Miracles of Herbal Phytomedicines as Potent Anti-Inflammatory Agents

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Received: 14-01-2023; Revised: 22-02-2023; Accepted: 28-02-2023; Published on: 15-03-2023.

ABSTRACT
The body uses inflammation as its main defense mechanism against injuries, infections, and other types of injury. Numerous diseases, including rheumatic and immune-mediated ailments, diabetes, cardiovascular accidents, and other conditions, are included in the broad category of pathologic states known as inflammation. However, in some circumstances, inflammation itself might be dangerous. For instance, many illnesses can keep inflammation elevated, which harms tissue. To reduce inflammation in the body, a variety of anti-inflammatory medications are available. Several nonsteroidal anti-inflammatory medicines have been demonstrated to lessen inflammation and pain by reducing the isoform of the cyclooxygenase enzyme’s ability to break down arachidonic acid, hence reducing the generation of prostaglandins. But they frequently have negative side effects, and sometimes they don’t work.

Medicinal plants and their secondary metabolites are being employed as complementary medicine to cure ailments. Certain herbal medicines contain natural ingredients that may also have anti-inflammatory properties. When compared to synthetic anti-inflammatory drugs, natural herbs are more secure, efficient, and preferable choices. The phytoconstituents are just as effective as synthetic compounds and have a similar mode of action. This review provides information on the anti-inflammatory properties of medicinal herbs, which will be useful for new researchers and practitioners in their seek for anti-inflammatory plants.

Keywords: Inflammation, medicinal plants, phytoconstituents, anti-inflammatory, NSAIDs, paw edema.

INTRODUCTION

Inflammation is defined as the local response of living tissue to injury due to any agent. It is a pathophysiological response and defensive mechanism of the body and it helps the body in protecting itself against injury, infection, burns, poisonous substances, allergies, and other harmful stimuli. Inflammation is characterized by four key symptoms: pain, redness, heat or warmth, and swelling. Inflammatory mediators like histamine, bradykinin, and prostaglandins are released when the inflammatory pathway is activated.

Inflammation can be either acute or chronic. Acute inflammation can be defined as an immediate or early response to injurious stimuli, microbes, or foreign substances, the critical function of which is to deliver leukocytes, plasma proteins, and antibodies to the site of injurious stimulus. It is a rapid, short-term response to cell injury. Chronic inflammation is defined as the prolonged process in which tissue destruction and inflammation occur at the same time.
have numerous drawbacks. They are expensive, have undesirable side effects, and are not widely available worldwide. The effects of using NSAIDs for a long time include erosion of the gastric mucosa, which leads to stomach ulcers, bleeding, and finally death. The risk factor multiples many times for those who are in their mid-70s. In addition to the danger of heart attack and stroke, there is also a risk of asthma and kidney damage. ¹

As an alternative, medicinal plants are looking promising and becoming more acceptable for the management of inflammatory disorders. They were efficient, inexpensive, readily available, and economical, and are gaining favor with the general public. Anti-inflammatory herbs are plants that have shown anti-inflammatory activity in traditional use, and clinical studies. As a result of the numerous health issues with synthetic anti-inflammatory drugs, they have recently become active research areas. These plants contain phytoconstituents that show anti-inflammatory properties. Numerous plants have been found effective in inflammation studies. These may have been appropriately assessed in clinical and experimental investigations or be of traditional use. Generally, the traditional method uses either the entire plant or parts of it, such as the root, stem, leaves, fruit, or flower, for medicinal purposes. The successful development of anti-inflammatory medications that occur naturally is largely dependent on a multidisciplinary approach to the search for new molecules. The goal of this review is to look at the fundamental aspects of many medicinal herbs’ anti-inflammatory properties. ³

1. *Tamarindus indica* (fabaceae)

Tamarind, which has origins in tropical Africa, has been imported and naturalized in more than 50 different nations. It is a versatile tree, and nearly every part has some value, whether for nutrition or medicine. The major production areas are in the Asian countries India and Thailand, but also in Bangladesh, Sri Lanka, etc. Each component of the *T. indica* plant, including the root, body, fruit, and leaves, is significant for industry and commerce in addition to having a wide range of medical applications and rich nutritional value.

According to the findings of the phytochemical investigation, *T. indica* contains phenolic substances such as catenin, procyanidin B2, epicatechin, tartaric acid, mucilage, pectin, arabinose, xylose, galactose, glucose, uronic acid, and triterpene. It contains a lot of vitamins, phytochemicals, and important amino acids. It has a long history of having numerous documented health advantages. Due to the high levels of potassium, tartaric acid, and malic acid in *T. indica* fruit, it is used as a laxative in traditional medicine. On ulcer model organisms, *T. indica* seed extract exhibits a dose-dependent protective effect. It possesses antimicrobial, antiparasitic, antifungal, antiviral, and antinematodal characteristics in addition to anti-diabetic, antioxidant, and anti-inflammatory effects.⁴

S.S. Bhadoria et al., used hydroethanolic extracts of *Tamarindus indica* leaves to study their anti-inflammatory properties. It was found that the hydroethanolic extract prevented paw edema in Wistar albino rats induced by carrageenan. These findings suggested that the HTI caused the inhibition of TNF alpha, neutrophil PG, and NO synthesis and also found that extract reduced WBC migration to the edema site.⁵

Borquaye et al., studied the anti-inflammatory and antioxidant properties of an ethanolic extract of the root and stem bark of *Tamarindus indica*. Using a carrageenan-induced paw edema model in chicks, ¹

Gupta et al., conducted a phytopharmacological study on extracts of *Tamarindus indica* root and performed anti-inflammatory activity in the carrageenan-induced rat paw edema model. It was discovered that the percentage inhibition against carrageenan-induced edema was 29.72%, 45.74% in the case of the aqueous extract at concentrations of 100 mg and 200 mg, and 32.43%, 37.83% in the case of the ethanol extract at a 5-hour interval. In comparison to aspirin. ⁶

2. *Vitis vinifera* (vitaceae)

The grape is the most widely grown fruit crop in the world, producing more than 67 million tonnes annually. In addition to in vitro activity against numerous cancer cell
lines, and hepatoprotective and cardioprotective properties, V. vinifera and its bioactive components have a variety of pharmacological actions including antioxidative, anti-inflammatory, and antibacterial capabilities. Proanthocyanidins, resveratrol, and quercetin, which are the active ingredients in grape seed extract, appear to be strong antioxidants. Grapes are a strong choice for the pharmaceutical and food industries because they are a good source of phenolic acids and flavonoids, which have a variety of biological actions that can stop the development of diseases and can be helpful for health. 7

Shafi et al., analyzed the anti-inflammatory properties of various Vitis vinifera leaf extract fractions by employing albumin denaturation, proteinase inhibition, and membrane stabilization techniques. They reported that the hydroalcoholic extract significantly reduced inflammation.8

Heba Handoussa et al., investigated the anti-inflammatory effects of two major components in the hydroethanolic extract of both Vitis vinifera and Carchorum ollitorius, and they found that the extract reduced carrageenan-induced rat paw edema.9

3. Terminalia chebula (Combretaceae)

Terminalia chebula is a medicinal plant that is found in the Middle East, Thailand, China, and India. Other common names for T. chebula include Black Myrobalan, Ink Tree, and Chebulic Myrobalan. Nowadays days, it is regarded as a valuable source of a number of natural components for the development of commercial products as well as medications to treat a range of ailments. T. chebula is a pyrogallol (hydrolyzable) type and contains 14 hydrolyzable tannins, including neochebulinic acid, gallic acid, chebulic acid, punicalagin, chebulacin, corilagin, ellagic acid, chebulegic acid, and chebulinic acid.

Figure 4: Terminalia chebula

T. chebula is regarded as the mother of medicine because of the wide range of nutritional and therapeutic qualities it offers. The entire plant is highly medicinal and has long been used to cure a variety of human illnesses. Folk medicine experts have utilized this plant to cure conditions like gout, bleeding piles, ulcers, bleeding gums, asthma, sore throat, vomiting, hiccupping, diarrhea, and dysentery. The plant has been shown to have a wide range of pharmacological and therapeutic properties, including anti-inflammatory, anti-mutagenic, anti-proliferative, anti-neoplastic, anti-arthritic, anti-anticaries, gastrointestinal motility, and wound healing action.10

Bag et al., studied the anti-inflammatory properties of the fruits of Terminalia chebula and discovered that the standardized extract at a dose of 250 mg/kg, p.o. caused a 69.96% reduction in carrageenan-induced rat paw edema and demonstrated a 96.72% protective effect on human RBC membrane stability.11

Yang et al., evaluated twelve chemicals that were extracted from the methanolic extract of Terminalia chebula fruits for their anti-inflammatory properties. Based on their capacity to inhibit inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) in LPS-stimulated macrophages, the activity of the substance was assessed.12

Sireeratatwong et al., reported that water extract from the fruits of T. chebula greatly decreased the licking time in the formalin test and the formation of edema that was caused by carrageenan and ethyl phenylpropiolate. The T. chebula extract exhibited analgesic and anti-inflammatory activities.13

4. Ficus carica (Moraceae)

It is often referred to as a "fig." Southwest Asia and the eastern Mediterranean are the native habitats of the common fig tree. Figs contain a lot of proanthocyanidins and other phenolic substances. The leaves, fruits, and roots of F. carica are used in traditional medicine to treat a wide range of illnesses, including inflammatory, cardiovascular, pulmonary, and gastrointestinal conditions. All fruits from the F. carica tree are edible, whether they are raw, dried, or jam-preserved. Figs are a great source of vitamins, minerals, carbohydrates, and dietary fibre because they are high in amino acids and low in fat and cholesterol. Additionally, it has been reported that figs have been traditionally utilized for their therapeutic advantages as a laxative, cardiovascular, pulmonary, antispasmodic, and anti-inflammatory therapies.14

Figure 5: Ficus carica
As a result of phytochemical studies on *Ficus carica*, phytosterols, anthocyanins, amino acids, organic acids, fatty acids, phenolic components, hydrocarbons, aliphatic alcohols, volatile components, and a few more groups of secondary metabolites have been isolated from the plant’s various parts.\(^\text{15}\)

**Figure 6:** phytoconstituents isolated from *Ficus carica*

Ali et al., reported that the hydro-alcoholic extract of *Ficus carica* leaves showed significant anti-inflammatory activity in carrageenan-induced paw edema in rats. The presence of steroids in the plant may be the cause of its enhanced anti-inflammatory effects.\(^\text{16}\)

Yan-Ping Liu et al., performed a phytochemical investigation on the fruits of *Ficus carica* which resulted in the isolation of 16 prenylated isoflavone derivatives including four new ones by analysing their inhibitory effect on NO generation, they also reported the anti-inflammatory efficacy of this separated compounds.\(^\text{17}\)

Yohiaoui et al., investigated the anti-inflammatory activity of *Ficus carica* L.latex from three cultivars and evaluated it through NO measurement. It was observed that the three cultivars exhibited a strong dose-dependent inhibitory effect on NO production. The obtained results signified that *Ficus carica* L. Latex may be exerted not only for the treatment but also for potent prevention against inflammation.\(^\text{18}\)

Vikas V. Patil et al., investigated the possible anti-inflammatory activities of extracts prepared from *Ficus carica* Linn leaves in petroleum ether (PEE), chloroform (CE), and ethanol (EE). The anti-inflammatory efficacy was tested using cotton pellet granuloma and carrageenan-induced rat paw edema techniques. The extracts were administered orally to healthy animals at doses of 300 and 600 mg/kg/day of body weight. The ethanolic extract (EEFC-II) 600 mg/kg had a maximum anti-inflammatory efficacy of 75.90% in acute inflammation and a 71.66% reduction in granuloma weight in chronic testing. The petroleum ether (PEE), chloroform (CE), and ethanol (EE) extract significantly suppressed the carrageenan-induced paw edema and cotton pellet granuloma method in rats. These extracts demonstrated a more potent anti-inflammatory effect than the common medication Indomethacin.\(^\text{19}\)

5. *Zingiber officinale* (zingiberaceae)

It is commonly known as ginger. It is a species of the Zingiberaceae family and one of the most important medicinal plants due to the many health benefits it provides, including nutritional, therapeutic, and ethnomedical ones. As a result, it is widely utilized as a spice, flavoring, and herbal treatment throughout the world. *Z. officinale* has been used for a very long time in the Ayurvedic, Siddha, Chinese, Arabian, African, and Caribbean medical systems to treat a wide variety of illnesses, including asthma, coughing, palpitations, inflammation, dyspepsia, loss of appetite, constipation, pain, and nausea and vomiting. The main phytochemical groups present in *Z. officinale* are thought to include essential oils, phenolic compounds, flavonoids, carbohydrates, proteins, alkaloids, glycosides, saponins, steroids, terpenoids, and tannins. Due to its ethno medical properties and nutritional value, the rhizome of *Zingiber officinale* is frequently utilized for both culinary and medicinal purposes worldwide. Recent developments in phytochemistry and ethnomedical research elaborate on ginger’s usefulness for physiological requirements, carcinogenic conditions, and viral infections.\(^\text{20}\) The gingerols were found to be the primary active ingredient in fresh ginger rhizomes, and they have been proven to be powerful anti-inflammatory agents.\(^\text{21}\)

**Figure 7:** *Zingiber officinale*
M. Thomson et al., examined the effectiveness of a ginger aqueous extract on preventing the production of PGE2 during ex vivo whole blood clotting of rats. Daily oral or intraperitoneal administration of an aqueous extract of ginger (50 and 500 mg/kg dosages) effectively suppressed the generation of PGE2 when measured ex vivo. These findings indicate that ginger could be used as an anti-inflammatory agent to reduce inflammation.

6. Moringa oleifera (Moringaceae)

In traditional folk medicine, Moringa oleifera is regarded as a valuable medicinal plant. Moringa oleifera (MO), also known as drumstick tree, and it is geographically distributed across South Asia, particularly in India, Sri Lanka, Pakistan, Bangladesh, and Afghanistan. Both as a food source and a medical treatment, moringa seeds and leaves have a wide range of applications. M. oleifera is known to have anti-inflammatory, anticancer, antioxidant, anti-obesity, anti-epileptic, antidiabetic, diuretic, wound-healing, antibacterial, immunomodulatory, and anti-diarrheal effects. Numerous phytoconstituents, including alkaloids, saponins, tannins, steroids, phenolic acids, glucosinolates, flavonoids, and terpenes, are present in different Moringa species. The variety of these phytochemicals throughout the genus adds to its many therapeutic benefits.

Young et al., extracted various compounds from the methanol extract of Moringa oleifera seeds, and they reported that some of the isolated compounds reduced the levels of TNF alpha, IL-6, and IL-1-beta that are produced by H1N1 infection.

Ruttiya Thongrung et al., examined the impact of M. oleifera leaf extract on inflammatory cytokine production in diabetic nephropathy (DN) rats. The findings revealed that M. oleifera leaf extract could reduce the mRNA expression of MCP-1, TNF-, and IL-1 in rats with STZ-induced DN. These findings show that M. oleifera leaf extract may minimize the chronic inflammatory process that contributes to the development of DN.

Liao et al., investigated the anti-inflammatory properties of beta-sitosterol (BSS) extracted from the Moringa oleifera and discovered that within a dose range of 7.5-30 micrometers, BSS inhibited the release of inflammatory factors from keratinocytes and macrophages caused by PGN, TNF-, or LPS, such as TNF-, IL-1, IL-6, IL-8, and ROS.

7. Glycrrhiza glabra (Fabaceae)

One of the most well-known medicinal plants in the Fabaceae family is Glycrrhiza glabra, also known as "Liquorice." This species is indigenous to the Mediterranean region, although it is currently found in China, India, and Russia. The herb is frequently used as a treatment for arthritis, bronchitis, cough, and digestive issues in traditional Chinese medicine. In particular, it is still frequently used in traditional medicine to treat gastritis, peptic ulcers, respiratory infections, and tremors. Numerous phytocompounds are present in this plant. The primary component of G. glabra is "glycyrrhizin," a chemical that is 50 times sweeter than sucrose and has cortisone-like actions. Others include isoflavones, glabrin A and B, and 18-glycyrrhetinic acid, which have shown a variety of pharmacological actions. Pharmaceutical research has shown that several extracts and pure chemicals from this species contain a variety of biological capabilities, including antibacterial, anti-inflammatory, antiviral, antioxidant, and antidiabetic actions.
Nirmala et al., examined the anti-inflammatory effects of hydroalcoholic extract of *G. glabra* (HAEGG) root against carrageenan-induced rat paw edema at dose levels of 100, 200, and 300 mg/kg orally. At a dose of 200 mg/kg, the HAEGG had a maximal inhibitory effect of 46.86% on carrageenan-induced paw edema and reduced leukocyte migration in a dose-dependent manner. The anti-inflammatory activity was comparable to that of the indomethacin (10 mg/kg) non-steroidal anti-inflammatory medicine.28

The anti-inflammatory properties of glycyrrhiza glabra extracts and purified components were examined by Luca Frattaruolo et al., in lipopolysaccharide (LPS)-stimulated RAW 264.7 murine macrophages. Even when employed at concentrations of 12.5 g/mL and 50 mM, extract of dried leaves and licoflavanone has shown effective anti-inflammatory activity without impairing cell viability. Furthermore, licoflavanone significantly reduced cyclooxygenase 2/inducible nitric oxide synthase and pro-inflammatory cytokines.29

Siracusa et al., investigated the anti-inflammatory activity of extract of licorice leaves by evaluating their effect on the release of TxB2 and PGE2 in human whole blood.30

8. *Ocimum basilicum* (Lamiaceae)

Basil (*Ocimum basilicum*), one of the most significant crops, contains phenolic acids, polyphenols, flavonoids, and essential oils. This annual plant is indigenous to tropical areas and is a member of the mint family. Basil leaves are also regularly added to rice, pork, stews, and soups and are known for their outstanding healing properties. It was once used to treat illnesses like malaria, earaches, anorexia, arthritis, earaches, irregular menstruation, renal issues, colds, and ear infections. It has also been used as a hemostatictic during childbirth. Basil has been proven to be useful against bacterial, fungal, viral, and other infections. Basil leaves have been used to treat fevers, coughs, the flu, asthma, bronchitis, influenza, and diarrhea.31 *O. basilicum* was found to contain glycoside, gums, mucilage, proteins, amino acids, tannins, phenolic compounds, triterpenoids, steroids, sterols, saponins, flavones, and flavonoids.

Figure 11: *Ocimum basilicum*

Aye et al., studied the anti-inflammatory action of ethanol extract of Basil (*Ocimum basilicum* L.) leaf and leaf callus in RAW 264.7 macrophage cells. The results revealed that the extract was non-cytotoxic and that it reduced NO generation in LPS-stimulated macrophages. These results indicate that Ocimum basilicum L. could be useful in reducing pathological inflammation.32

Osei Akoto et al., evaluated the anti-inflammatory effect of *Ocimum basilicum* Linn. fruit extracts by In Vitro Anti-Inflammatory Assay Using Egg Albumin Denaturation. These findings show that both hexane and ethanol extracts of *Ocimum basilicum* Linn. display anti-inflammatory characteristics, with their % inhibitions being 34.0 0.01 and 17.6 0.04 g/mL, respectively.33

9. *Mimosa pudica* (fabaceae)

The most prevalent herb in all regions of Bangladesh is *Mimosa pudica*, which has a long history of use as a medicinal plant. It is sometimes referred to as the humble plant. In addition to its local and traditional uses, it has a wide range of recognised pharmaceutical uses, including ovulation suppression, anticonvulsant, antidepressant, anti-diabetic, antibacterial, wound healing, snake venom-induced hyaluronidase and protease inhibition, snake venom neutralisation, and antioxidant activity.34 The *M. pudica* leaf extract was subjected to a preliminary phytochemical screening, which revealed the presence of bioactive substances like terpenoids, flavonoids, glycosides, alkaloids, quinines, phenols, tannins, saponins, and coumarins.35

Figure 12: *Mimosa pudica*

*Mimosa pudica* was studied by Azam et al., for its phytochemical components, in vitro free radical content, and anti-inflammatory potency. The anti-inflammatory properties of an ethanolic extract of *Mimosa pudica* were evaluated using a carrageenan-induced paw edema assay and cotton wool granuloma in rats. An hour after carrageenan treatment, the extract significantly lowers paw volume by nearly 50% at a dose of 300 mg/kg.34
Mistry et al., used the carrageenan-induced paw edema and cotton pellet granuloma approach on albino rats to study the anti-inflammatory efficacy of ethanolic extract of *Mimosa pudica* leaves at doses of 200 and 400 mg/kg. In comparison to the control group, the extracts demonstrated considerable action in a dose-dependent manner. The findings indicated that the *M. pudica* leaf extract was helpful in both acute and chronic inflammation. 36

10. *Rosmarinus officinalis* (Lamiaceae)

The plant known as rosemary, or *R. officinalis* L., is a member of the Lamiaceae family and is thought to have originated in the Mediterranean area. But it may be found everywhere. It is an aromatic perennial plant. It is possible to separate many phytocompounds with pharmacological properties from *R. officinalis* extracts and essential oils. Caffeic acid, carnosic acid, chlorogenic acid, monomeric acid, oleanolic acid, rosmarinic acid, and other phytocompounds are among the most commonly reported. The pharmacological effects of *R. officinalis* L. include the prevention of asthma, atherosclerosis, cataract, renal colic, hepatotoxicity, peptic ulcer, inflammatory disorders, ischemic heart disease, and the antioxidant and anti-inflammatory properties of rosmarinic acid. 37

Benincá et al., studied the anti-inflammatory properties of *Rosmarinus officinalis* crude extract, and isolated components such as carnosol, betulinic acid, and ursolic acid, in the mouse pleurisy model produced by carrageenan. *R. officinalis* L. has shown significant anti-inflammatory efficacy by inhibiting mediators and a pro-inflammatory enzyme that promotes inflammation in addition to leukocytes and exudation (MPO, NOx, IL-1b, and TNF-a). The results of the current investigation suggested that the compounds carnosol, betulinic acid, and ursolic acid may be responsible for this anti-inflammatory activity. 38

Rahbardar et al., examined the possible anti-inflammatory properties of *Rosmarinus officinalis* and rosmarinic acid in a rat model of sciatic nerve chronic constriction injury (CCI)-induced neuropathic pain. By measuring the levels of some spinal inflammatory markers, such as cyclooxygenase-2 (COX2), prostaglandin E2 (PGE2), interleukin 1 beta (IL-1b), matrix metallopeptidase 2 (MMP2), and nitric oxide (NO) production via Griess reaction on days 7 and 14 post-surgery, the anti-inflammatory effects of *R. officinalis* extract and rosmarinic acid were evaluated. The findings demonstrated that COX2, PGE-2, IL1b, MMP2, and NO levels were significantly elevated in CCI rats on days 7 and 14 and both days. On days 7 and 14, the levels of the inflammatory markers were reduced by rosmarinic acid and an ethanolic extract of *R. officinalis*. 39

Rocha et al., examined the anti-inflammatory characteristics of rosmarinic acid and an *R. officinalis* extract in local inflammation (carrageenin-induced paw oedema model in the rat), and they also examined the protective effect of rosmarinic acid in rat models of systemic inflammation, including liver ischemia-reperfusion (I/R) and thermal damage models. In the local inflammation model, male Wistar rats were given rosmarinic acid at doses of 10, 25, and 50 mg/kg (p.o.) and the extract at dosages of 10 and 25 mg/kg (equal doses to rosmarinic acid groups). With a dose-response effect, the administration of rosmarinic acid and extract at a dose of 25 mg/kg decreased paw edema at 6 hours nearly 60%, indicating that rosmarinic was the primary factor in the anti-inflammatory effect. When rosmarinic acid was given at a dose of 25 mg/kg (i.v.) 30 minutes before the onset of ischemia in the hepatic I/R model, the serum concentrations of transaminases (AST and ALT) and LDH were significantly lowered. When rosmarinic acid was given at a dose of 25 mg/kg (i.v.) five minutes before the onset of injury in the thermal injury model, it dramatically decreased the markers of multi-organ dysfunction (liver, kidney, and lung) by modulating NF-jB and metalloproteinase-9. Since it significantly reduces inflammation, rosmarinic acid has been found to have anti-inflammatory potential. 40

CONCLUSION

Inflammation serves as the body’s primary line of defense against wounds, infections, and other sorts of harm.
Rheumatic and immune-mediated illnesses are examples of diseases that fall under the broad group of pathologic conditions known as inflammation. Natural herbs are safer, more effective, and a better option than synthetic anti-inflammatory medications. The information in this review about the anti-inflammatory characteristics of medicinal herbs will be helpful to new researchers and practitioners looking for anti-inflammatory plants.

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Source of Support: The author(s) received no financial support for the research, authorship, and/or publication of this article.

Conflict of Interest: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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