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A REVIEW ON THE EVALUATION AND PHARMACOLOGICAL EFFECTS OF SWERTIA CHIRATA ON VARIOUS ANTIMICROBIAL RESISTANT STRAINS

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ABSTRACT

The global rise in antibiotic resistance has made it necessary to look for alternative treatments because it has compromised the efficacy of conventional antimicrobial therapy. While certain bacteria develop antibiotic resistance spontaneously, antibiotic overuse and the emergence of novel resistant forms through mutation are the main causes of antibiotic resistance in other bacteria. Plants have long been the primary source of medications and complementary therapies for the treatment of illnesses. Valuable secondary metabolites, including flavonoids, terpenoids, quinones, tannins, alkaloids, and polyphenols, are abundant in plants. Plant secondary metabolites are the subject of numerous investigations as a possible source for the development of antibiotics. They can act through a variety of processes and possess the necessary structural qualities. In addition to examining phytochemicals from various classes that have been shown to have antimicrobial activity against resistant bacteria, either on their own or in conjunction with conventional antibiotics, this review examines the antibiotic resistance mechanisms developed by multidrug-resistant bacteria. The current investigation sought to ascertain Swertiachirata's antibacterial efficacy against a number of antibiotic-resistant bacterial pathogens, including *Escherichia coli*, *Pseudomonas aeruginosa,* Bacillus species, and *Staphylococcus aureus*. At a Minimum Inhibitory Concentration (MIC), *Swertiachirata* demonstrated strong antimicrobial efficacy against a range of antimicrobual resistant bacteria. It might therefore be evolved into a superb broad-spectrum antibacterial agent.

To sum up, the results are encouraging and indicate that Swertia chirata may be useful in treating a range of microbial infections.

Keywords:Antimicrobial resistance, *Swertiachirata*, medicinal plant, MIC

1. INTRODUCTION

A significant increase in the frequency of bacterial infections that cause antibiotic-associated multidrug and antimicrobial resistance has occurred in the last few decades. The misuse, abuse, and overuse of antimicrobial medications are the main reasons why bacteria develop resistance genes. A resistance gene may be acquired by the bacterium as a result of horizontal gene transfer or bacterial DNA changes, in addition to these other factors, which could result in antibiotic resistance (WHO, 2018). Antimicrobial resistance is a complex and significant issue that impacts global health. To combat it, a multidisciplinary approach including partners from all health sectors, including the scientific community and public health authorities, is required. Resistant infections are now the third most common cause of mortality worldwide, according to a 2016 WHO report. Current figures show that antimicrobial resistance (AMR) costs the European healthcare system approximately EUR 1.5 billion annually and results in over 25,000 fatalities each year in Europe (European Commission, 2017). AMR has made it more difficult to manage major procedures, such as caesarean sections, cancer chemotherapy, organ transplants, and diabetes (WHO, 2018). According to estimates, drug-resistant diseases would kill 10 million more people annually than cancer by 2050. If appropriate measures are not taken to address this threat, the world economy would suffer a $100 trillion USD loss.

In February 2017, the World Health Organization (WHO) published a list of bacteria that have been connected to human diseases. The list made it clear how urgently new antibiotics are needed to tackle infections that are hard to treat. In healthcare facilities that have been designated as critical for antimicrobial resistance (AMR), the pathogens Acinetobacter baumannii, *Pseudomonas aeruginosa*, carbapenem-resistant Enterobacteriaceae, and Methicillin-resistant *Staphylococcus aureus* (methicillin-resistant) are particularly dangerous. Antimicrobial resistance (AMR) was the subject of a UK parliament debate in July 2014, during which the prime minister announced an extensive examination of AMR in an effort to identify new treatment approaches. It has also been taken into account in the "UK Five Year Antimicrobial Resistance Strategy 2013 to 2018" (Department of Health, 2013). It is essential to find alternative drugs to treat infectious infections.

Especially in the past ten years, more thorough studies on natural remedies have been conducted. It has been shown that plants are an excellent source of natural substances that support human health. Currently, phytochemicals are being continuously used for medicinal purposes in many countries. According to the World Health Organization (WHO), medicinal plants are the best source of a broad variety of drugs. The use of crude extracts of plant components and phytochemicals with proven antibacterial properties may be crucial in medical therapy. Many plants have been used for their antibacterial qualities, which are derived from the secondary metabolites the plants produce. The active components in these products, which include phenolic and tannin compounds present in essential oils, are widely known. Plants generate a wide variety of secondary metabolites, which are used as direct precursors or lead chemicals in the pharmaceutical industry. Plant extracts that target locations other than antibiotics are expected to be useful against drug-resistant bacteria.

As secondary metabolites, bioactive molecules are typically accumulated by all plant cells. However, the concentration of these substances varies depending on the part of the plant, the season, the climate, and the growth stage. The leaf is one of the plant parts that has the highest concentration of these compounds, which is why most people utilize it medicinally. A few of the active components stop the growth of disease-causing microorganisms, either alone or in combination. The most important of these plant bioactive substances include flavonoids, phenolic compounds, tannins, and alkaloids. Comprehending the correlation between phytoconstituents and plant bioactivity is imperative for the synthesis of molecules possessing specific activities intended for the management of diverse ailments, encompassing chronic conditions. Plants must undergo this form of preliminary phytochemical screening to discover and produce novel therapeutic compounds with greater efficacy, considering the significance of the previously described context. Other research groups throughout the world have also reported on these types of investigations. Therefore, the current study investigates the antibacterial activity of medicinal plants, particularly *Swertiachirata*, against gram-negative *Escherichia coli* and gram-positive *Staphylococcus aureus* bacteria.

1.2 Mechanism of Microbial Resistance

Numerous theories have been proposed to explain bacterial resistance to conventional antimicrobial treatments, and around 20,000 resistance genes have been found in bacteria. The 1950s saw the discovery of the first antibiotic resistance involving E. coli, Shigella, and Salmonella species. It took two decades to identify this growing issue, as multiple examples of penicillin, tetracycline, and chloramphenicol were documented in the 1970s. Clinical trials were rarely conducted to evaluate the hypothesized causes of bacterial resistance. It is unclear whether multiple bacteria share a common pathway to generate resistance or if each microbe has its own mechanism.

While certain bacteria may develop antibiotic resistance spontaneously, antibiotic overuse and the emergence of novel resistant strains are the main ways in which bacteria gain antibiotic resistance. Antibacterial resistance can be caused by a variety of mechanisms, such as bacterial efflux pumps that speed up the release of antibiotics, changes in the amount of time it takes for medication to diffuse inside bacteria, structural changes in bacterial porins that reduce permeability to antibiotic influx, hydrolytic enzymes that break down antibacterial agents, and modifications to antibiotic binding sites. Bacteria can develop resistance to antibiotics by combining multiple drugs or by resisting just one. In order to determine potential targets for future effective medicine, it is imperative to comprehend the processes of resistance.

1.3 Botanical description of genus *Swertia*

The Dutch gardener Emanuel Sweert (1552–1612; also written Swert) is honored by the name Swertia. These plants belong to the genus of herbs that are typically annual, biennial, or perennial and range in height from 2.5 cm to 1.5 m. Roots of Swertia species can be fibrous or woody. Stems might be terete, striate, angled, winged, simple, or occasionally branched, scapiform, well-developed, ascending, or erect. Most leaves are sessile, petiolate, or opposite; occasionally, they are rosulate, whorled, or alternating. Every Swertia L. species has a complete leaf edge. The inflorescences of these plants resemble cymes, and they usually form paniculate or simple thyrses. They can sometimes be solitary or raceme-like, although they are rarely absolutely dichotomous. A pair of sessile, opposing, leaf-like bracts serves as the primary support for pedicellate, four- or five-merous blooms. The calyx and corolla rotate, tubes less than 3 mm in diameter and lobed bases. Each corolla lobe has one or two nectaries, which can be naked, coated in scales or flaps, fringed, fimbriate, or glabrous. The number of corolla lobes is equal to the number of stamens that are attached at the base of the sinuses surrounding the corolla lobes and occasionally ringed by long hairs. The ovary has styles that range in duration from brief to long. The fruit is a flattened or oval capsule with a persistent calyx and corolla that split into two valves; the stigma is divided into two halves. Typically, Swertia L. seeds range in size from a few to numerous.

1.4 Effect of Swertiachirata on antimicrobial-resistant micro-organism

The chemistry of natural and synthetic medicinal products is very different, with natural products having a wider range of chemical constituents. Natural products are higher in molecular complexity, scaffold variation, stereochemistry, ring system diversity, and carbohydrate content, and lower in nitrogen, phosphorus, sulfur, and halogen (Schmidt et al., 2008). Natural plant extracts provide a variety of diverse phytochemicals that prevent the development of resistance. Plant extracts can combat diseases through numerous pathways due to the availability of multiple phytochemicals in a single plant.It has been claimed that *Swertiachirata* works well against a variety of infections. *Swertiachirata* contains natural plant extracts and chemicals that, in addition to having several modes of action, can be used in conjunction with conventional antibiotics to boost their antibacterial efficacy. The antibacterial efficacy of the Swertia species that are presently being studied varies depending on the type of bacterial strain. As stated by Srinivasan and colleagues (2001). This activity might indicate that Swertia species either widespread metabolic poisons or contain compounds that function as broad-spectrum antibiotics. Phytochemical analysis has demonstrated the presence of steroids, flavonoids, tannins, and phenols in Swertia species. has demonstrated antimicrobial properties of tannins and flavonoids. The antibacterial activity against certain bacterial strains could be attributed to these phytochemicals. Similar results were obtained from a previous study that looked at various Swertia species. Numerous studies have reported the antibacterial activity of differentSwertia species against various microbial strains, including *Swertiachirata* (Sultana et al., 2007; Ahirwal et al., 2011; Kweera et al., 2011; Ghosh et al., 2012; Roy et al., 2015), S. ciliata (Saeed et al., 1998), S. corymbosa (Ramesh et al., 2002; Kweera et al., 2015), and S. Petiolata (Bader, 2014).

1.5 Evaluation and Pharmacological activity of *Swertiachirata*

Numerous pharmacological studies have been initiated as a result of the diverse ethnobotanical applications of *Swertiachirata*. According to earlier studies, the biological activities of the *Swertiachirata* extracts include antibacterial, antifungal, antiviral, anticancer, anti-inflammatory, and other properties like antidiabetic and antioxidant properties (Verma et al., 2008). The pharmacological characteristics of *Swertiachirata* have been assessed using a wide variety of in vitro and in vivo test systems. Evidence-based laboratory research has demonstrated some intriguing pharmacological effects of *Swertiachirata* extracts in aqueous, alcoholic, and methanolic forms. For its antibacterial and antifungal properties, the entire *Swertiachirata* plant has been observed to be utilized. The anti-hepatitis B viral activity of *Swertiachirata* extracts was studied using HepG cell lines.

The entire *Swertiachirata* plant has been reported to possess hypoglycemic and anti-inflammatory properties. Chen et al. (2011) investigated the antioxidant activity of a 70% ethanolic extract of *Swertiachirata* using antioxidant tests such as the beta-carotene assay and reducing power. The results indicated that extracts containing 70% ethanol had a significant DPPH scavenging effect (IC_{50} = 267.80 μg/mL).

Evaluation of the biological activities of *Swertiachirata*.

Bioactivity evaluated,	Plant part(s) tested,	Test system,	Extracting solvent,	Test Organism/Models,	Resistance for drug,	Toxicity test.
Antibacterial	Whole plant	*In vitro*	Ethanol	*Escherichia coli* ATCC 26922	Ciprofloxacin	None
				Klebsiella pneumonia ATCC 15380		
				Pseudomonas aeruginosa ATCC 25619		
				Proteus vulgaris ATCC 6380		
Anti-bacterial	Stem	*In vitro*	Methanol	*Bacillus subtilis* ATCC 6633	Ceftriaxone, Ceftriaxone sodium, Cefuroxine, Ciprofloxacin, Gentamycine, Levofloxacin, Metronidazole, andTranexamic acid	None
				Enterococcus faecalis (ATCC 14506)		
				Staphylococcus aureus (ATCC 6538)		
				Pseudomonas aeruginosa (ATCC 27853)		
				Salmonella typhi (ATCC 14028)		
Antibacterial	Whole plant	*In vitro*	Methanol	*Bacillus subtilis* MTCC 736	Gentamycin	None
				Bacillus polymyxa		
				Staphylococcus aureus MTCC 3160		

				Escherichia coli MTCC 723		
				Salmonella typhi MTCC 3216		
				Vibria cholera MTCC 3906		
				Streptococcus pyogenes MTCC 1927		
				Proteus mirabilis MTCC 1429		
				Providentiaalk alifaciens		
				Pseudomonas aeruginosa MTCC 7837		
Antibacterial	Whole plant	*In vitro*	DCM; Ethanol	*Staphylococcus aureus*	Kanamycin 30 µg/disc	None
Antibacterial	Stem	*In vitro*	Ethanol	*Staphylococcus aureus*	Chloramphenicol 30 µg/disc	Brine shrimp assay–positive
				Bacillus subtilis		
				Salmonella typhi		
				Shigella flexeneriae		
				Sarcina lutea		
				Bacillus megaterium		
Antifungal	Whole plant	*In vitro*	Methanol	*Aspegillusniger* MTCC 1881	Amphotericin	None
				Aspergillus flavus MTCC 1883,		
				Cladosporium oxysporum MTCC 1777		

Swertiachirata presents a plethora of promising opportunities for both traditional and contemporary treatments. *Swertiachirata* seems to have a wide range of applications as a herbal medicine. An overview of the current use of *Swertiachirata* in ethnobotany, phytochemistry, pharmacological characteristics, safety evaluation, and human conservation status is given in this article. However, as no serious adverse effects or toxicity have been reported to date, more toxicological research is needed. To further substantiate the safety of these diverse plant-derived compounds. Toxicological, mutagenic, and biological activity in vivo attributes need to be assessed. Clinical trials are most likely required to determine the effectiveness of employing *Swertiachirata* in medicine. Due to its many applications, demand is always rising on both domestic and foreign markets. The population has drastically decreased as a result of overexploitation and habitat loss. Any proposed research has to be considered in a larger context that encompasses sustainable raw plant supply and conservation methods in order for this critically endangered medicinal plant to be successfully commercialized. Innovative methods that make use of biotechnological interventions—such as cryopreservation, micropropagation, and bioreactors—will be needed for both conservation and increasing commercial production. In order to enable commercial use, more comprehensive research is required in the field of synthetic seed technology, mainly to enhance the frequency of synthetic seed germination and the subsequent growth in soil. Hairy root technology has the potential to be used as a model system in the near future and will give plant biotechnologists powerful tools to improve *Swertiachirata*'s advantageous phytochemicals. Despite the development of efficient micropropagation methods, more studies on the biology of seeds and methods to increase the amount of bioactive secondary metabolites in *Swertiachirata* cultures would be helpful for their commercialization. Furthermore, to prevent *Swertiachirata* from being misidentified and perhaps adulterated, quality control methods must be followed.

1.6 Biological and pharmacological screening

There are various methods designed to investigate the biological activity of a targeted natural compounds. An optimal procedure must fulfil several criteria: fast, simple, reliable, high sensibility and selectivity, availability and low cost. Bioactivity evaluation for a plant extraction (plant fraction) is usually performed through *in vitro* or/and *in vivo* studies. Most often, *in vitro* studies are focused on the evaluation of specific cell biology (cell count, growth rate, metabolic rate, cell function and protein expression). *In vitro* tests are conducted on various animal or human cell cultures, enzymes, depending on targeted natural compound biological activity. For instance, the bioassays for antitumor activity are conducted on tumor experimental models. Complementary, the immunological activity on normal cell culture should be monitored. The cells will be analyzed by fluorescence microscopy and will be quantified to establish the degree of apoptosis and implicitly the cell viability. Also, the time lapse video microscopy can be used to evaluate the bioactive phytochemicals. The *in vivo* bio tests are applied on animals (mice, rats, pigs, etc.).

Antimicrobial Resistance (AMR)

Antimicrobial Resistance (AMR) occurs when microorganisms develop resistance to antimicrobial medications such as antivirals and antibiotics. AMR is increasingly becoming a global threat, both economically as well as in terms of health. AMR can lead to the treatments becoming ineffective, making it more difficult to treat infections, and can then cause an increase in the risk of the disease spreading. Particularly, diseases such as tuberculosis, malaria, HIV and Influenza are developing more drug resistant cases, leading to higher healthcare costs and a longer duration of illness. Within the European Union alone, the average yearly additional costs caused by AMR between 2015 and 2030 are estimated to be $252,215 USD per 100,000 persons per year.

Factors causing AMR

Several factors have been found to cause AMR. Human use of antimicrobial drugs, particularly antibiotics, is recognized as one of the primary drivers of AMR.

• Antibiotics are among the most familiar of medicines by the public, and the global consumption of antibiotics has been estimated at more than 35 billion daily doses at 2015.

• Several studies have found a positive association between antimicrobial use and AMR.

• Although in the past AMR research has focused on direct public consumption of antimicrobial drugs, drugs use in livestock are an increasingly concerning issue.

• Antibiotics are an integral part of industrial agriculture to ensure healthy livestock and promotion of growth.

• The Food and Agriculture Organization (FAO) expects that two-third of the future growth of antimicrobial use will be linked to animal production. Human consumption of these animals can lead to resistant microorganism transmission between hosts. Tis can then in turn impact the wider environment through animal and human waste affecting soil and land.

Other factors causing AMR

• Over-prescription of antibiotics

• Patients not finishing the entire antibiotic course

• Overuse of antibiotics in livestock and fish farming

• Poor infection control in health care settings

• Absence of new antibiotics being discovered

Table 1: Medicinal plants used for the treatment of antimicrobial disease

Sr No.	Botanical Name	Family	Part Used
1	*Acacia nilotica*	Mimosaceae	Stem
2	*Achyranthes aspera*	Amaranthaceae	Leaves
3	*Acorus calamus*	Araceae	Rhizome
4	*Aegelemarmelos*	Rutaceae	Leaves
5	*Aervalanata*	Amaranthaceae	WP
6	*Ageratum conyzoides*	Asteraceae	Leaves

7	*Alangiumsalvifolium*	Alangiaceae	Fruit
8	*Andrographis alata*	Acanthaceae	Leaves
9	*Andrographis echioides*	Acanthaceae	Leaves
10	*Andrographis paniculata*	Acanthaceae	Leaves
11	*Andrographis serpyllifolia*	Acanthaceae	Leaves
12	*Annona squamosa*	Annonaceae	Leaves
13	*Aristolochia bracteolate*	Aristolochiaceae	Leaves
14	*Azadirachtaindica*	Meliaceae	Leaves
15	*Calotropis gigantean*	Asclepiadaceae	Latex
16	*Carissa carandas*	Apocynaceae	Leaves
17	*Curcuma longa*	Zingiberaceae	Rhizome
18	*Cynodandactylon*	Poaceae	Root
19	*Euphorbia hirta*	Euphorbiaceae	Latex, Leaves
20	*Justicia adhotada*	Acanthaceae	Leaves
21	*Leucas aspera*	Lamiaceae	Leaves
22	*Mangiferaindica*	Anacardiaceae	Bark
23	*Mimusopselengi*	Sapotaceae	Leaves
24	*Plectranthuscoleoides*	Lamiaceae	Leaves
25	*Psidium guajava*	Myrtaceae	Leaves
26	*Scantalum album*	Santalaceae	Stem
27	*Sesbania grandiflora*	Fabaceae	Leaves
28	*Solanum surattense*	Solanaceae	Fruit
29	*Sphaeranthus indicus*	Asteraceae	Seed
30	*Tribulus terrertris*	Zygophyllaceae	Whole plant
31	*Tridaxprocumbens*	Asteraceae	Leaves
32	*Vitex negundo*	Verbenaceae	Leaves
33	*Zingeberofficinale*	Zingiberaceae	Rhizome [86-145]

CONCLUSION

The dramatic rise in infections in recent years has led to a chronic issue of antibiotic resistance. The antibacterial efficacy of different Swertia species against various bacterial strains varies, according to current research. As stated by Srinivasan and colleagues (2001). This activity might indicate that Swertia species either general metabolic poisons or contain broad-spectrum antibiotic chemicals. Phytochemical analysis has demonstrated the presence of steroids, flavonoids, tannins, and phenols in Swertia species. has demonstrated the antimicrobial properties of tannins and flavonoids.The antibacterial activity against certain bacterial strains could be attributed to these phytochemicals. To sum up, a lot of study has been done on *Swertiachirata* in the fields of phytochemistry, biological activity, ethnobotany, taxonomy, and conservation. However, new findings, may increase the therapeutic utility of *Swertiachirata* today and promote its continued use in modern medicine. More biotechnological approaches are required for conservation efforts.

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