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Table of Contents

Pharmacological effects of *Sesamum indicum*; Systematic review

Running Title: *Sesamum indicum*; Systematic review

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ABSTRACT

Sesamumindicum L. is a wildly used medicine in Ayurveda and traditional medicine in Sri Lanka. This study aims to analyse the most recent research findings about the pharmacological effects of S. indicum. The PubMed, Scopus, and Cochrane library databases were searched extensively and systematically for papers published between January 2011 and May 2022. We considered the PRISMA Statement to provide a good structure for systematic reviews. The keywords used to search for articles included "Sesamumindicum." Other filters were selected as the limit to medicine, open access, full-text articles, journal articles, and written English. All the data were recorded in an excel sheet, and the following number of research articles were found in the various databases; PubMed (n=03), Cochrane library (n=39), and Scopus (n=75). After removing duplicates, there were 114 articles. Those articles were further screened, firstly by reading topics and abstracts and secondly by reading the full text, and which did not match the inclusions were removed. After removing those articles, there were 27 articles, and after adding 03 additional articles, 30 articles were included in the systematic review. Finally, 08 clinical trials, 11 in-vivo, and 15 in-vitro research were analysed. According to those studies, its anti-cancer activity, antioxidant activity, antibacterial activity, antiatherosclerosis activity, anti-inflammatory activity, analgesic activity, anti-allergic activity, menstrual bleeding-inducing effect, skin whitening effect, neuroprotective activity, etc., have been proven scientifically. Limitations such as limited clinical research, not claiming all pharmacological actions, and not testing some medicinally used parts were identified.

Keywords: Pharmacological effect, Sesamumindicum, Systematic review

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INTRODUCTION

Sesamum indicum L. (*S. indicum*) is usually known as sesame in English, "*Tila*" in Sanskrit, and "*Thala*" in Sinhala. It is one of the world's oldest oilseed crops. It is used for nutritional, medical, and industrial applications worldwide. *S. indicum* is a wildly used medicine in Ayurveda and traditional medicine in Sri Lanka. Stem, Leaves, Seeds, and Oil have medicinal values.

This study aims to analyze the most recent research findings about the pharmacological effects of *S. indicum*.

METHODOLOGY

A systematic review of published full research papers reporting the pharmacological effects of *Sesamum indicum* was designed based on the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyzes) statement guidelines (Tricco *et al.*, 2018). Eligibility criteria are based on the PICO (Population, Intervention, Comparison, Outcomes) approach, study design, Language, and date.

Types of Studies

In vitro, in vivo, and clinically proven pharmacological effects were explored in this systematic study.

Inclusion Criteria

All the published full research papers from 2011 to May 2022, written in English, studied the pharmacological effects of *S. Indicum* were included.

Exclusion Criteria

Other than English, research articles were written in various other languages; Research papers published before 2011, abstract-only papers, journals with no full text available, case reports, case series, systematic review studies, and literature reviews were all eliminated.

Types of Outcomes

The primary outcome was the pharmacological effect, and the secondary outcome was the safety or adverse effects of *S. indicum*

Search Strategy

A comprehensive search of previously published research articles was conducted in PubMed, Scopus, and Cochrane library databases for studies published between January 2011 and May 2022. The keywords used to search for articles included "*Sesamum indicum*." Other filters were selected as the limit to medicine, open access, Full-text articles, journal articles, and written English.

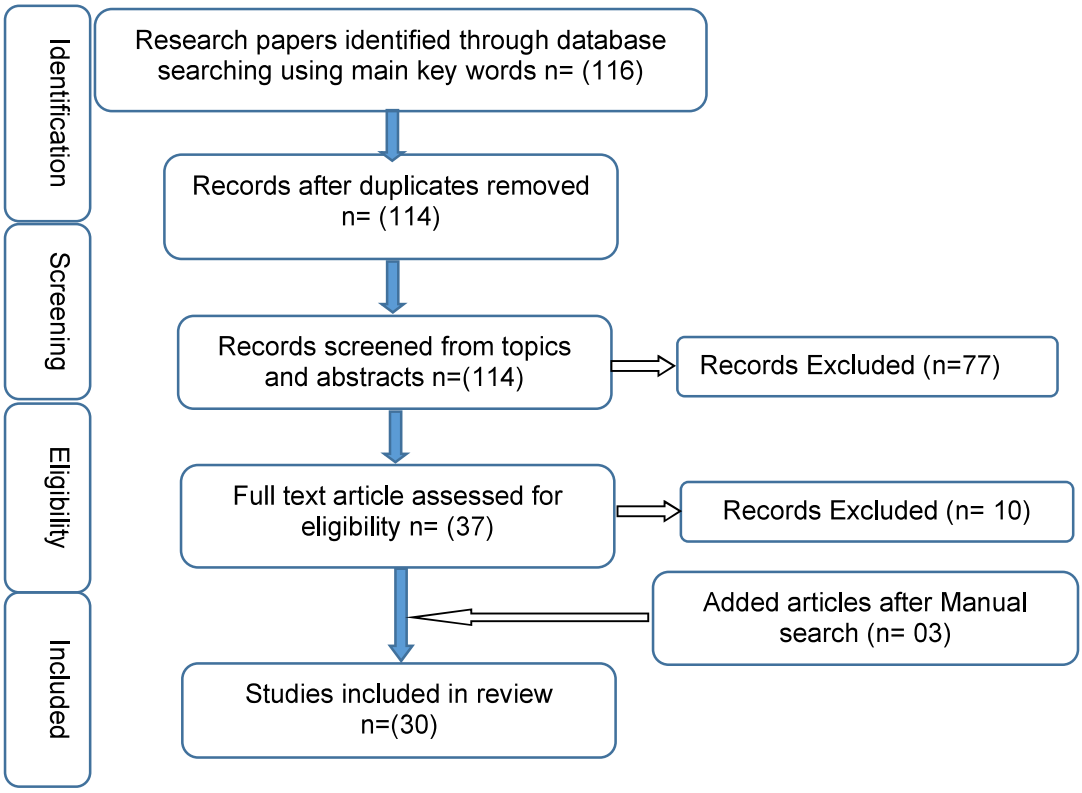

Figure 1: Search strategy

Evaluation of Article Quality

Two authors independently assessed the quality and acceptance of the articles and discrepancies were discussed until an agreement was reached.

Data Extraction

Information related to the study was collected, including the pharmacological activity, type of extract/used part, test method, laboratory organism/animal used, and Reference.

RESULTS AND DISCUSSION

Using the above-mentioned search parameters, the following number of research articles were found in the various databases; PubMed (n=03), and Cochrane library (n=39) and Scopus (n=75). After removing duplicates there were 114articles and those articles were further screened firstly by reading topics and abstracts and secondly reading full text and which did not match with the inclusions were removed. After removing those articles there were 27 articles and after adding 03 additional articles finally 30 articles were included in systematic review. Figure 1 summarizes the search approach. Finally, 08 clinical trials (Table 01), 11 in vivo studies (Table 02), and 15 in vitro research (Table 03) were analyzed (Some researchers conducted more than one study).

Table 1: Clinical Studies

	Pharmacological Activity	Used Part	Test Method	Reference
01	Analgesic effect	sesame oil	Randomized clinical trial	(Shamloo *et al.,* 2015)
02	Reduce muscle damage and oxidative stress	White Sesame seeds paste	Experimental, randomized, and placebo controlled. study	(Barbosa *et al*., 2017)
03	Inducing menstrual bleeding and maintaining regular menstruation	Powdered sesame	A single-blind randomized controlled clinical trial	(Yavari *et al.,* 2016)
04	Removal of retained. products of conception and the reduction of the severity of pain and vaginal bleeding	Sesame grinding powder	An open label randomized controlled clinical trial	(Aghababaei *etal*., 2021)
05	Analgesic effect	Sesame oil	A randomized controlled trial	(Shamloo *et al.,* 2019)
06	Effects on knee osteoarthritis	Sesame seeds powder	A randomized clinical trial	(Sadat *et al.,* 2013)
07	Effect on Lipid disorders	Paste of sesame seeds	A randomized clinical trial	(Mirmiran *et al.,* 2013)
08	Induce menstrual bleeding	Powdered sesame	Pilot study	(Yavari *et al.,* 2014)

Table 2. In-vivo Basic Experimental Studies

	Pharmacological Activity	Type of extract/ Used part	Laboratory Organism/ Animal Used	Reference
01	Anti-rheumatoid activity	Ethanolic extract of seeds	Wistar albino rats	(Ruckmani *et al.*, 2018)
02	Anti-Atherosclerotic action	Sesame oil	female LDLR - / - mice	(Narasimhulu *et al.,* 2015)
03	Anti-Inflammatory action	Sesame oil	female LDLR - / - mice	(Narasimhulu *et al.,* 2015)
04	Anti-Inflammatory and Antioxidant Activities	Sesame oil aqueous extract	Swiss Webster mice	(Selvarajan *et al.,* 2015)
05	Diminishes bone mass and bone formation	Methanol extracts of sesame seeds	Ovariectomized Female Wistar rats	(Tachibana *etal.,* 2020)
06	Diabetes-induced cardiac dysfunction	Sesamin dissolved in olive oil	STZ-induced type I diabetes rat model	(Thuy *et al.,* 2016)
07	Anti-cancer effect	Sesamol (one of the lignans in sesame seeds	6 weeks old male min mice, Apc mutant mice	(Shimizu *et al.,* 2015)
08	Reduced dementia	Sesamin and sesamolin (lignans in *S.indicum*)	Five-week-old male Slc:ddy mice	(Matsumura *et al.,* 2016)
09	Protects the femoral head from Osteonecrosis	Sesamin, isolated from *S.*	male Sprague-Dawley	(Deng *et al.,*2018)

		*indicum*seeds	rats	
10	Increased vitamin K concentrations	Sesamin extracted from white sesame seeds	male Wistar rats	(Hanzawa *etal.,* 2013)
11	Induced growth and development of mammary gland tissue	Pellets with sesame seeds	female Albino rats	(Al-Bazii *et al.,* 2019)

Table 3. In-Vitro Studies

	Pharmacological Activity	**Type of extract**	**Test method/ Laboratory Organism**	**Reference**
01	Anti-helicobacter pylori Activity	Ethanol extract of Leafe	*Helicobactor pylori*	(Masadeh *et al.,* 2014)
02	Anti-bacterial effect	Hexane, Ethyl acetate, and Ethanol extracts of seeds	*Staphylococcus aureus, Enterococcus faecalis, Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae, and Acinetobacter baumannii*	(Hossan *et al.,*2018)
03	Anti-Cancer effect	Dichloromethane extract of leaves	Human myeloid leukemia, human hepatocellular carcinoma, human lung carcinoma, human breast adenocarcinoma, and human Colon cancer cell lines	(Iweala *et al.,* 2015)
04	Free radical scavenging activity	Ethanolic extract of *S. indicum*leaves	DPPH free radical scavenging activity	(Iweala *et al.,* 2015)
05	Anti-Inflammatory and	Sesame oil aqueous	RAW 264.7 cell s and	(Selvarajan *et al.,*

	Antioxidant Activities	extract	human umbilical vein endothelial cells (HUVECS)	2015)
06	Pancreatic lipase inhibition and reducing total body fat	*S. indicum* extract (70%)	Pancreatic lipase (Pancreatic lipase assay)	(Badmaev *et al.,* 2015)
07	Anti-cancer activity (Colon cancer)	Sesamol (one of the lignans in sesame seeds	Human colon cancer cells	(Shimizu *et al.,* 2015)
08	Impacts on T and B lymphocyte activities	sesame seeds oil and sesamol	spleen cells of 8-10 weeks old female or male Balb/c mice	(Khorrami,Daneshmandi & Mosayebi, 2018)
09	Antioxidant and hypoglycemic activities	Ethanolic and aqueous extracts of *S. indicum* seeds	DPPH radical scavenging assay and Glycogen phosphorylase enzyme assays	(Hilmi *et al.,* 2014)
10	Antioxidant and antiproliferative activities	Six sesame seed varieties (Three black and three white)	Oxygen Radical Absorbance Capacity (ORAC) and antiproliferative activity (EC50) against HepG2 Cells	(Zhou *et al*., 2016)
11	Antioxidant and Anti-Colon Cancer Activities	Ethanol extract of *S. indicum*leaf	DPPH assay, FRAP and cell viability assay. Human colon cancer cell lines	(Kim *et al.,* 2021)
12	Pro osteoblastic and anti-osteoclastic	Methanolic extract of *S. indicum*	Osteoblastic MC3T3-E1 cells (mouse calvarial	(Suzuki *et al.,*2018)

	activity		origin)	
13	Alleviate neurodegeneration	Sesamin, isolated from *S. indicum* seeds	Rat pheochromocytoma (PC12) cells	(Udomruk *et al.,* 2020)
14	Anti-melanogenesis activity	Sesamol, an active lignan isolated from *S. indicum*	The melan-a melanocyte line	(Baek and Lee, 2015)
15	Anti-allergic activities	Fermented Sesame	The human keratinocyte HaCaT cell line	(Jung et al., 2018)

Since ancient times, the S. indicum has been crucial in helping treat many disease problems in humans. According to the research studies, its anti-cancer, antioxidant, antibacterial, anti-atherosclerosis, anti-inflammatory, analgesic, anti-allergic, menstrual bleeding inducing, skin whitening, neuroprotective, etc. activities were all scientifically demonstrated. Bioactive compounds, especially lignans (Samin, Sesamin, Sesamolin, Sesamol, Saminol, Sesaminol, Sesamolactol, Sesamolinol, etc.) are responsible for pharmacological activities. Three types, black, white, and red, are used in conventional medicine and Ayurvedic medicine to treat various medical conditions, including gynecological disorders, rectal disorders, and urinary tract disorders. Further, several plant organs, especially seeds, seed oil, flowers, stem, and the entire plant, are utilized to make various medicinal preparations, including decoctions, powders, oils, alkalizes/Kshara, etc. (Anonymous, 1994). According to this study different plant organs, Seeds, leaves, seed extracts and oil were tested. Most clinical trials frequently used seed paste or powder, and roots had yet to be evaluated. Six types of sesame seeds were evaluated by Zhou et al., who concluded that the black variety outperformed the other five varieties as an antioxidant supplement. Likewise, Ayurveda claims that black seeds have more therapeutic benefits (Anonymous, 1994).

CONCLUSION

Sesamum indicum's pharmacological properties are primarily highlighted in this review and many pharmacological effects of Sesamum indicum were scientifically proven by in vitro and in vivo studies. More clinical research must be done to fully understand its therapeutic potential and need to conduct scientific safety assessments further. Especially many gynecological disorders, Urinary and rectal diseases are treated with S. indicum, particularly in traditional and Ayurvedic medicine; nevertheless, there are very few clinical studies on such illnesses or ailments. Sesamum indicum was also used to treat diseases in Ayurveda and traditional medicine as a raw drug and in various pharmacological preparations. Thus, studies using those pharmacological formulations are also needed to prove their therapeutic value. Hence, limitations were identified in those studies, such as limited clinical research, not claiming all pharmacological actions, and not testing some medicinally used parts.

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   - SI units should be used.
   - A single space should be left between the numerical value and the unit.
8. Acronyms and Abbreviations
   - All acronyms should be written in full at the first time of appearance. Abbreviations can be used subsequently.

- The full stop should not be included in abbreviations. Where abbreviations are likely to cause ambiguity or may not be readily understood by readers, the units should be mentioned in full.

9. On being informed of the acceptance, the manuscripts should be revised as per the reviewers' suggestions and re-submitted to the Editor – SLAAS. The accepted manuscripts will be published in the inaugural Journal of the SLAAS. Manuscripts that do not confirm to the above guidelines will not be accepted.
10. Acknowledgements Only the essential individuals and/or organizations/institutes should be include
11. Need to attach the manuscripts both as 1. with names and affiliations of the author and 2. Without with names and affiliations of the author

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