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# Evaluation of Physicochemical and Antibacterial Properties of Ethanolic and Gel Extracts of Common Wireweed (*Sida acuta* Burm.f.)

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**ABSTRACT:** Man has used medicinal plants as remedies for several human diseases for centuries. This paper therefore evaluates the physicochemical and antibacterial properties of ethanolic and gel extracts of common wireweed (*Sida acuta* Burm.f.) using appropriate standard techninques. The filtrate was concentrated to a semi-solid mass (extract) and the antibacterial activity of the extract against *Staphylococcus aureus, Staphylococcus epidermidis, Pseudomonas aeruginosa*, and *Escherichia coli* were assessed using the agar well diffusion technique. The gels have good homogeneity, and spreadability, and are easily washable. The pH ranges between 5.8 and 6.3 and is within the normal skin pH range (4.0-6.8). The extrudability ranges from 45 to 70%. The viscosity of the gels is between 6178.6 mPas and 59,343 mPas and they are shear thinning systems. The gels prepared using *Sida acuta* ethanolic extract have antibacterial activity that is comparable to that of the extract alone. Gells formulated using carbopol were comparable to those prepared using HPMC.

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Plants have been a great source of medicinal substances. Herbal medicines make great use of medicinal plants. Medicinal plants have been utilized as remedies for several human diseases by man for centuries (Okafo *et al*., 2021). Some synthetic or orthodox medicines originated from medicinal plants. Medicinal plants produce many secondary metabolites or phytochemicals that may be utilized for therapeutic purposes (Arekemase *et al*, 2019; Okafo *et al*, 2023a). The World Health Organization (WHO) stated that about 80% of the developing world make use of traditional medicines obtained from medicinal plants (Arekemase *et al*, 2019; Strompfová *et al*, 2024). There is a recent surge in the utilization of herbal medicines. This may result from the belief in the safety of herbal medicines and that they have negligible or zero side effects when compared to conventional medicines, that they are not expensive and are easily available (Arekemase *et al*, 2019; Okafo *et al*, 2023a). Traditional medicines are utilized as antimicrobials, antiulcers, anticonvulsants, anti-inflammatories, antioxidants, and antidiabetics. One plant may be utilized in the treatment of different diseases (Okafo *et al*., 2021; Strompfová *et al*, 2024). Many plants

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contain active ingredients that possess antimicrobial effects (Arekemase *et al*, 2019). Antimicrobial agents are substances (natural or synthetic) utilized in killing or inhibiting the growth of microbes such as fungi, bacteria, and algae (Okafo *et al*, 2022a). Plants, fungi, and animals are natural sources of antimicrobials. Plants-derived antimicrobials are of major therapeutic importance because of their use in the treatment of contagious diseases as well as in ameliorating the negative side effects that result from the utilization of synthetic antimicrobials (Okafo *et al*, 2022a; Popova *et al*, 2022). Antimicrobial resistance occurs when microorganisms do not respond to antimicrobial medicines any longer. This makes antibiotics as well as other antimicrobial drugs ineffective, making it hard or unfeasible to treat infections and, enhancing the risk of spread of disease, causing severe illness, disability, and death (WHO, 2023). Synthesis of β-lactamase is a key mechanism by which bacteria develop antibiotic resistance (Egbule, 2016). Since some herbal medicines have antimicrobial activity against multidrug-resistant bacteria, their use is soaring in the context of the increasing resistance of microorganisms to antibiotics (Strompfová *et al*, 2024; Popova *et al*, 2022). Most current researches are geared towards the possibility of replacing antibiotics in this drug resistance crisis. One of the merits of treatment with plant-derived compounds is that they usually do not cause resistance (Strompfová *et al*, 2024). Herbal extracts prepared from plant parts are added to various skin and hair care cosmetic creams, lotions, gels, and ointments. Herbal cosmetics can prevent the skin from developing different skin conditions, skin allergic reactions, and skin diseases (Venkatachalam *et al*, 2019; Okafo *et al*, 2020). A gel is a semisolid preparation composed of a cross-linked network of structural materials interpenetrated by a liquid. The structural materials consist of small inorganic particles or large organic macromolecules, mainly polymers (Kaur and Guleri, 2013). Physical and/ or chemical cross-linking may be involved (Okafo *et al*, 2022b). This leads to the division of gels into chemical and physical gel systems. Permanent covalent bonding is involved in chemical gels, whereas relatively weaker and reversible bonding occurs in physical gels. The weak and reversible secondary intermolecular forces include hydrogen bonding, electrostatic interactions, dipole-dipole interactions, Van der Waals forces, and hydrophobic interactions (Kaur and Guleri, 2013). The clarity or turbidity of the gel is determined by the solubility of the ingredients it contains. Different ingredients may have varying solubility in the gel system. The gelling agents are utilized at concentrations less than 10% and usually at 0.5 to 2.0% (Crowley, 2005). Gels are usually utilized in pharmacy because they are semisolid in nature, very clear, easily applied, and removed (Okafo *et al*, 2022b; Crowley, 2005). Gels are a better healing alternative than liquid because they allow longer drug contact time than liquid, and could protect wounds from external influence. This dosage form is easy to use and spreads quickly on the skin. Appropriate and effective gel formulations are expected to reduce and prevent wound infection (Lestari *et al*, 2024). The topical delivery with gels can increase the resident time of the drug on the skin and improve the delivery and release of the substance (Dantas *et al*, 2016). Topical gels are usually thixotropic, greaseless, spread easily, easily removable, emollient, non-staining, compatible with several excipients, and water-soluble or miscible (Tanwar, 2017).

*Sida acuta* Burm. F is a shrub from to the Malvaceae family. The plant is commonly found in the subtropical regions, predominantly in bushes, farms, and near habitations. *Sida acuta* is a plant of wide usage in traditional medicine (Okafo and Chukwu, 2017a; Okafo and Chukwu, 2017b; Okafo *et al*, 2023b). The plant is an erect, perennial under shrub or shrub, 1.5 m high with linear to lanceolate leaves and flowers, yellow solitary or in pairs (Okafo *et al*, 2023b). The plant is utilized in folk medicine to treat diseases like fever, diarrhea, and dysentery. Studies were done to validate if the plant can produce *in vivo* the activities claimed by traditional practices. Such pharmacological properties include antimicrobial, cytotoxic activities, antioxidant, and many other properties (Karou *et al*, 2007). Herbal drugs are safer to use than synthetic drugs. They are non-toxic, cheap, biodegradable, and easily available (Arekemase *et al*, 2019; Okafo *et al*, 2023a). *Sida acuta* leaves are easily available and accessible, therefore, formulation of *Sida acuta* as a herbal drug will be of great economic and health benefit to the patient. This study was conducted to assess the antimicrobial activity of ethanolic extract of *Sida acuta leaves*, and that of the gels formulated using the extract as the active ingredient.

## MATERIALS AND METHODS

*Materials:* Ethanol (GH TECH- Guangdong Guanghua Sci-Tech Co., Ltd.), carbopol 940 (Corel Pharma Chem, Gujarat, India), hydroxypropyl methylcellulose (HPMC) (BDH Chemicals Ltd Poole England), glycerol (Merck Schuchardt OHG, Hohenbrunn, Germany), methylparaben (Organic Limited Gujarat, India), propylparaben (Zhajong Shenxia Chemicals Company, China), Mueller Hinton agar, antibiotic disk (Celtech diagnostic products, Bangalore, India), antibiotics (cefepime), Nutrient broth,

*Microorganisms used: Staphylococcus aureus, Staphylococcus epidermidis, Pseudomonas aeruginosa,* and *Escherichia coli.*

*Collection of plant:* Collection of the plant was done early in the morning from Madonna University school compound. The plant was authenticated by a plant taxonomist. The *Sida acuta* leaves were washed and air-dried under shade for three weeks. The leaves were pulverized using a blender and passed through a 300 µm sieve.

*Preparation of plant extract:* A 100 g of the pulverized leaves was macerated in 500 ml of ethanol for 72 hours. It was filtered using a muslin cloth and the filtrate was concentrated at $60^{o}$C for 24 hours using a water bath. After completing the evaporation of the solvent, the concentrate was weighed and preserved at 4°C in an airtight container. The percentage yield of the extract was calculated using equation 1.

$$\%\,Y = \frac{Quantity\ of\ extract\ (g)}{Quantity\ of\ the\ pulverized\ leaves\ (g)}\ x\ 100 \quad . \quad 1$$

Where %Y = Percentage Yield

*Antibacterial sensitivity testing of the crude extract:* The antibacterial activity of the ethanol extract of *Sida acuta* leaves was determined by agar well diffusion method. Parallel analysis with conventional antibiotic discs was conducted to determine the possible multidrug-resistant (MDR) nature of the isolates and to compare the potency of the crude ethanol extract to the conventional antibiotics. A 6.84 g of Mueller Hinton nutrient was weighed and transferred into a round bottom flask. 180 ml of distilled water was added to it and stirred using a stirring rod. It was covered tightly and placed in the autoclave for 20 min. A 20 ml of the nutrient agar was poured respectively into the Petri dishes (double plating) that were labelled with test organisms (*S. aureus, S. epidermidis, P. aeruginosa,* and *E. coli*) and allowed to solidify. The standardized inoculum of test organisms equivalent to McFarland's turbidity standard were smeared uniformly on the surface of the Mueller Hilton agar with the aid of a swab stick. Holes were made in the agar dishes using a 7 mm diameter sterile cork borer. A 60 µl of the six different concentrations of the extract derived from 2-fold serial dilution method as follows: 600, 300, 150, 75, and 37.5 mg/ml were aseptically added to the different labelled wells. Cefepime (50 µg/ml) was utilized as the standard drug. The extracts were allowed to diffuse into the agar for 1 hour before incubation at 37°C for 18-20 hours in an incubator (ESCO-Isotherm Forced Convection Laboratory Incubator, Singapore). After the incubation period, the zone of inhibition was measured in millimeters using the transparent meter rule.

*Preparation of Sida acuta ethanol extract gels:* Seven different gels were made using the formula in Table 1. The extract concentration of 300 mg/ml was used for the preparation of the gels because its antibacterial activity was comparable to that of 600 mg/ml, though slightly lower, however, it was more economical to use. The required quantities of SAEE, glycerol, methyl paraben, and propyl paraben were solubilized in distilled water. The respective gelling agent (Carbopol or HPMC) was introduced to the mixture. Proper mixing of the gel was ensured, not only to avoid lumps and bubbles but also to produce uniform and consistent gel of desired viscosity. The gels were kept for 24 h to hydrate properly for its final consistency and uniformity. They were stored in respective containers.

**Table 1:** Composition of the *Sida acuta* ethanol extract gels.

| Ingredients | F1 | F2 | F3 | F4 | F5 | F6 | F7 |
|---|---|---|---|---|---|---|---|
| SAEE (g) | 12 | 12 | 12 | 12 | 12 | 12 | _ |
| Carbopol (g) | 0.4 | 0.4 | 0.6 | 0.6 | _ | _ | 0.6 |
| HPMC (g) | _ | _ | _ | _ | 0.6 | 0.6 | _ |
| Glycerol (ml) | _ | 2 | _ | 2 | _ | 2 | _ |
| Methyl Paraben (g) | 0.12 | 0.12 | 0.12 | 0.12 | 0.12 | 0.12 | 0.12 |
| Propyl Paraben (g) | 0.04 | 0.04 | 0.04 | 0.04 | 0.04 | 0.04 | 0.04 |
| Water to (ml) | 40 | 40 | 40 | 40 | 40 | 40 | 40 |

Key: SAEE: *Sida acuta* ethanol extract gel

*Physicochemical evaluation of the gels:* The pH, spreadability, homogeneity, viscosity, and extrudability of the gels were assessed.

*pH of the gels:* The pH of the various gels was assessed using a digital pH meter (HI 2211 pH/ORP meter, Hanna Instruments). A 0.2 g of each of the gel was dissolved in 20 ml of distilled water and stirred. The average value obtained from three different pH measurement of each gel was calculated.

*Homogeneity of the gels:* The test was done by pressing a little amount of the gel between the index fingertips and the thumb. The smoothness of the gel was checked. This was done three times for each of the gels.

*Viscosity of the gels:* Brookfield viscometer (model NDJ-55, Shanghai Technology Co. Ltd) was used to measure the viscosity of the gels at a temperature of 28ºC. The viscosity was measured using spindle 4 at different speeds (shear stress), 6, 12, 30, and 60 rotations per minute. The dial reading for each speed was recorded.

*Spreadability of the gels:* Having good spreadability is an ideal quality of a gel. It shows the extent or area of the skin or affected part that a gel easily spreads to, when it is applied. The spreading value of a gel also dictates its therapeutic efficacy (Khan *et al*, 2022; Latif *et al*, 2023). A 0.5 g of the gel was put between two glass slides, and a 100 g weight was put on top of the upper glass slides for 5 min. The initial and final diameters of the films produced by the gel were recorded. Equation 2 was used to calculate the spreadability.

$$Spreadability = \frac{(FD - ID)}{ID} x\ 100 \quad 2$$

Where: FD = final diameter; ID = initial diameter

*Ease of removal of the gels:* This test is performed to know how easily the gel washes off from the skin after application. A little quantity was collected from each of the gels and applied to the back of the hand after which it was washed under running water. The ease and extent of wash-off with water were observed and recorded. A good gel washes off easily.

*Extrudability of the gels:* The weight of the collapsible tube ($w_1$) was recorded and 10 g of gel ($w_2$) was put inside it. A 100 g weight was dropped on the tube and the cover was removed. The quantity of the gel that was extruded ($w_3$) was recorded. This test was performed for all the gels. Equation 3 was used to calculate the % extrudability.

$$\%\ extrudability = \frac{w_3}{w_2} x\ 100 \quad . \quad . \quad 3$$

*Antibacterial activity of the gels:* Four gel formulations (F2, F4, F6, and F7) were chosen based on the outcome of the physicochemical evaluation test and were subjected to the antibacterial activity test. A 3.192 g of Mueller Hinton agar was added to 84 ml of water. It was stirred with a glass rod, covered properly and placed in an autoclave (Health Team Instruments, England) for 45 min. A 20 ml of the agar was added to the Petri dishes which were labelled with the names of the test organisms. They formed gels and were allowed to solidify. The standardized inoculum of *Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus,* and *Staphylococcus epidermidis* equivalent to McFarland's turbidity standard were streaked evenly on the surface of the Hilton Mueller agar with the aid of a swab stick. Holes were made in the Petri dishes using a 7 mm diameter cork borer. A 60 µl of the different concentrations of the extract was added into the holes and allowed to diffuse. After 24 hours, the zone of inhibition was measured in millimetres and recorded.

## RESULTS AND DISCUSSION

The results obtained are shown in Tables 2-4 and Figure 1. The percentage yield of the extract was 18.47%. From the results shown in Table 2, *Sida acuta* ethanolic extract has antibacterial activity that is concentration-dependent against the test bacteria (*Pseudomonas aeruginosa, Staphylococcus aureus, Staphylococcus epidermidis,* and *Escherichia coli*). The highest activity was witnessed at 600 mg/ml and the least activity was produced at 37.5 mg/ml. The 300 mg/ml concentration of the extract was utilized in the preparation of the gels because it has comparable activity to that produced by 600 mg/ml and will involve use of lower amount of the active ingredient. This will save costs, as well as, result in a lower incidence of side effects. The negative control (water + DMSO) had no activity against the test organisms but the positive control (cefepime) had higher activity than all the concentrations of SAEE used in the study. A study by Anani *et al* (2020), showed that the methanolic extract of *Sida acuta* had a significant activity on *S. aureus, E. coli, Bacillus subtilis,* and *Mycobacterium phlei*, but was not active on *Streptococcus faecalis, Klebsiella pneumoniae, Salmonella thyphimurium, Pseudomonas aeruginosa,* and *Candida albicans* (Karou et al, 2007; Anani *et al*, 2020). This was in consonance with the present study except that, unlike the study by Anani *et al* (2020), *Pseudomonas aeruginosa* was susceptible in the present study. From the results in Figure 1, the viscosity of the gels showed a non-Newtonian flow (pseudoplastic flow) pattern. The viscosity of the gels reduced with rising shear stress (from 6 to 60 rpm). This makes the gel to be stable in the container but readily spreadable on the skin when applied. Like elastic materials, the rheological characteristics of gels vary and show reversible deformation instead of flowing at low shear stresses. They flow like liquids at the yield value or yield stress, when a specific shear stress is exceeded (Chellathurai *et al*, 2023). The viscosity of a gel is the manifestation of the consistency of its gel compositions. The rheological property helps in determining consistency and influences the diffusion rate of a drug from a gel (Chellathurai *et al*, 2023).

**Table 2:** Inhibitory zone diameter (mm) produced by the controls and different concentration of the crude extract

| Drug | Zone of inhibition (mm) | | | |
|---|---|---|---|---|
| | ***Staphylococcus aureus*** | ***Staphylococcus Epidermidis*** | ***Pseudomonas aeruginosa*** | ***Escherichia coli*** |
| SAEE 600 mg/ml | 11 | 18 | 18 | 13 |
| SAEE 300 mg/ml | 9 | 11 | 16 | 8 |
| SAEE 150 mg/ml | 7 | 9 | 13 | 2 |
| SAEE 75 mg/ml | 5 | 8 | 11 | 1 |
| SAEE 37.5 mg/ml | 3 | 6 | 5 | 0 |
| Cefepime 50µg/ml (+) | 26 | 25 | 19 | 28 |
| Water + DMSO (-) | 0 | 0 | 0 | 0 |

*Key – SAEE: Sida acuta ethanolic extract; DMSO: Dimethyl sulfoxide, + positive control, - negative control*

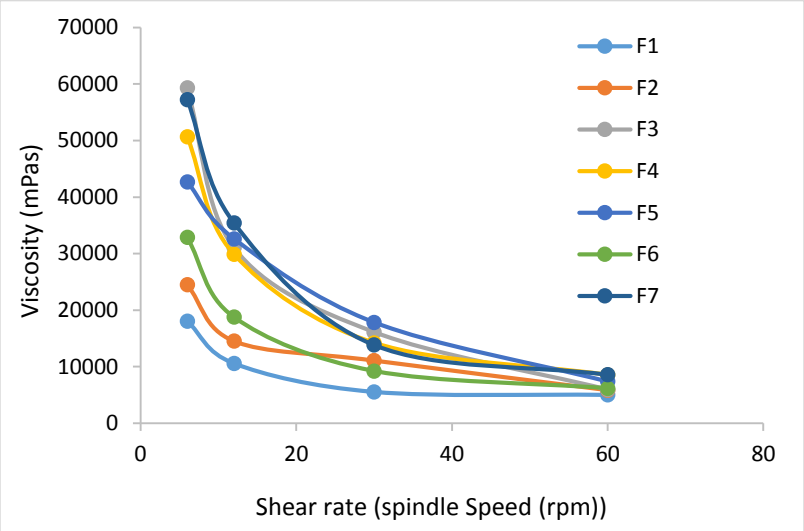


**Fig 1:** Viscosity result of the gels at 28ºC using spindle 4

**Table 3:** Physicochemical properties of gels

| | F1 | F2 | F3 | F4 | F5 | F6 | F7 |
|---|---|---|---|---|---|---|---|
| pH | 6.0 | 6.1 | 5.8 | 6.0 | 6.0 | 6.0 | 6.3 |
| Exrudability | 70% | 57% | 45% | 53% | 56% | 49% | 46% |
| Spreadability | 25% | 17.4% | 13% | 22.7% | 8% | 8.3% | 8% |
| Washability | good | Good | Good | Good | good | Good | Good |
| Homogeneity | smooth | smooth | Smooth | Smooth | smooth | smooth | Smooth |

The viscoelastic behaviour of the gel upon applied stress makes it easier for the gel to flow from the container to the applying area and suck back to the container upon the release of stress (Chellathurai *et al*, 2023). Topical products should be acidic and have a pH between 4 and 6. The pH of the skin varies from 4 to 6.8, and sweat and fatty acids secreted from sebum influence the pH of the skin surface (Dantas *et al*, 2016, Lestari *et al*, 2024). From the results shown in Table 3, the pH of the gels was between 5.8 and 6.3, therefore, the gels' pH was within the acceptable range. This shows that the cream will not irritate the skin (Okafo *et al*, 2021). The homogeneity of the gels was good and acceptable (Table 3). A good gel is supposed to be smooth to the touch and without lumps. This showed that the creams were properly mixed and no lumps were present (Okafo *et al*, 2021). All the gels have good spreadability (Table 3). The gels were easily spreadable. The spreadability is often used to express the level or area to that the topical preparation can readily spread upon application (Khan *et al*, 2022; Ordu *et al*, 2023). The spreadability value of a topical preparation affects its therapeutic effectiveness (Khan *et al*, 2022; Latif *et al*, 2023). Spreadability is a vital factor for enhancing patient compliance with the use of gel because those formulations that have good spreadability value produce more comfortable and uniform application over inflamed areas of skin (Khan *et al*, 2022). The extrusion of a topical preparation from its container with small shear stress is enhanced by optimum spreadability (Latif *et al*, 2023). From the results in Table 3, all the gels have good washability and were washed off easily. A good gel should be easily washes off skin with water to avoid staining. All the gels had good extrudability (Table 3). The spreadability and extrudability of gels are dependent on the viscosity of gels. Therefore, the viscosity of formulated gels should be characterized and ensured that they produce gels with optimum spread and extrudability (Ansong *et al*, 2023). Mechanical

property such as extrudability plays an important role in the selection, packing, and removal of a gel from its container. Therefore, extrudability should be quantified in order to determine how readily topical products, like creams, and gels could be removed and applied (Chellathurai *et al*, 2023).

**Table 4:** Inhibitory zone diameter (mm) using the gel

| | F2 | F4 | F6 | F7 |
|---|---|---|---|---|
| *Pseudomonas aeruginosa* | 15 | 13 | 17 | 7 |
| *Staphylococcus aureus* | 14 | 10 | 13 | 6 |
| *Staphylococcus epidermidis* | 17 | 18 | 15 | 12 |
| *Escherichia coli* | 14 | 13 | 12 | 8 |

The results in Table 4, showed that gels that contained SAEE (F2, F4 and F6) have inhibitory zone diameter (IZD) higher the same extract concentration (300 mg/ml) alone. They all retained the antibacterial property of SAEE and the higher activities noticed may be as a result of the additional antibacterial effect of the preservatives (methyl and propyl paraben). Formulation F7 that did not contain any extract had some inhibitory activity against the test organisms, though the activities were lower than that of the extract alone. The activity may be as a result of the presence of preservatives in the gel formulation.

*Conclusion***:** *Sida acuta* ethanolic extract (SAEE) has concentration-dependent antibacterial activity against the test bacteria, *Pseudomonas aeruginosa, Staphylococcus aureus, Staphylococcus epidermidis,* and *Escherichia coli.* The gels formulated using SAEE as the active ingredient retained the antibacterial activity of SAEE. They even showed comparably higher activity, possibly due to the preservatives' augmenting effect. Gels prepared using carbopol and hydroxypropyl methylcellulose (HPMC) as gelling agents have comparable antibacterial effects against the test bacteria.

*Declaration Of Conflict Of Interest:* The authors declare no conflict of interest.

*Data Availability Statement:* Data are available upon request from the corresponding author

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