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FORMULATION AND EVALUATION OF NANOMIEMGEL OF *SAMADERA INDICA*

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Abstract

The goal of Novel drug delivery system of herbal extract is to reduce toxicity, to improve drug efficacy, to improve better therapeutic effect, etc. Novel Drug Delivery System is better than conventional drug delivery system. After the collection of leaves prepared extract for experimental work by using Soxhlet apparatus. Preformulation study of extract was studied following parameters such as Preliminary phytochemical screening, % yield of extract, SEM, antifungal study. Solvent evaporation method was used to developed nanomiemgel. Characterisation of NMG was done by pH was 6.7, By Transmission Electron Microscopy (TEM), By Scanning Electron Microscopy (SEM). Viscosity, Spreadibility, Skin Irritation was not present, Homogeneity, Gritiness, drug release of Nanomiemgel was optimized. Purpose of this study minimising toxic effect, reducing dosing frequency, better therapeutic effect, increase bioavailability, etc

***Keywords*:** Nanomiemgel, Nanoemulsion, Nanomicelle, *Samadera Indica*.

Introduction

Novel Drug delivery System (NDDS) refers to the approaches, formulations, technologies, and systems for transporting a pharmaceutical compound in the body as needed to safely achieve its desired therapeutic effects. NDDS is a combination of advance technique and new dosage forms which are far better conventional drug delivery system (Dwivedi *et al.,* 2014; Nishiyama *et al.,* 2016; Somagoni *et al.,* 2014). Synthetic pharmaceuticals drugs are found out to be relatively more expensive and produce numerous undesirable side-effects despite their strong pharmacological action. Thus people nowadays are shifting back to herbal drugs, which are originated from the nature and claim to be safer (Waisi *et al.,* 2012; Jolly *et al.,* 2014).

Gels are biphasic swollen networks occupying both the cohesive characteristics of solids, and the diffusive transport properties of liquids. In contrast to ointments and creams, gels often grant immediate release of active pharmaceutical ingredient, regardless of the water solubility of the drug (Jamadar & Husen 2017; Deepa & Rama 2015). They have limited risk of inflammation and unwanted reaction and are remarkably biocompatible. Gels are easy to apply on the skin and there is no need to remove it. Gels for skin application possess various agreeable characters. They are thixotropic and non-greasy having emollient action. Gels are readily spreadable that can be conveniently wiped out upon washing since the gels are washable with water (Yadav *et al.,* 2012).

A gel is a semi-solid that can have properties ranging from soft and weak to hard and tough. Gels are defined as a substantially dilute cross-linked system, which exhibits no flow when in the steady-state. A gel has been defined phenomenologically as a soft, solid or solid-like material consisting of two or more components, one of which is a liquid, present in substantial quantity (Viswanand *et al.,* 2012; Diazdellavalle *et al.,* 2011).

Materials and Method

Plant Material

Plant was obtained and procured from DKC Agrotech Pvt. Ltd., New Delhi, India.

Chemicals

All chemicals obtained and procured from laboratory of Department of Pharmacy, Dr. APJ Abdul Kalam University, Indore, [M. P.], India.

Plant Profile

Common name: *Samadera Indica*

Synonyms: Karinjotta, QuassiaIndica, Lokhandi, Niepa bark tree

Preparation of Extract

Firstly leaves were carefully collected and separate out and washed to remove impurities then leaves were dried in sunlight, blend in the mechanical grinder and powder then passed through sieve no 40. The extraction process was done by hot extraction method using soxhlet apparatus. Take a 50gm of fine powder in round bottom flask were soaked in 250ml of methanol for 24 hours with intermittent shaking. This process was continued until the solvent became clear and collected the sample in container, then evaporating the solvent until the extract given in crude form.

Determination of Extraction Yield (% Yield)

The yield (%W/W) from the dried extracts was calculated as

$$\%\text{Yield} = (W_1 \text{ X } 100)/W_2$$

Where W_1 is the weight of extract after evaporation of solvent and W_2 is the weight of the plant powder.

Preliminary phytochemical investigation

After the crude drug obtained methanolic extract was used in preliminary phytochemical studies for presence of various phytochemical constituents. The extract of *Samadera indica* leaves present some bioactive compounds such as flavonoids, tannins, alkaloids, phenolic compounds, triterpenes, resins, proteins etc.

Antifungal study

In antifungal study firstly prepared different concentrations of methanolic extracts of *Samadera indica*. Comparison of methanolic extract with standard sample of fluconazole. There are strains of fungi such as *Aspergillus niger, Candida albicians.*

Antifungal properties by MIC method

The culture of saboraud dextrose agar medium (Fungi) plates and stored in slants as stock cultures and incubated at 27^{o} C for 48 h for fungi. The test of such substances against *Aspergillus niger* and *Candida albicans.* It was determined by liquid broth method of two fold serial dilution technique. In this assay, the minimum concentration of each test substances required to inhibit the growth of microorganism was determined by the production of turbidity. The standard used in the study was fluconazole.

Table 1: Antifungal activity

Organism	Zone of inhibition (mm)			
	Standard (Fluconazole)	MethanolicExtract		
		10ug/ml	20ug/ml	30ug/ml
Candida Albicans	17.9±0.02	-	-	10.28±0.29
Aspergillus Niger	20.22±0.02	-	11.9±0.16	15.20±0.62

Formulation

Formulation of nano-emulsion

Nanoemulsion (NEM) was prepared by first dissolving Extract (800 mg) in 8 mL of olive oil and miglyol (1:1), followed by the addition of 6 mL of "Polysorbate 80 and Transcutol" mixture (1:1). The oil and surfactant mixture-containing drug were sonicated for about 15 minutes to get clear oil & surfactant mixture. To the mixture, 11 mL of deionised water was added while homogenizing to get a primary emulsion. The obtained o/w emulsion was homogenized further for 5 minutes at 3000 rpm to obtain a micro emulsion.

Formulation of nanomicelle

Nanomicelle was prepared with Vitamin E TPGS using the solvent evaporation method where the organic solvent was removed through evaporation. The Vitamin E TPGS (7.55 gm), Extract (800 mg) were added to 2 mL of acetone. When a clear solution was obtained, 25 mL of distilled water was added. Then the organic solvent was removed gradually through evaporation. Change of solvent quality and hence, selectivity, from organic to aqueous was gradual; the polymer and the extract were able to aggregate into micelles rather than precipitating from the solution into the bulk. The solvent of choice was acetone, due to its high water miscibility and low vapor pressure, which simplified the solvent removal.

Preparation of nanomiem gel

50 mL of purified distilled water and propylene glycol (1:1) were put into a beaker and heated up to 70°C. EDTA (0.5%) and pluronic F-127 (0.5%) were added into the warmed purified water with continuous stirring after which the mixture was cooled down to 50°C. The mixture was then added to carbopol (1 g) under continuous low rpm stirring to form a uniform gel that was free from lumps and bubbles. The pH of gel was then neutralized with triethanolamine (TEA). After cooling the gel phase to 40°C, the NEM and NMI formulations were incorporated into the carbopol gel and mixed uniformly to obtain the NMG. The NEM and NMI were dispersed into the carbopol gel to achieve the final concentration of extract at 2 % respectively, whereas the final concentration of carbopol was maintained at 2 %. This NMG was used for the drug release, skin permeation and other *in vivo* studies.

Evaluation Parameters

pH

The pH of gel formulations was determined by using digital pH meter. One gram of gel was dissolved in 100 ml distilled water and stored for two hours. The measurement of pH of formulation was done in triplicate and average values are calculated. The value of pH of nanomiem gel is 6.7 by using glass electrode based pH meter. pH must be recorded without any dilution.

Scanning Electron Microscopy

This study discusses the strategies on sample preparation to acquire images with sufficient quality for size characterization by scanning electron microscope (SEM).

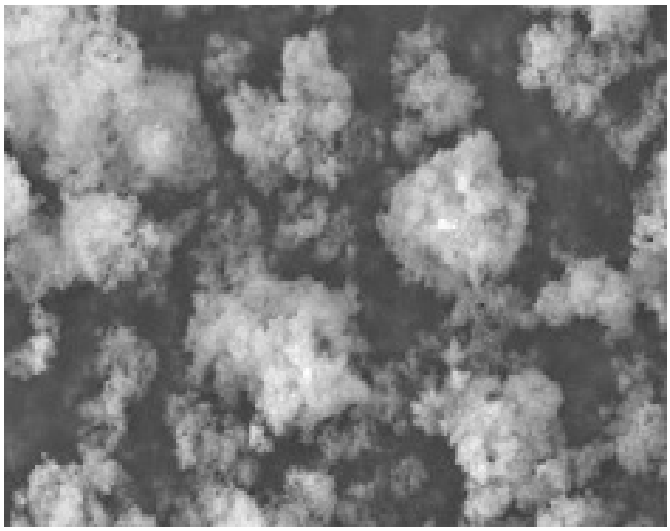

Fig. 1: Scanning electron microscopy of Nanomiemgel.

Transmission electron microscopy

Ultrathin sections of the lysozyme and ovalbumin gels fixed with solvent also show the presence of aggregated structures as judged from the transmission electron microscopy observations.

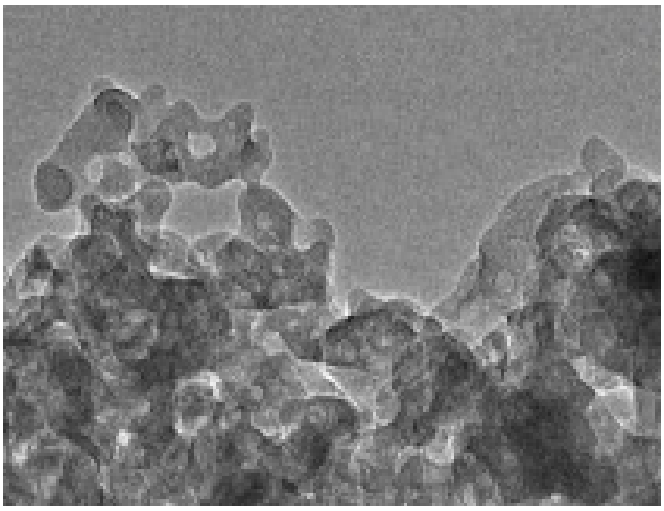

Fig. 2: Transmission electron microscopy of Nanomiemgel.

Viscosity

The measurement of viscosity of the prepared gel was done with a Brookfield Viscometer. The gel was rotated at 0.3, 0.6 and 1.5 rotations per minute. At each speed, the corresponding dial reading was noted. The viscosity of the gel was obtained by multiplication of the dial reading with factor given in the Brookfield Viscometer.

Table 2: Determination of Viscosity

S. No.	Formulations	Viscosity
1.	NEM	45100
2.	NMI	57300
3.	NMG	51600
4.	SI	47800

NMG=Nanomiemgel, NEM= Nanoemulsion, NMI= Nanomicelle SI= *Samedera indica*

Spreadibility study

Spreadability of semisolid formulations, that is, the ability of a gel to evenly spread on the skin, plays an important role in the administration of a standard dose of a medicated formulation to the skin and the efficacy of a topical therapy. The spreading values, that is, diameters observed for the formulations, after one minute. The values refer to the extent to which the formulations readily spread on the application surface by applying a small amount of shear. Results indicated that gel had comparable spreadability.

Table 3: Determination of Spreadibility

S. No.	Formulations	Spreadibility
1.	NEM	5.00
2.	NMI	4.09
3.	NMG	5.50
4.	SI	3.99

NMG=Nanomiemgel, NEM= Nanoemulsion, NMI= Nanomicelle SI= *Samedera indica*

Skin irritation

The prepared herbal gel was evaluated for its skin irritant effect, where no erythema or edema was observed for the formulations (Table 4), even after 10 days of study, indicating that the prepared herbal gel formulation was found to be safe.

Table 4: Determination of skin irritation

S. NO.	Formulation	Test
1.	NEM	-
2.	NMI	-
3.	NMG	-
4.	SI	-

NMG=Nanomiemgel, NEM= Nanoemulsion, NMI= Nanomicelle SI= *Samedera indica*

Homogeneity

One of the most important factors which influencing the gel homogeneity is the gel temperature. Temperature differences in different parts of the gel cause the monomers diffusion and result in gel in homogeneity.

Table 5: Determination of Homogeneity

S. No.	Formulation	Result
1.	NEM	H
2.	NMI	H
3.	NMG	H
4.	SI	H

NMG=Nanomiemgel, NEM= Nanoemulsion, NMI= Nanomicelle SI= *Samedera indica*

Grittiness

All the formulations were evaluated microscopically for the presence of any appreciable particulate matter which was seen under light microscope. Hence obviously the gel preparation fulfils the requirement of freedom from particular matter and from grittiness as desired for any topical preparation

Table 6: Determination of Grittiness

S. No.	Formulation	Result
1.	NEM	NG
2.	NMI	NG
3.	NMG	NG
4.	SI	NG

NMG=Nanomiemgel, NEM= Nanoemulsion, NMI= Nanomicelle SI= *Samedera indica* NG=Non gritty

Drug Release of NMG

In-vitro drug release was determined using Franz diffusion cell and synthetic membrane. 1 g of test sample was dispersed uniformly on membrane surface; finally, it was fixed on cell. cell receiver phase contained phosphate buffer, pH 6.8. The temperature of 37°C was controlled by pumped water bath circulating between 2 shells encompassed the chamber.

Franz diffusion cell was placed at receiver phase space by a magnetic stirrer to obtain sink conditions. This set was also put on a magnetic mixer then the cell mouth was covered by para film to avoid evaporation from donor phase. A volume of 1 ml samples were taken at specified time intervals. After each sampling, the aliquots were replaced by fresh phosphate buffer, pH 6.8 subsequently to gain the same volume of receiver phase during the experiment. The test was

repeated three times for each sample, and the absorbance was measured by standard curve of apparent concentration after performing. Apparent concentration is converted to actual concentration by equation below:

$$C_n = C + (C_{n-1})\ V/V_t$$

C_n: Actual concentration in sample *n*

C: Apparent concentration in sample *n*

C_{n-1}: Actual concentration in sample $n - 1$

V_t: Volume of receive phase

V: Sample volume

Table 7: Percentage drug release

Time (mts)	% Release
0	0
10	10.89
20	21.10
30	44.31
40	57.28
50	79.16
60	85.91
120	90.01
180	95.17
240	97.32
300	99.09

Result and Discussion

Proposed methodology was too developed as per the plan of work of the research project. The selection of plant and biodegradable polymer/ Excipients for formulation has been done. Preformulation parameters were successfully performed such as first we done extraction of plant by using soxhlet apparatus, then determination of extraction (% Yield), preliminary phytochemical investigation. After preformulation study of Nanomiem gel characterization was done by following evaluation parameters are pH, SEM, TEM, Viscosity study, Spreadibility, Skin irritation, Homogeneity, Grittiness, Drug release study was done and result discuss in experimental work.

Conclusion

As per the exhaustic literature survey was develop combination therapy in the form of nanomiemgel for the treatment of skin disease. Using a new combination of two different drug delivery systems (NEM+NMI), the absorption of the combined system (NMG) was found to be better than either of the individual drug delivery systems due to the utilization of the maximum possible paths of absorption available for that particular drug.

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