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Review Article

Boswellia serrata for the management of cerebral ischemic stroke: a preliminary review

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Abstract

Objective: To explore the neuroprotective effects of *Boswellia serrata* and its active ingredients, boswellic acids, in the management and prevention of cerebral ischemic stroke.

Materials and Methods: A comprehensive review of both *in vitro* and *in vivo* studies was conducted to assess the efficacy of *B. serrata* in alleviating cerebral ischemic stroke. The mechanisms of action investigated include neuroprotection, anti-apoptotic, anti-inflammatory, and antioxidant pathways.

Results: *B. serrata* and the active ingredients, based on *in vitro*, *in vivo*, and limited clinical data, have shown promising results in reducing oxidative stress, inflammation, and apoptosis associated with cerebral ischemic stroke. The active compounds of *B. serrata* demonstrate significant neuroprotective characteristics, indicating potential therapeutic benefits.

Conclusion: While the findings highlight the potential of *B. serrata* as a preventive and therapeutic agent against cerebral ischemic stroke, challenges remain in translating these preclinical results into clinical practice. Further research is necessary to fully understand the mechanisms of action and any potential toxic effects on other organs, alongside the need for related clinical trial studies.

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Introduction

Stroke ranks among the main causes of death worldwide and the primary cause of long-term disability in developed countries. Significant advancements in the diagnosis and treatment options to lessen the effects of acute ischemic stroke have been made throughout the recent years (Najjary et al. 2024; Nezami et al. 2025; Phipps and Cronin 2020).

Most strokes (nearly 80%) are ischemic strokes and brain cells are not receiving adequate oxygen and glucose due to an acute decrease of cerebral blood flow brought on by a blockage of vital cerebral arteries. Currently available management of cerebral ischemic strokes is done by means of physiotherapy, injection of recombinant tissue plasminogen activator, and removing clots by mechanical thrombectomy.

However, not all stroke patients receive either of these treatments. Therapeutic time window is important in cerebral ischemic strokes which is limited to 3-6 hr after stroke and attribute as a limiting factor in effective management of ischemic stroke (Forouzanfar et al. 2019; Koyama and Shichita 2023).

The limitations of current pharmacological treatments for ischemic stroke have sparked increased interest toward herbal therapy. A World Health Organization (WHO) report indicates the popularity of traditional medicine in developing countries (WHO 2019). These restrictions have prompted the creation of ground-breaking novel therapies. Numerous studies are beginning to acknowledge the significance of herbal formulation in the field of medicinal research (Balarastaghi et al. 2022; Moshirian-Farahi et al. 2025). Herbal therapy has emerged as one of the numerous effective therapeutic methods for the management of ischemic stroke (Azami and Forouzanfar 2023; Azami and Forouzanfar 2024; Azami et al. 2021; Danaei et al. 2022). With recent studies indicating that *Boswellia serrata*, a valued herbs of family Burseraceae may have an impact on cerebral ischemia (Forouzanfar et al. 2016), and *B. serrata* is becoming an attractive alternative for the prevention and treatment of stroke. *B. serrata* extract has previously been used as an effective treatment in the management of an experimental model of Parkinson's disease (PD). An animal study reported that *B. serrata* resin extract protects nigrostriatal dopaminergic neurons and can improve motor impairments in PD. The model study using adult rats showed that extract doses of 125 and 250 mg/kg were effective in improving motor behavior and motor dysfunction (Doaee et al. 2019). In another study, positive effect of *B. serrata* gum resin was shown on spatial learning in aged rats. Hippocampal examination showed that herbal therapy using aqueous extract of *B. serrata* can reduce memory deficits (Hosseini-Sharifabad et al. 2016).

We aimed to cite fruitful instances of *B. serrata* and review the most recent studies on the efficacy of this herb in treating and preventing cerebral ischemia.

Materials and Methods

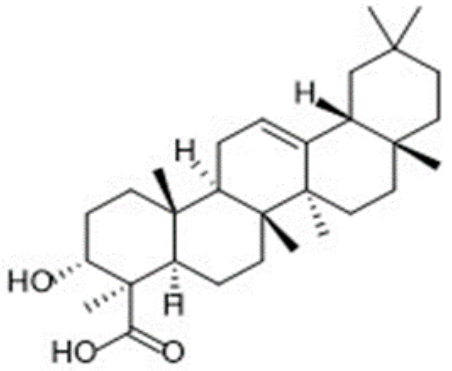
This review provides a detailed summary of current research on the management of ischemic stroke, including cell lines, animal, and human studies. The literature search was conducted on various scientific databases such as PubMed, Web of Science, and Google Scholar, focusing on recent articles published in the past 10 years to mid-2024 at the time of writing the article. The search terms included were "*Boswellia serrata*", "*B. serrata*", "management", "treatment", and "ischemic stroke".

Results

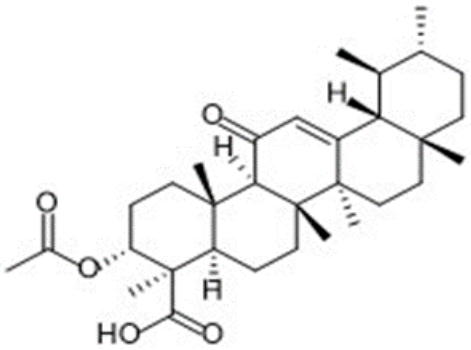
Boswellia serrata and boswellic acids

Twenty studies were included in this review, examining the neuroprotective effects of *B. serrata* extracts and boswellic acids as its active constituents. *B. serrata*, is a deciduous tree family Burseraceae (Iram et al. 2017). Boswellic acids are important bioactive components of *B. serrata* extracts (Figure 1) (Krüger et al. 2008). Chemically boswellic acid is 3-hydroxyurs-12-ene-23-oic acid. *Boswellia* species contain different amounts of boswellic acids. The main boswellic acids are α and β-boswellic acids (10–21%), acetylated α and β-boswellic acids (0.05–6%), 11-keto-β-boswellic acid (KBA) (2.5–7.5%), and 3-O-acetyl-11-keto-β-boswellic acid (AKBA) (0.1–3%). Commercially available standardized extracts range in boswellic acid concentration from 37.5 to 65% (Iram et al. 2017). The two most effective, strong, and potentially useful anti-inflammatory compounds among all of boswellic acids are AKBA and KBA (Table 1). However,

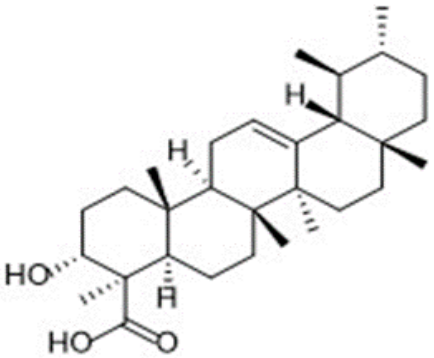
their pharmaceutical development has been limited due to their poor oral bioavailability (Gomaa et al. 2021). According to the literature, *B. serrata* gum resin extract has been utilized in the treatment of diverse inflammatory disorders like arthritis and rheumatic diseases, cancer, diabetes, asthma, and inflammatory bowel disease (de Oliveira et al. 2021; Gomaa et al. 2021; Roy et al. 2019).



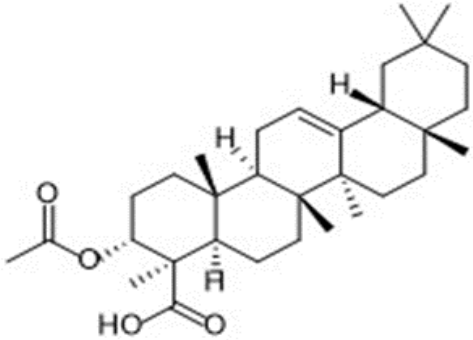
beta-boswellic acid



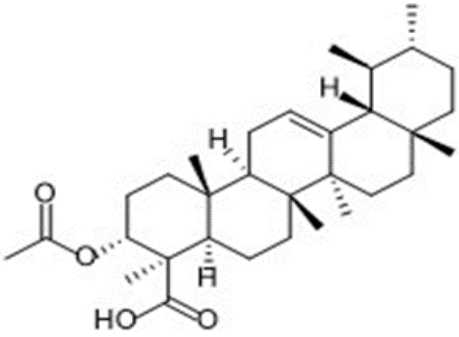
3-O-acetyl-11-keto-beta-boswellic acid



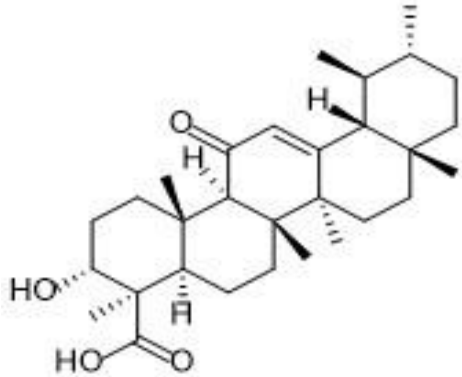
alpha-boswellic acid



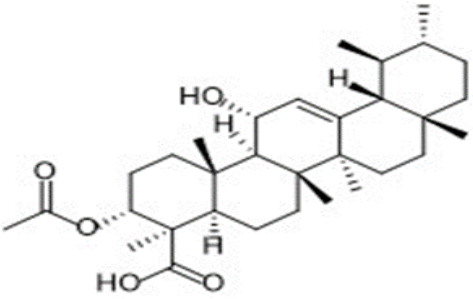
acetyl-alpha-boswellic acid



3-acetyl-beta-boswellic acid



11-keto-beta-boswellic acid



3-O-acetyl-11-hydroxy-beta-boswellic acid

Figure 1. Chemical structure of boswellic acids

Table 1. Name, formula, and molecular weight of the studied boswellic acids (Trivedi et al. 2023)

Entry	Compound	Chemical formula	Molecular weight (g/mol)
1	11-keto-α-boswellic acid	$C_{30}H_{46}O_4$	471
2	3-O-acetyl-11-keto-boswellic acid	$C_{32}H_{48}O_5$	513
3	α-boswellic acid	$C_{30}H_{48}O_3$	457
4	β-boswellic acid	$C_{30}H_{48}O_3$	457
5	3-O-Acetyl-α-boswellic acid	$C_{32}H_{50}O_4$	499
6	11-hydroxy-boswellic acid	$C_{30}H_{48}O_4$	473
7	11-keto-β-boswellic acid	$C_{30}H_{46}O_4$	471

Ischemic stroke pathophysiology

An overview of the ischemic stroke etiology can be helpful in studying the neuroprotective effects of *B. serrata*. An ischemic stroke is neurological impairment caused by a disturbance in the circulation of blood to the brain. When there is a decrease in cerebral blood flow, it leads to an immediate deprivation of oxygen and glucose, which disrupts cellular homeostasis, reduces the production of adenosine triphosphate (ATP) at the molecular level, and induces lactic acidosis. Excessive lactate production disturbs the brain's normal acid-base balance, causing cell injury (Haupt et al. 2023). Furthermore, ATP-dependent ion pumps deteriorate in the absence of ATP, depolarizing cells and opening voltage-gated Ca^{2+}, Na^{+}, and K^{+} channels. Increased influx of Ca^{2+}, Na^{+}, and K^{+} combined with an outflow of K^{+} releases glutamate. This process leads to extracellular toxicity mediated by glutamate (Haupt et al. 2023). The main mechanisms of free radical genesis comprise of reactive oxygen species (ROS) and reactive nitrogen species (RNS) production also occur simultaneously during cerebral ischemia. Initially, hypoxia causes the mitochondrial respiratory chain to stop its oxidative phosphorylation activity which depolarizes the mitochondria and raises the O_2^{-}level. At the same time, acidic conditions resulting from hypoxia accelerate the conversion of oxygen into ROS. The higher extracellular glutamate stimulates the N-methyl-D-aspartate (NMDA) receptors. This leads to rises in calcium influx. Elevated calcium influx exacerbates mitochondrial dysfunction and triggers the activation of cellular lipases and proteases (He et al. 2021). Furthermore, nitric oxide synthase (NOS) is activated by NMDA receptors. NOS enzyme synthases the creation of nitric oxide (NO) from amino acid L-arginine, which increases the synthesis of $ONOO^{-}$ radical. The elevated ROS level is also caused by other oxidase enzymes, such as diminished nicotinamide adenine dinucleotide phosphate (NADPH) oxidase and xanthine oxidase (He et al. 2021). In addition, oxidative stress signals cause disruptions to Ca^{2+} homeostasis and oxidative stress. Stress in the endoplasmic reticulum and Golgi apparatus is involved in the progression of oxidative stress. Overproduction of ROS and RNS can directly cause the release of inflammatory mediators and this can in turn activate the inflammasomes. Consequently, an inflammatory cascade invariably follows oxidative stress in neural tissues, with both processes leading to apoptosis via tanglesome pathways including p53, p38 mitogen-activated protein kinase (MAPK), extracellular signal-regulated kinase 1/2 (ERK1/2), and the Keap1– nuclear factor erythroid 2-related factor 2 (Nrf2) pathway. Furthermore, because ROS and RNS overproduction can cause vasodilatation and enhance vascular endothelial cell permeability, they often worsen the blood brain barrier (BBB) breakdown (He et al. 2021).

More importantly, RNS-induced caveolin-1 and matrix metalloproteinase (MMP) signaling pathways drive neuroinflammation and breakdown of the BBB. Following cerebral ischemia, microglia function as primary responders and become activated. Later, neutrophils, lymphocytes, dendritic cells, and

macrophages accumulate in the peri-infarct area (He et al. 2021; Iadecola and Anrather 2011). Macrophages and brain-resident microglia can release proinflammatory mediators of interleukin-1 (IL-1), tumor necrosis factor-α (TNF-α), cell adhesion molecules, and proteases, which can worsen tissue damage and inflammatory activity (George and Steinberg 2015; He et al. 2021). Additionally, NADPH oxidase and inducible NOS (iNOS) are produced by macrophages and microglia, which leads to the excessive generation of ROS and RNS and the progression of oxidative stress (He et al. 2021).

There are several possible targets for neuroprotective strategies given the chain of events that precede ischemic stroke, which includes neuroinflammation, free radical-mediated toxicity, opening of the BBB, cellular injury, and death (Haupt et al. 2023; Shaheryar et al. 2021). Pharmacotherapy can certainly be used as a neuroprotective strategy targeting these pathophysiological processes. Various protective substances have been proposed in this regard. For example, activin A plays a neuroprotective role in ischemic stroke, possibly by promoting white matter remyelination and reducing infarct size. Using a mouse model of ischemic stroke, it was demonstrated that activin A is able to inhibit autophagic degradation by the regulation of the STING1-dependent signaling network. Such neuroprotective effects and improvement of cell survival may be a potential therapeutic target for ischemic stroke (Liu et al. 2023). Accordingly, we discuss the neuroprotective effects of *B. serrata* here.

In vitro studies on the effectiveness of *B. serrata* in ischemic stroke

In one study, the protective function of AKBA in oxygen–glucose deprivation (OGD)/reperfusion model was examined using bEND.3 cells. Treatment (5 and 20 μM) decreased cell death and ROS (Figure 2). Additionally, OGD raised the expression of the complement C3a receptor (C3aR), TNF-α, and ICAM-1, and downregulated the content of tight junction proteins ZO-1 and occludin. There was an increase in ERK 1/2 phosphorylation in the bEND.3 cells in the OGD group. Following OGD, AKBA therapy dramatically reduced the expression levels of mentioned inflammatory markers, pERK 1/2 expression and inhibited ZO-1 and occludin from degrading (Ahmad et al. 2019). Another study investigated the neuroprotective effects of *B. serrata* as well as AKBA against ischemic conditions induced by OGD. Both bioactive compounds increased the viability of ischemic PC12 cells in a concentration-dependent changes while reducing free radicals, lipid peroxidation, and DNA damage. The findings suggested the neuroprotective effect of *B. serrata* and AKBA through attenuating oxidative stress (Sadeghnia et al. 2017).

In vivo studies on the effectiveness of *B. serrata* in ischemic stroke

Animal models have long been used to evaluate toxic/therapeutic effects of natural compounds/pharmaceutics (Aramjoo et al. 2021; Balali-Mood and Sadeghi 2021; Danaei et al. 2022; Farahi et al. 2025; Karimi et al. 2023). One study evaluated the efficacy of KBA (25 mg/kg) in preventing cerebral ischemia damage on Sprague-Dawley rats subjected to middle cerebral artery occlusion (MCAO) one hour after reperfusion. Decrease of apoptotic cells and infarct volumes, and improvement of the neurologic scores was achieved. Moreover, KBA reduced the levels of malondialdehyde (MDA), restored superoxide dismutase (SOD) activity, and elevated the expression of the proteins Nrf2 and heme oxygenase 1 (HO-1). KBA protected against oxidative stress caused by OGD via upregulating the expression of Nrf2 and HO-1 (Figure 2). While knockdown of Nrf2 or HO-1 reduced the protective effect of KBA in rats (Ding et al. 2015). A similar animal model of cerebral ischemia showed that treatment

with AKBA in MCAO rats could alleviate the upregulating the expression of HO-1 and Nrf2, reduce the infarct sizes and apoptotic cells, as well as raising the neurologic scores. This caused neuroprotection against oxidative damage generated by OGD. Furthermore, Nrf2 binding activity to antioxidant-responsive elements was enhanced by AKBA treatment. One again, knockdown of Nrf2 or AKBA reduced its protective impact (Ding et al. 2014). Another study examined the preventive properties of *B. serrata* extracts and AKBA in MCAO model. AKBA (50 mg/kg) and *B. serrata* aqueous extract and *B. serrata* ethanolic extracts (125, 250, and 500 mg/kg) were given intraperitoneally shortly after the induction of MCAO. In the cerebral cortex after a stroke, AKBA and *B. serrata* aqueous and ethanolic extracts alleviated neurological impairment and decreased brain infarction, neuronal death, and apoptosis. Moreover, the bioactive compounds decreased lipid peroxidation and increased SOD activity and glutathione (GSH) content. Apoptosis inhibition was achieved via regulating caspase-3 and bax/bcl-2 expressions (Forouzanfar et al. 2016). Underlying mechanisms of neuroprotective benefits of β-boswellic acids in cerebral ischemia/reperfusion injury was investigated using rat neuronal OGD/R. The findings demonstrated that β-boswellic acid reduced necrotic neurons, infarct volume, and neurological impairments shielding neurons from damage caused by OGD/R. Furthermore, β-boswellic acid markedly elevated the expression of HO-1, the translocation of nuclear factor erythroid 2-like 2, and the phosphorylation of protein kinase C epsilon (PRKCE) at S729 (Wang et al. 2022).

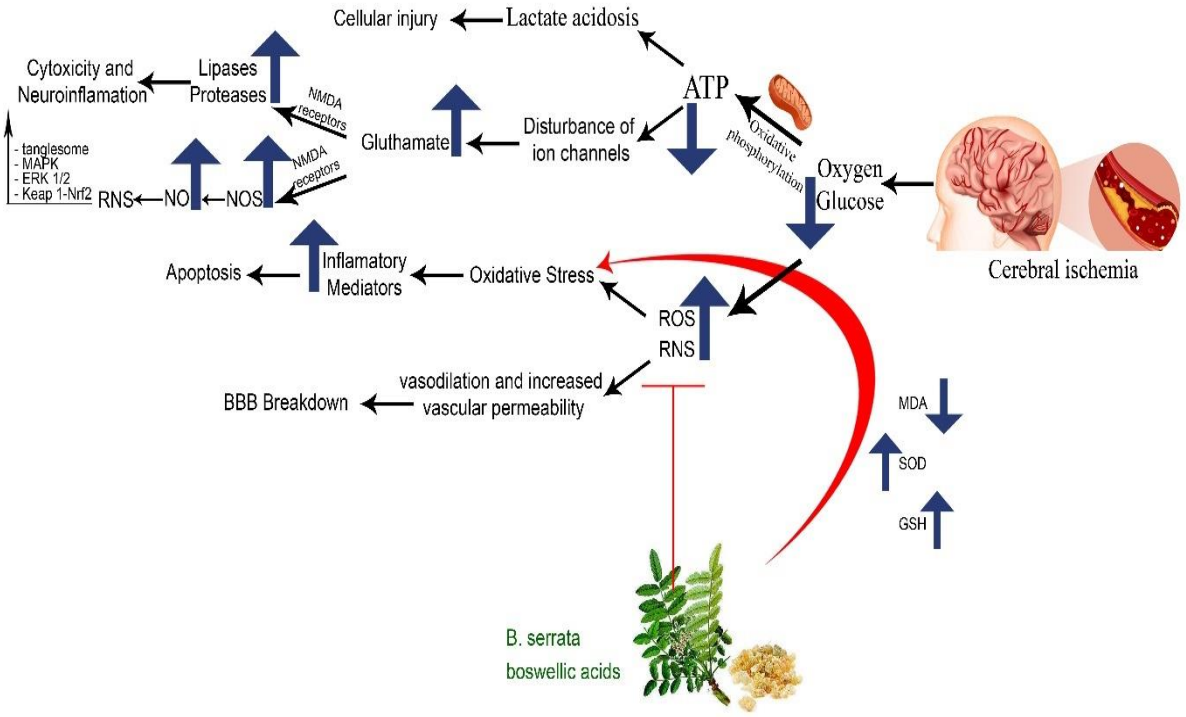


Figure 2. Possible anti-oxidant, anti-inflammatory, and anti-apoptotic of Boswellia serrata and boswellic acids on cerebral ischemic stroke. ROS: Reactive Oxygen Species; RNS: Reactive Nitrogen Species; MDA: Malondialdehyde; SOD: Superoxide dismutase; GSH: Glutathione; NMDA: N-methyl-D-aspartate; NO: Nitric Oxide; NOS: Nitric Oxide Synthase; MAPK: Mitogen Activated Protein Kinases; ERK: Extracellular Signal-Regulated Kinase; Nrf2: Nuclear factor erythroid 2-related factor 2

The poor solubility of AKBA in aqueous solvent limits its bioavailability and therapeutic efficacy for the treatment of cerebral ischemia-reperfusion injury. Therefore, nanoparticle drug delivery system could be a candidate to enhance its potency. A pharmacodynamic study showed that AKBA-nanoparticles have better neuroprotection compared to AKBA in primary neurons in the oxygen-glucose deprivation model as well as in the MCAO animal model. Such improvement in the efficacy is through AKBA-nanoparticles modulating antioxidant and anti-inflammatory pathways more effectively than AKBA by increasing the expression of Nrf2 and HO-1. This could also be achieved by decreasing the expression of nuclear factor kappa B and 5-lipoxygenase (Ding et al. 2016).

Neuroinflammation occurs following ischemic stroke affecting both the disease's acute and chronic phases. The inflammation is associated with BBB breakdown, neuronal injury, and worse neurological outcomes. To alleviate neurological dysfunction in cerebral ischemic stroke, one treatment approach could focus on inflammatory responses. *B. serrata* has been shown to protect against ischemic injury by modulating the inflammatory process. The lipopolysaccharide (LPS)-treated mice received AKBA 5 mg/kg for 7 days. The neuroprotective effect of AKBA was shown as a reduction in LPS-induced neuroinflammation by influencing the expression of miRNA-155, a pro-inflammatory mediator, mainly from inhibition of 5-lipoxygenase (Sayed et al. 2018).

Clinical trials studies on the effectiveness of *B. serrata* in ischemic stroke

A blind randomized study examined boswellic acids as supplemental therapy in stroke. Within 72 hr of the beginning of neurological symptoms, 80 ischemic stroke patients (aged 40–80) with a 4–20 score on the National Institutes of Health Stroke Scale (NIHSS) were randomized and followed for one month. Patients in the intervention group were given two 400 mg capsules of boswellic acids three times a day orally. The levels of immune-inflammatory cytokines and chemokines circulating in plasma were also evaluated. Participants receiving boswellic acids experienced a statistically significant improvement in their neurological function at the one-month follow-up against the placebo-controlled group. The boswellic acids group experienced a significant decrease in plasma inflammatory mediators (IL-1β, IL-6, IL-8, TNF-α, and prostaglandin E2 (PGE2) following a 7-day intervention (Baram et al. 2019). A placebo-controlled clinical trial of patients who had recently suffered a traumatic brain injury used *B. serrata* extract for a 3-month management period to treat neuropsychiatric problems. Assessment of cognitive changes showed significant improvements in patients' cognitive function using *B. serrata* (Meshkat et al. 2022). On the other hand, an investigation of the clinical efficacy of *B. serrata* extract among patients with ischemic stroke did not show significant effects. Sixty patients were recruited into a randomized clinical trial in two groups where movement and speech strength of subjects were evaluated before treatment, the first week after treatment, and after one month. Intervention group received four capsules of 500 mg powdered extract daily. Taking *B. serrata* together with the conventional treatment only improved muscle strength of stroke patients in the second stage while showed no improvement of muscle strength of right limbs or speech (Jivad et al. 2015).

Discussion

This paper reports the first review of the literature concerning the use of *B. serrata* in ischemic stroke. Our review showed a number of noteworthy findings that are crucial for future planning and

stroke prevention and treatment research. The complicated pathophysiology of stroke and the multifaceted effects of *B. serrata* and its ingredients suggest that natural medicine for stroke may have a bright future. It is thought that its anti-oxidant, antiapoptotic, and anti-inflammatory work well as a therapeutic. Herbal medications have anti-oxidant, anti-inflammatory, vascular protective, neuroprotective, and anti-apoptotic properties that are thought to be effective in treating stroke. Compared to allopathic therapy, herbs usually have fewer documented negative effects and might be safer to take over an extended length of time. While some herbal medicines demonstrate potential complementary therapeutic benefits for chronic conditions, current research suggests their efficacy varies and requires further rigorous investigation. Herbal interventions support conventional treatments in specific chronic diseases like stroke. In experimental studies, including *in vitro* and *in vivo* models, a number of therapeutic plants and their active ingredients exhibit encouraging outcomes. Nevertheless, the application of herbal medicine for stroke has faced significant challenges due to the inability to translate animal research from the lab to clinical trials (Gaire 2018). Numerous investigations have demonstrated that the progression of ischemic stroke is mostly driven by processes including oxidative stress, cell death, inflammation, and excitotoxicity (Shirley et al. 2014). The anti-oxidant, anti-inflammatory, and antiapoptotic properties of *B. serrata* extract have been found to be regulated by distinct mechanisms in both *in vitro* and *in vivo* contexts. The extract from *B. serrata* gum resin enhanced the antioxidant markers, NAD(P)H: quinone oxidoreductase 1 (NQO-1) and HO-1, as well as the Nfr2 in a rat model of endometriosis. Additionally, *B. serrata* boosted GSH levels, decrease lipid peroxidation, and raised SOD and glutathione peroxidase activity (D'Amico et al. 2022). *B. serrata* extract also decreased apoptotic pathway by downregulating Bcl-2 expression and raising the levels of Bax and cleaved caspase 9 (D'Amico et al. 2022). *B. serrata* extract was also shown to decrease caspase-3, cholinesterase, GSK-3β, TNF-α, IL-1β, IL-6, and MDA in the hippocampus. Additionally, *B. serrata* extract markedly increased hippocampal levels of SOD, GSH, and glutamate receptor expression (GluR, NR1, NR2 A, and NR2B) in diabetic rats induced by an enriched fat/fructose diet combined with streptozotocin administration (Gomaa et al. 2019). Treatment of microvascular endothelial cells with *B. serrata* extract revealed anti-inflammatory properties via the inhibition of TNFα-induced MMP-3, MMP-10, and MMP-12 activity (Roy et al. 2006). In rats with collagen-induced arthritis, *B. serrata* extract decreased inflammatory markers of IL-1β, TNF-α, IL-6, IFN-γ, and PGE2 while elevating the IL-10 levels (Umar et al. 2014). Furthermore, prior research has demonstrated that boswellic acids and *B. serrata* extracts attenuate the LPS-induced inflammatory response in peripheral blood mononuclear cells and macrophages (Cuaz-Pérolin et al. 2008; Henkel et al. 2012; Syrovets et al. 2005). Key findings of neuroprotective effects of *B. serrata* and boswellic acids are summarized in Table 2. Figure 3 shows a flowchart of pathophysiological mechanisms of ischemic stroke and intervention points for *B. serrata* and boswellic acids.

In summary, the present review explores the fundamental knowledge on the molecular pathways and possible underlying mechanisms related to the beneficial properties of *B. serrata* extracts and boswellic acids through the regulation of oxidative stress, inflammation, and apoptosis in ischemic stroke. Further research is needed to elucidate the exact mechanisms underlying *B. serrata* and boswellic acids. While preclinical studies

suggest promising neuroprotective potential of *B. serrata* and boswellic acids in ischemic stroke, still critical research gaps remain. Current gap includes limited human clinical trials, inadequate data on potential adverse interactions, and safety and long-term profile which requires further comprehensive investigation.

One main limitation of this study was the lack of comprehensive clinical data in the clinical studies section. The absence of such data restricted the ability to provide an in-depth analysis and robust discussion regarding the therapeutic effects of *B. serrata* in the clinical management of stroke. This highlights the need for future research on well-designed clinical trials that evaluate the efficacy, safety, and mechanisms of action of *B. serrata* in stroke patients.

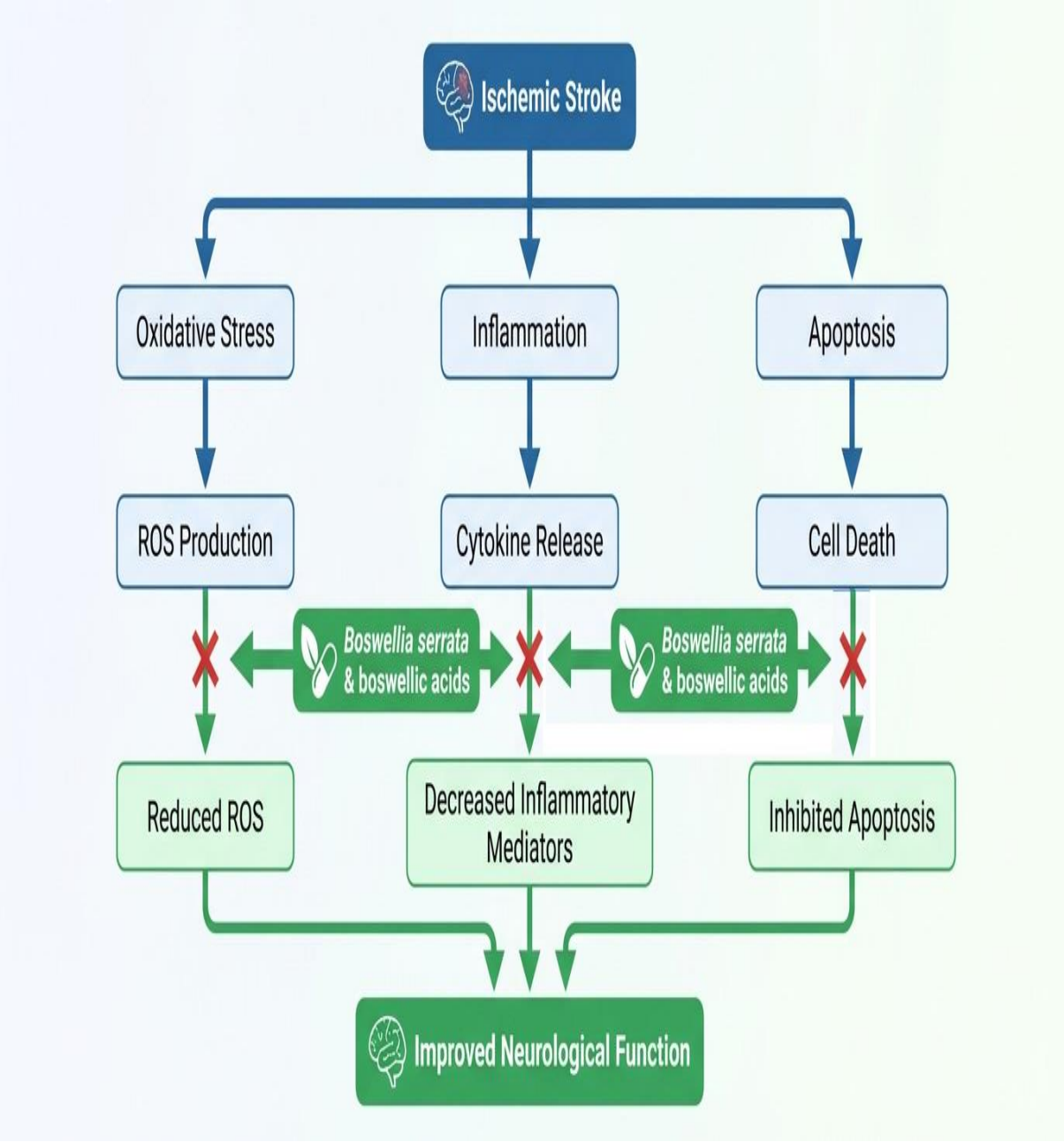


Figure 3. Diagram of effects of ischemic stroke on neurological function and possible neuroprotective properties of *Boswellia serrata* and boswellic acids through oxidative stress, inflammation, and apoptosis. ROS: Reactive Oxygen Species; *B. serrata*: *Boswellia serrata*

Table 2. Key findings from studies on *B. serrata and boswellic acids*

Study Design	Compound	Dose / Concentration	Administration	Population	Key Findings	References
In Vitro	AKBA	5 and 20 µM	Cell line treatment	bEND.3 cells	AKBA reduced cell death and ROS in OGD/reperfusion models, decreased inflammatory markers, and prevented degradation of tight junction proteins.	(Ahmad et al. 2019)
	B. serrata extract and AKBA	AKBA 40 µg/mL; extract 0–400 µg/mL	Cell line treatment	PC12 cells	*B. serrata* and AKBA increased neuronal cell survival and reduced oxidative damage	(Sadeghnia et al. 2017)
In Vivo	KBA and AKBA	25 mg/kg	PO	Rats	KBA and AKBA reduced infarct volumes and apoptosis in MCAO rat models, improved neurological scores, and enhanced expression of HO-1 and Nrf2.	(Ding et al. 2015)
	AKBA	20 mg/kg	ip	Rats	AKBA reduced infarct volume, improved neurological scores, and decreased neuronal apoptosis.	(Ding et al. 2014)
	AKBA	50 mg/kg	ip	Rats	β-boswellic acid significantly reduced necrotic neurons, infarct volume, and neurological impairments.	(Wang et al. 2022)
	B. serrata extract and AKBA	AKBA 50 mg/kg; extract 125–500 mg/kg	ip	Rats	*B. serrata* and AKBA reduced neuronal death and oxidative stress; improved neurological function	(Forouzanfar et al. 2016)
	AKBA	10 mg/kg	iv	Rats	AKBA-nanoparticles enhanced neuroprotection through antioxidant and anti-inflammatory pathways	(Ding et al. 2016)
	AKBA	5 mg/kg	ip	Mice	AKBA decreased neuronal apoptosis and reduced neuroinflammation	(Sayed et al. 2018)
Clinical Trials	Boswellic acids	2400 mg per day	PO	Stroke patients	Boswellic acids improved neurological function and reduced plasma inflammatory mediators in ischemic stroke patients.	(Baram et al. 2019)
	B. serrata extract	2000 mg per day	PO	Stroke patients	Partial clinical benefit of *B. serrata* in enhancing muscle strength	(Jivad et al. 2015)

AKBA: 3-O-acetyl-11-keto-β-boswellic acid; ROS: reactive oxygen species; OGD: oxygen–glucose deprivation; KBA: 11-keto-β-boswellic acid; PO: per os i.e., by mouth; MCAO: middle cerebral artery occlusion; HO-1: t heme oxygenase 1; Nrf2: Nuclear factor erythroid 2-related factor 2; ip: intraperitoneal; iv:intravenous

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Conflicts of interest

The authors declare that they have no competing interests.

Availability of data and material

The present study is a review article and data sharing are not applicable to this article.

Authors' Contributions

FF designed the study and conducted the literature search. MS provided the table and figures. FF and MS drafted the manuscript and co-developed the full text of the review. Both authors read and approved the final version of the manuscript.

Abbreviations

ATP: adenosine triphosphate. BBB: blood–brain barrier. C3aR: complement C3a receptor. HO-1: heme oxygenase 1. IL-1: interleukin-1. iNOS: inducible NOS. MAPK: mitogen-activated protein kinase. MCAO: middle cerebral artery occlusion.

MDA: malondialdehyde. MMP: metalloproteinase. NADPH: nicotinamide adenine dinucleotide phosphate. NMDA: N-methyl-D-aspartate. NO: nitric oxide. NOS: nitric oxide synthase. NQO-1: NAD(P)H: quinone oxidoreductase 1. OGD: oxygen–glucose deprivation. RNS: reactive nitrogen species. ROS: reactive oxygen species. SOD: superoxide dismutase. TNF-α: tumor necrosis factor-α

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