Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(2), 1855-1863 | ISSN:2251-6727

An Evaluation of the Neuroprotective and Anti-Inflammatory Activity of Cold Macerated Methanol Extract of *Salvia Officinalis*.

Dr. Ravindra Chandrakant Sutar[1], Dr. Gulshan Kumar[2], Kishor Kumar Mahakur[3], Jitendra Pratap Singh[4*], Rajeev Kumar[5], Jitendra Kumar[6], Dr. Hitesh Vishwanath Shahare[7], Dr. Mayuri Gurav[8]

[1]Associate Professor & HOD Department of Pharmacology, SRES'S Sanjivani College of Pharmaceutical Education and Research (Autonomous), Kopargaon, Ahmednagar, Maharashtra. 423603
[2]Assistant Professor, Bhagat Phool Singh Mahila Vishwavidyalaya, Department of Pharmaceutical Education and Research, Sonipat, India
[3]Assistant professor, Dhanvantari College Of Pharmacy, Munnapatra, Chakla, Ormanjhi, Ranchi, Jharkhand. 835219
[4*]Associate Professor, Mahatma Gandhi Institute of Pharmacy, Lucknow, Uttar Pradesh.
[5]Assistant Professor Department Of Biotechnology, Shivpadraj Mahavidyalaya Auraiya, Affiliation with CSJM University, Kanpur, Uttar Pradesh.
[6]Project Manager, IORA- Regional Centre of Science and Technology Transfer Coordination Centre on Medicinal Plants, CSIR-Central Institute of Medicinal and Aromatic Plants, Lucknow, India.
[7]Associate Professor, SNJB's Shriman Sureshdada Jain College of Pharmacy, Chandwad, Nashik, Maharashtra, India. 423101
[8]Assistant Professor, IVM's Krishnarao Bhegade Institute of Pharmaceutical Education and Research, Pune, Maharashtra, 410507.

***Corresponding Author:** Jitendra Pratap Singh
*****Associate Professor, Mahatma Gandhi Institute of Pharmacy, Lucknow, Uttar Pradesh.

(Received: 07 January 2024 Revised: 12 February 2024 Accepted: 06 March 2024)

KEYWORDS
Neuroprotective, Anti-inflammatory, RAW264.7 cells, Lipoxygenase, SK-N-SH cells, *Salvia officinalis*

ABSTRACT:
This investigation evaluated the effects of a cold-macerated *Salvia officinalis* leaf extract in methanol on neuroprotection and inflammation. This extract's neuroprotective and anti-inflammatory properties were evaluated *in vitro* on the RAW264.7 and SK-N-SH cell lines. The extract was tested in this study at various doses in well controlled laboratory conditions. By measuring intracellular reactive oxygen species levels, cytokines, and lipoxygenase inhibition, the anti-inflammatory and neuroprotective qualities were assessed and evaluated. According to the study findings and results, the extract demonstrated a concentration-dependent inhibition of lipoxygenase, decreased the production of cytokines suggestive of an anti-inflammatory activity, and revealed a neuroprotective impact in terms of improvement in intracellular reactive oxygen species levels. The current work clearly shows that cold-macerated methanolic leaf extract from *Salvia officinalis* possesses anti-inflammatory and neuroprotective effects *in vitro*.

INTRODUCTION

Increased rates of morbidity and death are associated with neurodegenerative illnesses. The field of medicine has advanced significantly in its comprehension of the processes associated with the advancement of neurodegenerative diseases. Every condition has a specific apoptotic route with self-mechanisms that lead to the development of new treatment modalities for each instance. The severe symptoms and development of many diseases remain difficult to control even with the availability of several western drugs. In the treatment of several neurological conditions, including epilepsy, neurodegenerative, neuro-metabolic, vascular, and psychosomatic illnesses, memory loss, depression, and neuroinflammation continue to be obstacles(Shoulson and Parkinson Study, 1998, Jain, 2011). The number of people suffering from age-related illnesses such as memory and learning impairments rises with age. The relevance of illness incidence, prevalence, morbidity, mortality, and trauma to clinical public health practise and health policy has grown. In addition to the widely used conventional western medications, Ayurveda can yield better outcomes with fewer side effects. The development of ayurvedic medications requires a thorough analysis that includes standardising the active biomolecules of herbal-mineral mixtures and providing scientific validation(Jain, 2011).

Neuroinflammation is a kind of inflammation that is classified as CNS gliosis due to immune system activation. Numerous medications, including NSAIDs, NMDA receptor antagonists, opioid antagonists,

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(2), 1855-1863 | ISSN:2251-6727

selective COX inhibitors, and seldom antibiotics, are used to treat neuronal inflammation. Despite its effectiveness in reinstating inflammation and analgesia, such allopathic medications have paradoxical consequences. For example, NSAIDs cause stomach discomfort, nausea, cramps, abdominal pain, disorientation, ringing in the ears, and decreased sperm motility, whereas opioid antagonists cause side effects such anxiety, nausea, dizziness, and lack of appetite. It is commonly believed to be persistent in contrast to CNS acute inflammation(Shabab et al., 2017, DiSabato et al., 2016).

Inflammatory chemicals, tissue deposition, and activation are the main indicators of acute inflammation, which usually occurs immediately after CNS damage. Chronic inflammation is characterised by the ongoing activation of glial cells and the recruitment of other immune cells into the brain. Viruses, bacteria, traumatic brain injury, spinal cord damage, toxic metabolites, autoimmune, and ageing are all linked to chronic inflammation. Despite the fact that many neurodegenerative illnesses are linked to neuroinflammation, there is growing interest in determining if reducing inflammation would have the opposite effect(DiSabato et al., 2016). Inhibiting inflammatory processes, for example, lessens the death of neurons seen in neurodegenerative illnesses.Glatiramer acetate, interferon B, and mitoxantrone are among the treatments for multiple sclerosis (MS), which decrease or prevent the activation of but have an impact on systemic immunosuppression. (Et al., Chiurchiu 2018). The usage of NSAIDs lowers the chance of developing AD. NSAIDs and glucocorticoids are used as treatments for AD. Prostaglandin H2 conversion to another (TX) is blocked by NSAIDs, and (PGs). These two increase microvascular permeability and function as mediators of inflammation(DiSabato et al., 2016, Lyman et al., 2014).

Numerous intricate connections exist between risk factors and the development, which can result in oxidative stress, vascular impairment, and brain damage. As soon as the event starts, neuroinflammation is increased, which damages cells and impairs neural function. Numerous stresses and damage reactions often trigger an immediate activation of the immune system, with some aspects thought to be neurotoxic and others neurotrophic. Increased amounts of (PGs) are associated with these inflammatory reactions in the brain, and these PGs are essential for brain disorders. The interaction between four and EP1, which are differently articulated on neuronal and glial cells across the central nervous system, mediates PGE2 signalling (Lyman et al., 2014).

As a result of inherent sterile damage or foreign stimuli like infections, the host responds by becoming inflamed. It is typified by the recruitment and deposition of immune cells in areas of injury as well as the generation of soluble mediators such as chemokines, lipid mediators, reactive oxygen and nitrogen species, and cytokines. Although they are necessary for regulating inflammation and promoting tissue healing, these mediators have the potential to worsen tissue injury. Through pattern recognition receptors (PRR), such as Toll-like receptors (TLRs) and NOD-like receptors (NLRs), among others, cells sense pathogen-associated molecular patterns (PAMPs) or damage-associated molecular patterns (DAMPs), which in turn triggers specific signalling pathways and initiates the inflammatory response. Based on the stimuli and the pattern of the induced immune response, macrophages are among the most significant cells involved in the resolution or worsening of inflammation. Interleukin (IL)-1β receptors (TNFR and IL1R, respectively) and tumour necrosis factor (TNF)-α receptors (TNFR) activate macrophages, which in turn produces inflammatory mediators such nitric oxide (NO), TNF-α, IL-1β, IL-6, and cyclooxygenase (COX)-2. Inducible nitric oxide synthase (iNOS) generates macrophage-derived NO, which possesses immunomodulatory, anti-tumoral, and anti-pathogenic properties that may be advantageous.Nonetheless, prolonged and elevated NO levels are harmful to the host and play a role in the aetiology of a number of illnesses. High amounts of TNF-α and IL-1β are also linked to inflammatory disorders. These substances affect immune cells autocrinely and paracrinely, intensifying the inflammatory response (Landskron et al., 2014, Zhang and An, 2007). The activation and nuclear translocation of nuclear factor-κB (NFκB) result from intracellular signalling pathways that are triggered by PRRs in various cell types, including macrophages. This process triggers the expression of most of the mediators previously mentioned. Additionally, the transcription of several genes involved in cellular adhesion, proliferation, apoptosis, stress response, and tissue remodelling is regulated by NFκBactivationSinceNFκB is implicated in a variety of human clinical illnesses, including both acute and chronic inflammation, it makes sense to target it when creating novel anti-inflammatory medications.

Depending on the nature of the illness, both acute and chronic inflammation might have different symptoms. Acute inflammation can be brought on by microbial infections, trauma, vibration, heat, cold, ionising agents, and chemical agents such as tissue necrosis, reducing agents, alkalis, and corrosive acids. Although chronic inflammation acts slowly at first, it does so for a very long time(Choi et al., 2023, Hamad et al., 2023, Mayangsari et al., 2023).Activated immunological or

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(2), 1855-1863 | ISSN:2251-6727

inflammatory cells trigger a variety of processes that lead to either acute or chronic inflammation. Activated inducible nitric oxide synthase (iNOS) and cyclooxygenase (COX)-2 produce pro-inflammatory cytokines and inflammatory mediators, such as reactive oxygen species (ROS), nitric oxide (NO), and prostaglandin E2 (PGE2), which are then overproduced by macrophages and play a major role in various immunopathological phenomena **(**Kataki et al., 2014**)**. In inflammatory conditions, adhesion molecule activation signals also stimulate immune cells, enhancing their migration to inflammatory tissue and eventually leading to the formation of heterotypic cell clustering (adhesion) between immune cells, endothelial cells, and inflamed cells. Pro-inflammatory cytokines and lipopolysaccharide (LPS) are two examples of inflammatory stimuli that cause immune cells to upregulate these inflammatory circumstances. For this reason, these stimuli are helpful targets for the development of novel anti-inflammatory medications as well as the investigation of a prospective drug's molecular anti-inflammatory mechanisms (Kataki et al., 2014, Zouhri et al., 2023, Pinto et al., 2024).

Owing to leukocytes' crucial function, cellular infiltration is a significant component of an inflammatory response. Leukocytes produce proteases and other lysosomal enzymes during inflammation as part of their protective functions, which further damages tissue and intensifies inflammation. A cell that has had damage to its membranes will be more vulnerable to further damage from lipid peroxidation caused by free radicals. Damage to the membrane will impair the ability of membrane proteins to regulate the volume and water content of cells via regulating the passage of sodium and potassium ions (Zouhri et al., 2023, Pinto et al., 2024, Sarma Kataki et al., 2012). Because the membranes of red blood cells and lysosomes are similar, understanding the inflammatory process may be gained by inhibiting red blood cell haemolysis. Stabilizing these cell membranes may prevent or postpone the lysis and subsequent release of the cytoplasmic contents, hence minimising tissue damage and the inflammatory response. Thus, it is crucial to have compounds that significantly protect cell membranes from harmful substances if you want to stop inflammation from spreading.

Salvia officinalis L. (Sage). Belongs to the Labiatae/Lamiaceae family is a perennial round shrub with important and noteworthy medicinal values. This family's biggest genus, Salvia, contains about 900 species. This plant genus is found all over the world, with the species *S. officinalis* being native to the Middle East and Mediterranean(Ghorbani and Esmaeilizadeh, 2017). In many regions of the world now, particularly in North America and Europe, it has been naturalised. The aerial parts of the *S. officinalis* shrub have long been used in traditional medicine and cuisine. Due to its flavour and seasoning capabilities, this plant is widely used in a wide range of culinary dishes (Miraj and Kiani, 2016). In Asian and Latin American traditional medicine, it has been used to treat a wide range of ailments, including epilepsy, ulcers, gout, rheumatism, inflammation, dizziness, tremor, paralysis, diarrhoea, and hyperglycaemia(Jakovljević et al., 2019). In European traditional medicine, *S. officinalis* has been used to treat mild dyspepsia, excessive sweating, age-related cognitive decline, and skin and neck inflammations (such as heartburn and bloating). The use of *S. officinalis* in medicine has been authorised by the German Commission E for a number of ailments, including inflammation and dyspepsia (Eidi et al., 2005). Considering these details, the current investigation set out to assess the anti-inflammatory and neuroprotective properties of cold-macerated methanolic leaf extract *Salvia officinalis*.

MATERIAL AND METHODS

Material

A botanist identified *Salvia officinalis*, which was collected from the Mandi area of Himachal Pradesh, India, between July and October of 2022. The voucher specimen, designated BKS-2022-209, is kept in our lab's herbarium. We purchased NG-monomethyl-l-arginine (N-MMA), lipopolysaccharide (LPS), and recombinant human interferon-α (IFN-α) from Sigma Aldrich, India. RPMI1640 and foetal bovine serum were purchased from Himedia (Mumbai, India). The ATCC provided RAW264.7 and SK-N-SH cell lines for purchase (Rockville, MD). The grade of all other compounds was of analytical grade from Sigma Aldrich and Loba Chem, India.

Solvent extraction

After 50 g of air-dried *Salvia officinalis* leaves were grinded to powder, 90 percent methanol (2×2 l) was used in a cold maceration process to extract the leaves at 25 °C. Following filtration, the extract was vacuum-concentrated and heated to dryness under low pressure. The methanolic extract was codenamed as SO-M.

Preliminary Phytochemical screening

The salvia extract (SO-M) was subjected to several standard test (Shaikh and Patil, 2020, Raaman, 2006)as preliminary phytochemical screening for detection of various phytocompound compound classes precent in the extract.

Cell culture

An appropriate medium (RPMI1640) supplemented with 100 U/ml penicillin, 100 g/ml streptomycin, and 10% foetal bovine serum was used to cultivate the SK-N-SH and RAW264.7 cell lines. Cells were grown in an environment with 5% carbon dioxide and humidified air at 37 °C.

Neuroprotective activity

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(2), 1855-1863 | ISSN:2251-6727

Cell culture and treatment

SK-N-SH cells, a human neuroblastoma cell line from American Type Cell Culture (ATCC), were cultured in DMEM supplemented with 10 percent (v/v) foetal bovine serum, 100 U/ml penicillin, and 100 µg/ml streptomycin to investigate the neuroprotective effects of WS. Ninety-six-well plates (Corning) containing SK-N-SH cells were plated at a density of 1.5 × 104 cells/well and incubated at 37°C. The media was entirely withdrawn from the cells after 24 hours after plating, and they were then maintained in DMEM containing antibiotics but no serum. Acrolein (20 µm) at hazardous concentrations was then applied to the cells for a whole day(Thummayot et al., 2016, Thummayot et al., 2014).

Intracellular reactive oxygen species level

By evaluating SO- M's capacity to scavenge ROS in SK-N-SH cells using the fluorescent dye DCF-DA as previously described, the antioxidant activity of the compound was verified. When cellular ROS are present, the cell-permeable dye DCF-DA is enzymatically transformed to the highly fluorescent molecule DCF, and the fluorescence intensity is directly correlated with the degree of intracellular ROS(Thummayot et al., 2014, Ramassamy and Singh, 2017).

Anti-inflammatory effect

Inflammatory marker cytokines including IL-1β, IL-6 and TNF-α

The *Salvia officinalis* extract (100 mg/ml) was diluted with RPMI1640 before to treatment, having been solubilized in 50% ethanol and 50% PBS. As was previously noted, the inhibitory effect of each fraction (100g/ml) on the LPS-treated RAW264.7 cells' cytokine production (IL-1β, IL-6, and TNF-α) was determined. Subsequently, supernatants were extracted and analysed using ELISA cytokine tests (Lee et al., 2006).

Lipoxygenase Inhibition Assay

The extract's lipoxygenase inhibitory activity was measured using a previously published technique, with a few amendments(Lee et al., 2006, Kataki et al., 2014). In a nutshell, 12 mL of the extract were treated with a combination of lipoxygenase (12µL, final concentration 8000 U/mL) and sodium borate buffer (1 mL, 0.1 M, pH 8.7) at room temperature (30 ± 2 °C) for five minutes. The procedure was initiated by adding 12 µL of linoleic acid substrate (12 mmol). A UV/VIS spectrophotometer was used to measure the reaction solution's absorbance at 235 nm (PerkinElmer). The percentage of lipoxygenase inhibition was calculated using the following formula, with phosphate buffer solution acting as the control:

% inhibition = 100 × (absorbance of the control − absorbance of the sample)/absorbance of the control

Statistical Analysis

For all investigated in vitro experiments, the data are shown as the mean ± standard deviation, and each analysis was carried out in triplicate. GraphPad Prism software was used to conduct a one-way analysis of variance (ANOVA), which was then used to compare the results of neuroprotective vs anti-inflammatory tests at a significance threshold of $p < 0.05$ (2-tailed).

RESULTS

Neuroprotective activity

***Salvia officinalis*extract decreases intracellular reactive oxygen species level**

Antioxidant potential of SO-M has been investigated since oxidative damages and ROS contribute to acrolein's toxicity. In SK-N-SH cells treated with H_2O_2 (500 µm), the SO-M extract was able to reduce the levels of ROS; a notable impact was seen at 6 µg/ml.

Table 1. Impact of SO-M in intracellular reactive oxygen species level

Control	**H_2O_2**	**SO-M Concentration (µg/ml)**				
	500 µm	**3**	**6**	**12**	**24**	**48**
100	297±5.67	296±4.89	256±4.39	238±3.99	178±2.08	174±2.14

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(2), 1855-1863 | ISSN:2251-6727

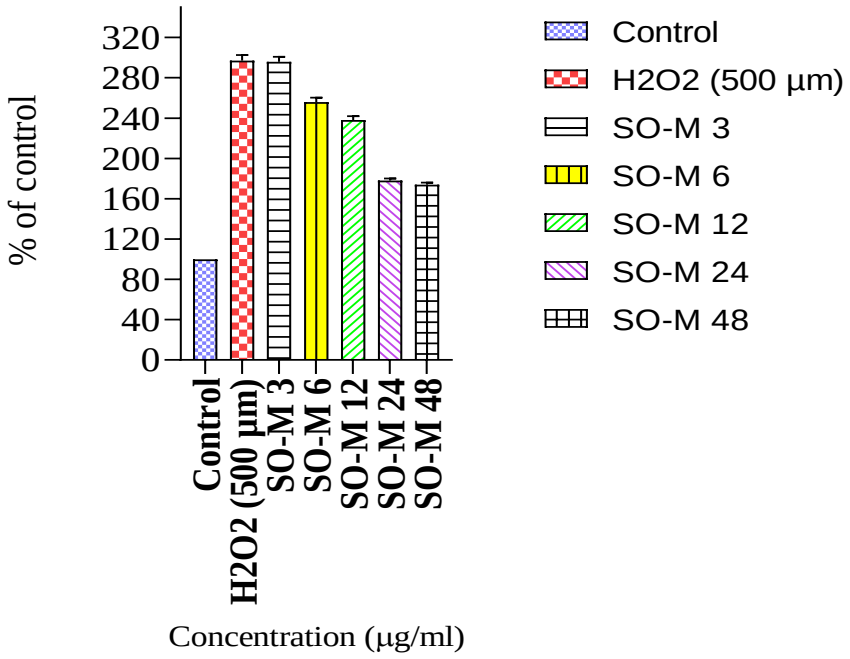

Figure 1.SO-M decreases intracellular reactive oxygen species level.

Anti-inflammatory effect

Inflammatory marker cytokines including IL-1β, IL-6 and TNF-α

It is well known that IL-1, IL-6, and TNF-are pro-inflammatory cytokines with a wide range of biological activities related to the immunopathology of autoimmune illnesses and acute or chronic inflammatory diseases such rheumatoid arthritis and septic shock. Therefore, we initially looked at the possibility that *Salvia officinalis* may prevent mouse macrophages (RAW264.7) from producing cytokines using the ELISA technique.Table 2 and figure 2 shows that the methanol extract(100µg/ml) significantly suppressed the production of IL-1, IL-6, and TNF- from RAW264.7 cells stimulated by LPS, up to 38.46 ± 1.02–52.88 ± 1.04%.*Salvia officinalis* may therefore regulate the translational amounts of pro-inflammatory cytokine production.

Table 2. Effects of 100 mg/ml *Salvia officinalis* extracts (SO-M) on RAW264.7 cells' production of pro-inflammatory cytokines

	Inhibition (%)		
Fraction	**IL-6**	**IL-1**	**TNF-α**
SO-M	52.88 ± 1.04**	38.46 ± 1.02**	44.91 ± 0.98**

* $p < 0.05$. ** $p < 0.01$

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(2), 1855-1863 | ISSN:2251-6727

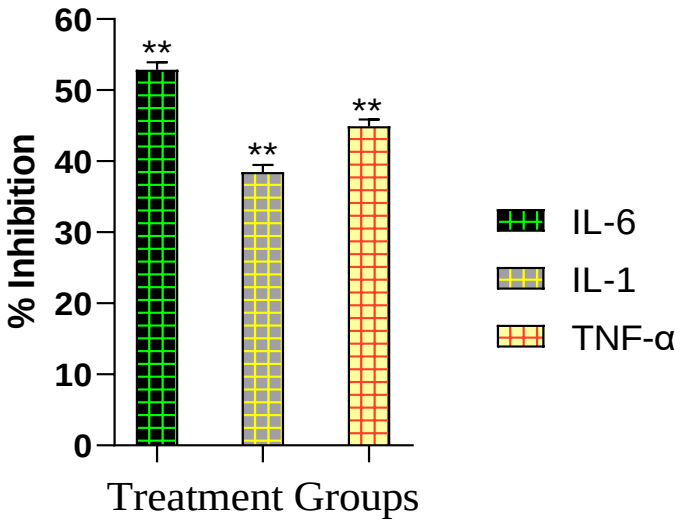

Figure 2. Impact of SO-M upon the production of pro-inflammatory cytokinesin RAW264.7 cells.

Lipoxygenase Inhibition Activity

Table 3 presents the extract's lipoxygenase inhibitory activity results visually. The concentration range of 30–150 µg/mL showed inhibition values between 4.297±0.02–69.99±1.52 percent. At a dosage of 150 µg/mL, the *Salvia officinalis* extract demonstrated an enhanced capacity to inhibit lipoxygenase activity, around 69.99±1.52 percent. Additionally, the study's findings demonstrated a strong anti-inflammatory (lipoxygenase activity) (Table 3). It was demonstrated that SO-M (150 µg/mL) reduced the 5-LOX enzyme's activity to a degree of 69.99±1.52%. It was discovered that the IC50 value for SO-M was 208.36 µg/mL(Table 3).

Table 3. Percentage inhibition of the 5-LOX by the extract.

Concentration (µg/mL)	**% Inhibition 5-LOX**
30	4.297±0.02
60	8.91±0.62
90	20.796±0.89
120	44.874±1.15
150	69.99±1.52
IC_{50}	208.36 µg/mL

DISCUSSION

Uncovering the therapeutic potential of *Salvia officinalis* (SO) extract, reveals its promising neuroprotective and anti-inflammatory activity. While neurological disorders such as Parkinson's and Alzheimer's disease belong to a long list of health conditions where its application could prove beneficial. In this article, we examine the implications of its neuroprotective activity, explore its anti-inflammatory effects, and its lipoxygenase inhibition activity, as evidenced in experimental studies. The first study supporting the neuroprotective activity of SO-M extract, demonstrates its ability to normalize intracellular reactive oxygen species (ROS) levels. Since oxidative damage and accumulation of ROS are central to multiple neurodegenerative processes, including acrolein-induced toxicity, the observation is of particular significance. The SO-M extract considerably reduced ROS levels in an experimental model employing SK-N-SH cells treated with hydrogen peroxide (H_2O_2); the most notable impact was shown at 6 µg/ml. This finding raises the possibility that SO-M extract protects brain cells from the oxidative stress associated with neurodegenerative diseases. The SO-M extract's down-regulation of the synthesis of pro-inflammatory cytokines further supports its anti-inflammatory properties.Pro-inflammatory mediators that play a crucial role in the pathophysiology of inflammatory and autoimmune disorders include pro-inflammatory cytokines including interleukin-1 (IL-1), interleukin-6 (IL-6), and tumour necrosis factor-alpha (TNF-α). Enzyme-linked immunosorbent assay

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(2), 1855-1863 | ISSN:2251-6727

(ELISA) investigation revealed that SO-M extract dramatically reduced their production by murine macrophages (RAW264.7 cells) challenged with lipopolysaccharide (LPS). The inhibition varied between 4.297±0.02–69.99±1.52 percent, indicating that SO-M extract may have the ability to control immunological responses and lessen diseases linked to inflammation.

Moreover, the lipoxygenase inhibition potential of SO-M extract has provided further support to its anti-inflammatory properties. Lipoxygenases are a class of enzymes involved in the biosynthesis of pro-inflammatory mediators and they represent attractive targets for anti-inflammatory therapies. The result of present study showed that the SO-M extract inhibited the lipoxygenase activity significantly in a concentration-dependent manner with the IC50 value of 208.36 µg/mL. This inhibition may help to infer that the SO-M extract has the potential to break the enzymatic cascade that is involved in the inflammatory mediator production and thereby keep inflammation to a low level. Leukotriene are series of inflammatory diseases, such as cancer, asthma, arthritis and allergy diseases are known to promoting agents, leukotriene A4 which is formed by lipoxygenase of inflammatory cell is a key enzyme for the formation of leukotriene. The metabolism of arachidonic acid is crucial step in the anti-inflammatory mechanism may be involved a number ofclasses of hormones, including prostaglandins, thromboxanes and leukotrienes (LOX-s). Membrane phospholipids emit arachidonic acid when neutrophils are properly stimulated in this route. It may then be handily changed into prostaglandins and leukotrienes respectively via the lipoxygenase and cyclooxygenase pathways. When polyunsaturated fatty acids are dioxygenated into trans, cis-conjugated diene hydroperoxides, lipoxygenase catalyses the production of significant mediators in several inflammatory processes, including leukotrienes. Our findings therefore suggest that SO- M may have a more powerful anti-inflammatory and neuro-protective effect in relation to the typical.With a mix of anti-inflammatory and antioxidant properties which might arise from the polyphenol and antioxidant substances present in the findings. Polyphenols have recently been demonstrated to inhibit lipoxygenase, and could thus interfere or stop the cascade process with the metabolism of arachidonic acid.

In conclusion, the findings from this series of experimental studies provide broad insights into the multifaceted therapeutic potential of *Salvia officinalis* extract. By virtue of its ability to reduce intracellular ROS levels, curb pro-inflammatory cytokine production, and inhibit lipoxygenase activity, SO extract dovetails well with the central dogma of neuroprotection and inflammation modulation. These pharmacological intricacies collectively conspire to position SO extract as an attractive candidate for development of pharmaceutical interventions for neurodegenerative disorders, autoimmune maladies, and other inflammatory maladies. The constellation of molecular targets and pathways modulated by SO extract in neuroinflammation and oxidative stress [8,9] mechanistically suggests that further exploration into its cascade of action seems readily feasible and warranted, potential yielding crucial data pertinent to the dissociation of novel agents with circumscribed (de)regulatory reach and improved safety/efficacy profiles.

In conclusion, the experimental evidence presented in this discussion underscores the therapeutic potential ofSalvia officinalis extract as a neuroprotective and anti-inflammatory agent. Further investigation is warranted to delineate the mechanisms of action, as well as the clinical applications in the management of neurological and inflammatory disorders, and this may lead to the development and implementation of the novel therapeutic strategies.

CONCLUSION

In conclusion, the findings obtained from the studies investigating the therapeutic potential of Salvia officinalis (SO) extract reveal interesting prospects for its application as a neuroprotectant and inflammation modulator considering: a) that the capability of SO extract to diminish intracellular levels of reactive oxygen species (ROS) indicates its capacity to counteract the effects of oxidative stress, which is pivotal in neurodegenerative processes; and b) that SO extract's inhibitory actions of pro-inflammatory cytokine production and lipoxygenase activity demonstrate its anti-inflammatory properties, and hence, its ability to potentially mitigate the pathologies associated with inflammation. These pharmacological features position SO extract as a candidate of interest to design therapies that can target a range of diseases, including neurodegenerative disorders, autoimmune conditions and chronic inflammatory pathologies. In addition to targeting oxidative stress, its ability to ward off inflammation broadens the spectrum of potential pathologies against which SO-M may be used and would help explain how a relatively simple extract might be therapeutic across a wide range of conditions. Much more research is required to elucidate the exact mechanisms of the SO-M extract — its safety and efficacy in any clinical setting, for example; the magnitude of its possible synergistic effects with the standard of care; how dosages could be optimized for maximal therapeutic benefit. Nevertheless, as the evidence in favour of the neuroprotective and anti-inflammatory effects of SO-M extract continues to build, and given the limitations of current options, it

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(2), 1855-1863 | ISSN:2251-6727

seems that this extract may be the first of its breed. Continued efforts to elucidate the mechanisms of action underpinning these therapeutic effects and to explore their clinical applications are essential to uncovering the full therapeutic potential of this natural remedy.

REFERENCE

1. CHOI, Y. G., CHOI, W. S., SONG, J. Y., LEE, Y., LEE, S. H., LEE, J. S., LEE, S., CHOI, S. R., LEE, C. H. & LEE, J. Y. 2023. Antiinflammatory effect of the ethanolic extract of Korean native herb Potentilla rugulosa Nakai in Bisphenol-a-stimulated A549 cells. *J Toxicol Environ Health A,* 86**,** 758-773.
2. DISABATO, D. J., QUAN, N. & GODBOUT, J. P. 2016. Neuroinflammation: the devil is in the details. *Journal of neurochemistry,* 139**,** 136-153.
3. EIDI, M., EIDI, A. & ZAMANIZADEH, H. 2005. Effect of Salvia officinalis L. leaves on serum glucose and insulin in healthy and streptozotocin-induced diabetic rats. *Journal of ethnopharmacology,* 100**,** 310-313.
4. GHORBANI, A. & ESMAEILIZADEH, M. 2017. Pharmacological properties of Salvia officinalis and its components. *Journal of traditional and complementary medicine,* 7**,** 433-440.
5. HAMAD, R. S., EL SHERIF, F., AL ABDULSALAM, N. K. & ABD EL-MOATY, H. I. 2023. Chlorogenic acid derived from Moringa oleifera leaf as a potential antiinflammatory agent against cryptosporidiosis in mice. *Trop Biomed,* 40**,** 45-54.
6. JAIN, K. K. 2011. *The handbook of neuroprotection,* Springer.
7. JAKOVLJEVIĆ, M., JOKIĆ, S., MOLNAR, M., JAŠIĆ, M., BABIĆ, J., JUKIĆ, H. & BANJARI, I. 2019. Bioactive profile of various Salvia officinalis L. preparations. *Plants,* 8**,** 55.
8. KATAKI, M. S., KAKOTI, B. B., BHUYAN, B., RAJKUMARI, A. & RAJAK, P. 2014. Garden rue inhibits the arachidonic acid pathway, scavenges free radicals, and elevates FRAP: role in inflammation. *Chinese journal of natural medicines,* 12**,** 172-179.
9. LANDSKRON, G., DE LA FUENTE, M., THUWAJIT, P., THUWAJIT, C. & HERMOSO, M. A. 2014. Chronic inflammation and cytokines in the tumor microenvironment. *Journal of immunology research,* 2014.
10. LEE, H. J., HYUN, E. A., YOON, W. J., KIM, B. H., RHEE, M. H., KANG, H. K., CHO, J. Y. & YOO, E. S. 2006. In vitro anti-inflammatory and anti-oxidative effects of Cinnamomum camphora extracts. *J Ethnopharmacol,* 103**,** 208-16.
11. LYMAN, M., LLOYD, D. G., JI, X., VIZCAYCHIPI, M. P. & MA, D. 2014. Neuroinflammation: the role and consequences. *Neuroscience research,* 79**,** 1-12.
12. MAYANGSARI, E., MUSTIKA, A., NURDIANA, N. & ARDHAYUDICVA, S. 2023. Potency antiinflammatory of ethanol extract gel of Kepok banana peel (Musa balbisiana). *Med J Malaysia,* 78**,** 488-490.
13. MIRAJ, S. & KIANI, S. 2016. A review study of therapeutic effects of Salvia officinalis L. *Der Pharmacia Lettre,* 8**,** 299-303.
14. PINTO, A., DE MELO NUNES, R., DE FREITAS CARVALHO, W. V., GIRÃO, V. C. C. & ROCHA, F. A. C. 2024. Systemic and local antiinflammatory effect of magnesium chloride in experimental arthritis. *Adv Rheumatol,* 64**,** 6.
15. RAAMAN, N. 2006. *Phytochemical techniques,* New India Publishing.
16. RAMASSAMY, C. & SINGH, M. 2017. In vitro screening of neuroprotective activity of Indian medicinal plant Withania somnifera. *Journal of Nutritional Science,* 6**,** e54.
17. SARMA KATAKI, M., MURUGAMANI, V., RAJKUMARI, A., SINGH MEHRA, P., AWASTHI, D. & SHANKAR YADAV, R. 2012. Antioxidant, hepatoprotective, and anthelmintic activities of methanol extract of Urtica dioica L. leaves. *Pharmaceutical Crops,* 3.
18. SHABAB, T., KHANABDALI, R., MOGHADAMTOUSI, S. Z., KADIR, H. A. & MOHAN, G. 2017. Neuroinflammation pathways: a general review. *International Journal of Neuroscience,* 127**,** 624-633.
19. SHAIKH, J. R. & PATIL, M. 2020. Qualitative tests for preliminary phytochemical screening: An overview. *International Journal of Chemical Studies,* 8**,** 603-608.
20. SHOULSON, I. & PARKINSON STUDY, G. 1998. DATATOP: a decade of neuroprotective inquiry. *Annals of neurology,* 44**,** S160-S166.
21. THUMMAYOT, S., TOCHARUS, C., PINKAEW, D., VIWATPINYO, K., SRINGARM, K. & TOCHARUS, J. 2014. Neuroprotective effect of purple rice extract and its constituent against amyloid beta-induced neuronal cell death in SK-N-SH cells. *Neurotoxicology,* 45**,** 149-158.
22. THUMMAYOT, S., TOCHARUS, C., SUKSAMRARN, A. & TOCHARUS, J. 2016. Neuroprotective effects of cyanidin against Aβ-induced oxidative and ER stress in SK-N-SH cells. *Neurochemistry International,* 101**,** 15-21.
23. ZHANG, J.-M. & AN, J. 2007. Cytokines, inflammation and pain. *International anesthesiology clinics,* 45**,** 27.
24. ZOUHRI, A., BOUDDINE, T., MENYIY, N. E., KACHKOUL, R., EL-MERNISSI, Y., SIDDIQUE, F., MOUBACHIR, R., KHALLOUKI, F.,

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(2), 1855-1863 | ISSN:2251-6727

SALAMATULLAH, A. M., WONDMIE, G. F., BOURHIA, M. & HAJJI, L. 2023. Ionomic analysis, polyphenols characterization, analgesic, antiinflammatory and antioxidant capacities of Cistus laurifolius leaves: in vitro, in vivo, and in silico investigations. *Sci Rep,* 13**,** 22890.