

Asian Journal of Phytomedicine and Clinical Research

Journal home page: www.ajpcrjournal.com

<https://doi.org/10.36673/AJPCR.2026.v14.i02.A05>



STIGMASTEROL: A COMPREHENSIVE REVIEW ON ITS NATURAL SOURCES, BIOLOGICAL ACTIVITIES AND MODERN DRUG DELIVERY STRATEGIES

S. Vishwa*¹ and E. Abraham Theodore Rajaselwin¹

^{1*}Department of Pharmaceutics, Sri Ramakrishna Institute of Paramedical Sciences, College of Pharmacy, (Dr M.G.R. Medical University), Sarojini Naidu Road, Coimbatore, Tamil Nadu - 641 044, India.

ABSTRACT

Stigmasterol is a naturally occurring phytosterol widely found in plant sources such as vegetable oils, legumes, nuts, and medicinal plants. It has gained considerable attention in pharmaceutical and biomedical research due to its diverse pharmacological properties. Studies have reported that stigmasterol possesses significant anti-inflammatory, antioxidant, antimicrobial and anticancer activities, making it a promising bioactive compound for therapeutic applications. Its anti-inflammatory effect is mainly associated with the regulation of important signaling pathways such as Nuclear Factor kappa B and Mitogen-Activated Protein Kinase, which are responsible for the production of inflammatory mediators. However, the practical application of stigmasterol is limited due to its poor water solubility and low bioavailability. Therefore, advanced drug delivery systems such as Niosomes are being explored to enhance its solubility, stability and therapeutic effectiveness in modern pharmaceutical formulations.

KEYWORDS

Stigmasterol, Phytosterol, Molecular mechanism and Pharmaceutical challenges.

Author for Correspondence:

Vishwa,
Department of Pharmaceutics,
Sri Ramakrishna Institute of Paramedical Sciences,
College of Pharmacy, (Dr M.G.R. Medical
University), Sarojini Naidu Road, Coimbatore,
Tamil Nadu - 641 044, India.

Email: abraham.theodore@gmail.com

INTRODUCTION

Stigmasterol is a naturally occurring phytosterol mainly present in plant-derived sources like vegetable oils, legumes, nuts, seeds, and therapeutic herbs. Its structure resembles that of cholesterol, featuring a tetracyclic cyclopenta [a] phenanthrene ring system, along with a distinct double bond at the C-22 position in its side chain, setting it apart from other plant sterols. Stigmasterol is a vital part of plant cell membranes, assisting in the regulation of membrane fluidity and permeability. Because of its similar structure to cholesterol, it competitively

blocks the absorption of cholesterol in the intestines, which helps produce its cholesterol-lowering effect. Moreover, stigmasterol demonstrates various biological and pharmacological effects, such as anti-inflammatory, antioxidant, anti-osteoarthritic and anticancer activities, primarily through the modulation of essential signaling pathways, including NF- κ B, MAPK and enzymes related to oxidative stress. Additionally, it acts as a key precursor in the formation of several steroid hormones, vitamin D₃ and pharmaceutical intermediates. Despite its potential as a therapy, the clinical use of stigmasterol is frequently hindered by its low solubility in water and poor bioavailability, prompting greater research focus on innovative drug delivery methods like nanoparticles and niosomes to improve its effectiveness^{1,2,3}.

SIGNIFICANCE

Natural Phytosterol

Stigmasterol is a naturally occurring plant sterol present in many plants, vegetable oils and medicinal herbs.

Anti-inflammatory Activity

It helps reduce inflammation by inhibiting inflammatory mediators and regulating pathways such as Nuclear Factor kappa B.

Antioxidant Property

Stigmasterol protects cells from oxidative stress by neutralizing harmful free radicals.

Cholesterol-Lowering Effect

It reduces intestinal absorption of cholesterol, thereby helping to maintain healthy blood cholesterol levels.

Pharmaceutical Importance

Due to its therapeutic potential but poor solubility, advanced delivery systems such as Niosomes are used to enhance its stability and bioavailability.

SOURCES AND EXTRACTION

NATURAL SOURCES

Like soybean oil, calabar beans and medicinal herbs.

Soybean oil

Soybean oil is a vegetable oil extracted from the seeds of *Glycine max*.

It is one of the richest natural sources of the phytosterol Stigmasterol.

Soybean oil contains several phytosterols such as stigmasterol, β -sitosterol and campesterol.

It is widely used in food, pharmaceutical and cosmetic industries because of its nutritional and therapeutic value.

The presence of phytosterols in soybean oil helps in reducing cholesterol levels and improving cardiovascular health.

Calabar beans

Commonly known as Calabar beans, is a tropical leguminous plant native to West Africa.

The seeds contain several bioactive compounds, including the phytosterol Stigmasterol.

Calabar beans also contain an important alkaloid called Physostigmine, which has medicinal and pharmacological significance.

Due to the presence of phytochemicals, the plant is studied for anti-inflammatory, antioxidant, and therapeutic properties.

However, Calabar beans are highly toxic if consumed improperly, so they must be handled carefully in medicinal and pharmacological research².

Medicinal herbs

Azadirachta indica – Commonly known as Neem, widely used for its anti-inflammatory and antimicrobial properties.

Calotropis gigantea – A medicinal plant used in traditional medicine for pain and inflammatory conditions.

Withania somnifera – Known as Ashwagandha, used for its antioxidant and anti-inflammatory effects.

Eclipta alba – Commonly called Bhringraj, used in herbal medicine for its pharmacological benefits.

Stigmasterol present in medicinal herbs contributes to anti-inflammatory, antioxidant and antimicrobial properties⁴.

ISOLATION TECHNIQUES METHODS

Isolation techniques like Solvent extraction methods, Saponification methods, Column chromatography, Thin layer chromatography, Recrystallization^{2,5,6}.

Thin Layer Chromatography (TLC)

Thin layer chromatography is commonly used for the identification and preliminary separation of Stigmasterol from plant extracts. It helps determine the R_f value and confirm the presence of stigmasterol.

Column Chromatography

Column chromatography is widely used for the purification of stigmasterol. The plant extract is passed through a silica gel column and eluted with suitable solvent systems to separate stigmasterol from other phytosterols.

High Performance Liquid Chromatography (HPLC)

HPLC is an advanced chromatographic technique used for the accurate separation, identification, and quantification of stigmasterol in plant extracts and pharmaceutical formulations.

Gas Chromatography (GC)

Gas chromatography is used for the analysis of sterols, including stigmasterol, especially after derivatization. It provides high sensitivity and precise separation.

Preparative Chromatography

Preparative chromatography is used to isolate larger quantities of purified stigmasterol from complex plant extracts for research and pharmaceutical applications.

SOLVENT EXTRACTION METHODS

Plant Preparation

Plant materials containing Stigmasterol are first dried and finely powdered to increase the surface area for efficient extraction^{4,7}.

Use of Organic Solvents

Non-polar or moderately polar solvents such as hexane, petroleum ether, chloroform, or ethanol are commonly used to dissolve stigmasterol from plant material.

Extraction Process

The powdered plant material is soaked or continuously extracted with the selected solvent using techniques like maceration or Soxhlet extraction.

Filtration and Concentration

After extraction, the solution is filtered and the solvent is evaporated to obtain a concentrated extract containing stigmasterol.

Purification

The extracted material may undergo saponification and chromatographic techniques to isolate pure stigmasterol from other phytosterols and impurities.

Physicochemical properties

Drug name: Stigmasterol

Chemical name: Stigmasta-5,22-dien-3 β -ol

Molecular formula: C₂₉H₄₈O

Molecular weight: 412.69g/mol

Drug class: Phytosterol

Appearance: White crystalline powder

Origin: phytosterol that occurs naturally and widely in the fats and oils of numerous plants such as soybeans, calabar beans and rapeseed.

Storage Temperature: -20°C (for long-term storage).

Shelf Life: At least 2 years when stored correctly.

Half life: 2-6 hr for animals.

Melting point: 160- 164°C

Boiling point: ~501–502°C

Solubility: Soluble in organic solvents.

Log p: ~7.80 to 10.07.

Dissociation constant(pka): ~15.03.

BIOLOGICAL ACTIVITIES

ANTI INFLAMMATORY

Mechanism involving inhibition of pro inflammatory cytokinase

Stigmasterol reduces inflammation by inhibiting the production of pro-inflammatory cytokines.

It suppresses cytokines such as Tumor Necrosis Factor alpha and Interleukin-6 that play a major role in inflammatory responses.

It regulates inflammatory signaling pathways like Nuclear Factor kappa B.

It also modulates the Mitogen-Activated Protein Kinase pathway, reducing the expression of inflammatory genes.

By decreasing cytokine release, stigmasterol helps reduce tissue inflammation and protect cells from inflammatory damage⁸.

ANTI CANCER

Effects on apoptosis and cell cycle arrest

Stigmasterol exhibits anticancer activity by inducing apoptosis (programmed cell death) in cancer cells.

It activates apoptotic signaling pathways and increases the activity of enzymes such as Caspase-3 and Caspase-9, which play a key role in the apoptosis process.

Stigmasterol promotes cell cycle arrest, preventing the uncontrolled proliferation of cancer cells.

It can arrest the cancer cell cycle at specific phases such as G0/G1 or G2/M phase, thereby inhibiting tumor cell growth.

Through apoptosis induction and cell cycle arrest, stigmasterol helps suppress tumor progression and cancer cell proliferation⁵.

Cholesterol lowering effects

Competition with cholesterol for micellar solubilization in the gut

Stigmasterol is a plant sterol that structurally resembles cholesterol.

In the intestine, stigmasterol competes with Cholesterol for micellar solubilization, which is necessary for absorption.

Due to this competition, the incorporation of cholesterol into micelles is reduced.

As a result, intestinal absorption of cholesterol decreases, leading to lower cholesterol levels in the bloodstream.

This mechanism contributes to the cholesterol-lowering and cardioprotective effects of stigmasterol^{2,6}.

ANTI DIABETIC

Emerging research areas

Stigmasterol has shown potential anti-diabetic activity in recent pharmacological studies.

It helps improve insulin sensitivity and regulate glucose metabolism.

It may protect pancreatic β -cells and support insulin secretion.

It reduces oxidative stress associated with Diabetes mellitus.

Due to these effects, stigmasterol is being investigated as a promising natural compound for diabetes management⁶.

MECHANISM OF ACTION

Stigmasterol produces anti-inflammatory effects by inhibiting COX-2 and 5-LOX enzymes, thereby reducing prostaglandin and leukotriene synthesis.

Inhibits activation of nuclear factor- κ B (NF- κ B).

Result in decreased the production of pro-inflammatory cytokines (TNF- α , IL-1 β , IL-6), iNOS and nitric oxide.

Suppresses MAPK signaling (ERK, JNK, p38) and reduces cytokine release and inflammatory cell activation.

Additionally its antioxidant and membrane-stabilizing actions limit oxidative stress, lysosomal enzyme release and immune cell activation resulting in reduced inflammation^{3,9,10}.

APPLICATIONS IN INDUSTRY

Pharmaceuticals: As a precursor for the synthesis of progesterone and Vitamin D₃

Stigmasterol is widely used in the pharmaceutical industry as a raw material for the synthesis of steroidal compounds.

It acts as a precursor for the synthesis of important hormones such as Progesterone.

Stigmasterol is also used in the production of Vitamin D₃, which is essential for bone health.

It is used as an intermediate in the manufacture of corticosteroids and other steroid-based drugs.

Due to its biological activities, it is studied in the development of anti-inflammatory and anticancer drugs.

Stigmasterol is also utilized in drug formulation research to develop new therapeutic agents.

It is used in biomedical and pharmaceutical research for studying phytosterol-based drug development.

Because of its natural origin and pharmacological potential, stigmasterol has become an important compound in modern pharmaceutical synthesis.

Food Science: Used as a food additive or in functional "heart-healthy" spreads

Stigmasterol is used as a functional food ingredient because of its health benefits.

It is commonly added to heart-healthy spreads and fortified foods to support cardiovascular health.

Stigmasterol helps reduce the absorption of Cholesterol in the intestine.

It is used in the development of nutraceutical products and dietary supplements.

It is incorporated into functional foods designed to manage cholesterol levels.

Stigmasterol is used in fortified dairy products and margarine to enhance their health benefits.

It contributes to the development of health-promoting food formulations.

Due to its phytosterol nature, it plays an important role in preventing cardiovascular diseases through diet.

It is also studied for use in dietary products aimed at improving lipid metabolism.

Because of its natural origin, stigmasterol is widely explored in modern food science and functional food development.

Table No.1: Mechanism of action

S.No	Biological Effect	Primary Target / Pathway
1	Anti-Osteoarthritis Activity	Inhibits Nuclear Factor- κ B (NF- κ B) signaling pathway, thereby reducing inflammatory mediators involved in cartilage degradation.
2	Anti-Inflammatory Activity	Suppresses Mitogen-Activated Protein Kinase (MAPK) signaling and reduces production of inflammatory mediators such as TNF- α and IL-6.
3	Cholesterol-Lowering Effect	Competes with the Niemann-Pick C1-Like 1 (NPC1L1) transporter, thereby decreasing intestinal cholesterol absorption.
4	Antioxidant Activity	Enhances endogenous antioxidant enzymes including Superoxide Dismutase (SOD) and Catalase, reducing oxidative stress.
5	Anticancer Activity	Induces programmed cell death through activation of caspase-3 and other apoptotic signaling pathways.
6	Anti-Diabetic Activity	Improves insulin sensitivity and regulates glucose metabolism, contributing to the management of diabetes mellitus.
7	Immunomodulatory Effect	Modulates immune responses by regulating cytokine production and inflammatory signaling pathways.
8	Anti-Hyperlipidemic Activity	Reduces lipid accumulation and improves overall lipid metabolism in metabolic disorders.
9	Hepatoprotective Activity	Protects hepatocytes against oxidative stress and inflammatory damage, supporting liver function.
10	Cardioprotective Effect	Promotes cardiovascular health by reducing cholesterol levels and preventing oxidative damage to cardiac tissues.

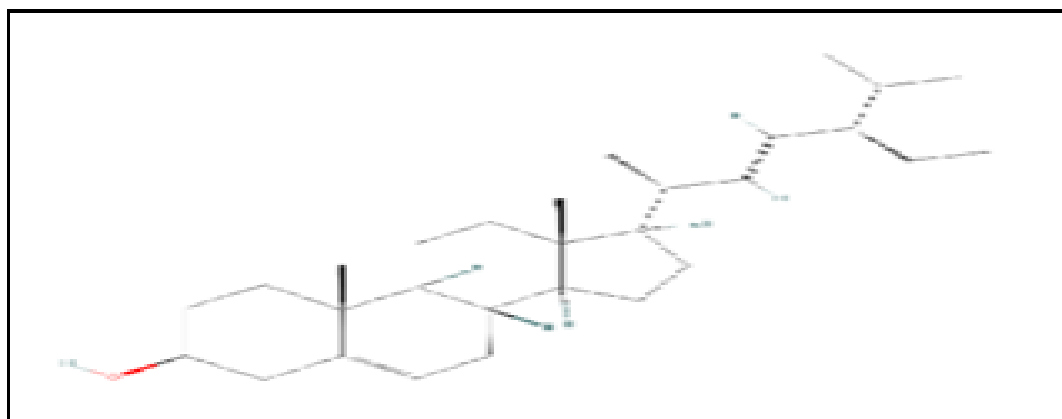


Figure No.1: Physicochemical properties

FUTURE PERSPECTIVES AND CONCLUSION

The growing body of literature highlights the compound's diverse pharmacological potential, ranging from metabolic regulation to anti-inflammatory and antioxidant effects. However, despite promising preclinical outcomes, translational success into clinical settings remains limited. One of the most persistent challenges is its poor bioavailability, as the compound is often rapidly metabolized and exhibits low absorption in the gastrointestinal tract. This discrepancy between experimental efficacy and clinical performance underscores the need for a more critical evaluation of study designs, including differences in dosage, delivery routes, and biological models used across research.

Another key issue lies in the inconsistency of reported outcomes across studies. While some investigations demonstrate significant therapeutic benefits, others report minimal or no effect under similar conditions. These variations may be attributed to factors such as differences in experimental models (*in vitro* vs. *in vivo*), formulation methods, or duration of treatment. A critical comparison of these findings suggests that standardization in methodology is essential for generating reproducible and clinically relevant data. Future studies should prioritize harmonized protocols to enable meaningful cross-study comparisons.

To overcome the limitations associated with bioavailability, emerging strategies such as nano-delivery systems offer a promising avenue. Nanoparticles, liposomes, and polymer-based carriers have shown potential in enhancing solubility, stability and targeted delivery of bioactive compounds. By improving absorption and protecting the compound from rapid degradation, these advanced delivery systems could significantly enhance its therapeutic efficacy. However, further research is needed to evaluate the safety, scalability, and long-term effects of such technologies before they can be widely implemented in clinical practice. In addition to formulation advancements, future research should also explore the compound's mechanisms of action at the molecular level. Integrating omics-based approaches, such as genomics, proteomics, and metabolomics, could provide deeper insights into its biological interactions and identify potential biomarkers for efficacy. Furthermore, well-designed clinical trials involving diverse populations are essential to validate preclinical findings and establish appropriate dosing regimens. Such efforts will be crucial in bridging the gap between laboratory research and real-world therapeutic applications. Finally, while the compound demonstrates significant potential as a therapeutic agent, its clinical translation is hindered by challenges related to bioavailability and inconsistent study outcomes. Addressing these limitations through innovative delivery systems, standardized research

methodologies and comprehensive clinical investigations will be key to unlocking its full potential. Continued interdisciplinary collaboration and a focus on recent, high-quality evidence will ensure that future research remains both relevant and impactful.

ACKNOWLEDGEMENT

The authors wish to express their sincere gratitude to Department of Pharmaceutics, Sri Ramakrishna Institute of Paramedical Sciences, College of Pharmacy, (Dr M.G.R. Medical University), Sarojini Naidu Road, Coimbatore, Tamil Nadu - 641 044, India for providing the necessary facilities to carry out this review work.

CONFLICT OF INTEREST

We declare that we have no conflict of interest.

BIBLIOGRAPHY

1. Harries A D, Kumar A M, Satyanarayana S, Bissell K, Hinderaker S G, Edginton M, *et al.* References for scientific papers: Why not standardise to one global style? *Public Health Action*, 3(3), 2013, 255-257.
2. Mallik S. How to Write and publish your article: Guidelines to the young researchers, *J Compr Health*, 5(1), 2020, 12-23.
3. Bakrim S, Benkhaira N, Bourais I, El Omari N, Sheikh R A, Aboulaghras S, *et al.* Health benefits and pharmacological properties of stigmasterol, *Antioxidants (Basel)*, 11(10), 2022, 1912.
4. Kambhampati S B S, Maini L. Formatting references for scientific manuscripts, *Indian J Orthop*, 53(3), 2019, 381-383.
5. Khopkar U, Madke B. Get set, write, *Indian J Dermatol Venereol Leprol*, 77(3), 2011, 392.
6. International Committee of Medical Journal Editors, Uniform requirements for manuscripts submitted to biomedical journals, *Philadelphia (PA): ICMJE*, 2007.
7. Bhardwaj P, Yadav R K. Harmonising format and style requirements for scientific and medical publications: Time to address a long-pending dream, *Sci Ed Publ*, 4(3-4), 2019, 189-196.
8. Trevethan R, Betta M. Academic referencing on university library websites: A call for clear, coherent and correct categorisation, *J Aust Libr Inf Assoc*, 66(1), 2017, 50-67.
9. N'Dri S J B, Adhikari S, Gupta P, Pandey S, Chini S, Gaur R, *et al.* Stigmasterol: An enigmatic plant stress sterol with versatile functions, *Int J Mol Sci*, 25(15), 2024, 8122.
10. Kaur N, Chaudhary J, Jain A, Kishore L. Stigmasterol: A comprehensive review, *Int J Pharm Sci Res*, 2(9), 2011, 2259-2265.
11. Li K, Yuan D, Yan R, Meng L, Zhang Y, Zhu M. Advances in stigmasterol on its anti-tumor effect and mechanism of action, *Front Oncol*, 12, 2022, 1101289.

Please cite this article in press as: Vishwa S *et al.* Stigmasterol: A comprehensive review on its natural sources, biological activities and modern drug delivery strategies, *Asian Journal of Phytomedicine and Clinical Research*, 14(2), 2026, 34-40.