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Formulation and Evaluation of Polyherbal Gel Using Catharanthus roseus for Wound Healing Activity

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ABSTRACT
This research aimed to develop a wound-healing gel using the methanolic extract of Catharanthus roseus (Madagascar periwinkle), rich in therapeutic alkaloids. The study focused on formulating the gel, analyzing its physicochemical properties, and evaluating its antibacterial efficacy, particularly against Staphylococcus aureus, as a natural wound care alternative. Catharanthus roseus leaves were obtained from Ch. Sambhajinagar, Maharashtra, India. A methanolic extraction was carried out using maceration and sonication techniques. To identify the presence of alkaloids, flavonoids, tannins, and saponins, phytochemical screening was conducted. Utilizing Carbopol 934 as the gelling agent, the methanolic extract was mixed with excipients such as propylene glycol, triethanolamine, and preservatives to produce the wound-healing gel. The gel was assessed for pH, spread-ability, viscosity, drug content, and antibacterial properties. The agar well diffusion method was used to determine the antibacterial efficacy against Staphylococcus aureus. The presence of bioactive compounds such as flavonoids, alkaloids, tannins, and saponins was verified by phytochemical analysis. The gel exhibited suitable physical properties, including a pH range of 6.62–7.08, good spread-ability (9.7 gm.cm/sec), and appropriate viscosity (5.51 Cps). The drug content was found to be 65.01%, as determined by UV spectrophotometry. The gel showed significant antibacterial activity, with a zone of inhibition of 21.26 mm against Staphylococcus aureus, closely matching the positive control (streptomycin) at 22.68 mm. The Catharanthus roseus wound-healing gel showed antibacterial properties and suitable physicochemical traits, offering a natural alternative to antibiotics.

Keywords: alkaloids, anti-cancer, bioactive compounds,Catharanthus roseus, gel, green chemistry,wound healing

I. INTRODUCTION

The periwinkle plant, known scientifically as Catharanthusroseus, is commonly referred to as Madagascar periwinkle. It is native to various regions of Europe, Africa, and Asia and is a member of the Apocynaceae family. This perennial or semi-evergreen plant is characterized by its dark green, opposite leaves and small, star-shaped flowers, which bloom in various colors, including pink, blue, purple, and white. It develops in rich, properly drained soils that have some shade, developing a height of 15–45 cm and spreading out 15–30 cm. subsequently has been proposed that the name "periwinkle" originates from the Russian word pervinka, which means "first," since it is one of the first flowers to blossom in the spring. [11]

The dried aerial parts of Catharanthus roseus are widely used as a biological source in traditional and modern medicine. Throughout ancient Mesopotamia[20], this plant was traditionally used medicinally from 2600 BC20Although potentially toxic, its roots and shoots have been used to treat a variety of illnesses in ancient Indian medicine, or Ayurveda.C. roseus is particularly notable for its production of around 130 alkaloids, including vincristine and vinblastine, which are critical in treating diseases like Hodgkin's lymphoma, breast cancer, and leukemia. [11]

International Journal of Pharmaceutical Research and Applications
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Leaves of Catharanthus roseus

Various pharmacological properties, including anticancer, antibacterial, antioxidant, antidiarrheal, and wound-healing characteristics, can be observed by the plant[18]. The wound-healing potential of C. roseus is especially noteworthy. The inflammatory phase, which begins tissue repair, the proliferative phase, which is characterized by the formation of granulation tissue and re-epithelialization, and additional phases constitute a component of the dynamic biological process of wound healing and the maturation phase, where the wound achieves tensile strength. Wounds can be categorized based on their nature and severity, such as open or closed wounds, or acute and chronic wounds, depending on the time required for healing. [17]

There are three main approaches to wound healing: primary intention, where wounds are closed surgically using stitches or adhesives; secondary intention, where healing occurs naturally without closure; and tertiary intention, where wound closure is delayed to allow drainage or prevent infection. Treatment strategies for wound care often include cleaning the wound, removing debris, applying dressings, vaccinating against tetanus if necessary, and, in severe cases, surgical intervention. These measures are aimed at preventing infection and promoting optimal healing. Given its pharmacological properties, C. roseus offers great potential in wound management, particularly due to its anti-inflammatory and antimicrobial effects. This study seeks to formulate and characterize an herbal wound-healing gel using C. roseus as a primary ingredient, presenting a natural and effective alternative for wound care solutions. [18]

II. MATERIALS AND METHODS

MATERIALS

The resources and chemicals applied to this research, including methanol, distilled water, phenolphthalein, potassium iodide, sodium thiosulfate, acetic acid, chloroform, Muller-Hinton agar, and remaining reagents were all analytical grade and had been purchased from HI MediaPvt. Ltd., India.

METHODOLOGY

1. Selection and collection of Catharanthus Roseus

Alkaloids occur in abundance throughoutCatharanthus roseus, an established medicinal plant in theApocynaceaefamily. The highest concentration of C. roseus's alkaloids can be observed in the root bark, which varies from 0.15 to 1.34% and, depending on strains, reaches as much as 1.79. Among the approximately 130 indole-group alkaloids found in the plant, 25 are dimeric. Vinblastine and vincristine, two dimeric alkaloids primarily found in the aerial parts, have been widely used to treat human neoplasms. Ajmalicine (raubacine), one of the monomeric alkaloids present in the roots, has been shown to have a wide range of uses in the management of circulatory disorders, particularly the alleviation of blockages in normal cerebral blood flow. The endemic species of plant C. roseus is native to Madagascar, although it was developed elsewhere as a visually appealing and healing plant. The leaves of C.roseuswere collected from the surrounding areas of Ch. Sambhajinagar, Maharashtra, India. The leaves were collected manually. The plant has been identified and authenticated by Dr. U. H. Patil, the Headof Department of Botany of BhogawatiMahavidyalaya, Kurukali by using “The flora of the presidency of Bombay”.

2. Preparation of plant leaf extract using methanol extract

For the purpose of to prepare the methanol extract from C. roseus leaves, use a mixture of maceration and sonication techniques to ensure optimal yield and preservation of bioactive compounds. Initially, all glassware was sterilized to prevent cross-contamination. 75 grams of a relatively coarse powder made from dried leaves were combined with 750 milliliters of a solvent that included 25% distilled water and 75% methanol. After being stored in a sealed container, the mixture was allowed to stand for seven days,

International Journal of Pharmaceutical Research and Applications
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sometimes stirring with a magnetic stirrer to improve blending. Afterward, the liquid extract was separated by straining, and the solid residue was pressed to recover the remaining solvent. The extract was then filtered to remove impurities, followed by evaporation to concentrate the extract. The final product (figure 1& 2) was stored under appropriate conditions to maintain its integrity, and percentage of the initial plant substance's weight was used to determine the extraction yield. [2]

Figure 1. Filtration of extractFigure 2.Evaporation of extract

3. Phytochemical Screening of Hydro-alcoholic extracts of Catharanthus Roseus Leaves Sample extract

After dissolving around 100 mg (0.1 gm) of the extract in 5 ml of distilled water, it is then filtered. The filtrate has been used in the following tests as a sample solution. Using standard qualitative tests, phytochemical analysis of plant extracts was performed to determine the presence of essential bioactive substances like alkaloids, avonoids, tannins, and saponins.[10]

A.Detection of Alkaloids

The assays constructed by Mayer's, Hager's, Dragendorff's, and Wagner's tests were used to determine alkaloids. In Mayer's test, when a few drops of Mayer's reagent were added to 1 ml of the sample, a yellow or white precipitate formed, which signified the presence of alkaloids.In Dragendorff's test,whenDragendorff's reagent was added to 2 ml of the sample, an orange-red precipitate formed, indicating the presence of alkaloids. In Wagner's test, when a prepared iodine-potassium iodide solution was added to the sample solution, the formation of a brown precipitate indicated alkaloids. In Hager's test, a yellow precipitate formed when a few drops of Hager's reagent were added to 2 ml of the extract, indicating the presence of alkaloids.[10]

B.Detection of Flavonoids

The sodium hydroxide, zinc-HCl reduction, lead acetate, and Shinod's tests were performed for screening detect flavonoids.In the sodium hydroxide test, 1 ml of the sample solution was mixed with a few drops of diluted sodium hydroxide, which produced a yellow tint that disappeared when diluted acid was introduced.When a small amount of zinc dust and a few drops of concentrated hydrochloric acid were added to the sample for the zinc-HCl reduction test, a magenta color developed, signifying the presence of flavonoids.In the lead acetate test, 10 mg of the extract was mixed with a few drops of a 10% lead acetate solution; the resulting formation of a yellow precipitate confirmed the presence of flavonoids. In Shinod's test, when 10 drops of diluted hydrochloric acid and a small amount of magnesium were introduced to 1 ml of the sample, and then the presence of flavonoids was confirmed by the appearance of an affluent pink color.[10]

C. Detection of Tannins

Tannins were detected through the ferric chloride test, matchstick test, gelatin test, and phenazone test. A few drops of ferric chloride solution were added to the tannin solution in order to perform the ferric chloride test, resulting in a blue, black, violet, or green precipitate, depending

International Journal of Pharmaceutical Research and Applications
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on the tannin type. The matchstick test involved heating a matchstick near a flame, which caused the wood to turn pink or red due to the formation of phloroglucinol. The occurrence of precipitates in the gelatin test confirmed the presence of tannins. The phenazone testing included adding sodium acid phosphate to an aqueous tannin solution and then a 2% phenazone solution, causing the precipitation of tannins as a bulky, coloured precipitate.[10]

D.Detection of Saponins

The ferric chloride, frothing, and foam tests were used to identify saponins. In the ferric chloride test, a few drops of 10% ferric chloride solution were added to the aqueous extract, and the development of a blackish-blue or green-black color indicated the presence of saponins. For performing the foaming test, 3 mL of the extract was mixed with 10 ml of distilled water, shaking vigorously for 5 minutes, and detecting the development of a froth that resembled honeycomb, which indicated the existence of saponins. 1ml of the extract solution, diluted with 20 ml of distilled water, was shaken in a graduated cylinder for 15 minutes in order to perform the foam test. [10]

4. Formulation of wound healing gel containing methanolic extract of Catharanthus Roseus

The formulation of the wound healing gel included the following ingredients in specific quantities: Catharanthus roseus extract (1 g) served as the primary active component. Carbopol 934 (1 g) was used as a gelling agent to provide the desired consistency. Forthe formulation to be stable and lasting, preservatives such propylparaben (0.11 g) and methylparaben (0.21 g) were used.Propylene glycol (5 ml) acted as a humectant, improving the gel's moisturizing properties. Triethanolamine (1.2 ml) was incorporated to adjust the pH of the gel, making it suitable for skin application. Finally, sufficient distilled water (q.s.) was added to the gel to obtain the volume required. This precise combination of ingredients ensured the gel's effectiveness, stability, and user-friendliness.[14]

Carbopol 934 was precisely weighed and then dissolved in 50 ml of distilled water in a beaker to begin the wound healing gel formulation procedure. To allow the Carbopol to swell, the mixture was allowed to stand undisturbed for 30 minutes. After that, it had been stirred for 30 minutes at 1200 rpm using a mechanical or lab stirrer. During the same a period of time 5 ml of propylene glycol and the required quantity of C. roseus extract were prepared separate.Properly weighed amounts of propyl and methyl paraben were combined with 5 ml of propylene glycol in a separate beaker and thoroughly swirled. During the preparation of the Carbopol dispersion, 1 g of the extract and the preservative solutions were added while being constantly stirred. Furthermore, the remaining distilled water was added to bring the volume reduced to 100 ml.Following that, dropwise additions of triethanolamine were performed to the formulation in order to ensure that the gel had a sufficient consistency and to obtain the ideal skin pH of 6.8–7. [14]

5. Evaluation Tests for Herbal Gel

A. Physical evolution of gel

The gel formulation was evaluated through various sensory and physical tests to assess its quality. To determine the gel's visual appeal, the color was first examined against a white background.Through mixing a small amount of the gel with water and smelling it, the odor was determined. After applying the gel to the skin and analyzing its texture and spread-ability, its consistency was determined. Greasiness has been examined by applying the gel to the skin to determine whether it left any oily residue. The formulation was also evaluated microscopically under 40x magnification to check for any particulate matter or aggregates, ensuring it was free of grittiness. Finally, homogeneity was tested by visually inspecting the gel after it had set in a container, ensuring it appeared uniform without any visible aggregates. [8]

B. pH Determination:

A digital pH meter was used to monitor the pH of a beaker containing around 20 mg of the formulation within 24 hours after manufacturing. [8]

C. Spread-ability:

The Periwinkle's spread-ability was measured by applying 0.5 g of the gel on a pre-marked, 2 cm diameter circle on a glass plate, and then using of a second glass plate. For 5 minutes, a half-kilogram weight was allowed to remain on the top of the glass plate. Following gel development, the circle's diameter was measured. [4]

Formula: M. L / T = S

Here,weight attached to the upper slide is denoted by M. L is the glass slide length. T is the period of time required to split the slides D.

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 1 Jan - Feb 2025, pp: 1626-1635 www.ijprajournal.com ISSN: 2456-4494

D. Viscosity test:

The Brook eld Viscometer was used to measure the prepared gel's viscosity. Prepared the gel with different concentrations. A level indicator can be used to set the instrument's base level. The spinning device was connected to the instrument after being cleaned. After that, the spinning device was turned around in the gel until the viscometer displayed a consistent reading. Compute the average value by repeating the procedure three times. [14, 16]

E. Drug Composition:

A precisely weighed amount of gel (1gm) in 100ml volumetric ask can be used to calculate the formulation's drug composition. After adding 70 ml of methanol, it was shaken. The volume was increased to 100 ml. A suitable filter paper was used to effectively filter the contents. A UV/visible spectrophotometer adjusted at 250 nm had been employed to measure the drug concentration (extract) after 1 ml of filtrate had been acquired and diluted.[16]

6. Chemical Tests:

A. Acid value amount: -

The acid value was determined by dissolving 0.5 grams of gel in 10 times pure alcohol. After 5 min of heating on a hot plate, when addition two to three drops of phenolphthalein indicator, the liquid was titrated with 0.1 N KOH until it taken up a light pink color. Acid Value = 56.11 × KOH Titre value × N/Sample Weight. [13]

B. Peroxide value amount: -

A solution of chloroform, 30 ml of acetic acid, and 5 grams of the control (base) gel sample and formulations were addedto a separate 200 ml flask and stirred gently. After that, 30 mL of water was added, and 0.5 mL of potassium iodide solution was added while being continuously shaken. After that, the mixture was agitated violently while a 0.1 M sodium thiosulfate solution was added to correct it. When the yellow color almost disappeared the titration's, consequence was seen. After adding 0.5 mL of 1% starch, the titration was vigorously shaken to evacuate most of the iodine from the chloroform layer until the blue color disappeared. [4]

Peroxide value amount = M × S × 1000/gm sample

Here,
S = Sodium thiosulfate ml.
M = sodium thiosulfate solution's molarity.

7. Antibacterial activity of polyherbal gel:

Using a slightly modified agar well diffusion method, the antibacterial activity of the developed blend was tested against a Gram-positive (S. aureus NCIM 2654) bacterial strain. During further studies, the corresponding test pathogen suspension has been prepared in sterile saline. Pathogens have been spread on plates using a sterile spreader after being inoculated on the surface of sterile Muller and Hinton agar for the antimicrobial activity test. A sterilized cork borer with a 0.6 cm diameter was then used to create the agar well aseptically. The test sample was then added to the several wells of the corresponding test pathogen at a weight of 25–100 mg/ml. After 20 minutes of sample diffusion in a culture medium at 4 °C, the plates were moved to an incubator adjusted at 37 °C for 24 hours. Additionally, as a positive control, the results were contrasted with the well containing 1000 mg/ml antibiotic Streptomycin.[14]

III. RESULTS:

A summary of the hydro-alcoholic extracts of C. roseus leaves that completed qualitative phytochemical screening are listed in table 1.

Table 1. Screening of Phytochemicals

Sr.no	Phytochemicalconstituents	Typeoftest	Result
1.	Alkaloids	Mayer'stest	+
		Dragandroff'stest	+
		Wagner'stest	+
		Hager'stest	+
2.	Flavonoids	Sodiumhydroxidetest	+
		Zinc-HClreductiontest	+

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 1 Jan - Feb 2025, pp: 1626-1635 www.ijprajournal.com ISSN: 2456-4494

		Leadacetatetest	+
		Shinod'stest	+
3.	Tannins	Matchsticktest/Catechintest	+
		Ferricchloridetest	+
		Gelatintest	+
		Phenazone test	+
4.	Saponins	Ferricchloridetest	+
		FrothingTest	+
		Foamtest	+

Physical evaluation of gel:
On the basis of Organoleptic properties ofher balextracti.e C. roseusfollowingobservationsare shown in table.2.

Table 2. Observations of organoleptic properties

Sr.no	Test	Observations
1	Color	Darkgreen
2	Odour	Characteristics
3	Greasiness	Non-greasy
4	Consistency	Smooth
5	Homogeneity	Homogenous

Formulation of wound healing gel containingmethanolic extract of Catharanthus Roseus:

The precisely measured Carbopol 934 has been submerged in 50 ml of distilled water and permitted swelling for 30 minutes. A mechanical stirrer was then used to frequently blend increasing amounts of Carbopol for 30 minutes at 1200 rpm. Separately, 5 ml of propylene glycol and 1 g of Catharanthus roseus methanolic extract were mixed. Also, 5 ml of propylene glycol was mixed until it was compatible after measured amounts of methyl paraben and propyl were added, which was subsequently mixed until it was uniform. During the full dispersion of Carbopol, the extract and preservative solutions were added while stirring continuously. In order to obtain an adequate gel consistency and the ideal skin pH (6.8–7), triethanolamine was added dropwise to the final volume, which was adjusted with distilled water to 100 ml. Using the extract of Catharanthusroseus's bioactive properties, the resultant gel was uniform and suitable for use in wound healing applications as showing in figure 3.

Figure 3. Gel formulation

pH Determination:

After 5 days of varying storage conditions, it was determined to be between 6.63 and 7.09. The base and formulations' pH were not significantly different after 5 days at 8°C, and the results were significantly higher than the control (base) over the duration of a month ($p < 0.03$). Curiously, the formulation showed a higher pH change (7.08) at 40°C, although the others stayed relatively constant over the course of the 5 days analysis. The following table 3 shows the formulation data at 40°C that were determined to be significant.

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 1 Jan - Feb 2025, pp: 1626-1635 www.ijprajournal.com ISSN: 2456-4494

Duration	Storagecondition	pH
1 day	8 ^{0}C	6.63±0.22
	40 ^{0}C	6.91±0.17
3 days	8 ^{0}C	6.87±0.19
	40 ^{0}C	6.93±0.23
5 days	8 ^{0}C	6.80±0.38
	40 ^{0}C	7.08±0.14

Table3.pH of the formulation at different storage condition

Spread-ability:

After analysis, the formulation's spread-ability was determined to be 9.7 gm.cm/sec. It was discovered that the formulation had significant spread-ability.

Viscosity test:

Subsequently was determined that the formulations' rheological and viscosity properties were 5.51 Cps. The data of viscosity in formulation were significant temperatures shown in Figure 4.

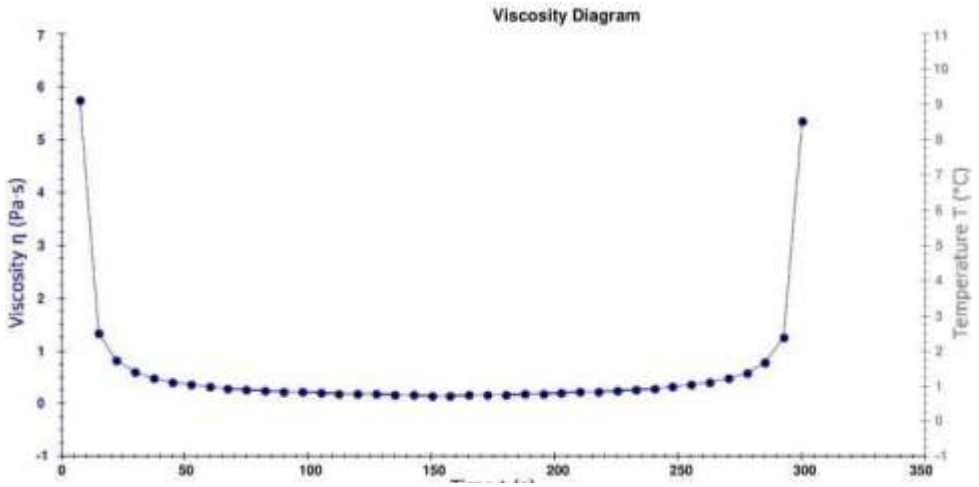

Figure4.Graph (viscosity vs time)

Drug content determination

The observations of Calibration curve and absorbance of herbal extract of C.roseusleaves shown in figure5. After the analysis of the extract release using UV spectrophotometer (UV – 1900, Shimadzu, Japan) at 410 nm, at dilutions of 10,20,30,40and 50 it was 65.01%.

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 1 Jan - Feb 2025, pp: 1626-1635 www.ijprajournal.com ISSN: 2456-4494

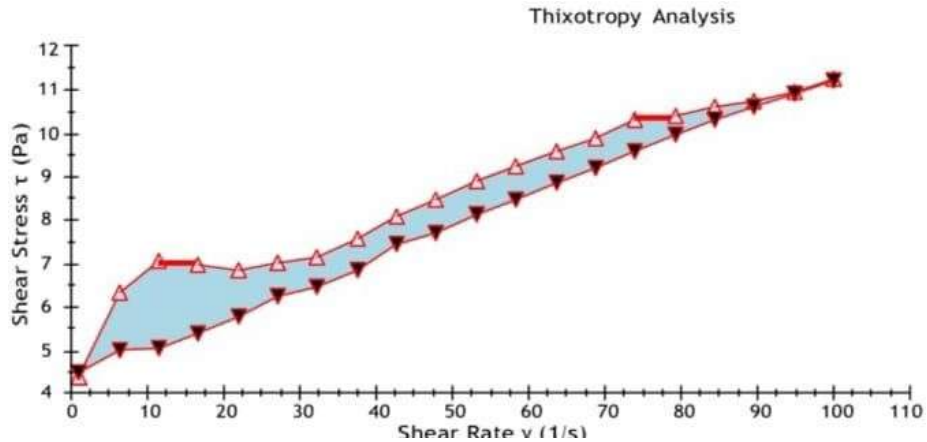

Figure 5. Graph (shear stress vs shear rate)

Chemical tests

Table 4 includes an explanation of the formulations' acid value, peroxide value, and overall fatty matter after 15 days of storage under various conditions. The acid value ranged from 2.65 to 2.91, the peroxide value ranged from 1.49 to 1.88, and the total fatty matter ranged from 15.01 to 15.5. Notably, there were significant variations ($p < 0.06$) between the peroxide value values for formulations maintained at 8°C and 40°C.

Table4.Calculatedvalues ofchemicaltests

Duration	Storage condition	Acid value	Peroxidevalue
5Days	8^0C	2.65	1.49
	40^0C	2.59	1.53
10Days	8^0C	2.63	1.55
	40^0C	2.74	1.62
15Days	8^0C	2.85	1.64
	40^0C	2.91	1.67

Anti bacterial activity of gel

The zone of inhibition of the herbal formulation against S. aureus, as presented in table 5, along with the control at varying concentrations. The data revealed a clear pattern, with the zone of inhibition increasing as the concentration of the herbal formulation was raised. When tested at the same concentration, streptomycin demonstrated an inhibition zone that was slightly larger than that of the polyherbal gel at 100 mg/ml. The herbal formulation produced a zone of inhibition of 21.26 mm, while streptomycin showed a zone of 22.68 mm. These findings, shown in Figures 6 and 7, suggest that the polyherbal gel could be a promising alternative to conventional antibiotics for treating S. aureus infections.

Table5.Zone of inhibition

Sample	Concentration of sample (mg/ml)	Zoneofinhibition (mm)
Herbal formulation	25	17.10
	50	18.05

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 1 Jan - Feb 2025, pp: 1626-1635 www.ijprajournal.com ISSN: 2456-4494

against S. aureus	75	19.75
	100	21.26
Streptomycin against S.aureus	100	22.68

Figure 6.Zone of inhibition of control and Herbal formulation against *S. aureus*

Figure7.Standard(streptomycin)

IV. DISCUSSION

The rats provided a 100 mg/kg/day ethanol extract showed decreased wound area, accelerated wound contraction, reduced epithelization period, and increased dry weight and hydroxyproline content in granulation tissue, indicating that C. roseus leaf extract had significant wound-healing activity. The herbal wound-healing gel formulated with methanolic C. roseus extract exhibited favourable physical properties such as appropriate pH, spread-ability, viscosity, and antibacterial activity against S. aureus, comparable to streptomycin at higher concentrations. These results suggest that the gel could serve as an effective topical alternative to conventional wound treatments, though further clinical studies are needed for validation.[11]

V. CONCLUSION

This study successfully formulated a wound-healing gel using the methanolic extract of C. roseus (Madagascar periwinkle), a plant renowned for its medicinal properties, including its antimicrobial, antioxidant, and wound-healing potential. The gel was made with adequate excipients and tested for a number of factors, such as pH, spreadability, viscosity, and medication content, which indicates that it is suitable for skin application.

The presence of several significant beneficial substances was confirmed by the phytochemical screening, including alkaloids, flavonoids, tannins, and saponins, which contribute to the plant's therapeutic effects. The gel exhibited a promising zone of inhibition against Staphylococcus aureus, a common pathogen in wound infections, with results comparable to those of streptomycin, suggesting its potential as an effective antimicrobial agent. Additionally, the formulation showed favorable physical characteristics, good spreadability, and stability across different storage conditions, making it a viable candidate for wound care. The antibacterial activity further supports its potential as an alternative to conventional antibiotics, particularly for managing S. aureus infections. An essential instrument in the development of herbal-based wound-healing products, the gel derived from C. roseus provides a safe, natural, and effective alternative for wound healing.

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