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Review Article on Biological Activities and Chemical Constituents of Genus *Senna*

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ABSTRACT

Senna is a Fabaceae family with approximately 250-300 approved species dispersed throughout tropical and subtropical areas. Senna spp. have a common use in Africa, Asia, Europe, and Latin America for their laxative, anti-bacterial and anti-inflammatory activities, which have been used in folk medicine to cure diabetes, microbiological diseases, and malaria. This review was developed by doing a thorough search of present publications. Most important active constituents in the genus include anthraquinones, steroids, alkaloids, tannins, flavonoids, glycosides, terpenoids, saponins, and essential oils. Senna extracts and metabolites exhibit a variety of pharmacological activities, including anti-diabetic, anti-microbial, antioxidant, wound healing, anti-lipogenic and anti-inflammatory activities. This review surveys some recent breakthroughs in phytochemical and pharmacological research investigations of Senna, offering a valuable resource for future research and medical uses. Senna species have long been applied for therapeutic intents, with potent traditional evidence supporting their activities. Further research should focus on identifying active constituents responsible for pharmacological actions, structural elucidation, and toxicological activities.

KEYWORDS: Senna spp., Leguminosae, Cassia spp., Phytochemistry, Pharmacology.

1. INTRODUCTION

Senna is one of perennial plants in the family Fabaceae. Nearly 250-300 acknowledged species distributed all over the world, with the majority observed in subtropical and tropical areas such as Asia, Africa, Latin America, and Europe. Senna spp. have been widely applied in traditional medicine for many years. Cassia and Senna are closely related genera but there are minor differences as in Cassia, three abaxial stamens of the outer whorl are enlarged and their firm, elastic filaments sigmoidally curved, while all other stamens are much smaller. In Senna, however, the two abaxial stamens of the inner whorl are larger [1]. Senna spp. are widely utilized in India, China, Brazil, Mexico, Africa, Thailand, and Malaysia to cure various illnesses and infections, including diabetes, STDs, measles, malaria, inflammation, abdominal pain, typhoid, and gonorrhea [2]. Senna spp. have been studied for their many bioactive constituents and biological and pharmacological properties, including bark, root, leaf, stem, fruit, and seed over the past decade. Senna spp. are annual or biennial shrubs with a particular odour. Senna spp. typically thrives in sunny, grassy, coastal, waste, and water-logged regions [3]. Most Senna spp. are tightly related based on morphological data, which shows differences in size and leaf alignment (or arrangement) [4,5]. The pharmacologically bioactive constituents of many Senna spp. have been studied lately. Additionally, researches have shown that Senna plants produce more than 120 structurally varied phytoconstituents including anthrones, terpenoids, glycosides, tannins, saponins, steroids, flavonoids, anthraquinones, and polyphenols [3]. The genus Senna's crude extracts, fractions, or isolated constituents have been shown in recent pharmacological researches to exhibit anti-malarial, anti-diabetic, anti-bacterial, antioxidant, anti-inflammatory, analgesic, anti-tumor, antinociceptive, and anti-cancer properties [6]. Significant advancements have been made thus far thanks to thorough phytochemical analysis of Senna, which have revealed phytoconstituents with intriguing pharmacological properties. However, there is not nearly enough phytochemical research to support the use of the species as medical bioresources. Therefore, to explore the medicinal potential of the genus Senna, highlight knowledge gaps, and evaluate future research opportunities that may yield the discovery of novel pharmacophore, this review is geared toward a thorough connection among the phytochemistry, traditional uses and pharmacology of Senna.

2. MATERIAL AND METHODS

This review carried out a thorough examination of accessible literature utilizing leading scientific databases like Scopus, PubMed, SciFinder, Science Direct, and Google Scholar. Pertinent informations were gathered from books on ethnopharmacology and taxonomy. These informations were obtained from the Plant List (http://www.theplantlist.org), Tropicos (http://www.tropicos.org) and floras books. Senna, pharmacology, uses of Senna, toxicological assessments and phytochemistry of the Senna are among the keywords selected to gather the published articles. Following the compilation of published articles, the findings underwent analysis and were categorized based on the review's or section's theme. A total of 22 published articles were collected and the library of publications that were downloaded had articles that were published from 1996 till 2021**.**

3. RESULTS AND DISCUSSION

3.1. Chemical Constituents Reported from *Senna*

Extensive phytoconstituents analysis of certain *Senna spp*. have made a noteworthy involvement to the identification of a wide range of bioactive constituents with distinct structural characteristics (Table 1). Anthraquinones, terpenoids and essential oils are among phytoconstituents that were extracted from several Senna spp [7]. Some of these phytochemicals shown significant in vivo and in vitro activities.

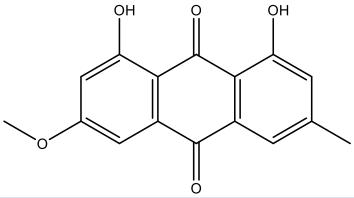
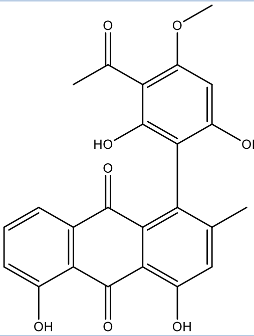
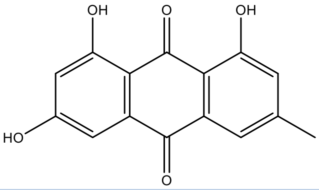
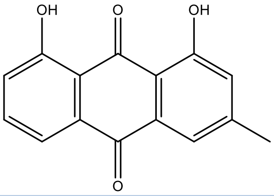
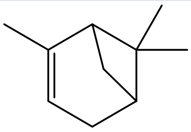
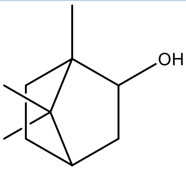
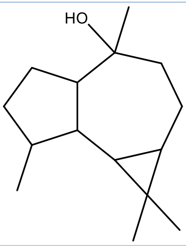
3.1.1. Anthraquinones

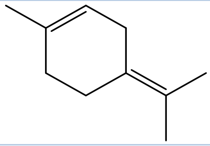
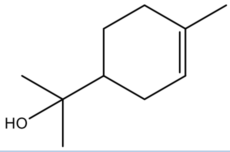
One of the main phytochemicals in *Senna* genus is anthraquinone. The hydroxyl-anthraquinone is the most often used scaffold. Physcion, knipholone, emodin, and chrysophanol were determined to be the known metabolites through a comparison of spectroscopic data with existing literature [5,8].

3.1.2. Terpenoids

Terpenoids are one of the major phytoconstituents of the *Senna* genus. the triterpenoids and sesquiterpenoids (Table 1). α-pinene, borneol, globulol, terpinolene, and terpineol are a few of the terpenoids that have been isolated from the genus *Senna* [9].

Table 5: Examples of some compounds isolated from *Senna*

Compound	Structure	Plant species	Plant part	References
Physcion		*S. didymobotrya*	Pod	[8]
knipholone		*S. didymobotrya*	Pod	[8]
Emodin		*S. didymobotrya*	Pod	[8]
Chrysophanol		*S. didymobotrya*	Pod	[8]
***α*-pinene**		*S. occidentalis*	Whole plant	[9]
Borneol		*S. occidentalis*	Whole plant	[9]
Globulol		*S. occidentalis*	Whole plant	[9]

Terpinolene		*S. occidentalis*	Whole plant	[9]
Terpineol		*S. occidentalis*	Whole plant	[9]

3.1.3. Volatile Oils

Most *Senna spp.* are grown for their volatile oils, and when milled, most of them have a disagreeable smell. Examples of volatile oils according to quantitative and qualitative investigations are *β*-caryophyllene, cyperene, *α*-terpineol, limonene, caryophyllene oxide, hexadecanoic acid, 2,5-dimethoxy-*p*-cymene, pentadecanal, borneol, linalool, and pentadecanal were found in *Senna spp*. [10-12].

3.2. Medical Effects Reported from *Senna*

It has been observed that crude extracts, fractions, and isolated constituents have a broad spectrum of medicinal effects (Fig.1).

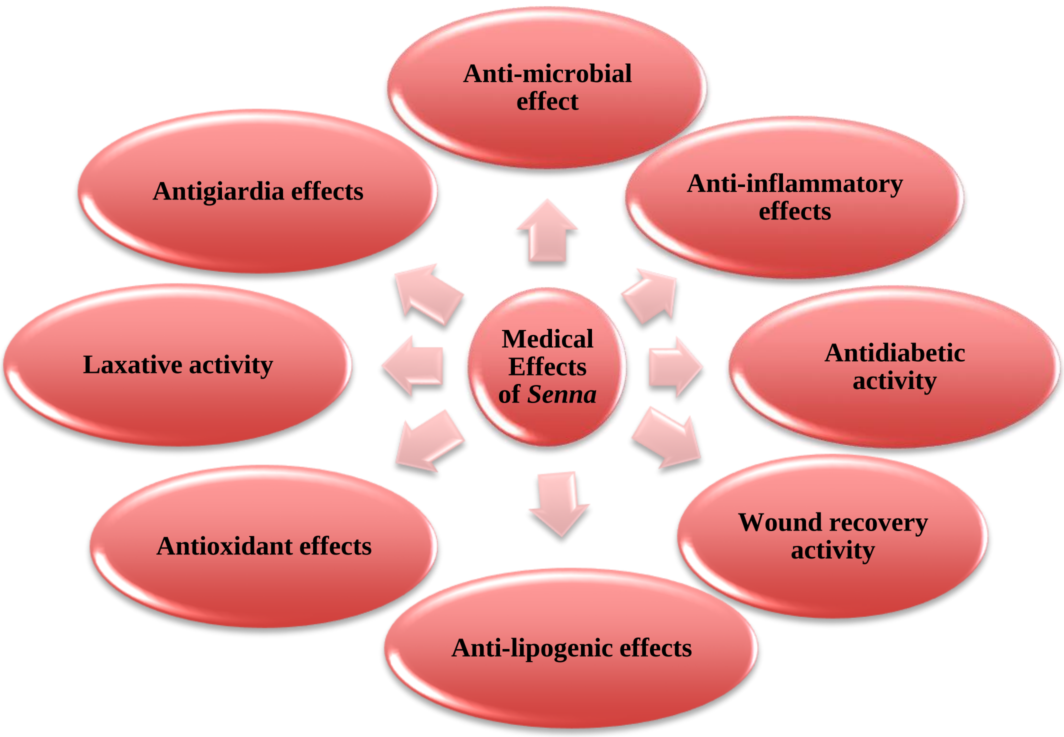


Fig. 53: Summary of medical effects of *Senna*

3.2.1. Anti-Microbial Effect

The genus *Senna's* antibacterial effects are thought to be its most researched medicinal use. The actions detailed in this section will be determined by the minimum bactericidal concentration (MBC) or minimum inhibitory concentration (MIC), which measures its value to human health. When tested using the agar overlay method, piceatannol, a stilbenoid found in *Senna skinneri* roots, demonstrated significant resistance against *Salmonella typhimurium* and *Escherichia coli* [13]. Essential growth inhibition was spotted for bacterial and fungal isolates with MICs of 5.0 mg/mL for *Candida albicans* and 2.5 mg/mL for 2.5 mg/mL for *Staphylococcus aureus* and *B. subtilis* and *Staphylococcus aureus,* due to the piperidine alkaloid (-)-cassine present in the leaves of *S. racemose* [14].

3.2.2. Anti-inflammatory Effects

Inflammation is body's physiological response to injury or disturbance. As to Allkin's research, the majority of the Leguminosae family, particularly the *Senna spp*., have been traditionally utilized in folk medicine as an anti-inflammatory [15]. The ethanolic extract of the aerial component of *S. septemtrionalis* was evaluated in vitro utilizing LPS-stimulated macrophages in the Carrageenan-induced paw and TPA-induced ear oedema test. Furthermore, nitric oxide (NO), ELISA kits, cytokines (IL-6, IL-1β, and TNF-α) and hydrogen peroxide (H_2O_2) were investigated. Considerable inhibitory activity was shown by the extract at concentrations of 154.7 mg/mL (H_2O_2), > 200 mg/mL (IL-1β, TNF-α, and NO), and 163.3 mg/mL (IL-6). In the TPA and carrageenan tests, the extract demonstrated strong inhibitory effect (in vivo) (ED_{50} = 137.8 mg/ kg) [16]. Through prevention of the upregulation of cyclooxigenase-2, phosphorylation of MAPK/ERK, and transcription factor NF-kB, the anti-inflammatory effect (-)-cassine isolated from *S. spectabilis* increases the interaction between TRPA1 and TRPV1 receptors.

3.2.3. Antidiabetic Activity

In folk medicine, the genus *Senna* has a long history of usage as a treatment for diabetes mellitus [17]. Male Sprague-Dawley mice that had been given T2D were used to test *S. singueana's* antidiabetic potential (in vivo). The acetone fraction (150 and 300 mg/kg) obtained from the alcoholic extract was administered using two body weights. After 28 days of administration, the fraction dramatically reduced non-fasting blood glucose concentration; however, the treated mice's glucose tolerance, liver glycogen, pancreatic β-cell function and serum insulin concentration were all regulated, with the effects being more remarkable than in the control group [6].

3.2.4. Wound Recovery Activity

Ethanol extract of *C. fistula* leaves in male albino rats wound healing profile was evaluated based on its effects on various healing parameters. For the 4th, 8th, 12th, and 16th days, the extract demonstrated 21 ± 2.24, 42.4 ± 3.05, 83.8 ± 2.86, and 96 ± 1.58% wound closure. On day 4, total bacterial count at the affected area was reduced from 109 to 104 CFU/g in treated animals compared to 107 in the control group. Protein concentrations in the rats treated increased remarkably from day 4 to day 16. Protein concentrations were 7.27 ± 0.41, 11.63 ± 0.53, 16.01 ± 0.28, and 28.03 ± 0.44 mg/100 mg of infected tissue on the 4th, 8th, 12th, and 16th days, respectively. The extract-treated rats demonstrated efficient tissue regeneration at the wound site, prominent wound closure and a strong correlation between histological examinations and biochemical studies concerning to wound healing, confirming a scientific logic for the use of *C. fistula* in the treatment of infected wounds without the use of synthetic antibiotics [18].

3.2.5. Anti-Lipogenic Effects
There is a paucity of research demonstrating the hypolipidemic and anti-obesity benefits of *Senna*. Sudden weight gain is linked to obesity because of disproportionate body fat accumulation, high-fat diets, and energy imbalances. In mice fed a high-fat diet, the anti-obesity or lipid metabolism management potential of *S. alata* leaves was studied. For three months, a high-calorie meal containing 45 kcal% fat was given. After 7 weeks, the aqueous extract was given for 6 weeks at body weights of 250 and 500 mg/kg/day. Leptin, triglycerides, hepatic triglycerides, serum total cholesterol, serum insulin, and high blood glucose levels all showed significant declines in the treated mice. Furthermore, there was a decrease in lipid buildup in liver tissue. On the other hand, the extract raised PPARz protein expression in liver tissue [19].

3.2.6. Antioxidant Effects
Senna's bioactive metabolites, including flavonoids and phenolic substances, are responsible for its free scavenging properties. The flower extract had a significant antioxidant effect of 0.479 ± 0.001 at 500 mg/L and a scavenging effect against 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical (90.20 ± 0.29%). The extract's activities may be attributed to its high total phenolic content (850.30 ± 13.81 mg/100 g) and flavonoid content (2.79 ± 0.23 mg/100 g) derived from flower extract [20].

3.2.7. Laxative Activity
Senna is commonly used in traditional medicine as a laxative due to its ability to stimulate contractions and improve intestinal motility without hindering stool release. *S. alata's* potential for bowel management was tested in patients with repaired anorectal abnormalities and constipation using Fischer's exact test. The clinical trials and washout duration in infants with complications were examined. The efficacy of *S. alata* extract was evaluated using three parameters: daily bowel movement, clean abdominal Xray and a fecal soiling. The extract considerably reduces the risk of fecal soiling and related wounds from stool discharge. Enhanced intestinal motility led to faster stool ejection [21].

3.2.8. Antigiardia Effects
Senna's antigiardia properties have not been extensively studied. Folk medicine has shown that Senna species can heal both acute and chronic diarrhea. The anti-giardia efficacy of *S. racemosa* stem bark was studied on Giardia intestinalis-induced diarrhea. Mice infected with *G. intestinalis* trophozoites were given a methanolic extract of *S. racemosa* stem bark (0.25-0.15 mg extract/kg body weight). The methanolic extract's bioactive metabolites, chrysophanol and physcion, effectively reduced the development of *G. intestinalis* in neonatal CD-1 mice (ED_{50} =1.14 mg/kg). This supports the folkloric usage of *Senna spp*. in treating diarrhea [22].

4. CONCLUSION

This review demonstrates a thorough evaluation of the genus Senna's phytochemistry, pharmacology, and traditional significance. Numerous studies on the pharmacology of the Senna genus supported the traditional uses that have been documented. Numerous phytoconstituents with considerable therapeutic promise for improving a range of infectious and degenerative disorders were revealed by the studies. Even though the genus Senna has been the subject of much research on phytochemistry, little is known about the chemical diversity within the species. Senna spp. may grow in many different types of environments and climates. The diversity of active constituents that plants produce may be influenced by the species' geographic range and capacity to adapt to different temperatures. In specific cases, the volatile components contribute significantly to the aroma that the species releases when milled. Understanding the diversity of chemicals in the world may help find relevant biomarker substances that may have therapeutic value. Studies have been conducted on the antibacterial, antidiabetic, antioxidant, anti-inflammatory, anti-obesity, and wound healing properties; however, additional research is required to precisely investigate the pharmacological actions using suitable models (in vivo). Therefore, it is important to carefully evaluate isolation and clinical trials as they may result in the identification of novel bioresources and satisfy scientists' biotechnological needs for safe therapeutic medications that could address today's health issues.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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APPENDIX A: LIST OF ABBREVIATIONS

STDs	Sexually transmitted diseases
Spp	species or species plural
MIC	Minimum inhibitory concentration
MBC	Minimum bactericidal concentration
B. subtilis	Bacillus subtilis
mg	Milligrams
ml	Milliliter
LPS	Lipopolysaccharide
TPA	Topical anti-inflammatory
ELISA	Enzyme-linked immunosorbent assay
TRPA1	Ion channel located on the plasma membrane of many humans and animal cells.
TRPV1	Nonselective cation channels that are sensitized from noxious stimuli
T2D	Type 2 diabetes millitus
Kg	Killogram
CFU	colony-forming unit
C. fistula	Cassia fistula
Spp.	species