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Review Article

In Vitro Evaluation of the Antimicrobial Activity of *Solenostemma argel* (Harjal) Extract Against Uropathogenic

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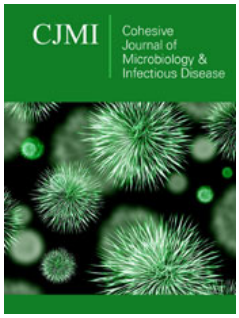

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Abstract

Background: Most uropathogenic bacteria exhibit multi-drug resistance, even with antibacterial medicines intended to treat urinary tract infections. These are causing an increasing amount of health and economic loss globally, so regional, national, and international action is required. Therefore, different strategies utilizing bioactive components from conventionally used medicinal plants are needed to address this issue.

Objectives: This study evaluated the *in vitro* antimicrobial activity of different concentrations of ethanolic *Solenostemma argel* (Harjal) extraction in the traditional treatment of urinary tract infections.

Methods: A cross-sectional study was done in Shendi Town, River Nile State, at the microbiology laboratory at Shendi University. Fifty samples from both sexes were collected randomly from different clinics in Shendi, from which eight strains of uropathogenic bacteria were isolated and identified using colonial morphology, Gram stain, and biochemical tests. We tested the ethanolic *Solenostemma argel* (Harjal) extract at concentrations of 100%, 50%, 25%, and 12.5% w/v, using the agar well diffusion method.

Results: Out of a total of 50 clinical specimens confirmed, 22 (44% of them) were men, and 28 (56%) were women. Of the total 50 clinical specimens, 15 (30%) were confirmed as *Staphylococcus aureus*, 20 (40%) *Escherichia coli*, 3 (6%) *Klebsiella pneumoniae*, 2 (4%) *Citrobacter*, 2 (4%) *Enterobacter*, 6 (12%) *Staphylococcus epidermidis*, 1 (2%) Staphylococcus saprophyticus, and 1 (2%) E. fecalies. The extract of *Solenostemma argel* has promising antibacterial activity against tested uropathogenic bacteria.

Conclusion: The *Solenostemma argel* possesses a remarkable antimicrobial effect on gram-positive and gram-negative bacteria. Of all extracts, the ethanolic and aqueous extracts of *Solenostemma argel* were the most active, whereas the aqueous extracts of all plants do not possess significant antibacterial activity both against standard and clinical strains. Ethanolic extracts of *Solenostemma argel* showed high antibacterial activity against Gram-positive and Gram-negative at low concentrations, whereas they were found to be ineffective at high actions. However, further studies are necessary to find active components in *Solenostemma argel* extract and to confirm its mechanism of action.

Keywords: *Solenostemma argel*; Uropathogenic; Antimicrobial activity; Herbal medicine; Bacterial infections

Introduction

150 million people worldwide are afflicted with Urinary Tract Infections (UTIs), which are among the most prevalent bacterial infections [1]. In elderly men, women of all ages, and newborn boys, Urinary Tract Infections (UTIs*)* are a major source of morbidity. Frequent recurrences, pyelonephritis with sepsis, preterm birth, kidney injury in young infants, and consequences from frequent use of antibiotics, such as high-level antibiotic resistance and *Clostridium difficile colitis*, are among the worst sequelae. UTIs are classified as either simple or

complicated clinically. People who are otherwise healthy and do not have any anatomical or neurological urinary system abnormalities are usually the ones who have simple UTIs [2,3]. Cystitis, a lower UTI, and pyelonephritis, an upper UTI, are two separate types of these illnesses. Several risk factors are associated with cystitis, including female gender, a prior UTI, sexual activity, vaginal infection, diabetes, obesity, and genetic susceptibility [3,4]. Both Gram-positive and Gram-negative bacteria, as well as some fungi, can cause urinary tract infections. Uropathogenic *Escherichia coli* is the most frequent cause of both simple and complex UTIs (UPEC). UPEC is the most common agent associated with uncomplicated UTIs, followed in prevalence by group B *Streptococcus* (GBS), *Proteus mirabilis, Pseudomonas aeruginosa, Staphylococcus aureus, Enterococcus faecalis,* and *Candida spp* [4-7]. Antibiotics are frequently prescribed to patients with symptomatic UTIs; nevertheless, these therapies have the potential to permanently alter the normal microbiota of the gastrointestinal tract and vagina and to foster the growth of microbe's resistant to multiple drugs. The possibility of multidrug-resistant uropathogen colonization can be heightened by the presence of niches that the changed microbiota has ceased to occupy. Significantly, the "golden age" of antibiotics is ending, which means that more carefully thought-out alternative treatments are required. Microbial infection is a major public health problem in developing countries. Antibiotics are used to treat these infections. Due to the misuse of antibiotics, the incidence of multiple antibiotic resistance among human pathogens is increasing, forcing scientists to search for new antimicrobial substances from natural sources [8].

In addition to the unfavorable side effects of antibiotics, the misuse of antibiotics "used to treat these infections" has led to an increase in the incidence of multiple antibiotic resistance among human pathogens, which is a major public health concern in both developed and developing nations. This has forced scientists to look for new antimicrobial substances from natural sources [9]. Plants possess active ingredients for defense against plant pathogens. Many of these antimicrobial substances were found to produce the same effects against human pathogens. Hence, researchers started screening plenty of plant extracts and essential oils against various human pathogens. Screening medicinal plants for antimicrobial activity has led to encouraging results. However, it is essential to investigate the toxicity of the plant. Antibiotics have undesirable side effects, while the emergence of previously uncommon infections is also a serious medical problem. Over 75% of the antimicrobials in clinical use are of natural origin, and most of them are obtained from fungal sources [10,11]. The important medicinal plants are mostly extracted from herbs, shrubs, and even trees. Herbs are defined as small plants with soft stems. People have discovered the benefit of using plants for medical purposes over time [12].

An estimated large population of half a billion people, mostly in the third world, use medicinal plants in various traditional ways [13]. Herbal medicine is becoming popular nowadays. Simply because they are available, cheap, and have no side effects, on one hand. In addition, the massively poor population cannot afford the expensive and sometimes infective imported medicine available in the market [13]. The wild herbal plant known as harjal (*Solenostemma argel*) is extensively distributed across various nations, including Sudan, Saudi Arabia, and Egypt. These plants' stems, leaves, and bark are used to treat illnesses of the urinary, gastrointestinal, and respiratory systems as well as to relieve pain [14]. In these countries, these portions have also been used to treat diabetes, cardiovascular disease, liver, and kidney problems [14]. Previous studies have shown that argel leaves, bark, the leaves, bark, and stems of argel have diverse medicinal applications and are traditionally being used for the treatment of numerous diseases such as pain, diabetes, respiratory tract infections, cardiovascular disorders, gastrointestinal problems, urinary tract infections, and kidney and liver diseases [15]. And stems have antispasmodic, anti-inflammatory, antinociceptive, antipyretic, anticancer, antioxidant, and antimicrobial activities [15]. Numerous phytochemicals were found in argel according to a phytochemical investigation. These included flavones (quercetin, (1)-catechin, naringenin, isorhamnetin, and kaempferol), glycosylated flavonoids (quercetin-3-rutinoside and apigenin-7-glucoside), polyphenols (catechol and resveratrol), b-carotene, b-sitosterol, monoterpenes, pregnenes, and pregnane [16-19].

After ingestion, therapeutics like probiotics have a positive impact on the host's gut microbiota and may be able to prevent a number of illnesses, including AD [20]. Even though Argel leaves have high quantities of phenolics with antioxidant and antimicrobial potentials, limited information is available on their use in meat and meat products for extending shelf life and preventing lipid oxidation [16]. This plant is regarded as the richest source in Sudan and is locally called Hargel; it is indigenous in the northern region [21] and widely spread in the places between Dongola and Barber, particularly around the Abu Hamad area [22]. Sudanese use the Hargel plant in traditional medicine as an anti-inflammatory, anti-spasmodic, anti-rheumatic agent, carminative, and anti-diabetic [23-26]. The plant can be used as an anti-nutrition factor [27] and anticancer [28]. *Solenostemma argel* is a desert medicinal plant indigenous to African countries. This research aims to study the pharmacological properties of the *Solenostemma argel* plant as an antimicrobial activity against uropathogenic isolates in Shendi City, Sudan (Figure 1).

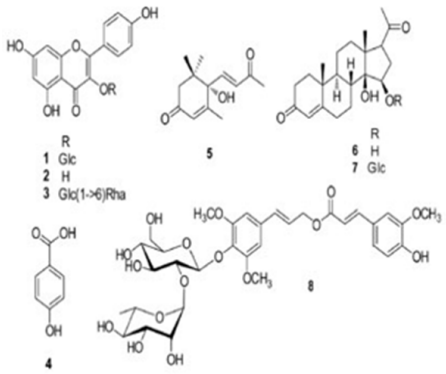

Figure 1: Structures of compounds 1-8 isolated from (*Solenostemma argel*) harjal [48].

Materials and Methods

Study design

This study was an analytical, cross-sectional, laboratory-based study. The samples were distributed between different hospitals and clinical centers located in Shendi locality, River Nile State, Sudan. Shendi is a town in northern Sudan, situated on the east bank of the Nile (150km) northeast of Khartoum. Shendi is also about 45 km southwest of the ancient cities of Meroawi and Napata, 250km to the northwest.

Samples collection

A total of fifty samples (n=50) of urine specimens were under aseptic status in Shendi town, River Nile, Sudan.

Bacterial isolation and identification

The isolated bacteria were identified by colony morphology, Gram stain, and biochemical tests. Full identification was done by using the Gram staining technique and specific confirmatory biochemical tests. After identification, stock cultures were made and then kept in the refrigerator at the optimum temperature.

Collection and preparation of *Solenstemma argel* (Harjal)

Solenstemma argel is collected from farmers in Shendi city. *Solenstemma argel* was dry in shadow and was cleaned from dust and grass, Samples were identified and extracted in the laboratory Research Institute at Shendi University. A hundred grams of the plant samples were ground using mortar and pestle and extracted by soaking in 80 % ethanol for about five days with daily filtration and evaporation. The solvent was evaporated under reduced pressure to dryness using a rotary evaporator apparatus and the extract was allowed to air till complete dryness and the yield percentages were calculated.

Concentrations of *Solenstemma argel* (Harjal): *Solenstemma argel* was used in different concentrations (100%, 50%, 25, and 12.5%) against isolated organisms.

Preparation of standard bacterial suspension: Clinical isolates were isolated from different samples in a sterile slope of nutrients and standard bacteria were brought from the microbiology department of the National Institute for Research, ten ml of normal saline were distributed in test tubes and sterilized in an autoclave at 121 °C for 15 minutes. A loop full of purified bacteria was inoculated in sterile normal saline. Inoculum density was compared with the McFarland standard solution.

The agar well diffusion method

The agar well diffusion method is widely used to evaluate the antimicrobial activity of plants or microbial extracts. Using a sterile wire loop, touch 3-5 well-isolated colonies of similar appearance to the test organism and emulsify in 3-4 ml of sterile physiological saline or nutrient broth. In a good light match the turbidity of the suspension to the turbidity standard (mix the standard immediately before use). When comparing turbidities, it is easier to view against a printed card or sheet of paper. Using a sterile swab, inoculate a plate of Mueller Hinton agar. Remove excess fluid by pressing and rotating the swab against the side of the tube above the level of the suspension. Streak the swab evenly over the surface of the medium in three directions, rotating the plate at approximately 60 to ensure even distribution. With the petri dish lid in place, allow 3-5 minutes for the surface of the agar to dry. Then, a hole with a diameter of 6 to 8 mm is punched aseptically with a sterile cork borer; honey is introduced into the well at the desired concentration [26]. Then agar plates are incubated under suitable conditions. By using a ruler on the underside of the plate measure the diameter of each zone of inhibition in mm. The endpoint of inhibition is where growth starts [29].

Data collection and analysis

A self-administered questionnaire was used and supported with coding numbers to facilitate the sorting of data. Data were entered, checked, and analyzed using Microsoft Excel 2007. The final results were presented as frequencies and percentages.

Result

(Tables 1-8), (Figure 2).

Table 1: The distribution of clinical specimens according to gender.

Gender	Frequency	Percentage
Male	22	44%
Female	28	56%
Total	50	100%

Table 2: The distribution of clinical specimens according to age.

Age	Frequency	Percentage
15-25 years	8	16%
26-50 years	24	48%
51-75 years	18	36%
Total	50	100%

Table 3: The frequency and percentage of clinical bacteria isolated from patients with UTI.

Isolate	Frequency	Percentage
E. coli	20	40%
S. aureus	15	30%
S. epidermidis	6	12%
S. saprophyticus	1	2%
E. faecalis	1	2%
K. pneumoniae	3	6%
Entereobacter	2	4%
Citrobacter	2	4%
Total	50	100%

Table 4: The antibacterial activity of reference drug against gram-positive bacteria.

Drug	Concentration Mcg	*S- aureus*	*S-epidermidis*	*S- saprophytic*	*E- fecalis*
Gentamicin	10	19	25	20	20
Ciprofloxacin	5	32	30	32	18
Amoxicillin	10	21	10	12	27
Vancomycin	30	23	20	12	22

Table 5: The antibacterial activity of reference drug against gram-negative bacteria.

Drug	Concentration Mcg	*E- coli*	*Citrobacter*	*Enterobacter*	*K. pneumoniae*
Gentamicin	10	19	18	20	18
Ciprofloxacin	5	24	30	37	32

Table 6: The sensitivity of selected bacteria to different concentrations of *Solenostemma argel*.

Bacteria	Concentration of ethanolic S-argal extract							
	100%		50%		25%		12.50%	
	S	R	S	R	S	R	S	R
E. coli	4	16	4	16	13	7	13	7
S. aureus	4	11	4	11	11	4	11	4
S. epidermis	2	4	2	4	6	0	6	0
S. saprophyticus	0	1	0	1	0	1	1	0
E. fecalis	0	2	0	2	2	0	2	0
Enterobacter	0	2	0	2	2	0	2	0
Citrobacter	1	2	1	2	3	0	3	0
K. pneumonia	0	1	0	1	1	0	1	0
Percentage	22%	78%	22%	78%	76%	24%	78%	22%

Table 7: The comparison of sensitivity between gram-positive bacteria to antibiotics and different concentrations of *S. argal* extract.

Pathogen	Gentamicin	Ciprofloxacin	Amoxicillin	Vancomycin	100%	50%	25%	12.50%
S. aureus	12 (80%)	15 (100%)	15 (100%)	10 (67%)	4 (27%)	4 (27%)	11 (73%)	11 (73%)
S. epidermis	6 (100%)	6 (100%)	6 (100%)	0 (0%)	2 (33%)	2 (33%)	6 (100%)	6 (100%)
S. saprophyticus	1 (100%)	1 (100%)	0 (0)	0 (0)	0 (0%)	0 (0%)	0 (0%)	1 (100%)
E. fecalis	1 (100%)	1 (100%)	1 (100%)	1 (100%)	0 (0%)	0 (0%)	1 (100%)	1 (100%)
Total	20 (87%)	23 (100%)	22 (96%)	11 (49%)	6 (26%)	6 (26%)	18 (78%)	19 (82%)

Table 8: The comparison of sensitivity between gram-negative bacteria to antibiotics and different concentrations of *S. argal* extract.

Pathogen	Gentamicin	Ciprofloxacin	100%	50%	25%	12.50%
E. coli	20 (100%)	16 (80%)	4 (20%)	4 (20%)	11 (55%)	11 (55%)
Citrobacter	2 (100%)	2 (100%)	0 (0%)	0 (0%)	2 (100%)	2 (100%)
Enterobacter	2 (100%)	2 (100%)	0 (0%)	0 (0%)	2 (100%)	2 (100%)
K. pneumonia	3 (100%)	3 (100%)	1 (33%)	1 (33%)	3 (100%)	3 (100%)
Total	27 (100%)	23 (85%)	5 (19%)	5 (19%)	18 (67%)	18 (67%)

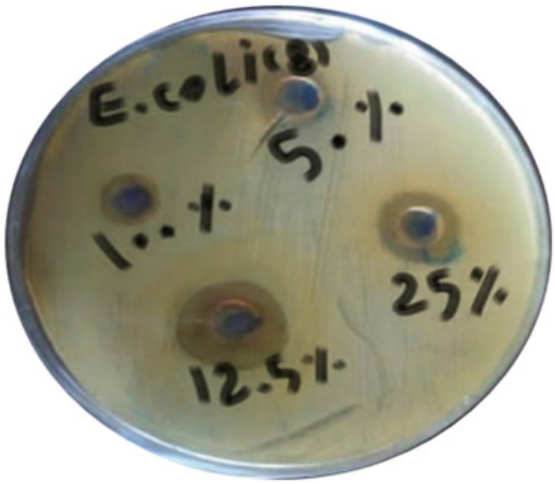

Figure 2: Show the activity of *Solenostemma argel* against *e. coli.*

Discussion

Natural medication is inexpensive, safe, and simple to take. The main benefit of these herbal medicines is that they do not cause bacterial resistance. These natural therapies can help with the resistance issue that results from using standard treatments. Bacteria, particularly Gram-negative ones like *Escherichia coli, Proteus species, Pseudomonas aeruginosa, Acinetobacter species, Klebsiella species, Enterobacter species, and Citrobacter species*, are frequently the cause of UTIs. Among Gram-positive bacteria, *Staphylococcus saprophyticus, Enterococcus* species, and Coagulase-negative *Staphylococcus* are a common, predictable spectrum of bacteria that are responsible for causing UTIs [30,31]. In our research study, the ratio of female patients with UTI was higher than that of males. This was inconsistent with the study by Kattel et al. [32] the higher prevalence of UTI among females is due to various factors that predispose women to UTI [33]. The most prevalent urinary tract pathogen in both genders in our study was *E. coli* and *K. pneumoniae,* in concordance with other studies from Saudi Arabia conducted by Ahmed et al. and Al-Tawfiq and Anani [34,35]. In the study of Haqgoo et al. [36], 72.3% of patients with positive urine cultures were women and 27.7% were men.

In the study of Jarsiah et al. [37], it was also observed that the number of positive cultures is higher in women than in men. In the study of Ramezanzadeh et al. [38], most of the bacteria were also isolated from women's samples. It was also reported in the Laupland et al. [39] study found that women had a greater incidence of urinary tract infections. All of the previously mentioned data corroborate the findings of this study, indicating that women may be more vulnerable to this disorder due to the shorter urethra and closer location of its outlet to the vagina and anus. This study reported that the main cause of UTI in the study population was *E. coli* (40%), followed by *S. aureus* (30%), *S. epidermidis* (12%), *K. pneumonia* (6%), *Enterobacter* and *Citrobacter* (4%), *S. saprophyticus, and E. faecalis* (1%). The suggestions state that the treatment of UTIs with empirical antibiotics is common. The purpose of antimicrobial therapy is to destroy pathogenic microorganisms. The type of infection, its severity, the prevalent bacteria in the location, and patterns of antibiotic resistance all influence the antibiotic that is selected. Trimethoprim, Sulfamethoxazole, Nitrofurantoin, Ciprofloxacin, Levofloxacin, Cephalexin, Ceftriaxone, Azithromycin, Doxycycline, and other antibiotics are frequently used to treat urine-related infections [40]. The most potent antibiotics in this study are isolated Gram-positive uropathogens that were tested, including Gentamicin, Ciprofloxacin, Amoxicillin, and Vancomycin. And Gentamicin and Ciprofloxacin for Gramme-negative uropathogens are isolated.

The number (percentage) of common Gram-negative urinary pathogens sensitivity (S) to antimicrobial agents. The common urinary pathogens, *E. coli, K. pneumoniae, Citrobacter,* and *Enterobacter,* showed high sensitivity when they were tested against Gentamicin (27%) and Ciprofloxacin (23%). In comparison, Gram-negative urinary pathogens sensitive *S. aureus, S. epidermis, S. saprophyticus, and E. fecalis* showed high sensitivity when they were tested against Gentamicin (20%), Ciprofloxacin (23%), Amoxicillin (22%), and vancomycin (11%). Both Gram-positive and Gram-negative bacteria exhibited antimicrobial resistance. The urine pathogen that was isolated had a high level of multiple resistances. Particularly in high concentrations of *Solenostemma argel*, the resistance rate is 78% in (100% and 50% of ethanolic *S-argal* extract concentration), while resistance rates are 24% and 22% in (25% and 12.5% of ethanolic *S-argal* extract concentration), respectively. In this study, the extract of *Solenostemma argel* had moderate activity against all the tested uropathogenic bacteria. These results were in agreement with those obtained by Sandhya B and his colleagues [41], who obtained moderate results and recommended that more research be done to investigate the role of *S. argal* in the biological activity of different herbal extracts, but there was no agreement in the effective concentration. On the other hand, our results differ from those obtained by Abdel Moneim E. Sulieman and his colleagues [42]. This variation may be due to a difference in the method of sensitivity testing.

The ethanol extraction of *Solenostemma argel* leaves exhibited high antibacterial activity against all uropathogenic bacteria at a concentration of 12.5%. This result decreases when the concentration is increased. A few bacteria showed the antibacterial activity of *Solenostemma argel* extract in concentrations of 100%, like *E. coli*, *S. aureus,* and *Staphylococcus epidermidis. S. epidermidis* and a moderate effect on *E. coli, S. aureus,* and *Citrobacter*, followed by *Klebsiella pneumonia and Staphylococcus saprophyticus*. Moreover, the results indicate that the most effective concentration was 12.5%, and the effect of *Solenostemma argel* extraction decreased dramatically when the concentration of *Solenostemma argel* was increased. It was observed that the ethanol *Solenostemma argel had* higher antibacterial activity against *S. aureus* and was resistant to vancomycin, and *Solenostemma argel* was resistant to amoxicillin and vancomycin. The four *S. argel* extracts that showed antibacterial properties on both bacteria Escherichia coli and Staphylococcus aureus could be due to the presence of phytochemical components composed of saponin, flavonoid, and

cardiac glycoside [12], reported similar results. He proved that certain plant constituents, such as alkaloids, tannins, saponins, and flavonoids, were associated with antibacterial activities. These results also agreed with the findings of Rose (1980) and [43], who reported different inhibitory effects of the above-mentioned components against bacteria and fungi.

The inactivity of the petroleum ether extracts from *S. argel* leaves observed could be because the chloroform used in the extraction process might have removed the compounds that act as soluble agents for the active constituents in the petroleum ether extracts. Another possibility that might explain this loss of activity could be the synergetic action of more phytochemical components present in different extract fractions. The low antibacterial activity in high concentration showed by *S. argel* extracts in our study is due to the resistance of the bacteria to the antibacterial constituent in the extract, which agreed with the findings of Sowofora [44], who documented the bacteria's resistance to a variety of pharmaceutical medications, in particular the clinical isolate of *Staphylococcus aureus* that shown a blatant resistance to benzoyl penicillium. This was found to be due to the production of β-lactam ring.

The phytochemical screening and TLC separation have been confirmed and complemented by the study results of Khalid et al. [45], who proved the presence of antibacterial ingredients such as kaempferol and cardiac glycoside; and those of Maharn (1967) and El Fishawi [46], who also proved the presence of the above-mentioned compounds as well as quercetin [47,48]. Natural bioactive components of potential medical use, such as antioxidants, antimicrobials, anti-inflammatory agents, and anticancer agents, are present in the methanolic extract of *Solenostemma argel* [49]. However, further detailed investigations are required for the complete chemical identification of active constituents of *S. argel* needed to produce new antibacterial agents from the plants. To fully understand these phytochemical modes of action, more investigation is required. To determine which phytoconstituents are responsible for treating uropathogenes, more research is required. Thus, you must carry out additional research on genetics and develop techniques to ascertain how phytoconstituents work to eradicate harmful microorganisms [50]. Dietary and pharmacological inhibition of neuron nuclear receptors will determine neuron proliferation and remodeling with excessive nuclear receptor inhibitor consumption related to protein aggregation in neurological diseases [51].

Conclusion

Depending on the extremity of the infection, different drugs are used to treat UTIs. However, the bacteria linked to UTIs are becoming tougher for medical experts to treat as a result of antibiotic treatment resistance. Herbal medicine is one type of alternative therapy that is one of the most successful therapeutic options and is seen to be a blessing for treating urinary tract infections. The *Solenostemma argel* possesses a remarkable antimicrobial effect on gram-positive and gram-negative bacteria [52]. Of all extracts, the ethanolic and aqueous extracts of *Solenostemma argel* were the most active, whereas the aqueous extracts of all plants do not possess significant antibacterial activity both against standard and clinical strains. Ethanolic extracts of *Solenostemma argel* showed high antibacterial activity against Gram-positive and Gram-negative at low centration, whereas they were found to be ineffective at high concentrations. However, further studies are necessary to find active components in *Solenostemma argel* extract and to confirm its mechanism of action.

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