

“A Review supporting Anti- Inflammatory effect of Boswellia Serrata and Capsaicin in Rheumatic Arthritis”

Shaffi Tangri*¹, G. gnanarajan², Pranshu Tangri³, Shivani kala⁴, Mrynal Chamoli⁵, Muskan Ranjan⁵, Riya Tyagi⁵

1. Assistant Professor, SPS, SGRR University, Dehradun, India.
2. Professor, SPS, SGRR University, Dehradun, India.
3. Professor, GRD (PG)IMT, Dehradun, India.
4. Assistant Professor, Maya College of Pharmacy, Dehradun, India.
5. Student, SPS, SGRR University, Dehradun, India.

Abstract:

Highlights of the literature on the anti-inflammatory properties of Boswellia and capsicums are presented in this article. Numerous review papers have been written in this area, however the majority of them offer a regional, constrained viewpoint on this crucial subject. This study provides a comprehensive analysis of the numerous review and research publications that have discussed the anti-inflammatory properties of extracts and/or pure substances obtained from Boswellia and capsicum. Additionally, some intriguing historically used medicinal herbs that have not yet been researched are identified in this analysis.

Keywords-Natural Products, anti-inflammatory, Boswellia, capsicums, plants extracts

Introduction

Inflammations

Infectious microorganisms like bacteria, viruses, or fungus commonly leads to inflammation when they come in contact with the body, live in specific tissues, or circulate in the circulation (1-3). Inflammation can also result from conditions such tissue damage, cell death, malignancy, ischemia, and degeneration. Inflammation is often created by a combination of the innate immune system and the adaptive immune system (4-9). The primary defensive mechanism against invasive microbes and cancer cells is the innate immune system, which involves the activity of many cells, including macrophages, mast cells, and dendritic cells. In the adaptive immune system, more specialized cells like B and T cells plays major role. They are in charge of destroying foreign infections and cancer cells by creating certain receptors and antibodies. Different forms of inflammatory reactions result in the synthesis and release of a variety of inflammatory mediators (5-9). Typically, pro- and anti-inflammatory mediators are used to categories inflammatory compounds. Some mediators, including interleukin (IL)-12, do, nonetheless, have the ability to both promote and reduce inflammation. Amid the inflammatory

mediators and cellular pathways that have been systematically investigated in connection with human pathological states are cytokines (such as interferons, interleukins, and tumor necrosis factor), chemokines (such as monocyte chemoattractant protein 1), eicosanoids (such as prostaglandins and leukotrienes), and the powerful transcription factor nuclear factor B that modulates inflammation (10).

Rheumatic arthritis

The chronic, symmetrical, inflammatory autoimmune illness rheumatoid arthritis (RA) first affects small joints, then bigger joints, and finally the skin, eyes, heart, kidneys, and lungs. Tendons and ligaments deteriorate, and joints' bone and cartilage are frequently lost (11). Deformities and bone erosion are brought on by all this joint deterioration, which is typically quite painful for the patient. The morning stiffness of the afflicted joints for longer than 30 minutes, weariness, fever, weight loss, sensitive, swollen, and heated joints, and rheumatoid nodules under the skin are common symptoms of RA. This illness often begins between the ages of 35 and 60, and it can go into remission or worsen. Juvenile RA (JRA), a condition comparable to RA in which the presence of the rheumatoid factor is absent, can also affect young children even before the age of 16. According to estimates, RA affects 1-2% of people in the West and 1% of people globally (12-17).



Boswellia Serrata

Plants and plant-derived items have served as mankind's main source of food, clothing, shelter, tastes, and scents for Aeon's. They have also been important sources of medicine-grade components. Natural resins have had a significant impact on this situation. Additionally, they have been employed as coating materials, adhesives, cosmetic preparation elements, ritual and religious ceremony perfumes, everyday ritual and ceremony fragrances, and for their many medicinal properties [18-20]. Natural resins were utilized for embalming and incense in ancient civilizations such as the Hindus, Babylonians, Persians, Romans, Chinese, and Greeks, as well as the inhabitants of old American civilizations. They were adamant that when these materials are exposed to flames, the smoke and scent they emit not only calm their spirits but also appease their gods. Their cultural life now heavily involved the burning of these natural resins. In order to protect their souls from the influence of bad spirits or to honor the deceased or alive, they burnt these resins during sacrifice rites and as part of their everyday rituals.

In arid mountainous areas of India, Northern Africa, and the Middle East, the *Boswellia serrata* (Salai/Salai guggul) (Family: Burseraceae; Genus: *Boswellia*) is a medium- to large-sized branching tree. In the plant kingdom, the Burseraceae family is represented by 600 species that

are found in all tropical climates in 17 genera. The *Boswellia* genus has around 25 species, the majority of which are found in Arabia, along the northeastern coast of Africa, and in India. Three of these species have traditionally been regarded as the "real Frankincense" producing trees (21-24).

The earliest species of *Boswellia*, *Boswellia sacra* Flueck, is found in South Arabia and is referred to by the Arabic term "maghrayt d' sheehaz"; the resin it produces is referred to as "luban dhakar." *Boswellia carterii* Birdw is a plant that grows in Somalia. In the local tongue, it is known as "moxor," and the resin it produces is referred to as "luban dhakar." Additionally, a Somali species, *Boswellia frereana* Birdw. is known as "jagcaar" in the local dialect, and the resin it produces is referred to as "loban majdi" or "maydi." This brand of resin is the priciest one available. *Boswellia serrata* Roxb., also known as Indian olibanum, Indian frankincense, dhup, salai, or salai guggul, is another species that produces resin. It is found in the central and northern regions of Eastern India. Since over 25 years ago, Shallaki has been used to market a high-quality extract of it in India (25-27).

Traditional uses

One of the most valuable and old herbs in Ayurveda is *Boswellia serrata*. A Sanskrit term for *Boswellia* called "Gajabhakshya" has been used occasionally, and it implies that elephants use this herb (28). The foundation of classical Ayurvedic science, which has its roots in India, is made up of three renowned ancient texts: Charka's *Charka Samhita* (c. B. C. 700), the first basic medical text; Susruta's *Susruta Samhita* (c. B. C. 600), which attempted to compile all of the medical knowledge with an emphasis on surgery; and the two-volume work *Astanga Samgraha* and *Astanga Hridaya Gugguls*, or gum resins from trees, are mentioned in the first two supports of Ayurveda as having antirheumatic (anti-arthritis) properties(29–32). This gummy resin is cited in traditional Ayurvedic and Unani texts as an effective treatment for arthritis in addition to its beneficial uses for diarrhoea, dysentery, ringworm, boils, fevers (antipyretic), skin and blood diseases, cardiovascular diseases, mouth sores, bad throat, bronchitis, asthma, cough, vaginal discharges, hair loss, jaundice, haemorrhoids, syphilitic diseases, irregular menses. Additionally, it is diaphoretic, astringent, diuretic, and stimulates both the interior and exterior nervous systems. Its usage as an anti-arthritic, anti-inflammatory, anti-hyperlipidemic (controls blood lipids), anti-atherosclerotic (anticoronary plaque), analgesic (pain-reliever), and hepatoprotective is well supported by modern medicine and pharm

Formulations Containing *Boswellia serrata*:

In 1991, Sabinsa Corporation introduced the US and European markets to Boswellin®, a recognised trademark. This comes in pill or tablet form, as well as a calming lotion that relieves pain and contains capsaicin. The recommended dosage for products containing boswellic acids is 150–250 mg/capsules or tablets, taken orally two–three times a day. As a Licensed User of the

Trade Mark owned by MMI Corporation, Himalayan Drug Company, Makali, Bangalore produces Shallaki®, which includes 125 mg of *Boswellia serrata* in each capsule and has great anti-inflammatory and analgesic effects that can help with joint discomfort. The dosage is 1 capsule twice day, at a cost of Rs. 75 for 60 capsules (Batch No. F297001G). The company's website may be found at www.himalayaheal.com.

Niltan® is an externally applied cream that comes in a 15 g tube. It is a blend of active herbal extracts and is made by Dr. Reddy's Laboratories Limited in Hyderabad (boswellin, arbutin, liquorice extract and coriander seed oil in a cream base). It lessens the skin's synthesis of melanin, which in turn lessens the development of dark skin, by reducing the activity of the tyrosinase enzyme within the skin.

Rheumatic-X®, produced by Sunrise Herbals in Varanasi, India, includes 20 mg of "Shallaki" in addition to other substances and is intended to treat rheumatoid, gouty, osteoarthritis, and sciatic pain. It should be used as prescribed by a doctor, two capsules twice day (33-34).



Capsaicin

The complicated action of capsaicin and its associated vanilloids on primary sensory neurons plays a significant part in the physiology of pain by detecting a high threshold to painful chemical and physical stimuli, which is the initial step in initiating the pain session (35). Capsaicin first causes their activation, which is characterized by a local burning and stinging sensation (36) and may be linked to hyperalgesia and allodynia after being exposed to heat and mechanical stimulation (37). Because of the neuropeptides that are produced by the peripheral sensory nerve fibers, these nociceptive effects are followed with a localized, transitory inflammatory response known as neurogenic inflammation. The analgesic/anti-nociceptive effect of topical application of capsaicin is primarily caused by the initial excitation of nociceptive neurons, which is followed by a loss of responsiveness, known as desensitization of nociceptive neurons (38) in cases of repeated or prolonged applications of capsaicin. To "defunctionalize" cutaneous nociceptors and cure painful disorders, low-concentration topical creams, gels, lotions, and patches containing capsaicin (0.025, 0.075, and 0.1%) were created (39). Capsaicin also inhibits the first inflammatory response and further depletes the neuropeptides from the sensory nerve terminals (40). When administered in high quantities or over an extended length of time, capsaicin can potentially cause a gradual neurotoxic degeneration of cutaneous nerves.

Capsaicin has been used to treat neuropathic pain (40-47), post-herpetic neuralgia (50), diabetic and/or HIV-related neuropathy (50-55), burning mouth syndrome, temporomandibular joint problem, chemotherapy-induced peripheral neuropathy, and fibromyalgia. Topical use of capsaicin demonstrated its efficacy and safety in trials involving patients with osteoarthritis and rheumatoid arthritis as an alternative to systemic analgesics, which frequently may result in major side effects.

Furthermore, capsaicin-induced local inflammation may be seen and measured using laser-Doppler flowmetry and more recently utilizing *in vivo* reflectance confocal microscopy, highlighting its potential diagnostic utility in a variety of functional abnormalities of cutaneous sensory nerve fibers (55-60).

More than 200 different species make up the genus *Capsicum*, and the fruits' size, shape, flavor, and level of heat vary greatly. *Capsicum annuum*, *Capsicum baccatum*, *Capsicum chinense*, *Capsicum frutescens*, and *Capsicum pubescens* are the five primary species mentioned in the literature. The Solanaceae family, which also includes peppers of significant economic importance, comprises peppers endemic to the tropical and humid regions of Central and South America (Govindarajan, 1986; Menichini et al., 2009). According to Meghvansi et al. (2010), they are frequently used as a spice or food as well as for a wide range of therapeutic uses in Indian, Native American, and Chinese medicinal traditions for the treatment of arthritis, rheumatism, stomach aches, skin rashes, dog bites, and wounds. According to Hervert-Hernandez et al. (2010), *Capsicum annuum*, *Capsicum chinense*, and *Capsicum frutescens* contain a variety of phytochemicals with well-known antioxidant properties, including carotenoids (Deli et al., 2001), capsaicinoids (Osa et al., 2002; Ochi et al., 2003; Pino et al., 2007), and Marin et al., 2004; Materska and Perucka; Howard et al., 2000;2005; Kappel and others (2008)). Due to its lipophilic nature and prominence as the primary representative of the pungent components, Clinical practice has made advantage of analgesic and anti-inflammatory properties.

Animal tests revealed that *Capsicum annuum* has hypocholesterolemia effects (Srinivasan, 2005; Aizawa and Inakuma, 2009). Recent research has shown that the etiology of atherosclerosis and, subsequently, the increased risk of cardiovascular illnesses are directly related to hyperlipidemia, inflammation, and oxidative stress (Libby, 2002; Arroyo and Iruela-Arispe, 2010). Therefore, a substance with antioxidant and anti-inflammatory properties will be helpful in preventing these illnesses. The chili pepper Brazil is one of the countries that consumes a lot of *Capsicum baccatum* var. *pendulum*, and the few reports on it that have been published in the literature have mostly dealt with its carotenoid and capsaicinoid contents as well as the antioxidant activity of its crude juice. In a preliminary investigation into the anti-inflammatory properties, Spiller et al. (2008) tested a crude extract of *Capsicum baccatum* administered intravenously and subcutaneously to rats at dosages of 0.2, 2 and 20 g/kg. Activity was seen with the final two dosages. To find the components responsible for the antioxidant and anti-inflammatory

properties, *Capsicum baccatum* was fractionated in the current investigation to produce an enhanced bioactive extract. In order to link these findings with the tested activity, we also determined the extracts' total phenolic component, flavonoid, and capsaicin contents.

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