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DEVELOPMENT AND CHARACTERIZATION OF SILVER NANOGEL CONTAINING HERBAL EXTRACT

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ABSTRACT

The present study was to develop a herbal Silver nanogel formulation using hydroalcoholic flowers extract of *Desmodium gangeticum*s so as to provide a natural herbal based antimicrobial, activity over the skin disease. Further the formulation developed should be effective, easy to use nonirritant and cosmetically acceptable. Herbal medicines get Preferences over modern medicines due to minimum side effects and also healthier Option for the patients. This novel way have overcome the issues by Improving absorption of drugs, sustained release of drug, controlled release of drugs, by reducing toxicity of drugs etc. Increasing demand for natural products, the development of Silver nano-formulations containing natural active ingredients requires in-depth knowledge of the substances used, methods of obtaining, and stability profiles to ensure product quality, efficacy, and safety. the study of medicinal plants to obtain active metabolites with therapeutic properties, as well as the different nano-systems responsible for carrying these molecules. Due to the wealth of biodiversity found in the world, many species are submitted to the extraction process for several purposes. However, identifying, classifying, and quantifying the constituents of herbal matrices are crucial steps to verify their therapeutic potential. In addition, knowing the techniques of production and elaboration of nanotechnology products allows the optimization of the incorporation of herbal extracts as an innovation target. For studies to be successful, it is necessary to exhaust experimental results that guarantee the efficacy, safety, and quality of natural nanosystems, with the objective of obtaining reliable answers in nanotechnology therapy.

KEYWORDS: Desmodium gangeticums flowers extract, Antimicrobial activity, Silver Nanoparticle, Silver Nanogel

1. Introduction

Nanogels are of nanoscale size and three-dimensional hydrogel materials formed by networks of cross-linked swellable polymer. They exhibit potential to hold water, without actually dissolving into the aqueous medium. Nanogels can be synthesized by using a variety of naturally occurring polymers, synthetic polymers, or a combination of the both. Nanogels gained greater attention as a carrier system due to their capability to entrap different types of drug molecules. The nanogel can be designed in such a way that it becomes compatible with small molecules including drugs and fluorophores, peptides, proteins, and nucleic acids as well as inorganic nanoparticles composed of gold, silver, or iron oxide.By modifications in chemical composition of the nanogels, their characteristics such as charge, size, porosity, amphiphilicity, degradability, and softness can be adjusted. They are mostly spherical in shape. They can be also designed to have either a core-shell or a core-shell-corona structure, with the cross-linked layer for structural integrity.

Being hydrophilic in nature, nanogels are highly compatible with the molecules with high-loading capacity. They acquire high water content, biocompatibility, as well as desirable mechanical properties. Nanogels offer targeted drug delivery in a controlled manner due to having characteristic properties such as softness, stimuli-responsive behavior, and swelling. They can successfully protect the cargo from elimination and degradation. Nanogels display distinctive advantages for polymer-based drug delivery systems. They have a large surface area for multivalent bioconjugation and a strong interior network that facilitates incorporation of biomolecules. Nanogels have an ability to hold biological molecules via electrostatic, van der Waals, and/or hydrophobic interactions or covalent bonding with the polymer chains. Compared to liposomes and polymeric micelles, this loading capacity of the nanogel is high. After drug loading, nanogels collapse and form a stable nanoparticle which encapsulates the biological agents. During the collapse of the drug-nanogel complex, hydrophilic polymer chains becomeexposed at the surface and form a protective layer around the nanogel.

Silver is a soft white lustrous element. Metallic silver itself is insoluble in water, but metallic salts such as $AgNO_3$ and silver chloride are soluble in water. AgNPs are unique in nanoscale system due to the ease in its synthesis and chemical modifications. AgNPs are used in the development of new technologies in the areas of electronics, material sciences and medicine and because of their extensive applications in various areas more research is being conducted on the AgNPs by the scientists throughout the world.

2. MATERIALS AND METHODS

2.1 Collection of plant material

Leaves of *Desmodium gangeticum* were collected from Vindhya Herbal Nursery Bhopal in the month of September, 2022. Drying of fresh plant parts was carried out in sun but under the shade. Dried Leaves of *Desmodium gangeticum* were preserved in plastic bags, closed tightly and powdered as per the requirements.

2.2 Extraction procedure

Leaves of *Desmodium gangeticum* were shade dried at room temperature. The shade dried plant material was coarsely powdered and subjected to extraction with petroleum ether by maceration. The extraction was

continued till the defatting of the material had taken place. Dried powdered Leaves of *Desmodium gangeticum* has been extracted with hydroalcoholic solvent (ethanol: water: 75:25) using maceration process for 48 hrs, filtered and dried using vacuum evaporator at 40°C.

2.3 Determination of percentage yield

The percentage yield of each extract was calculated by using following formula:

$$\text{Percentage yield} = \frac{\text{Weight of Extract}}{\text{Weight of powdered drug}} \times 100$$

2.4 Phytochemical Screening

The *Desmodium gangeticum* extract acquire was subjected to the precursory phytochemical analysis following standard methods by Khandelwal and Kokate. The extract was screened to identify the presence of various active principles of Carbohydrate, alkaloids, glycosides, phenols, flavonoids, Terpenoids, Saponins, Tannin.

2.5 Biosynthesis of Silver nanoparticles

AgNO3 powder was dissolved in distilled water to prepare 10 mM AgNO3 stock solution from which a series of 1 mM, 2 mM and 3 mM AgNO3 solutions were prepared59. The AgNO3 solutions were mixed with the aqueous extract of Leaves of Desmodium gangeticum at a ratio of 1:1, and 1:2 to a volume of 50 mL in a flask. The flask was wrapped with an aluminum foil and was then heated in a water bath at 60°C for 5 hours. Furthermore, the mixture was stored in the refrigerator for the further use.

Table 2.1: Different formulation of Silver nanoparticles

Formulation Code	Extract (mg)	AgNO3 (mM)	Ratio
F1	500	1	1:1
F2	500	2	1:1
F3	500	3	1:1
F4	500	1	1:2
F5	500	2	1:2
F6	500	3	1:2

2.6 Characterization of synthesized silver nanoparticles formulations

2.6.1 Microscopic observation of prepared silver nanoparticles

An optical microscope with a camera attachment was used to observe the shape of the prepared silver nanoparticle formulation.

2.6.2 Percentage Yield

The prepared silver nanoparticle with a size range of 200-300nm were collected and weighed from different formulations. The measured weight was divided by the total amount of all non-volatile components which were used for the preparation of the microspheres.

$$\% \text{ Yield } = \frac{\text{Actual weight of product}}{\text{Total weight of drug and polymer}} x\ 100$$

2.6.3 Entrapment efficiency

Entrapment efficiency was determined by dialysis method. Silver nanoparticle entrapped extract were isolated from the free drug using dialysis method.

2.6.4 Surface charge and vesicle size

The particle size and size distribution and surface charge were obtained by Dynamic Light Scattering method. Zeta potential measurement of the silver nanoparticles was based on the zeta potential that was estimated according to Helmholtz–Smoluchowsky from electrophoretic mobility. For measurement of zeta potential, a zeta sizer was used with field strength of 20 V/cm on a large bore measures cell. Samples were diluted with 0.9% NaCl adjusted to a conductivity of 50 lS/cm.

2.7 Formulation development of gel

Measured amounts of methyl paraben, glycerin, polyethylene glycol and Silvernanoparticle of *Desmodium gangeticum* leavess extract were dissolved in about 100 ml of water in a beaker and stirred at high speed using mechanical stirrer (or sonicator). Then Carbopol 940 was slowly added to the beaker which contained above liquid while stirring. Neutralized the solution by adding a slow, constantly stirring triethanolamine solution until the gel formed.

Table 2.2: Formulation of gel

Ingredients (mg)	**F1**	**F 2**	**F3**
***Desmodium gangeticum* extract**	500	500	500
Carbopol 940	500	1000	2000
Glycerin	10	10	10
Polyethylene Glycol 600	0.2	0.2	0.2
Methyl Paraben	0.08	0.08	0.08
Triethanolamine	1.0	1.0	1.0
Distilled Water	100 ml	100ml	100ml

2.8 Evaluation of gel

A. Appearance and consistency:

The physical appearance was visually checked for the texture of gel formulations and observations reported.

B. Washability

Prepared formulations were added to the skin and then manually tested for ease and degree of washing with water, and findings were recorded.

C. Extrudability determination of formulations

The gel formulations were filled into aluminium collapsible tubes and sealed. The tubes were pressed to extrude the material and the extrudability of the formulation was noted.

D. Determination of Spreadability

Spreadability is a concept defined to denote the degree to which the gel applies readily to the skin upon application. A formulations medicinal potency also depends on its spread-value. Spreadability is expressed in terms of the time taken by two slides in seconds to slip off the surface, put between them, under the application of a certain load. The less time required for two slides to separate, the greater the spreadability. The experiment was repeated and the average of 6 such determinations was calculated for each formulation.

$$\boldsymbol{Spreadability} = \frac{m * l}{t}$$

Where, S=Spreadability (gcm/sec)

m = weight tied to the upper slide (20 gram)

l= length of glass slide (6cm).

t = time taken is seconds.

E. Determination of pH

Digital pH meter had calculated the pH of the gels. Measurements of pH were repeated twice for each formulation.

F. Drug content

The composition of the medication was measured by taking 1gm of gel mixed with methanol in 10 ml volumetric flask. 3 ml of stock solution has been mixed with 1 ml $AlCl_3$ solution of 2 %. The mixture was vortexed for 15s and allowed for the color production to stand at 40°C for 30min, using a spectrophotometer the absorbance was measured at 420 nm.

G. Viscosity

The viscosity of the prepared gel was determined by a Brookfield digital viscometer. The viscosity was assessed using spindle no. 6 at 10 rpm at ambient room temperature of 25-30^{o}C. ***In* H. *vitro* diffusion profile**

In vitro diffusion experiments were performed using Franz diffusion cell for all formulations. A weighed quantity of formulation equivalent to 1g of gel was taken on to the rat skin and was immersed slightly in 100 ml of receptor medium, which was continuously stirred. The whole network had been held at 37±1^{o}C. At different time intervals of up to 4 hours, an aliquot of 5 ml was extracted, and spectrophotometrically measured at 295 nm. The diffusion media was replaced with an equal volume of fresh diffusion medium after each withdrawal. For each time period the total percent release was measured.

2.9 Antimicrobial activity of Silver nanoparticle gel

The antimicrobial sensitivity test is employed on to the all the microbes used under present study with extract and silver nanoparticles obtained from Leaves of *Desmodium gangeticum.* For this experiment 6 mm diameter wells, stock of 100 mg/ml of extract separately applied on it. A nutrient agar plate is seeded with particular microbes with the help of spread plate technique prior and left for 5 minutes then incubated for 24 hours at 37ºC. After incubation, plates were observed to see the sensitivity of extracts towards test bacteriums at particular concentration in the form zone of inhibition. The well diffusion method was used to determine the antimicrobial activity of the extract prepared from the Leaves of *Desmodium gangeticum* using standard procedure. There were 3 concentration used which are 25, 50 and 100 mg/ml for each extracted phytochemicals in antibiogram studies.

3. RESULTS AND DISCUSSION

3.1 Determination of Percentage Yield

Table 3.1: % Yield of flowers of *Desmodium gangeticum*s

S. No.	Solvents	% Yield
1.	Pet ether	8.92
2.	Hydroalcoholic	10.47

3.2 Phytochemical screening of extract

Table 3.2: Phytochemical screening of extract *of* flowers of *Desmodium gangeticum*s

S. No.	Constituents	Hydroalcoholic Extract
1.	**Alkaloids**	
	Mayer's Test	+ve
	Wagner's Test	+ve
	Dragendroff's Test	+ve
	Hager's Test	+ve
2.	**Glycosides**	
	Modified Borntrager's Test	-ve
	Legal's Test	-ve
3.	**Flavonoids**	
	Lead acetate	+ve
	Alkaline test	-ve

4.	**Phenol** Ferric chloride test	 +ve
5.	**Proteins** Xanthoproteic test	 -ve
6.	**Carbohydrates** Molisch's Test Benedict's Test Fehling's Test	 +ve -ve -ve
7.	**Saponins** Froth Test Foam Test	 -ve -ve
8.	**Diterpenes** Copper acetate test	 -ve
9.	**Tannins** Gelatin Test	 +ve

3.3 Result of Herbal extract and excipient compatibility

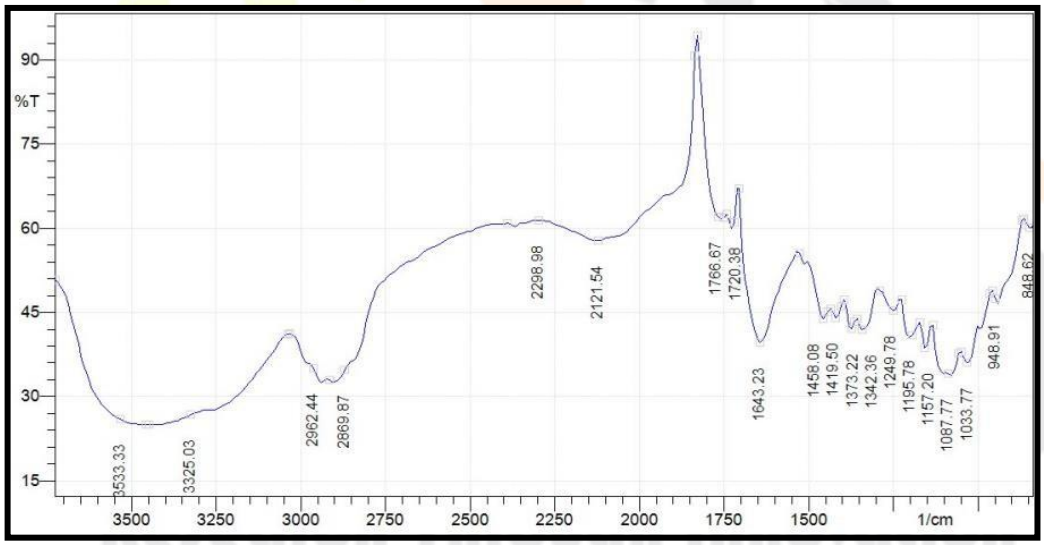

Figure 3.1: FTIR Spectrum of silver nanoparticle and Carbopol 934 *Desmodium gangeticum*s hydroalcoholic extract AgNPs + Carbopol 934

3.4 Characterization of Optimized formulation of Silver nanoparticles

a. Percentage Yield

Practical yield of the prepared silver nanoparticles was in the range of 61.51±0.73 to 68.64±0.21.

Table 3.3: Determination of % yield of prepared formulations

Formulation	% Yield
F1	67.28±0.75
F2	62.75±0.27
F3	67.18±0.46
F4	68.64±0.21
F5	61.51±0.73
F6	65.85±0.49

b. Results of % Entrapment efficiency

The EE was found to be in the range from 0.631±0.049 to 0.909±0.028%.

Table 3.4: Determination of entrapment efficiency of prepared formulations

Formulation	Percentage entrapment efficiency (Flavonoid mg/100mg quercetin equivalent)
F1	0.735±0.025
F2	0.685±0.077
F3	0.784±0.073
F4	0.909±0.028
F5	0.631±0.049
F6	0.829±0.024

c. Microscopic observation of prepared silver nanoparticles optimized formulation F4

Scanning Electron Microscope analysis was carried out to study the morphology of synthesized *Desmodium gangeticum*s silver nanoparticles are found to be discrete and spherical shape.

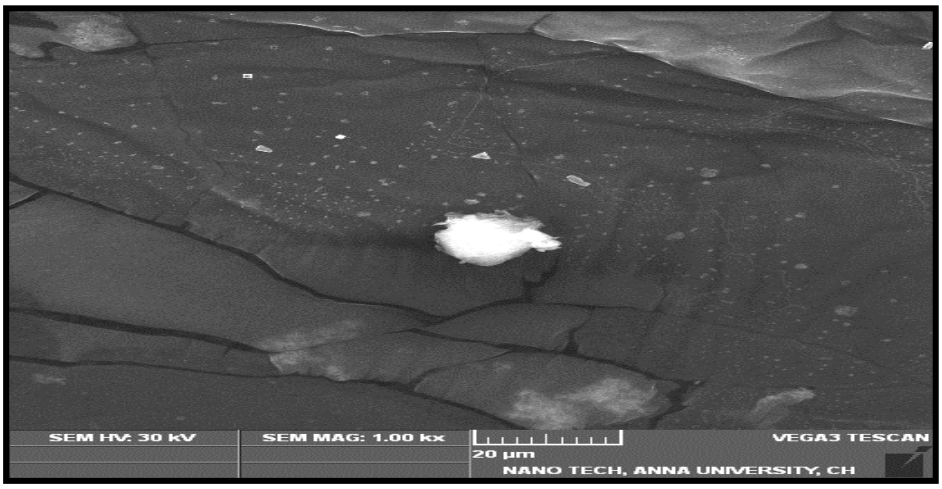

Figure 3.2: Different magnification SEM of prepared silver nanoparticles optimized formulation F4

d. Average particle size and zeta potential

Average particle size of nanoparticles was found to be 229.3 nm. Zeta potential of prepared nanoparticles was found -39.7 mV. It was found that higher the zeta potential less will be the particle aggregation, due to electric repulsion and hence more will be the stability of nanoparticles.

Table 3.5: Characterization of Optimized formulation of silver nanoparticles for average particle size and zeta potential

Formulation	Average Particle size (nm)	Zeta Potential (mV)
F4	229.3	- 39.7 mV

3.5 Results of Evaluation of formulated Silver Nanogel

3.5.1 Results of Physical Characteristics

Table 3.6: Results of Physical Characteristics

Formulation	Colour	Clogging	Homogeneity	Texture	Washability	Extrudability
F1	Brown	Absent	Good	Smooth	Good	Good
F2	Brown	Absent	Good	Smooth	Good	Good
F3	Brown	Absent	Good	Smooth	Good	Good

3.5.2 Results of Spreadability

Table 3.7: Results of spreadability of Silver Nanogel

Formulation	Spreadability* (gcm/sec)
F1	9.27±0.25
F2	8.79±0.55
F3	7.27±0.85

*Average of three determinations (n=3 ±SD)

3.5.3 Results of Viscosity

Table 3.8: Results of Viscosity of Silver Nanogel

Formulation	Viscosity* (cp)
F1	3497
F2	3176
F3	3064

*Average of three determinations (n=3 ±SD)

3.5.4 Results of flavonoid Content

Table 3.9: Results of flavonoid content of Prepared Silver Nanogel using $AlCl_3$ method

Formulation	Flavonoid Content (mg/100mg)
F1	0.647±0.071
F2	0.788±0.045
F3	0.817±0.085

*Average of three determinations (n=3 ±SD)

3.5.5 Results of pH

Table 3.10: Results of pH of gel

Formulation	pH
F1	6.98±0.02
F2	7.12±0.01
F3	7.03±0.02

*Average of three determinations (n=3 ±SD)

3.5.6 Results of *In Vitro* Drug Release Study

Table 3.11: *In vitro* drug release study of prepared gel formulation

S. No.	Time (hr)	% Cumulative Drug Release		
		F1	F2	F3
1	0.25	17.45	14.14	10.23
2	0.5	32.98	29.56	22.56
3	1	49.98	44.98	35.25
4	1.5	65.58	58.74	45.56
5	2	81.56	71.95	57.32
6	2.5	94.65	84.98	69.26
7	3	99.85	92.23	84.45
8	4	-	98.02	99.27

3.6 Antimicrobial activity of extract and prepared silver nanoparticles gel

Table 3.12: Antimicrobial activity against selected microbes

S. No.	Name of drug	Microbes	Zone of inhibition		
			25 mg/ml	50 mg/ml	100 mg/ml
1.	Extract	*Staphylococcus aureus*	10±0.71	13±0.83	18±0.86
2.	Silver nano gel		11±0.27	14±0.16	20±0.04

SUMMARY AND CONCLUSION

AgNPs are also known to have unique properties in terms of toxicity, surface plasmon resonance, and electrical resistance. Based on these, intensive works have been conducted to investigate their properties and potential applications for several purposes such as antimicrobial agents in wound dressings, anticancer agents, electronic devices, and water treatment. Small portion of the dried extracts was subjected to the phytochemical tests using standard methods. Phytochemical screening reveals that presents of various phytoconstituents such as saponins, flavonoids, phenol, tannin, carbohydrates and proteins separately for hydroalcoholic extract of *Desmodium gangeticum*s. The total Practical yield of the prepared silver nanoparticles was in the range of 61.51±0.73 to 68.64±0.21. The yield of nanoparticles decreased with increasing the concentration of extract and silver nitrate, which might be due to generation of stickiness by extract. The EE was found to be in the range from 0.631±0.049 to 0.909±0.028%. It was observed that the encapsulation efficiency depends on the concentration of extract and silver nitrate ratio. On the basis of high yield, and encapsulation efficiency batch F4 was observed as optimized batch for the preparation of silver nanoparticles.

The Optimized gel formulation F3 release approx 10.23 percent drug within 15 minutes and approx 99.27 percent of drug release in 4 hours. When the regression coefficient values were compared, it was observed that 'R^2' values of first order were maximum i.e. 0.981hence indicating drug releases from formulation follow first order release kinetics. In low concentrations, silver has been indicated as non-toxic material to humans, and it has been assessed as a promising material in pharmaceutical and biomedical fields. Although silver nanoparticles have been investigated for their superior physical, chemical, and biological properties, some issues related to synthesis methods, potential risks to health and the environment and scale-up production still require future works to promote a safer and more efficient use of the nanoparticles. Antibacterial study of the developed formulation showed higher inhibitory activity against *Staphylococcus aureus*, when compared to the extract. The results of our study concluded that silver nanoparticle of Desmodium gangeticums in aqueous gel base may be used for the treatment of Skin infection.

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