IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

A – Review on Senna Occidentalis L. Root Extract GCMS and LC-MS Metabolite antimicrobial Activity

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Abstract

Senna occidentalis L. is a medicinal plant known for its traditional use in various therapeutic applications. In this study, we aimed to elucidate the metabolite profile of *Senna occidentalis* L. root extract using Gas Chromatography-Mass Spectrometry (GC-MS) and Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS). The phytochemical compositionof the extract was analyzed to identify and characterize the bioactive compounds present. TheGC-MS analysis revealed a diverse array of volatile and non-volatile compounds in the *Sennaoccidentalis* L. root extract, including alkaloids, terpenoids, flavonoids, and other secondary metabolites. LC-MS/MS further provided a comprehensive identification of the polar and non-polar constituents, allowing for a more in-depth understanding of the chemical composition. To explore the potential therapeutic applications of the identified compounds, the antimicrobial activities of the *Senna occidentalis* L. root extract was evaluated against a panel of pathogenicmicroorganisms. The extract exhibited notable antimicrobial effects, demonstrating its efficacy against both Gram-positive and Gram-negative bacteria, as well as fungi. The findings from this study contribute valuable insights into the chemical composition of *Senna occidentalis* L.Roots and highlight its potential as a source of bioactive compounds with antimicrobial properties. Further research is warranted to isolate and characterize specific compounds responsible for the observed activities, paving the way for the development of novel pharmaceuticals or natural products for therapeutic applications.

Keywords: Gas Chromatography-Mass Spectrometry (GC-MS), Liquid Chromatography- Mass Spectrometry (LC-MS/MS), Phytochemical, Antimicrobial properties.

Introduction

A microscopic organism is known as a microorganism or microbe. The term "microbiology" refers to the study of microorganisms. Bacteria, fungi, archaea, and protists are all examples of microorganisms. Prions and viruses are not considered microbes because they are considered non-living in general(Tamang et al., 2016).

Currently, there is a lot of debate over how life is organized and categorized, especially when it comes to the study of microorganisms. The essential division between prokaryotes (cells lacking internal membrane-bound organelles, the Monera, including the majority of microbes) & eukaryotes (cells containing membrane-bound organelles - protists, fungi, plants, & animals) separates living beings into two groups. The two kingdoms of plants and animals were a convenient division of living things before the invention of the microscope. But this division was inadequate what about fungi Today's kingdom taxonomists have established five or six kingdoms (Monera, Protoctista, Fungi, Plantae, & Animalia, with Archaea as the sixth), neither of which include viruses (or prions). Viruses are thought to straddle the living and non-living spectrum. The question of whether or not viruses are live things. Because they don't fulfill all the requirements of the widely recognized definition of life, the majority of virologists consider them to be non-living. For instance, many viruses do not react to environmental changes, which is a defining characteristic of living things. Additionally, viruses can only multiply by invading a host cell. As a result, they are unable to reproduce on their own. A recently identified infectious agent is called prion. They are proteins that can change properly folded proteins into abnormally folded ones because of their abnormal folding (folding is a feature of proteins that allows them to take a shape that is crucial for their function). The development of genetic analysis has both made the issue simpler and more complicated. Dr. Carl Woeser discovered using DNA sequence analysis in the 1970s to suggest the split of life into three domains: bacteria, archaea, & eukaryota. The tree of life he derived from the sequence data reveals the reasons behind this divide. This tree of life demonstrates unequivocally that microorganisms make up the vast bulk of life on earth. 99% of the microbes on earth, according to scientists, have not yet been named (Mishra et al., 2021).

Types of microorganism

- **Bacteria**: - You probably hear the most about the category of microorganisms presentlyknown as "eubacteria" or "true bacteria" to distinguish them from archaebacteria. Theyare the kind most likely to make you ill, which is why. The majority of skin infectionsare brought on by bacteria, which are also responsible for many other illnesses like foodpoisoning, pneumonia, and strep throat. But bacteria can also be incredibly beneficial to people. Our digestive tracts' "good bacteria" aid in the digestion of our food and in the defense against potentially harmful pathogens (Kirillova et al., 2019).

Fig.1 Bacteria

- **Archaea: -** It was originally believed that archaea, also known as archaebacteria, belonged to the bacterial family. Recent studies have revealed that they differ significantly from eubacteria & could be even more closely connected to humans as they are to SS bacteria. In a number of the same areas that bacteria are found, includingwater, soil, and our stomachs, where they support our health, archaea are also present. The fact that many bacteria survive in extremely hot, cold, acidic, or salty settings means that they can also be discovered in some unexpected locations. They may so easily survive in heated springs and other environments where other species find it difficult to thrive.

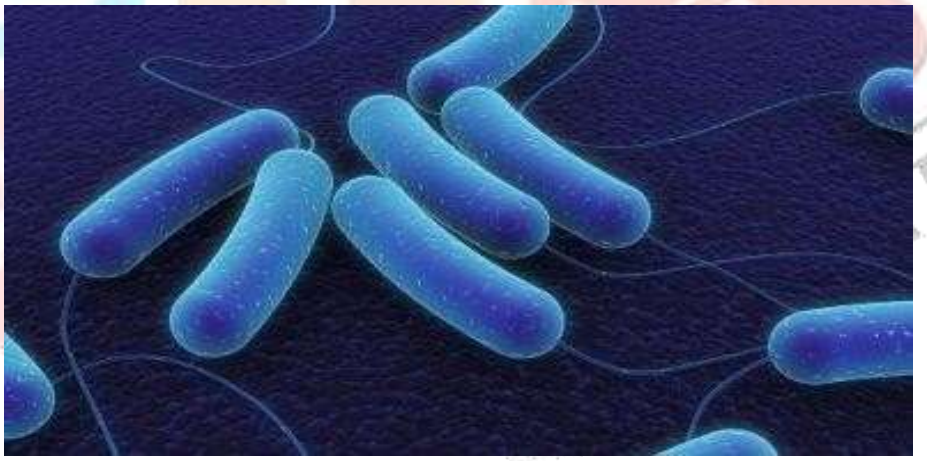

Fig. 2 Archaea

- **Animals: -** Several types of animals come in microscopic varieties, including:

    1. Arthropods (dust mites, spider mites, microscopic crustaceans)
    2. Rotifers (a type of zooplankton)
    3. Loricifera (microscopic animals that live in ocean sediments)
    4. Nematodes

- **Protozoa: -** A varied class of unicellular eukaryotic creatures known as protozoa. Theyare single-celled, like microbes and archaea, but their cells more closely resemble thatof animals & plants than those in bacteria or archaea. African "sleeping sickness," Chagas disease, toxoplasmosis, giardia, malaria, and other serious human illnesses areall brought on by protozoa.

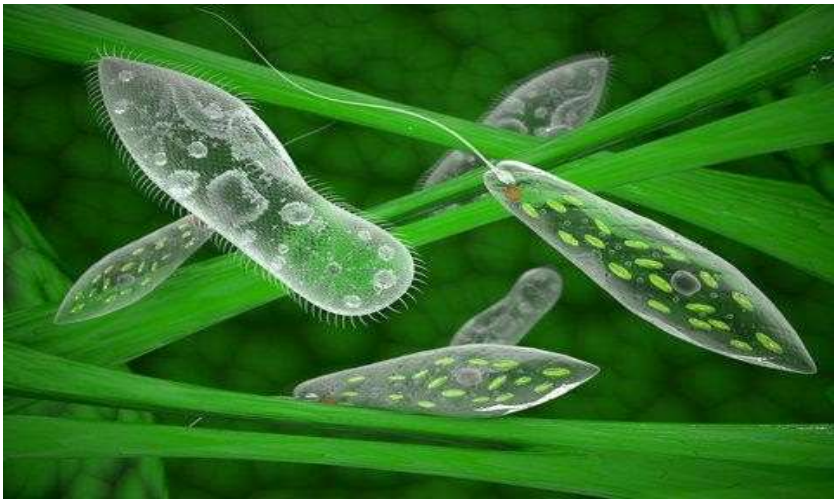

Fig.3 Protozoa

- **Fungi: -** Despite the fact that some tiny fungi can infect people similarly to bacteria or protozoa, yeast is one type of microscopic fungi that most people enjoy eating. The fungus known as yeast is also what gives wine, beer, and other alcoholic beverages theircharacteristic rise. Food sugars are utilized by yeast, which uses them to produce carbondioxide and, yep, ethyl alcohol. If yeasts are bottled given a high concentration if sugar,the alcohol can accumulate to intoxicating levels and the carbon dioxide makes your bread and cakes airy.

Fig. 4 Fungi.

Molds: - Molds is microorganisms that resemble fungi in certain ways but are not actual fungi.Among these are pathogenic molds, which have infected plants and led to catastrophic crop failures like the Great Irish the famine in the 1840s. They also comprise the incredibly bizarreclass of slime molds, which are single-celled organisms with cooperation abilities so astounding that, at one point in their life cycle, a large number of slime mold cells congregateand function like a single organism. Because of the remarkable intercellular cooperation found in slime molds, researchers have begun utilizing them to examine intelligence and problem- solving.

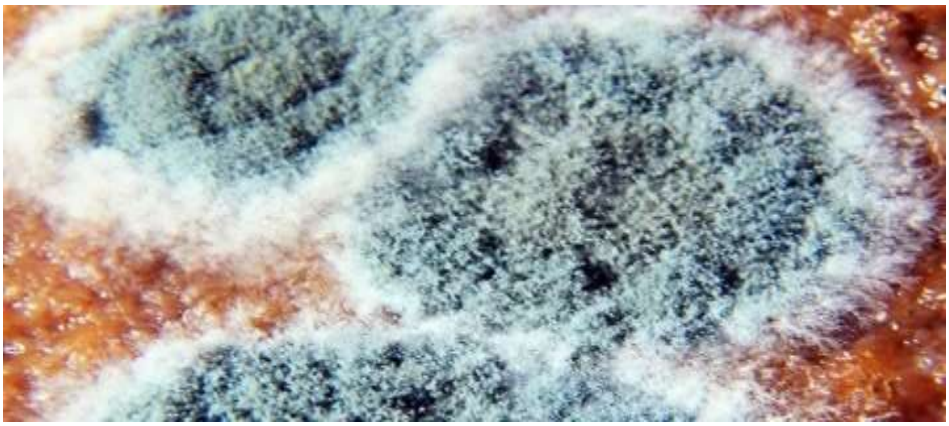

Fig.5 Molds

- **Algae: -** Algae, which are microscopic, were once assumed to be plants, and more recentresearch has disproved this. Instead, it is believed that these single-celled photosynthetic creatures are descended from the group that gave rise to land plants. Algae have been significant photo synthesizers for a very long time. They probably developed before land plants existed, and together their ancestors, the cyanobacteria, they assisted in supplying oxygen to the Earth's atmosphere. Today, algae can both benefit and harm humans. While certain species purify the water and create oxygen, others produce toxic byproducts that can contaminate our food supply and drinking water.

Fig. 6 Algae.

Diseases Caused by Microorganisms

Microbial infections can spread from a number of environmental causes. Therefore, understanding the diseases and how they spread is essential to taking the necessary precautions.The list of diseases brought on by microbes and the method of transmission are provided below.

Table 1 Diseases Caused by Bacteria

Name of Diseases	Causative agent	Mode of transmission	References
Tuberculosis	Mycobacterium Tuberculosis	Air	(Xu 2019)

Typhoid	Salmonella Typhi	Water	(Nitsch-Osuch, Choroszy-Król, and Wardyn 2007)
Pneumonia	HaemophilusInfluenza andStreptococcus pneumoniae	ets of sneeze in theair	(Felma Mosse, Prasetyaningsih,and Adityarini 2021)
Cholera	Vibrio cholera	Food and water	(Zhu et al., 2017)
Anthrax	Bacillus anthrax	Contact with contaminated meat	(Zhu et al., 2017)
Diphtheria	Corynebacterium Diphtheriae	or contact with aninfected agent	(Komives 2022)
Citrus canker	anthomonas axonopodis	Air	(Nasution, Mardina, and Wibowo 2021)
Acne vulgaris	ropionibacterium Acnes	Direct contact with the infected person	(Debelian, Olsen, and Tronstad 1994)
Plague	Yersinia pestis	Air and direct contact	(Luchi, Ioos, and Santini 2020)
Peptic ulcers	Helicobacter pylori	N/A	(Amariucai-Mantu et al. 2022)

Table 2 Disease caused by the virus

Name of Diseases	**Causative agent**	**Mode of transmission**	**References**
Chicken pox	Varicella zoster virus	Air and direct contact	(Wong et al., 2022)
Small pox	riola major andminor	Air, water, and direct contact with an infected agent	(Evallo, Taguiam,and Balendres 2021)

Cold, cough, and flu	Rhinoviruses	iratory droplets inthe air	(CHIPPA and SUVARNA 2021)
AIDS	Human immunodeficiency virus	Exchange of blood, semen, and vaginal and rectal fluids breast milk	Mieres-Castro etal. 2021)
Dengue	Flavivirus	Aedes mosquito(female)	(Quito-Avila et al. 2022)
Ebola	Ebola virus	Infected animal	(Wong et al., 2022)
Chikungunya	Chikungunya virus	Aedes aegypti andAedes Albopictus mosquito	(Wan et al. 2020)
Hepatitis B	Hepatitis B virus	Blood exchange or sexually transmitted	(Tuhumury and Amanupunyo 2018)
Polio or poliomyelitis	Poliovirus	Water, mouth, or body waste	(Yudin et al. 2018)
Zika	Zika virus	Aedes aegypti and Aedes Albopictus mosquito	(Yuki, Fujiogi, and Koutsogiannaki 2020)
Measles	Measles virus	Air	(Li et al. 2021)
Oral and foot diseases	Picornavirus or Genus aphthovirus	Animal and close contact with the infected agent	(Tada and Senpuku 2021)
Covid-19	Coronavirus	Respiratory droplets in the air and direct contact	(Kurubanjerdjit et al. 2021)

Table 3 Disease caused by fungi

Name of diseases	Causative agent	Mode of transmission	references
Rust of wheat	Micro Trichophyton Epidermophytonfungi	Contact with infectedskin	Pérez-Jiménez2008)
Ringworms	Puccinia rust fungus	Air and seeds	(Lima, dos Reis, and de Souza 2015)

Table 4 Disease caused by protozoa

Name of diseases	Causative agent	Mode of transmission	references
Malaria	Plasmodium malaria, Plasmodium vivax and Plasmodium falciparum	pheles mosquito(female)	(Agudelo Higuita etal. 2021)
Dysentery	Leishmania	N/A	
Sleeping sickness	Trypanosoma	Infected tsetse fly	(Derda and Hadaś 2015)
Ladies' finger or yellow vein	Yellow vein mosaic virus	Insect	Morais-Braga et al. 2016)
Amoebic Dysentery and amoebiasis	Entamoeba Histolytica	Impure water and food	(Kihel et al. 2021)
Visceral leishmaniasis or kala-azar	Leishmania genus	sandflies	(De Oliveira and Brodskyn 2012)

Antimicrobials Drugs

One of the significant medical developments of contemporary medicine is the introduction theantimicrobial medicines into routine clinical use. Many novel antimicrobials entered clinical usage in the latter part of the century, giving clinicians a wide range of options when treating various infectious infections. Antimicrobial resistance is a problem that has existed since the advent of antibiotics, although it has only recently gained

in significance. Clinicians are observing a rise in intrinsically resistant organisms such as infections in immune compromisedhosts as well as rising in vitro resistance rates among formerly susceptible species. The availability of treatments for several critical and potentially fatal diseases has been constrainedby the rise of resistance. In order to stop the emergence and spread of antibiotic resistance, require both the discovery and creation of novel agents, as well as the preservation of existingantimicrobials through their proper application. While there is a need for novel agents, some major pharmaceutical companies have made the decision to stop developing antimicrobials, particularly antibacterial drugs. This essay will look at the development of antimicrobial drugsthroughout history, how it has affected the current state of affairs, where we are right now, andsome potential solutions for promoting further antimicrobial growth and development, including the reaction of regulatory organizations like the Food and Drug Administration of theUnited States (FDA) (Cheng et al. 2016).

Table 5 History of Antibacterial Drug Introductions and Approval

Year	Introduced of Drug
1935	Sulfonamides
1941	b-lactams (Penicillin)
1944	Aminoglycosides
1949	Chloramphenicol
1950	Tetracyclines
1952	Macrolides／Lincosamides／Streptogramins
1956	Glycopeptides
1957	Rifamycins
1959	Nitromidiazoles
1962	Kefauver-Harris Amendments
1962	Quinolones
1968	Trimethoprim
2000	Oxazolidinones
2003	Lipopeptides

Before the year 2000, the final novel class of antibiotics was first described. Since then, the bulk of antimicrobials have been developed by chemical alterations of medication classes thathad already been identified. This demonstrates the difficulties involved in finding novel agents.It's also vital to remember that the bulk of antibacterials were developed before to the FD&C Act's 1962 effectiveness requirement. Drug developers continue to add new agents to existingclasses despite the absence of new agent classes. Some of these medications were effective against disorders brought on by germs that were impervious to earlier "generations" of their class. Additionally, when compared to earlier medications, some of the treatments showed better efficacy in treating specific disorders In this case, third-generation cephalosporins are more effective than first-generation cephalosporins in treating conditions such acute bacterial meningitis and those brought on by Gram-negative bacteria. Although they displayed a distinctsafety record or a more practical dosing schedule, other medicines demonstrated comparable efficacy. However, they did provide practitioners a wider variety of treatment options. Other medicines launched at this time offered modest improvements over earlier agents in the class(Biegański et al., 2021).

When one looks at the story of the FDA's clearance of antibacterial medicines, it is clear that numerous new medication classes have not been developed since the 1960s. The FDAauthorized 29 novel antibacterial medications between 1980 and 1989. 24 of those 29 agents were b-lactams, with cephalosporins accounting for nearly two-thirds of them. The FDA accepted 22 new antibacterial medications between 1990 and 1999, with nine of the treatmentsbeing in the quinolone class and eight falling under the b-lactam class. Due to the absenceof new drugs and the approval of a growing number of agents in classifications Thus, it may not be surprised that antibacterial drug development has reached a saturation point. The FDA approved 2.9 new antibacterial medicines annually in the 1960s, 2.2 drugs annually in the 1990s, and 1.6 pharmaceuticals annually as of the year 2000. The number of new drugs filed to the FDA overall has decreased during this time, thus this fall is not specific to antibacterial medications(Kurubanjerdjit et al., 2021).

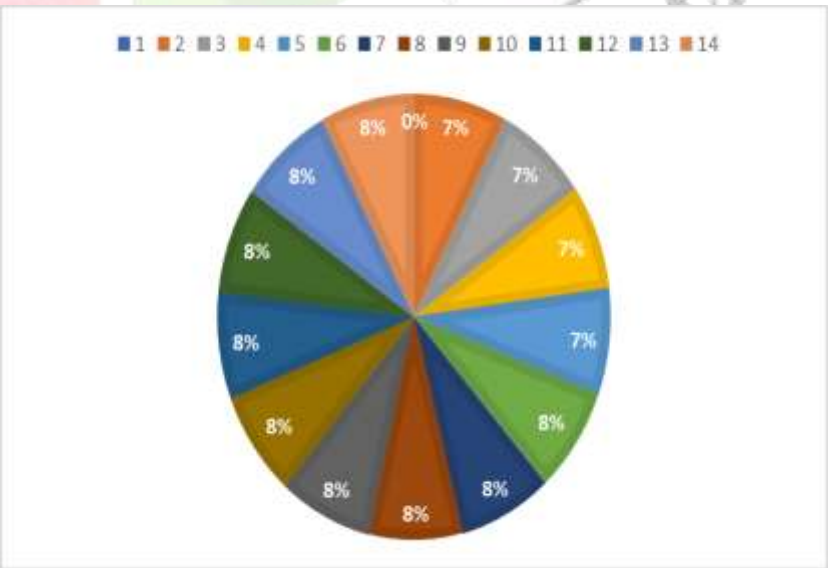

Fig. 7 Drug approvals by class systemic antibacterial. (1980 to 2004*)*

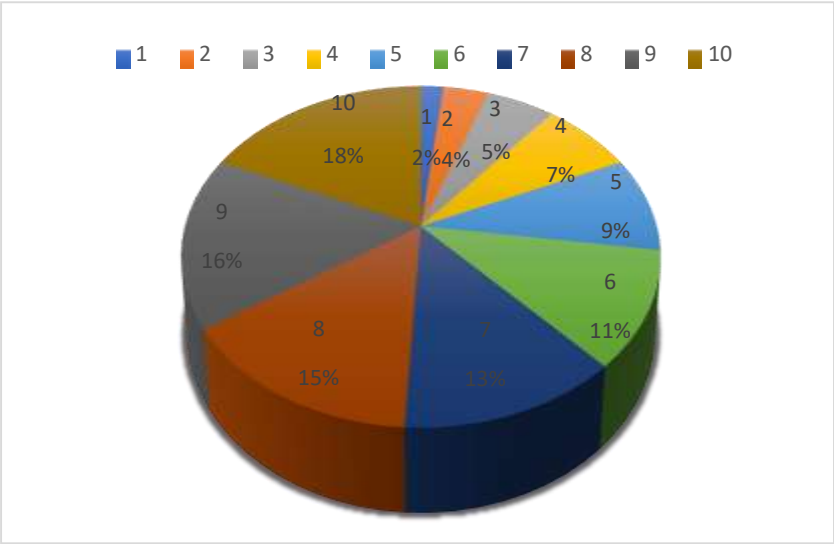

Fig. 8 Drug approvals by class systemic antibacterial. (2005 to2022)

With an increase in funding for biomedical research. This illustrates the inherent difficulties infinding and creating novel medications across all therapeutic classes(Brown & Wright, 2016).

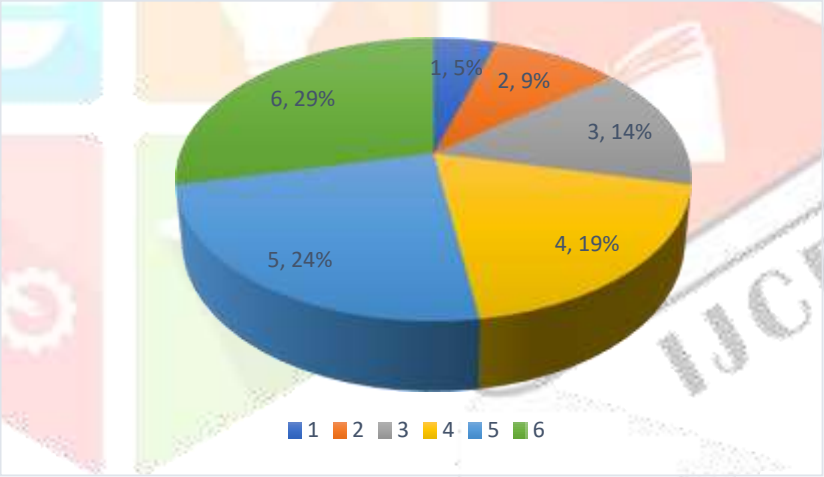

Fig 9 Ten-year trend in drug and biological new molecular entity (NME) (1993 to2003)

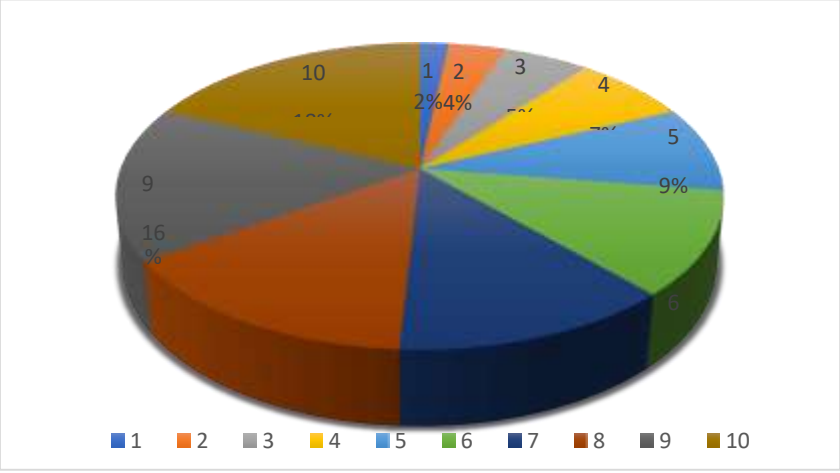

Fig. 10 Ten Year trend by in drug and biological new molecular entity (NME) (2004to2023)

Plant Profile

Senna occidentalis is a thin, erect, herbaceous at sub-woody plant or small shrub, growing to aheight of 0.5-2 m, with yellow flowers & glossy green foliage. The leaves are compound, alternating, and comprise 4-6 pairs of opposing leaflets with a pointy apex and a downy underside and edge.

Botanical Origin	**:**	*Senna occidentalis*
Family	**:**	Fabaceae, Caesalpinioideae

Taxonomy:

Kingdom	**:**	Plantae
Phylum	**:**	Magnoliophyta
Class	**:**	Magnoliopsida
Subclass	**:**	Rosidae
Order	**:**	Fabales
Family	**:**	Fabaceae
Subfamily	**:**	Caesalpinioideae
Tribe	**:**	Cassieae
Genus	**:**	Senna
Subject	**:**	Senna occidentalis (L.) Link

Fig. 11 Seena occidentalis

Pharmacological Activities

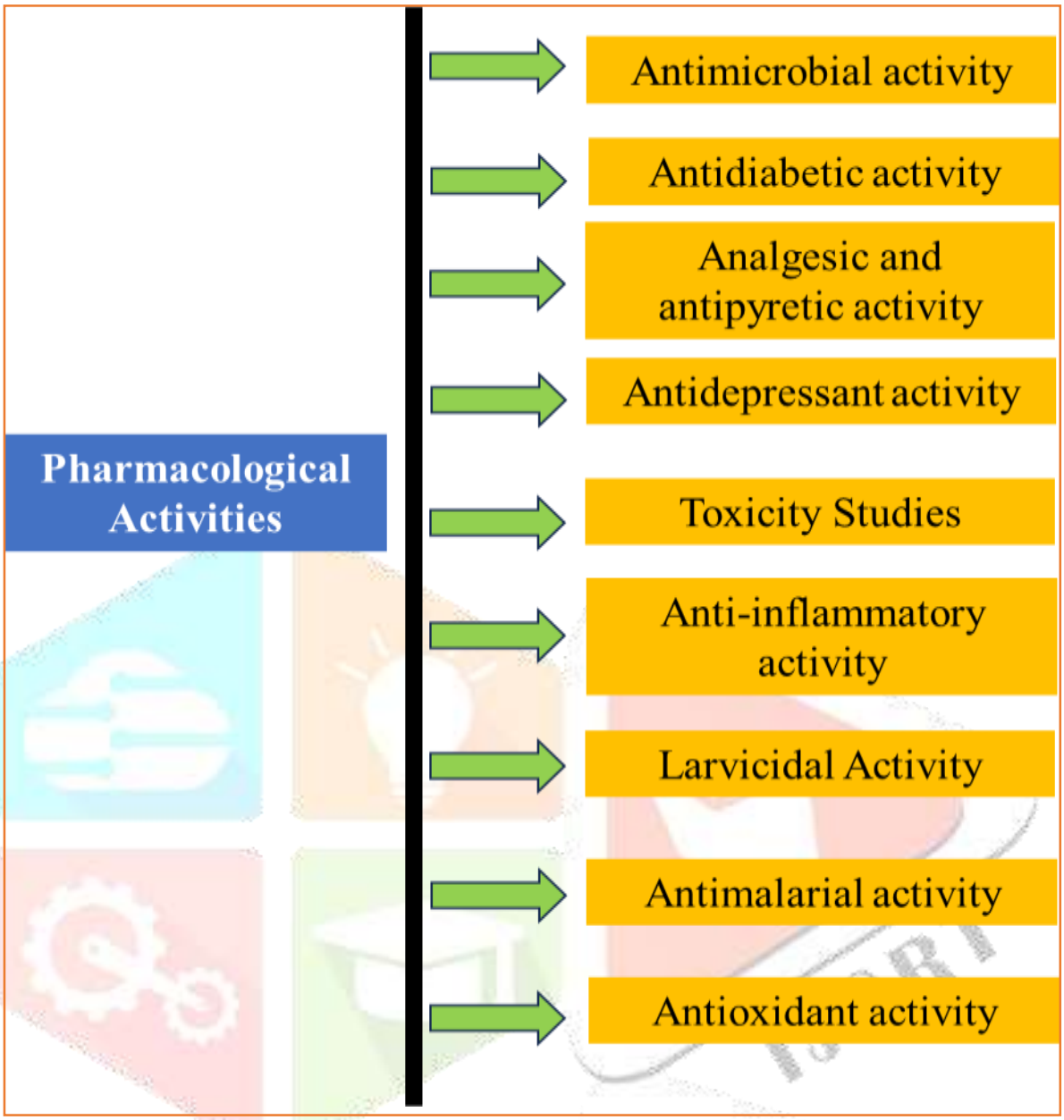

Fig. 12 Pharmacological Activities

Antimicrobial activity

A study was carried out on senna occidentalis antimicrobial properties. The test was conducted with four different extracts such as methanol, aqueous, benzene, petroleum ether, and chloroform extract. Among these methanol extract showed positive against P. aeruginosa, K. pneumonia, P. mirabilis, E. coli, S. aureus, and S. epidermidis; the aqueous extract was effective against P. vulgaris, K. pneumoniae, and P. aeruginosa; benzene and petroleum ether extracts were active against P. mirabilis and E. coli; chloroform extract was found to be very inactive against all tested strains. Another study reported maximum activity against Salmonella typhi and minimum with Shigella spp. This study concluded that the antibacterial activity of senna occidentalis leaves of ethanol and water extract was increased with higher concentrations. A report with Cassia

occidentalis flower extract showed maximum inhibition against Klebsiella pneumonia and no activity against Staphylococcus aureus, Streptococcus pneumoniae, and Pseudomonas aeruginosa. Thus, the flower extract of senna occidentalis can be used to treat Klebsiella-associated ailments such as pneumonia, bronchitis, and other diseases known to be caused by K. pneumonia. A report states that E. coli was sensitive to methanol, hexane, chloroform, and aqueous extract of leaves of senna occidentalis. Similarly, Jain and his coworkers observed that the metabolite-rich fraction of (anthraquinones) leaves, pods, flowers, and callus were effective against E. coli.

Antioxidant activity

The aqueous-ethanolic extract of leaves of senna occidentalis was tested for hepatoprotective activity on liver damage in rats which was induced by paracetamol and ethyl alcohol by monitoring serum transaminase, alkaline phosphatase, serum cholesterol, serum total lipids, and histopathological alterations. They found that the leaf extract had shown significant hepatoprotective activity. Some other observations found that the seed extracts of senna occidentalis limit the DNA degradation caused by iron (II)-driven Fenton reaction. Notably, inhibition of DNA damage may be due to their capability of strong ferrous ion chelation. Further, they proposed that the scavenging activity towards free radicals might be the reason. Senna occidentalis is an ingredient in Himoliv, a polyherbal ayurvedic formulation. It has also proved that it prevents carbon tetrachloride-induced hepatotoxicity in rats. Based on the observation they suggested that Himoliv increases the protective enzymes superoxide dismutase (SOD) and catalase in the liver homogenate of rats.

Antimalarial activity

Senna occidentalis plant extract was proved to have effective antimalarial activity. In a study with ethanolic, dichloromethane, and lyophilized aqueous extracts Senna occidentalis of root bark was tested for antimalarial activity against Plasmodium burgher ANKA. They tested its toxicity by treating the orally and found that there was no toxic effect or mortality in mice with a single dose, of 500 mg/kg of body weight, or the same dose given twice weekly for 4 weeks. The extracts produced significant chemo suppressions of parasitemia with a 200 mg/kg dose when administered orally. Senna occidentalis was found to be potential with 60% chemo suppression. They also found that the ethanolic extract is more active than the lyophilized aqueous extract Senna occidentalis leaf extract with ethanol and chloroform was found to possess better antimalarial activity. When tested with 6 µg/ml concentration more than 60% inhibition was observed against the parasite.

Larvicidal Activity

In a study using Anopheles Stephensi larvae, the larvicidal & pupicidal properties of Senna occidentalis were investigated. Both larva and pupa were observed to respond better to the ethanol extract of Senna occidentalis. It was discovered through the smoke toxicity testing that it's more efficient against Anopheles stephensi. Compared to those who were not exposed, gravid females exposed to smoke oviposited fewer eggs. An increase of the morbidity of C. maculatus eggs is caused by seed oil, according to yet another study. Numerous tests using pure substances led to the conclusion that the culprits are the fatty acids (linoleic, oleic, & stearic). The western Senna occidentalis oils at 10 ml/kg of seed did not affect the oviposition in C. maculatus.

Anti-inflammatory activity

A carrageenan-induced rat paw edema model was used to assess the anti-inflammatory effects of Senna occidentalis leaf powder and the effects of Cardiospermum halicacabum aerial components with ethanol extract. Senna occidentalis was shown to be most active at a dose of 2000 mg/kg, whereas the lowest effective dose of halicacabum was determined to be 500 mg/kg. The effectiveness of these medications was evaluated using a cotton pellet granuloma assay, and it was found that they inhibited the transudative, exudative, & proliferative aspects of chronic inflammation. These medications reduced the amount of lipid peroxide, glutamyl transpeptidase, and phospholipase activities in the exudate of the cotton pellet granuloma. Alkaline phosphatase activity was observed to be higher and the plasma A/G ratio to be lower in rats with normalized cotton pellets granulomatous rats following therapy. A human erythrocyte membrane might be protected from hypotonicity-induced lysis by the use of Senna occidentalis powders and C. halicacabum extract. These medications may likely block phospholipase A2, which reduces the availability of arachidonic acid, which is a precursor to prostaglandin formation, and/or stabilize the lysosomal membrane system, to exercise their anti-inflammatory effects.

Toxicity Studies

Senna occidentalis underwent an acute toxicity test, and it was discovered that neither dangerous symptoms nor death occurred in this plant. Senna occidentalis doesn't alter hematological and biochemical profiles, food and water intake, or body weight growth with sub-acute treatment. Additionally, neither the macroscopical nor microscopic characteristics of the animal organs changed. They draw the conclusion that Senna occidentalis isn't harmful when administered acutely or subacutely. A histopathological study of both the liver or kidney revealed no signs of necrosis, inflammation, or cell death. Thus, at the doses supplied, it has been determined that the plant's leaves are harmless and have no negative effects on the liver or kidney functions. Another investigation examined the effects of oral Senna occidentalis treatment on pregnant Wistar female

rats. They discovered that there were no no statistically significant differences between the control and test groups in the weights of the fetuses, placentae, and ovaries; the number of corpora lutea in the ovaries; or the rates of pre- and post- implantation loss.

Antidepressant activity

Anxiety and depression are common psychiatric disorders that affect about 5% of people worldwide. Years ago, anxiety and depression were treated with herbs and formulas. In a recent investigation, it was examined how the aqueous and ethanolic extracts of Senna occidentalis leaves affected rodents' levels of anxiety and depression. Actophotometer antianxiety activity and raised plus maze model exposure to novel aversion in rats were tested. Less repulsion from fear causes anti-anxiety behavior. The despair swim test and the tail suspension test were used to evaluate the antidepressant activity. Antidepressant action is elicited by decreased immobility period. They come to the conclusion that senna occidentalis leaf extracts in both ethanolic and aqueous form have antidepressant and anti-anxiety properties. Senna occidentalis leaf ethanolic extract shown more notable action as the aqueous extract.

Analgesic and antipyretic activity

Analgesic and antipyretic properties of Senna occidentalis Linn. were studied. Senna occidentalis leaf extracts were examined for their effects on rats and mice using the yeast- induced pyrexia method as well as the hot plate & tail immersion assays. They discovered that senna occidentalis had antinociceptive and antipyretic effects in both its ethanol and water extracts. 300 mg/kg was discovered to be the maximum inhibitory dosage. According to the findings, pyrexia caused by yeast was significantly affected by both the ethanolic and aqueous extracts of Senna occidentalis.

Antidiabetic activity

When the aqueous extract or Senna occidentalis was investigated for antidiabetic efficacy, it was found that both normal or alloxan-induced diabetic rats had significantly lower fasting blood glucose levels. In addition, they tested for additional extracts such petroleum ether as well as chloroform extracts and came to the conclusion that the activities examined were from days 14 and 7, respectively. When compared to diabetes control and normal animals, aqueous extract treated-diabetic animals showed distinct differences in blood lipid profiles (cholesterol as triglyceride), serum protein, and shifts in body weight. According to histopathological investigations, the animals' pancreas displayed regrowth caused earlier necrosed extracts [32].

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