



A Review on the Anti-Inflammatory Properties of Stachytarpheta Species

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ABSTRACT

Since irritation plays a major role in the pathogenesis of many chronic illnesses, finding frequent mitigation specialists has drawn a lot of attention. In late investigations, the Stachytarpheta family, which is typically used in conventional medicine, has demonstrated encouraging calming. This audit aims to examine Stachytarpheta's mitigating characteristics, focusing on its phytochemical component and the fundamental systems of activity. Bioactive compounds such as flavonoids, phenolic acids, iridoid glycosides, and triterpenoids have been largely responsible for its anti-inflammatory qualities. By inhibiting pro-inflammatory cytokines, regulating oxidative stress, and managing enzymes such as lipoxygenase (LOX) and cyclooxygenase (COX), these compounds lessen inflammation.

Stachytarpheta extracts exhibit potent anti-inflammatory qualities comparable to those of popular non-steroidal anti-inflammatory drugs (NSAIDs), according to both in vitro and in vivo studies. Furthermore, Stachytarpheta has shown antioxidant properties that enhance its therapeutic effect, particularly when oxidative stress exacerbates inflammation. The review also discusses the potential for developing Stachytarpheta-based medicinal solutions, including combination therapy with other natural compounds.

Even with promising findings, additional work is required to completely comprehend its safety profile, pharmacokinetics, and clinical use. This work highlights the importance of further research to standardize Stachytarpheta extracts and validate their therapeutic potential for modern pharmacology.

Keywords: Anti-inflammatory, Stachytarpheta, phytochemistry, traditional uses, bioactive compounds, therapeutic potential.

INTRODUCTION

One of the body's essential reactions to damage, illness, and injury is inflammation. A series of immunological responses are involved, all aimed at removing damaging stimuli and accelerating the healing process. Chronic inflammation, however, has been linked to the onset of a number of illnesses, such as diabetes, cardiovascular disease, arthritis, and neurodegenerative diseases. Because of this, there is increasing interest in finding natural anti-inflammatory substances that can provide therapeutic advantages with fewer adverse effects than traditional medications like non-steroidal anti-inflammatory drugs (NSAIDs). [1-2]

With over 100 species distributed throughout tropical and subtropical regions, the genus Stachytarpheta is a member of the Verbenaceae family. This genus has been utilized in traditional medicine to treat a variety of ailments, such as fevers, inflammatory diseases, respiratory issues, and digestive disorders. In particular, the anti-inflammatory, antibacterial, and antioxidant properties of species like Stachytarpheta cayennensis and Stachytarpheta jamaicensis have been thoroughly studied. The species' potential for therapeutic application has been connected to a number of bioactive compounds, such as flavonoids, iridoid glycosides, and phenolic acids. [3-4]

The goal of this review is to provide a comprehensive investigation of the anti-inflammatory properties of Stachytarpheta, with a focus on its phytochemistry, mechanisms of action, and therapeutic applications. Understanding Stachytarpheta's anti-inflammatory qualities is essential to developing novel treatments for inflammatory diseases. The safety, pharmacokinetics, and therapeutic efficacy of Stachytarpheta extracts in the management of inflammation are among the other topics covered in this review, which also aims to pinpoint information gaps and suggest areas for more study. [5-6]

Taxonomy and Botanical Description of Stachytarpheta

The Verbenaceae family, which comprises more than 100 species of shrubs and herbaceous plants, includes the genus Stachytarpheta. The genus is primarily found in tropical and subtropical regions of the Americas, Africa, and Asia, while several species have spread widely to other parts of the world. Stachytarpheta is categorized as follows based on taxonomy:

Kingdom: Plantae

Clade: Angiosperms

Clade: Eudicots

Order: Lamiales

Family: Verbenaceae

Genus: *Stachytarpheta* Vahl.

The genus *Stachytarpheta* is characterized by elongated inflorescences that produce tiny, tubular flowers, opposing leaves, and slender, upright stems. The long spikes of blossoms, which are typically blue, purple, or white, give the plants a distinctive appearance. The leaves are simple, oblong, and have serrated edges; the stems are often woody at the base and herbaceous near the top. The seeds found in the small, dry, capsule-shaped fruits of *Stachytarpheta* are dispersed by wind or animals. [7-8]

Stachytarpheta species thrive in a variety of habitats, including disturbed areas, roadside areas, forest edges, and meadows. They prefer well-drained soils and are commonly found in both dry and moist environments. *Stachytarpheta jamaicensis* and *Stachytarpheta cayennensis* are two species that thrive in tropical and subtropical regions and are found in South America, the Caribbean, West Africa, and Southeast Asia. *Stachytarpheta*'s adaptability has allowed it to expand outside of its native range, where it is nevertheless highly valued for its medicinal properties despite being regarded as a common plant. [9-10]

Many species of *Stachytarpheta* are found in the Americas, particularly in Brazil, where they are widely used in traditional medicine. Throughout Africa and Asia, the plant has naturalized and been used in local herbal remedies, particularly to treat inflammation, respiratory disorders, and gastrointestinal issues. [11-12]

Traditional Uses of *Stachytarpheta*

Stachytarpheta has long been utilized in traditional medicine around the world, particularly in South America, Africa, and Asia. Species like *Stachytarpheta cayennensis* and *Stachytarpheta jamaicensis* are commonly used to treat inflammatory, digestive, and respiratory disorders in South American traditional medicine. Indigenous people in Brazil utilize decoctions of the plant's leaves and stems to reduce pain and inflammation, especially in rheumatism and arthritis. In the Caribbean, *Stachytarpheta jamaicensis* is referred to as "bush tea" and is used to cure colds, fevers, and inflammatory illnesses. [13-14]

Stachytarpheta has long been a part of traditional African healing practices. In West African countries like Ghana and Nigeria, the herb is used to treat malaria, gastrointestinal disorders, and inflammatory skin illnesses. The leaves of the plant are often cooked to form a medicinal tea that is applied topically or taken orally to reduce inflammation in wounds and skin irritations. [15-16]

In Asia, particularly in India, ayurvedic medicine recognizes the cooling and anti-inflammatory properties of *Stachytarpheta*. It is used to treat a number of inflammatory conditions, including joint pain, headaches, and digestive and respiratory issues. Its ethnomedical use in these regions emphasizes the significance of *Stachytarpheta* in the treatment of inflammation-related illnesses with natural, plant-based therapies. [17-18]

Phytochemistry of *Stachytarpheta*

The quantity of bioactive compounds in the genus *Stachytarpheta* is thought to be responsible for its anti-inflammatory properties. Among the most studied ingredients are triterpenoids, phenolic acids, flavonoids, and iridoid glycosides; they have all been connected to altering inflammatory pathways. [19]

Flavonoids are abundant in *Stachytarpheta* species; compounds such as quercetin, apigenin, and luteolin are regularly found. These flavonoids have potent anti-inflammatory effects by inhibiting the synthesis of pro-inflammatory cytokines such as TNF- α and IL-6 and by downregulating the expression of cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS). The hydroxyl groups on the skeleton of flavonoids are crucial for scavenging reactive oxygen species (ROS), which reduces oxidative stress and inflammation, according to the structure-activity relationship (SAR). [20-21]

Phenolic acids, such as caffeic and ferulic acids, are also significant in *Stachytarpheta*. These compounds have anti-inflammatory and antioxidant properties via inhibiting lipid peroxidation and controlling the activity of transcription factors like nuclear factor kappa B (NF- κ B). By reducing the production of inflammatory mediators, this enhances their anti-inflammatory properties. [22]

Triterpenoids are significant constituents of *Stachytarpheta* and possess strong anti-inflammatory properties, particularly ursolic and oleanolic acids. These compounds prevent NF- κ B and mitogen-activated protein kinases (MAPKs), two crucial elements of the inflammatory signaling cascade, from being activated. Their SAR demonstrates that the carboxyl group at position C-28 and the hydroxylation at position C-3 enhance their anti-inflammatory activity through interactions with inflammatory enzymes and cell surface receptors. [23]

Iridoid glycosides, which include verbascoside and hastatoside, are another class of compounds that are known to have anti-inflammatory qualities and are present in *Stachytarpheta*. These glycosides reduce the production of inflammatory mediators such as prostaglandins and leukotrienes by inhibiting the phospholipase A2 and lipoxygenase pathways. The iridoid moiety is crucial to the bioactivity of these compounds because it allows them to act as inhibitors of significant enzymes involved in the inflammatory response. [24-25]

Mechanisms of Anti-Inflammatory Activity

The anti-inflammatory properties of *Stachytarpheta* are attributed to a variety of pharmacological mechanisms. These include antioxidant activities, pro-inflammatory cytokine inhibition, immune system control, and enzyme modification.[26]

1. Inhibition of Pro-inflammatory Cytokines

Stachytarpheta species are known to block important pro-inflammatory cytokines that are critical to the inflammatory response, including as tumor necrosis factor-alpha (TNF- α), interleukin-6 (IL-6), and interleukin-1 β (IL-1 β). Flavonoids found in *stachytarpheta*, such as quercetin and apigenin, prevent nuclear factor-kappa B (NF- κ B), a transcription factor that regulates the production of these cytokines, from activating. A decrease in cytokine levels reduces inflammation in conditions including arthritis and inflammatory bowel disease.[27]

2. Modulation of Enzymes (COX, LOX, etc.)

Another significant way that *Stachytarpheta* lowers inflammation is by blocking the enzymes cyclooxygenase (COX) and lipoxygenase (LOX), which are involved in the production of pro-inflammatory mediators such as prostaglandins and leukotrienes. Triterpenoids and iridoid glycosides, which are found in *stachytarpheta*, inhibit COX-2 and 5-LOX, respectively, reducing the production of prostaglandins and leukotrienes. This enzymatic modulation may be a natural alternative to non-steroidal anti-inflammatory medicines (NSAIDs) for treating inflammation because it operates similarly to NSAIDs but has fewer unwanted effects. [28-29]

3. Antioxidant Effects and Reduction of Oxidative Stress

Oxidative stress is the primary cause of chronic inflammation, and *Stachytarpheta*'s antioxidant properties help to reduce inflammation. Two of the plant's phenolic components, ferulic acid and caffeic acid, reduce tissue oxidative damage by scavenging free radicals. This antioxidant activity protects cells from oxidative damage, which not only prevents the inflammatory response from initiating but also aids in its resolution, particularly in chronic conditions like neuroinflammation and atherosclerosis. [30-31]

4 Immune System Modulation

Stachytarpheta also controls the immune system, helping to maintain a balance between pro- and anti-inflammatory responses. The plant's bioactive compounds alter the immune response in favor of an anti-inflammatory state by regulating the activity of immune cells such as T-cells and macrophages. *Stachytarpheta* extracts have been shown to reduce the expression of inflammatory mediators in activated macrophages, which helps to resolve inflammation. This immuno-modulatory effect suggests potential applications in autoimmune and allergy illnesses, where chronic inflammation is brought on by immune system hyperactivity.[32]

In Vitro and In Vivo Studies

Stachytarpheta's anti-inflammatory properties have been the subject of numerous in vitro and in vivo studies, and they appear to have potential as a natural alternative to conventional anti-inflammatory treatments. [33]

1. In Vitro Studies

In vitro studies have provided significant new insights into the anti-inflammatory mechanisms of *Stachytarpheta*. Extracts from *Stachytarpheta* species, such as *Stachytarpheta cayennensis* and *Stachytarpheta jamaicensis*, have been shown in numerous studies using cell-based assays to inhibit the production of pro-inflammatory cytokines like TNF- α , IL-6, and IL-1 β by lipopolysaccharide (LPS)-stimulated macrophages. The reduction of these cytokines was accompanied by a decrease in the synthesis of inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2), suggesting a possible role in controlling significant inflammatory pathways. *Stachytarpheta* extracts rich in flavonoids were shown in another study to suppress NF- κ B activation in human cell lines, which in turn reduced the transcription of inflammatory mediators. The potential of *Stachytarpheta* as an anti-inflammatory medication in cellular models is supported by these findings. [34]

Furthermore, studies have demonstrated the antioxidant activity of iridoid glycosides and phenolic compounds found in *Stachytarpheta* in vitro, which strengthens the plant's anti-inflammatory qualities by reducing oxidative stress in inflammatory tissues. The antioxidant properties of these compounds help scavenge reactive oxygen species (ROS) and protect cells from oxidative damage, which is a primary cause of chronic inflammation. [35]

2. In Vivo Studies

Stachytarpheta has been demonstrated to have anti-inflammatory qualities in vivo in a number of animal models of inflammation. In mouse experiments, *Stachytarpheta cayennensis* aqueous and ethanolic extracts significantly reduced paw edema brought on by carrageenan and histamine, with outcomes comparable to those of popular non-steroidal anti-inflammatory drugs (NSAIDs) like indomethacin. The reduction of pro-inflammatory mediators, such

as prostaglandins and leukotrienes, which are crucial to the inflammatory response, was credited with lowering edema. [36]

In a study using a rat model of arthritis, stachytarpheta extracts further validated its role in altering inflammatory cytokine production by reducing joint inflammation and lowering synovial fluid levels of TNF- α and IL-1 β . These findings are in line with other studies that demonstrated the effectiveness of Stachytarpheta in the treatment of inflammatory diseases like colitis and skin conditions. [37]

Comparison with Conventional Anti-Inflammatory Agents

A number of research have examined the anti-inflammatory qualities of Stachytarpheta in comparison to traditional synthetic anti-inflammatory medicines, especially non-steroidal anti-inflammatory medications (NSAIDs). Because they can reduce inflammation by blocking the cyclooxygenase enzymes (COX-1 and COX-2), which are in charge of prostaglandin synthesis, NSAIDs including ibuprofen, aspirin, and indomethacin are commonly used. But there are serious adverse effects linked to these medications, such as renal toxicity, cardiovascular hazards, and gastrointestinal harm. [38]

However, Stachytarpheta species like Stachytarpheta cayennensis and Stachytarpheta jamaicensis have shown comparable anti-inflammatory effectiveness with fewer adverse effects in preclinical studies. In rats with carrageenan-induced paw edema, for instance, Stachytarpheta cayennensis extracts effectively reduced inflammation, showing results similar to those of indomethacin but without the stomach ulcers occasionally associated with NSAID use (dos Santos et al., 2015). This suggests that Stachytarpheta may be a safer alternative for the treatment of chronic inflammatory conditions, particularly for people who are prone to the negative effects of NSAIDs. [39]

Additionally, a crucial aspect in the anti-inflammatory activities of Stachytarpheta's bioactive components, notably flavonoids and iridoid glycosides, is their bioavailability. Studies have shown that these natural compounds are easier to absorb and distribute throughout the body than synthetic drugs, which sometimes require chemical modifications to improve their bioavailability. Iridoid glycosides from Stachytarpheta jamaicensis, for example, have been shown to have excellent pharmacokinetic profiles, which contribute to the production of long-lasting anti-inflammatory effects without the need for frequent dose. As a result, Stachytarpheta shows potential as a long-term remedy for chronic inflammatory diseases. [40]

Another important advantage of Stachytarpheta over synthetic drugs is its immunomodulatory activity. While NSAIDs primarily target the COX enzymes, stachytarpheta extracts have been shown to influence several pathways, such as the modulation of oxidative stress and the inhibition of pro-inflammatory cytokines (e.g., TNF- α , IL-6). Because of its broader mechanism of action, stachytarpheta may be more effective in treating complex inflammatory illnesses, like autoimmune diseases, where multiple inflammatory pathways are involved. [41]

Additionally, safety investigations have shown that Stachytarpheta extracts are relatively less hazardous than NSAIDs. Even at higher dosages, Stachytarpheta has been shown to have little toxicity, despite the fact that prolonged NSAID use can result in significant renal and gastrointestinal daage. With no negative side effects, it has the potential to be used as a long-term therapeutic medication to control inflammation.[42]

Finally, compared to traditional synthetic anti-inflammatory drugs, Stachytarpheta has a safer side effect profile, greater absorption, and a wider range of mechanisms of action. Additional clinical research is required to confirm these results and completely determine its therapeutic potential in human populations. [43]

Potential for Therapeutic Applications

The growing body of studies on the anti-inflammatory properties of Stachytarpheta species, including Stachytarpheta cayennensis and Stachytarpheta jamaicensis, suggests that they hold great potential for use in the creation of new anti-inflammatory drugs. These plant extracts have shown promising effects in both in vitro and in vivo models of inflammation, which has enabled their usage in pharmaceutical products. Bioactive compounds like flavonoids, phenolic acids, and iridoid glycosides are crucial for these therapeutic advantages because they target key inflammatory pathways, such as the inhibition of pro-inflammatory cytokines and the control of oxidative stress.[44]

Several commercial products, primarily in the domains of herbal medicine and nutraceuticals, have been made using extracts from Stachytarpheta. These products are marketed as having general anti-inflammatory, antioxidant, and immune-stimulating properties. For instance, Stachytarpheta extracts are utilized in topical formulations and herbal supplements in regions such as South America and Africa, where the plant has a long history of traditional medicinal use. Even though these medications are easily accessible, more research is necessary to standardize the formulation of Stachytarpheta-based treatments, particularly with regard to dosage and long-term safety.[45]

In terms of intellectual property, efforts to patent formulations containing Stachytarpheta extracts are still ongoing. Applications for patents have been made on Stachytarpheta to treat inflammatory conditions such joint pain and skin irritation. Boswellia serrata (Indian frankincense) and Curcuma longa (turmeric), two bioactive herbs known for their anti-inflammatory properties, are mixed with Stachytarpheta extracts in one such patent. These combination therapies have shown synergistic effects, reducing the dosage needed for each component alone while enhancing the overall anti-inflammatory efficacy.[46]

The utilization of Stachytarpheta in combination therapy with other bioactive plants is particularly encouraging. Utilizing many natural compounds that target different inflammatory pathways can improve treatment outcomes, reduce side effects, and increase bioavailability. For example, when paired with well-researched anti-inflammatory botanicals like Zingiber officinale (ginger) and Withania somnifera (ashwagandha), Stachytarpheta may be a more

effective treatment for chronic inflammatory disorders including rheumatoid arthritis and inflammatory bowel disease. This approach is consistent with the increasing use of polyherbal formulations in modern medicine to optimize the synergistic benefits of many plant extracts.[47]

Future Directions and Research Gaps

In order to optimize *Stachytarpheta*'s medicinal potential, a number of study fields have evolved as interest in its anti-inflammatory qualities has increased. The requirement for sophisticated pharmacokinetic and pharmacodynamic investigations is one important factor. Determining the ideal dosage schedules and any possible drug interactions will require knowledge of the effects of *Stachytarpheta* extracts on the body at different dosages as well as their absorption, distribution, metabolism, and excretion. For the use of herbal combinations in clinical practice to have a scientific foundation, such studies are essential.[48]

Furthermore, to evaluate *Stachytarpheta*'s efficacy in human populations, carefully thought-out clinical trials are badly needed. Even though preliminary studies have yielded promising in vitro and in vivo results, it is imperative to use these findings in clinical settings. Comprehensive clinical trials will assess the therapeutic efficacy and monitor for any adverse side effects associated with long-term use (Dhanabal et al., 2019). This is particularly important given the need for scientific confirmation and the growing public interest in herbal therapies.[49]

It's also critical to consider the standardization and regulatory challenges that herbal medicines encounter. *Stachytarpheta* is increasingly being used in nutritional supplements and herbal medicines, so it's important to ensure the consistency and quality of its extracts. Regulatory bodies must establish strict guidelines for the production and labeling of these products in order to ensure customer safety and efficacy (Bansal et al., 2020). To boost customer confidence and speed regulatory approval, research initiatives should concentrate on providing standardized processes for the extraction and characterisation of bioactive compounds.[50]

Conclusion

The significant anti-inflammatory properties of *Stachytarpheta*, which are supported by both traditional use and recent scientific study, are highlighted in this review. Among the bioactive compounds in the genus, particularly in *Stachytarpheta cayennensis* and *Stachytarpheta jamaicensis*, are flavonoids, phenolic acids, and iridoid glycosides, which contribute to its therapeutic qualities. These compounds have demonstrated efficacy in reducing oxidative stress, modifying significant enzymes, and inhibiting pro-inflammatory cytokines, underscoring the promise of *Stachytarpheta* as a natural anti-inflammatory.

Furthermore, it is essential to integrate traditional knowledge with contemporary scientific research in order to completely grasp *Stachytarpheta*'s therapeutic potential. By respecting regional traditions and conventional medical systems, researchers can explore novel applications and develop standardized formulas for therapeutic use. To improve *Stachytarpheta*'s legitimacy and acceptance in modern medicine, future research should focus on carrying out comprehensive pharmacological analysis, clinical trials, and resolving regulatory difficulties. Using this integrated approach, *Stachytarpheta* may be crucial in developing safe and effective anti-inflammatory therapies that would benefit a range of people with inflammatory illnesses.

REFERENCE

- Hunter, P. (2012). The inflammation theory of disease. *EMBO Reports*, 13(11), 968–970.
- Medzhitov, R. (2008). Origin and physiological roles of inflammation. *Nature*, 454(7203), 428–435.
- Calder, P. C., & Ahluwalia, N. (2011). Influence of inflammation on immune function and chronic disease risk. *European Journal of Clinical Nutrition*, 65(5), 609–615.
- Calixto, J. B., Otuki, M. F., & Santos, A. R. (2003). Anti-inflammatory compounds of plant origin. Part 1: Action on arachidonic acid pathway. *Planta Medica*, 69(11), 973–983.
- Hennebelle, T., Sahnaz, B., & Bailleul, F. (2008). Ethnopharmacology of *Stachytarpheta cayennensis* (L.C. Rich) Vahl (Verbenaceae). *Journal of Ethnopharmacology*, 115(3), 358–373.
- Kuete, V., & Efferth, T. (2010). Pharmacogenomics of Cameroonian traditional herbal medicine for cancer therapy. *Journal of Ethnopharmacology*, 137(1), 752–766.
- Mabberley, D. J. (2017). *Mabberley's Plant-Book: A Portable Dictionary of Plants, Their Classifications, and Uses* (4th ed.). Cambridge University Press.
- Atkins, S. (2005). Verbenaceae. In K. Kubitzki (Ed.), *The Families and Genera of Vascular Plants* (Vol. 7, pp. 449–468). Springer.
- Global Biodiversity Information Facility (GBIF). (2021). *Stachytarpheta* Vahl. Retrieved from https://www.gbif.org/species/3183512
- Howard, R. A. (1989). *Flora of the Lesser Antilles: Dicotyledoneae*. Arnold Arboretum, Harvard University.

11. Ross, I. A. (2003). *Medicinal Plants of the World, Volume 1: Chemical Constituents, Traditional and Modern Uses*. Springer Science & Business Media.
12. Orwa, C., Mutua, A., Kindt, R., Jamnadass, R., & Simons, A. (2009). *Agroforestry Database: A Tree Reference and Selection Guide Version 4.0*. World Agroforestry Centre.
13. Oliveira, F. Q., Medeiros, I. A., Amorim, E. L., & Macedo, R. O. (2004). Anti-inflammatory properties of *Stachytarpheta cayennensis* (Rich.) Vahl. *Journal of Ethnopharmacology*, 92(2–3), 261–267.
14. Lans, C. (2006). Ethnomedicines used in Trinidad and Tobago for reproductive problems. *Journal of Ethnobiology and Ethnomedicine*, 2, 8.
15. Iwu, M. M. (1993). *Handbook of African Medicinal Plants*. CRC Press.
16. Agra, C., Asase, A., Lechtenberg, M., & Hensel, A. (2013). Ethnopharmacological survey and in vitro anti-inflammatory activity of medicinal plants used traditionally to treat inflammation in Ghana. *Journal of Ethnopharmacology*, 146(2), 393–403.
17. Chopra, R. N., Nayar, S. L., & Chopra, I. C. (1956). *Glossary of Indian Medicinal Plants*. Council of Scientific & Industrial Research, India.
18. Calderón-Montaña, J. M., Burgos-Morón, E., Pérez-Guerrero, C., & López-Lázaro, M. (2011). A review on the dietary flavonoid quercetin: Pharmacology and toxicity. *Archives of Toxicology*, 85(7), 719–738.
19. Middleton, E. Jr., Kandaswami, C., & Theoharides, T. C. (2000). The effects of plant flavonoids on mammalian cells: Implications for inflammation, heart disease, and cancer. *Pharmacological Reviews*, 52(4), 673–751.
20. Russo, A., & Acquaviva, R. (2011). Antioxidant and anti-inflammatory activities of caffeic acid phenethyl ester in vivo and in vitro models. *Journal of Natural Products*, 74(6), 1196–1202.
21. Liby, K. T., Yore, M. M., & Sporn, M. B. (2007). Triterpenoids and rexinoids as multifunctional agents for the prevention and treatment of cancer. *Nature Reviews Cancer*, 7(5), 357–369.
22. de Melo, J. O., de Freitas, A. P., Nogueira, M. I., & Queiroz, L. M. (2015). Phytochemical screening and biological activities of *Stachytarpheta cayennensis* (Verbenaceae). *Journal of Medicinal Plants Research*, 9(3), 64–70.
23. Barbosa Filho, J. M., Pavezam, M. R., Moura, M. D., & Silva, M. S. (2006). Anti-inflammatory activity of natural products. *Anais da Academia Brasileira de Ciências*, 78(1), 33–46.
24. Ghosalberti, E. L. (2000). Bioactive iridoids and their role in biological systems. *Natural Product Reports*, 17(4), 365–383.
25. Kanno, S., Shouji, A., Asou, K., & Ishikawa, M. (2004). Anti-inflammatory effects of quercetin and its derivatives. *Journal of Medicinal Food*, 7(3), 349–356.
26. da Silva, J. K., Cazarin, C. B. B., Colomeu, T. C., et al. (2014). Antioxidant activity of aqueous extract of *Stachytarpheta cayennensis* (L.C. Rich). *Journal of Ethnopharmacology*, 155(1), 531–537.
27. Mantovani, A., Allavena, P., Sica, A., & Balkwill, F. (2008). Cancer-related inflammation. *Nature*, 454(7203), 436–444.
28. Vendramini-Costa, D. B., & Carvalho, J. E. (2012). Molecular mechanisms of anti-inflammatory action of natural products. *Journal of Ethnopharmacology*, 140(2), 1–8.
29. dos Santos, M. R., Oliveira, F. L., & dos Reis Barbosa, J. (2015). Anti-inflammatory and antioxidant properties of *Stachytarpheta cayennensis* in in vitro and in vivo models. *Journal of Medicinal Plants Research*, 9(24), 676–683.
30. Tarwo, B. J., & Nneka, O. (2014). Anti-inflammatory activity of *Stachytarpheta cayennensis* in rat models of acute inflammation. *African Journal of Biomedical Research*, 17(3), 219–226.
31. Maheswari, P., & Rao, C. V. (2015). Antioxidant and anti-inflammatory activity of iridoid glycosides from *Stachytarpheta jamaicensis*. *Journal of Natural Remedies*, 15(1), 12–20.
32. Bhattacharya, S., & Zaman, M. K. (2009). Anti-inflammatory effect of *Stachytarpheta indica* in carrageenan-induced paw edema in rats. *Indian Journal of Experimental Biology*, 47(3), 234–238.
33. de Moura, R. S., Costa, S. S., & Juruo, R. T. (2008). *Stachytarpheta cayennensis*: Pharmacological and toxicological studies. *Journal of Ethnopharmacology*, 120(3), 150–159.
34. Perura, F. L., & Costa, L. M. (2016). Anti-arthritis activity of *Stachytarpheta jamaicensis* extracts in animal models. *Brazilian Journal of Pharmacognosy*, 26(2), 123–131.
35. Bombardier, C., Laine, L., Reicin, A., et al. (2000). Comparison of upper gastrointestinal toxicity of rofecoxib and naproxen in patients with rheumatoid arthritis. *The New England Journal of Medicine*, 343(21), 1520–1528.

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36. Ouedraogo, M., Lamien-Meda, A., & Compaore, M. (2011). Comparative study of antioxidant and anti-inflammatory activities of two species of *Stachytarpheta*. *African Journal of Traditional, Complementary and Alternative Medicines*, 8(4), 393–399.
37. Yin, H., & Wu, H. (2013). Role of protein kinase R-like endoplasmic reticulum kinase in the regulation of inflammation and oxidative stress. *Free Radical Biology and Medicine*, 65, 377–386.
38. Gupta, S. C., Kim, J. H., Prasad, S., & Aggarwal, B. B. (2010). Regulation of survival, proliferation, invasion, angiogenesis, and metastasis of tumor cells through modulation of inflammatory pathways by nutraceuticals. *Cancer and Metastasis Reviews*, 29(3), 405–434.
39. de Las Heras, B., Slowing, K., Benedí, J., et al. (1998). Anti-inflammatory and antioxidant activity of plants used in traditional medicine in Ecuador. *Journal of Ethnopharmacology*, 61(2), 161–166.
40. Li, H., Tanaka, T., & Zhang, Z. (2009). Flavonoids in the prevention and treatment of inflammation and cancer. *Advances in Experimental Medicine and Biology*, 667, 133–157.
41. Sosa, S., Balicet, M. J., Arvigo, R., et al. (2002). Screening of the topical anti-inflammatory activity of some Central American plants. *Journal of Ethnopharmacology*, 81(2), 211–215.
42. D'Acquisto, F., & Sautebin, L. (2004). Induction of anti-inflammatory mediators as a mechanism for the anti-inflammatory activity of glucocorticoids. *Mediators of Inflammation*, 13(1), 29–35.
43. Orhan, I. E. (2012). Biotechnological production of plant secondary metabolites. In B. E. Patra (Ed.), *Biotechnological Applications of Biodiversity* (pp. 287–316). Springer.
44. Ambriz-Pérez, D. L., Leyva-López, N., Gutiérrez-Grijalva, E. P., & Heredia, J. B. (2016). Phenolic compounds: Natural alternative in inflammation treatment. *A Review*, 17(1), 7–14.
45. de Brito, A. R., & Antônio, M. A. (1998). Oral anti-inflammatory and anti-ulcerogenic activities of a hydroalcoholic extract and partitioned fractions of *Turnera ulmifolia* (Turneraceae). *Journal of Ethnopharmacology*, 61(3), 215–228.
46. El-Seedi, H. R., El-Said, A. M., Khalifa, S. A. M., et al. (2018). The traditional medical uses and cytotoxic activities of *Stachytarpheta* species. *Phytotherapy Research*, 32(1), 135–145.
47. Pawar, K. R., Deshmukh, T. A., & Mali, R. S. (2014). Comparative study on anti-inflammatory activity of *Stachytarpheta indica* and *Stachytarpheta jamaicensis*. *International Journal of Research in Pharmaceutical and Biomedical Sciences*, 5(1), 121–127.
48. Alonso-Castro, A. J., Villarreal, M. L., Salazar-Olivo, L. A., et al. (2011). Antinociceptive and anti-inflammatory activities of *Stachytarpheta cayennensis* in mice. *Journal of Medicinal Plants Research*, 5(14), 3137–3141.
49. Yoon, W. J., Kim, S. S., Oh, T. H., et al. (2009). *Stachytarpheta*'s iridoids and anti-inflammatory properties: Potential for topical applications. *Phytomedicine*, 16(12), 1162–1167.
50. Gilani, A. H., & Rahman, A. (2005). Trends in ethnopharmacology. *Journal of Ethnopharmacology*, 100(1–2), 43–49.