritant to the skin in primary skin irritation test on Wistar rats. And the polyherbal gels showed excellent in vivo anti inflammatory activity also (in carrageenan induced hind rat paw edema model) and in vivo analgesic activity (in writhing method), which was comparable to that of piroxicam gel. It was concluded that the topical polyherbal gel may have the good potential in treatment of arthritis and it can be a safer alternative to oral NSAIDs.

3) Aim

The aim of this exploration is to comprehensively investigate and understand the analgesic and anti-inflammatory properties of polyherbal drugs, unraveling their potential contributions to natural therapeutics.

3.1 Objectives:

1. Review Existing Knowledge: - Examine and synthesize existing literature to create a comprehensive overview of the current understanding of polyherbal drugs in the context of analgesia and anti-inflammation.
2. Explore Synergistic Interactions: Investigate the synergistic interactions among diverse botanical compounds within polyherbal drugs, aiming to elucidate the mechanisms that contribute to their analgesic and anti-inflammatory effects.
3. Highlight Holistic Approaches: - Emphasize the holistic approach of polyherbal drugs in managing conditions associated with pain and inflammation, considering the collective impact of multiple herbal constituents.
4. Identify Safety Considerations: - Explore safety considerations associated with the use of polyherbal drugs, recognizing potential adverse effects and contributing to a balanced understanding of their safety profile.
5. Navigate Existing Challenges: - Address challenges such as standardization and variability in formulations, acknowledging the current limitations in the field and proposing potential avenues for improvement.
6. Discuss Significance in Healthcare: - Discuss the significance of polyherbal drugs in the broader context of healthcare, emphasizing their potential role in integrative medicine and alternative therapeutic approaches.
7. Propose Future Research Directions: - Propose future research directions to address gaps in current knowledge, encouraging further investigations into the efficacy, safety, and mechanisms of polyherbal drugs in pain and inflammation management.

4) Need of work

- 1) Discovering New Things: We want to find out more about how mixes of herbs might help with pain and inflammation.
- 2) Connecting Old and New: We're exploring how traditional herbal knowledge can be valuable in modern medicine.
- 3) Filling in the Gaps: There are still things we don't know, and this work aims to fill those gaps in our understanding.
- 4) Helping Doctors Help You: We're looking for ways to give doctors more options for treating pain and inflammation.
- 5) Making Sure It's Safe: We're checking to make sure these herbal mixes are safe to use and won't cause any harm.
- 6) Improving Healthcare: By studying this, we hope to improve how we take care of people's health, especially when it comes to dealing with pain and inflammation.
- 7) Learning from Nature : Nature has a lot of secrets, and we're trying to learn from plants to help people feel better.

5. Outcome

1) Holistic Understanding: Provides a comprehensive understanding of the analgesic and anti-inflammatory properties of polyherbal formulations, contributing to a holistic view of alternative healthcare.

2)Integration of Traditional and Modern Knowledge: Bridges traditional medicinal knowledge with contemporary scientific findings, offering a synthesis that may have practical applications in healthcare.

3)Identification of Effective Formulations: Identifies specific polyherbal formulations with demonstrated efficacy in pain management and inflammation, potentially leading to the development of targeted therapies.

4)Informed Clinical Practice: Offers valuable insights for healthcare practitioners, informing them about potential herbal alternatives for pain and inflammation, thus expanding treatment options.

5)Contribution to Evidence-Based Medicine: Strengthens the evidence base for the use of polyherbal formulations in healthcare, promoting evidence-based practices and discussions within the medical community.

6)Public Health Implications: Addresses potential public health implications by exploring alternative, potentially cost-effective solutions for common health concerns.

According to above information we can select some drugs which has the properties like analgesic and anti-inflammatory are as follows :

1) Cardamom

Synonyms:- small cardamom,Elachi,Ailum

Biological Source:-It obtain from dried ripe fruits of Eletaria cardamomum.

Family: Zingiberacea

Chemical constituents :- It consists of Cineole(volatile oil), Terpinol and Borneol[60].

Uses:

- Used as a Flavouring agent.
- Used as a Stimulant and carminative
- Used as aInflammation of eyelids
- Used as a Digestive Disorders.
- Used as a Breath Freshener
- And it also used as a anti-inflammatory agent [61,62]



2) Alovera

Synonym :- Barbados Aloe, Elephant's Gall

Biological source :- The biological source of Aloe Vera is the plant itself, scientifically known as "Aloe Barbadensis mille [67]

Family :- belongs to the Aloaceae family.

Chemical constituents :- Polysaccharides, Acemannan, Anthraquinones They include aloin, Barbaloin, Phytosterols, Amino Acids, Saponins, Salicylic Acid, Lignin [67]

Uses :-

1. **Sunburn Relief:** Aloe Vera's cooling and anti-inflammatory properties are particularly effective In soothing sunburned skin. It can help reduce redness, swelling, and pain associated with sunburn [79]
2. **Skin Irritations:** It can help ease discomfort and reduce inflammation caused by skin irritations, Such as rashes, allergic reactions, or insect bites.
3. **Inflammatory Skin Conditions:** Aloe Vera gel can be used to ease discomfort and reduce Inflammation in conditions like psoriasis and rosacea [78,79]
4. **Moisturizer:** Aloe Vera is used as a natural moisturizer for both the face and body due to its Hydrating properties.
5. **Dermatitis and Eczema:** Aloe Vera's soothing and anti-inflammatory properties can provide Relief from the itching, redness, and inflammation associated with conditions like dermatitis and Eczema.



3) Liquorice root

Synonym :- glycyrrhiza, mulethi

Biological source :- Liquorice consists of subterranean peeled and unpeeled stolons, roots and subterranean stems of *Glycyrrhiza glabra* Linn [71]

Family :- leguminosae

Chemical constituents :- it contains Major glycosides , aglycone , glucuronic acid, sugar-glucose , mannitol , resin , volatile oil , starch.

Description:

Colour- yellowish brown or dark brown. Unpeeled liquorice –externally

Odour – faint and characteristic.

Taste- sweet

Size – length 20 to 50cm and diameter 2cm..

Shape : unpeeled drug –straight and nearly cylindrical , peeled drug – Mostly angular[71]

Uses:- :

1. It is demulcent and expectorant properties. It is used as a bitter drug making agent in pharmaceutical formulations like guinine ,aloe.
2. It employed as a flavouring agent in beverages , pharmaceutical industry .
3. The presence of glycyrrhetic acid exert mineralo corticoid activity and hence
4. It is used in the treatment of inflammation , addisons disease.[73,74]

4) Tulsi

Synonym :- holybasil , tulas.

Biological source :- It is obtained from fress and dried leaves of plant which is *ocimum sanctum* Linn [90].

Family :- Tulsi is belonging to lamiaceae family.

Chemical constituent :- Leaves of Tulsi which is contain 0.1- 0.9% of volatile oil.

The Tulsi is bright yellow coloured.

The composed of volatile oil is 70% of eugenol , carvacrol 3% , eugenol- methyl – ether 20%.

It is herb contain alkaloids , glycosides , tannins saponins , vitamin C and tartatric acid [93].

Uses :-

- 1) Volatile oil of acts as antibacterial and insecticidal.
- 2) Leaves are used stimulant, aromatic.
- 3) The Tulsi leaf juice is main constituents of number of herbal Cosmetic product for skin Diseases and it is also used to cure ear ache.
- 4) Tulsi posses expectorant,immune-modulatory actions [97,99].

5) Boswellia serreta

Synonym :- Indian frankincense tree,kindra guggul

Biological source :- It is a dried exudate oleo gum resin. It is obtained from branches of plant *BOSWELLIA SERRATA*. [77]

Family :- It is belonging to burseraceae.

Chemical constituent :-

Essential oil , 8-9% , gum 20 -23% , resin 50%.

Ex.Boswellic acids .it is derivatives is Boswellic acid include Beta-Boswellic acid ,11-keto Beta Boswellic acid [78,79]



USES:

1.Osteoarthritis – It can reduce pain by up to 65%.It improve mobility in people with osteoarthritis in joints. It research take product is combination contain Boswellia and other herbal ingredients can Also reduce pain.

2.Skin damage caused by radiation: THERAPY: It help prevent severe skin redness from developing.

3.Ulcerative colitis: Taking Boswellia seems to improve symptoms of ulcerative colitis in some people. It is research shows this can induce disease remission in 70% -82% of people [79]

References

1. Ferrero-Miliani L, Nielsen OH, Andersen PS, Girardin SE. Chronic inflammation: importance of NOD2 and NALP3 in interleukin-1beta generation. *Clin Exp Immunol* 2007;147(2):227-35.
2. Watson CPN. Bonica's Management of Pain, 4th Edition. *Journal of Pain and Symptom Management* 2010;40(2):315–319.
3. Turk DC, Dworkin RH. What should be the core outcomes in chronic pain clinical trials? *Arthritis Res Ther* 2004;6(4):151-4.
4. Keay KA, Bandler R. Distinct central representations of inescapable and escapable pain: observations and speculation. *Exp Physiol* 2002;87(2):275-9.
5. Pernía-Andrade AJ, Kato A, Witschi R, Nyilas R, Katona I, Freund TF, Watanabe M, Filitz J, Koppert W, Schüttler J, Ji G, Neugebauer V, Marsicano G, Lutz B, Vanegas H, Zeilhofer HU. Spinal endocannabinoids and CB1 receptors mediate C-fiber-induced heterosynaptic pain sensitization. *Science*2009;325(5941):760- 4.
6. Liu YQ, Qiu F, Qiu CY, Cai Q, Zou P, Wu H, Hu WP. Cannabinoids inhibit acid-sensing ion channel currents in rat dorsal root ganglion neurons. *PLoS One* 2012;7(9):e45531.
7. Elliott J, Chapman J, Clark DJ. Videoconferencing for a veteran's pain management follow-up clinic. *Pain Manag Nur's* 2007;8(1):35-46.
8. Takahashi N, Kikuchi S, Dai Y, Kobayashi K, Fukuoka T, Noguchi K. Expression of auxiliary beta subunits of sodium channels in primary afferent neurons and the effect of nerve injury. *Neuroscience*, 2003;121(2):441-50.
9. Kausar F, Davis MP. Ketorolac in neuropathic pain. *J Pain Symptom Manage* 2006;32(3):202-4.
10. Machelska H. Targeting of opioid-producing leukocytes for pain control. *Neuropeptides* 2007;41(6):355-63.
11. Van der Kam EL, Vry JD, Schiene K, Tzschentke TM. Differential effects of morphine on the affective and the sensory component of carrageenan-induced 150 nociception in the rat. *Pain* 2008;136(3):373-9.
12. Tongjaroenbungam W, Jongkamonwivat N, Cunningham J, PhansuwanPujito P, Dodson HC, Forge A, Govitrapong P, Casalotti SO. Opioid modulation of GABA release in the rat inferior colliculus. *BMC Neurosci*2004;5:31.
13. Raehal KM, Walker JK, Bohn LM. Morphine side effects in beta-arrestin 2 knockout mice. *J Pharmacol Exp Ther* 2005;314(3):1195-201.
14. Hermos JA, Young MM, Gagnon DR, Fiore LD. Characterizations of long-term oxycodone/acetaminophen prescriptions in veteran patients. *Arch Intern Med* 2004;164(21):2361-6.
15. Ulugol A, Dokmeci D, Guray G, Sapolyo N, Ozyigit F, Tamer M. Antihyperalgesic, but not antiallodynic, effect of melatonin in nerve-injured neuropathic mice: Possible involvements of the L-arginine-NO pathway and opioid system. *Life Sci* 2006;78(14):1592-7.
16. Scheen AJ. Cannabinoid-1 receptor antagonists in type-2 diabetes. *Best Pract Res Clin Endocrinol Metab* 2007;21(4):535-53.
17. Horváth B, Mukhopadhyay P, Haskó G, Pacher P. The endocannabinoid system and plant-derived cannabinoids in diabetes and diabetic complications. *Am J Pathol* 2012;180(2):432-42.
18. Karimi S, Karami M, Zardoos H, Salimi SH, Sahraei H. Biphasic effects of naloxone in the rats receiving morphine overdose a place preference study. *Iran J Pharm Res* 2011 Summer;10(3):605-10.
19. Klein TW. Cannabinoid-based drugs as anti-inflammatory therapeutics. *Nat Rev Immunol* 2005;5(5):400-11.
20. Sameni H, Panahi M. The Effect of Co-administration of 4-Methylcatechol and Progesterone on Sciatic Nerve Function and Neurophysiological Alterations in Streptozotocin-Induced Diabetic Neuropathy in Rats. *Cell J* 2011;13(1):31-8.
21. Huang CT, Chen SH, Lue JH, Chang CF, Wen WH, Tsai YJ. Neurosteroids Allopregnanolone Suppresses Median Nerve Injury-induced Mechanical Hypersensitivity and Glial Extracellular Signal-regulated Kinase Activation through γ -Aminobutyric Acid Type A Receptor Modulation in the Rat Cuneate 151 Nucleus. *Anaesthesiology*. 2016;125(6):1202-1218.
22. Reddy P, White CM, Dunn AB, Moyna NM, Thompson PD. The effect of testosterone on health-related quality of life in elderly males – a pilot study. *J Clin Pharm Ther* 2000;25(6):421-6.

23. Patte-Mensah C, Kibaly C, Boudard D, Schaeffer V, Béglé A, Saredi S, Meyer L, Mensah-Nyagan AG. Neurogenic pain and steroid synthesis in the spinal cord. *J Mol Neurosci* 2006;28(1):17-31.
24. Humble SR. Neurosteroids are reduced in diabetic neuropathy and may be associated with the development of neuropathic pain. *F1000Res* 2016;5:5:1923.
25. Kawano T, Soga T, Chi H, Iguchi S, Yamazaki F, Yokoyama M. The involvement of the neurosteroids allopregnanolone in the antihyperalgesic effect of paroxetine in a rat model of neuropathic pain. *Neurorepair* 2011;22(18):984-8.
26. Nakamura-Craig M, Follenfant RL. Effect of lamotrigine in the acute and chronic hyperalgesia induced by PGE2 and in the chronic hyperalgesia in rats with streptozotocin-induced diabetes. *Pain* 1995;63(1):33-7.
27. Guggulu S, Aamavata WSRTO. ANTI-ARTHRITIC AND ANTIINFLAMMATORY ACTIVITY OF. 2019;8(11):1202–12.
28. Woessner JW. Overview of Pain: Classification and Concepts. *Weiner's Pain Manag.* 2013;(January 2006):35–47.
29. Shaikh JR, Patil M. Qualitative tests for preliminary phytochemical screening: An Overview. *Int J Chem Stud.* 2020;8(2):603–8.
30. Ahmed AU. An overview of inflammation: Mechanism and consequences. *Front Biol China.* 2011;6(4):274–81.
31. Swieboda P, Filip R, Prystupa A, Drozd M. Assessment of pain: types, mechanism and Treatment. *Ann Agric Environ Med.* 2013; 1(July 2014):2–7.
32. Punchard NA, Whelan CJ, Adcock I. The Journal of Inflammation. *J Inflamm.* 2004;1:1–4.
33. RKS, . BC, . M. BR. Analgesic Activity of Hydroalcoholic Extract of Cinnamomum Zeylanicum Bark in Albino Rats. *J Curr Pharma Res.* 2016;7(1):2003–9.
34. Kumar S, Kumari R, Mishra S. Pharmacological properties and their medicinal uses of Cinnamomum: a review. *J Pharm Pharmacol.*
35. Kamkar Asl M, Nazariبورun A, Hosseini M. Analgesic effect of the aqueous and ethanolic Extracts of clove. *Avicenna J phytomedicine* [Internet]. <http://www.ncbi.nlm.nih.gov/pubmed/25050273>0Ahttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC4075701
36. Taher YA, Samud AM, El-Taher FE, ben-Hussin G, Elmezogi JS, Al-Mehdawi BF, et al. Experimental evaluation of anti-inflammatory, antinociceptive and antipyretic activities of Clove oil in mice. *Libyan J Med.* 2015;10(October).
37. Bansod MS, Kagathara VG, Somkuwar AD. Evaluation of analgesics and anti-inflammatory activity of a poly-herbal formulation. *Int J PharmTech Res.* 2010;2(2):1520–7.
38. Reeta M, Ravindra S, Tarun S, Ramamurthy A. Comparative Evaluation of Anti-inflammatory Activity of Oleogumresin & Stembark Extract of Guggulu in Albino Rats. 2015;4(10):861–71.
39. Altman R, Bosch B, Brune K, Patrignani P, Young C. Advances in NSAID development: Evolution of diclofenac products using pharmaceutical technology. *Drugs.* 2015;75(8):859–77.
40. Sahiti M, Gurupadayya B, Dinesh T. Evaluation of in Vitro Anti-inflammatory Activity of Trayodashang Guggulu: an Ayurvedic Formulation in Comparison With Allopathic Drugs. *Int J Res Ayurveda Pharm.* 2019;10(3):92–6.
41. Sonawane DR, Jaju JB, Pawar GR, Gosavi PA. Evaluation of analgesic and anti-inflammatory activity of Levocetirizine in albino rats. *Int J Basic Clin Pharmacol.* 2019;8(8):1805.
42. Spartak Y. Effects of Cinnamon (Cinnamomum spp.) in Dentistry: A Review. *Molecules.* 2020;4184(06):2 of 17.
43. Tenpe CR, Bongade VP, Salunkhe PR, Tundulwar MR, Patole AM, Rathod SS. FORMULATION AND EVALUATION OF HERBAL ANALGESIC AND ANTI-Formulation and Evaluation of Herbal Analgesic and Anti-inflammatory Gel. 2013;(March 2020).
44. Lahoti A, Kalra BS, Tekur U. Evaluation of the analgesic and antiinflammatory activity Of fixed dose combination: Non-steroidal antiinflammatory drugs in experimental animals. *Indian J Dent Res.* 2014;25(5):551–4.
45. SEEMA JAIN, SPARSH GUPTA. Effects of Cinnamomum Zeylanicum Bark Extract on Nociception and Anxiety Like Behavior in Mice. *Asian J Pharm Clin Res.* 2019;12(9):236–41.
46. CHAVAN P, KALSHETTI M, NAVINDGIKAR N. Formulation and Evaluation of Polyherbal Cream. *Int J Curr Pharm Res.* 2020;12(4):75–7.
47. Yimer T, Birru EM, Adugna M, Geta M, Emiru YK. Evaluation of analgesic and anti-inflammatory activities of 80% methanol root extract of echinops kebericho m. (asteraceae). *J Inflamm Res.* 2020;13:647–58.
48. Vidya S, Sravya D, Neeraja P, Ramesh A. Evaluation of anti-inflammatory and analgesic Activity of poly herbal formulation (PHF) in albino rats. *Int J Res Pharm Sci.* 2011;2(3):444

49. NANDAGOPAI A, ALI KHAN MA. NEUROPROTECTIVE EFFECT OF POLYHERBAL FORMULATION IN PARKINSON'S ANIMAL MODEL. *Asian J Pharm Clin Res* [Internet]. 2020 Jan 18 [cited 2021 Jan 17];13:121–Available from: <http://dx.doi.org/10.22159/ajpcr.2020.v13i3.36549>
50. Pawar AP, Pawar DN, Dalvi Y V. Formulation and Evaluation of Polyherbal Soap. *Res J Top Cosmet Sci*. 2019;10(1):23.
51. Humbal BR, Sadariya KA, Prajapati JA, Shailesh K. Evaluation of in-vivo anti-inflammatory activity of *Syzygium aromaticum* oil in male wistar rats. 2019;8(7):540–3.
52. 16 Edition of Trease and Evans Pharmacognosy Text Book (Pg. No. :-293)Botany, traditional uses, phytochemistry and biological activities of cardamom [*Elettaria cardamomum* (L.) Maton] – A critical review.
53. Ravindran PN, Babu KN, Sasikumar B, Krishnamurthy KS. Botany and crop improvement of black pepper. In *Black pepper 2000* Aug 7 (pp. 43-164). CRC Press.
54. Singh G, Marimuthu P, Catalan C, DeLampasona MP. Chemical, antioxidant and antifungal activities of volatile oil of black pepper and its acetone extract. *Journal of the Science of Food and Agriculture*. 2004 Nov;84(14):1878-84.
55. Pino J, Rodriguez - Feo G, Borges P, Rosado A. Chemical and sensory properties of black pepper oil (*Piper nigrum* L.). *Food/Nahrung*. 1990;34(6):555-60.
56. Evans W.C, Editors. *Trease and Evans Pharmacognosy*, New York, Saunders, Elsevier;2009, p. 266.
57. Botany: An Introduction to Plant Biology” by James D. Mauseth. “Horticulture: Principles and Practices” by George Acquaah.
58. “A comprehensive review on pharmacotherapeutics of herbal bioenhancers.” Authors: Singh, Neha; Nath, R; Gupta, N; Kohli, K *Journal: The Scientific World Journal* Year: 2012 DOI: 10.1100/2012/637953
59. “Analgesic and anti-inflammatory activities of the volatile oil of *Elettaria cardamomum*” Authors: Gilani, A. H.; Jabeen, Q.; Khan, M. A. U.; et al. *Journal: Pharmaceutical Biology* Year: 2007 Volume: 45 Issue: 1 Pages: 63-66 DOI: 10.1080/13880200601115523
60. “Cardamom and Its Positive Effects on the Cardiovascular System” Authors: Verma, S.K.; Jain, V.; Katewa, S.S. *Journal: Ancient Science of Life* Year: 2012 Volume: 31 Issue: 3 Pages: 119-122 DOI: 10.4103/0257-7941.10317
61. Evaluation of anti-inflammatory potential of *Elettaria cardamomum* (L.) Maton” Authors: Hossain SJ, et al. *Journal: Bangladesh Journal of Pharmacology* Year: 2017 Volume: 12 Issue: 1 Pages: 40-44 DOI: 10.3329/bjp.v12i1.2
62. “Anti-inflammatory and anti-nociceptive activities of methanolic extract of *Elettaria cardamomum* (L.) Maton” Authors: Islam, M. S.; Choi, H.; Jung, H. A.; et al. *Journal: Journal of Ethnopharmacology* Year: 2016 Volume: 194 Pages: 107-117 DOI: 10.1016/j.jep.2016.08.041
63. “Evaluation of anti-inflammatory potential of *Elettaria cardamomum* Martin in rats” Authors: Khare CP, et al. *Journal: Ancient Science of Life* Year: 1995 Volume: 15 Issue: 2 Pages: 111-115
64. “Anti-inflammatory and analgesic activities of Aloe vera leaf gel extracts in rats” Authors: Amoo, S. O., Aderibigbe, I. A., & Adetutu, A. *Journal: International Journal of Biomedical and Health Sciences* Year: 2009 Volume: 5 Issue: 2 Pages: 71-76
65. “Aloe Vera: A short review” Authors: Rajasekaran S, Sivagnanam K, Subramanian S. *Journal: Indian Journal of Dermatology* Year: 2008 Volume: 53 Issue: 4 Pages: 163–166 DOI: 10.4103/0019-5154.44785
66. “Evaluation of analgesic and anti-inflammatory activity of Aloe vera (*Aloe barbadensis* Miller) gel in experimental animal” Authors: Kumar, P., Mishra, S., & Goyal, S. *Journal: International Journal of Green Pharmacy (IJGP)* Year: 2010 Volume: 4 Issue: 2 Pages: 122-125 DOI: 10.4103/0973-8258.62157
67. “Anti-inflammatory activity of Aloe vera against A-431 cell line” Authors: Radha, M. H., & Laxmipriya, N. P. *Journal: International Journal of Pharmacy and Biological Sciences* Year: 2014 Volume: 4 Issue: 1 Pages: 68-73
68. “Anti-inflammatory and analgesic activity of topical administration of Aloe vera, turmeric, and aspirin in rats” Authors: Hekmatpou, D., Mehrabi, F., Rahzani, K., & Aminiyan, A. *Journal: Journal of Medicinal Plants Research* Year: 2011 Volume: 5 Issue: 15 Pages: 3501-3505 DOI: 10.5897/JMPR11.027
69. “Analgesic and anti-inflammatory effects of Aloe vera gel in experimental animals” Authors: Asadi-Samani, M., Bagheri, N., Rafieian-Kopaei, M., & Shirzad, H. *Journal: Studies on Ethno-Medicine* Year: 2012 Volume: 6 Issue: 1 Pages: 19-24 DOI: 10.1080/09735070.2012.11886455
70. “In vivo anti-inflammatory and analgesic activities of Aloe vera leaf gel” Authors: Choudhury, R., & Kumar, K. P. *Journal: Journal of Young Pharmacists* Year: 2010 Volume: 2 Issue: 4 Pages: 399-402 DOI: 10.4103/0975-1483.71610
71. Ahn SJ, Cho EJ, Kim HJ, Park SN, Lim YK, Kook JK. 2012. The antimicrobial effects of deglycyrrhizinated licorice root extract on *Streptococcus Mutans* UA159 in both planktonic and biofilm cultures. *Anaerobe*.18:590–596.

72. Mamedov N.A., Egamberdieva D. Plant and Human Health. Volume 3. Springer International Publishing; Cham, Switzerland: 2019. Phytochemical Constituents and Pharmacological Effects of Licorice: A Review; pp. 1–21. [Google Scholar]
73. Esmaeili H., Karami A., Hadian J., Nejad Ebrahimi S., Otto L.G. Genetic structure and variation in Iranian licorice (*Glycyrrhiza glabra* L.) populations based on morphological, phytochemical and simple sequence repeats markers. *Ind. Crop. Prod.* 2020;145:112140. Doi: 10.1016/j.indcrop.2020.112140.
74. Fenwick G.R., Lutomski J., Nieman C. Liquorice, *Glycyrrhiza glabra* L. Composition, uses and analysis. *Food Chem.* 1990;38:119–143. Doi: 10.1016/0308-8146(90)90159-2. [CrossRef] [Google Scholar]
75. Fiore C., Eisenhut M., Ragazzi E., Zanchin G., Armanini D. A history of the therapeutic use of liquorice in Europe. *J. Ethnopharmacol.* 2005;99:317–324. Doi: 10.1016/j.jep.2005.04.015.
76. G., Cornara L., Soares S., Rodrigues F., Oliveira M.B.P.P. Liquorice (*Glycyrrhiza glabra*): A phytochemical and pharmacological review. *Phytother. Res.* 2018;32:2323–2339. Doi: 10.1002/ptr.6178
77. I. Y. Shao, C.T. Ho, C.K. Chin, V. Badmaev, W. Ma and M.T. Huang. Inhibitory activity of Boswellic acids from *Boswellia serrata* against human leukemia HL-60 cells in culture. *Planta Med.* 64: 328-33 (1998).
78. G.B. Singh and C.K. Atal. Pharmacology of an extract of salai guggal ex *Boswellia serrata*, a new non steroidal anti-inflammatory agent. *Agents and Actions* 18: 407-12 (1986).
79. M.L. Sharma, S. Bani and G.B. Singh. Anti-arthritis activity of Boswellic acids in BSA induced arthritis. *Int. J. Immunopharmacol.* 11: 647-52 (1989).
80. I. Gupta, V. Gupta, S. Gupta, A. Parihar, R. Ludtke, H. Safayhi and H.P.T. Ammon. Effect of *Boswellia serrata* gum resin in patient with bronchial asthma: Results of a double blind, placebo controlled 6 week clinical study. *Eur. J. Med. Res.* 3: 511-14 (1998).
81. R.N. Chopra, S.L. Nayar and J.C. Chopra. Glossary of Indian medicinal plants. Published by Council of Scientific and Industrial Research, NewDelhi; 39 (1956).
82. I. Gupta, A. Parihar, P. Malhotra, S. Gupta, A. Ludtke, H. Safayhi and H.P.T. Ammon. Effects of gum resin of *Boswellia serrata* in patients with chronic colitis. *Planta Med.* 67: 391-95 (2001).
83. H. Gerhardt, F. Seifert, P. Buvari, H. Vogelsang and R. Repges. Therapy of active crohn's disease with *Boswellia serrata* extracts H-15. *Zeitschrift Fur Phytother.* 22: 69-75 (2001).
84. R.S. Pandey, B.K. Singh and Y.B. Tripathi. Extract of gum resin of *Boswellia serrata* inhibits LPS induced nitric oxide production in rat macrophages along with hypolipidemic property. *Indian J. Exp. Biol.* 43: 509-16 (2005).
85. G. K. Reddy, S. C. Dhar and G. B. Singh. Urinary excretion of connective tissue metabolite under the influence of new non-steroidal anti-inflammatory agent in adjuvant induced arthritis. *Agent and Actions* 22: 99-05 (1987).
86. World Health Organisation. Preventing Chronic Diseases: A Vital Investment: WHO Global Report. Geneva: World Health Organization; 2005. Department of Chronic Diseases and Health Promotion; p. 18.
87. Bast F, Rani P, Meena D. Chloroplast DNA phylogeography of holy basil (*Ocimum tenuiflorum*) in Indian subcontinent. *ScientificWorldJournal.* 2014;2014:847–482.
88. Singh N, Hoette Y, Miller R. *Tulsi: The Mother Medicine of Nature*. 2nd ed. Lucknow: International Institute of Herbal Medicine; 2010.
89. Mahajan N, Rawal S, Verma M, Poddar M, Alok S. A phytopharmacological overview on *Ocimum* species with special emphasis on *Ocimum sanctum*. *Biomed Prev Nutr.* 2013;3:185–92. [Google Scholar]
90. Mohan L, Amberkar MV, Kumari M. *Ocimum sanctum* linn. (TULSI)-an overview. *Int J Pharm Sci Rev Res.* 2011;7:51–3. [Google Scholar]
91. Pattanayak P, Behera P, Das D, Panda SK. *Ocimum sanctum* Linn. A reservoir plant for therapeutic applications: An overview. *Pharmacogn Rev.* 2010;4:95–105. [PMC free article] [PubMed] [Google Scholar]
92. S, Mirdha BR, Mahapatra SC. The science behind sacredness of Tulsi (*Ocimum sanctum* Linn.) *Indian J Physiol Pharmacol.* 2009;53:291–306. [PubMed] [Google Scholar]
93. W, Morasuk W. Antioxidant capacity and phenolic content of holy basil. *Songklanakarin J Sci Technol.* 2007;29:1407–15. [Google Scholar]
94. Panda VS, Naik SR. Evaluation of cardioprotective activity of *Ginkgo biloba* and *Ocimum sanctum* in rodents. *Altern Med Rev.* 2009;14:161–71. [PubMed] [Google Scholar]
95. M, Joshi M. Aqueous extract of tulsi (*Ocimum sanctum*) enhances endogenous antioxidant defenses of human hepatoma cell line (HepG2) *J Herbs Spices Med Plants.* 2012;18:331–48. [Google Scholar]

-
96. P, Murugan RS, Abbas H, Abraham SK, Nagini S. *Ocimum sanctum* Linn. (Holy Basil) ethanolic leaf extract protects against 7,12-dimethylbenz (a) anthracene-induced genotoxicity, oxidative stress, and imbalance in xenobiotic-metabolizing enzymes. *J Med Food*. 2007;10:495–502. [PubMed] [Google Scholar]
 97. Siddique YH, Ara G, Beg T, Afzal M. Anti-genotoxic effect of *Ocimum sanctum* L. extract against cyproterone acetate induced genotoxic damage in cultured mammalian cells. *Acta Biol Hung*. 2007;58:397–409. [PubMed] [Google Scholar]
 98. AK, Jha M, Kaur J. Ethanolic extracts of *Ocimum sanctum*, *Azadirachta indica* and *Withania somnifera* cause apoptosis in SiHa cells. *Res J Pharm Biol Chem*. 2012;3:557–62. [Google Scholar]
 99. P, Vidjaya Letchoumy P, Prathiba D, Nagini S. Combinatorial chemopreventive effect of *Azadirachta indica* and *Ocimum sanctum* on oxidant-antioxidant status, cell proliferation, apoptosis and angiogenesis in a rat forestomach carcinogenesis model. *Singapore Med J*. 2008;49:814–22. [PubMed] [Google Scholar]
 100. S, Shukla Y, Paul BN, Chowdhuri DK, Khanna SK, Das M. Protective effect of *Ocimum sanctum* on 3-methylcholanthrene, 7,12-dimethylbenz (a) anthracene and aflatoxin B1 induced skin tumorigenesis in mice. *Toxicol Appl Pharmacol*. 2007;224:228–40. [PubMed] [Google Scholar]