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DEVELOPMENT AND VALIDATION OF HERBAL DRUG-LOADED TOPICAL NIOSOMAL GEL FOR TREATMENT OF ECZEMA

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Abstract:
To create and validate a straightforward, accurate, and affordable UV-visible spectrophotometric method for calculating Calendulla officinalis and nelumbo nucifera in accordance with ICH Q2 (R1) guidelines. A UV-spectrophotometric technique has been devised for the simultaneous quantification of calendulla officinalis and nelumbo nucifera in a formulation of niosomal gel for the treatment of dermatitis. The stock solution is made using methanol as a solvent, and subsequent dilutions are made in distilled water. Calendula officinalis and nelumbo nucifera calibration standards were created, and absorbance was measured at the wavelength of maximum absorption. The linearity and range of the calibration curve of concentration vs. absorbance were computed. Additionally, it demonstrates that nelumbo nucifera and Calendulla officinalis both display absorption maxima at 320 nm and 254 nm, respectively. In the concentration ranges of 2–10 g/ml for Calendulla officinalis and 10–50 g/ml for nelumbo nucifera, respectively, the system followed Beer's law. According to ICH standards, the method was verified for linearity, range, accuracy, precision, and recovery studies. The routine examination of Calendulla officinalis and nelumbo nucifera in the formation of niosomal gel was therefore found to benefit from the suggested method's rapidity, specificity, precision, accuracy, and cost-effectiveness as a quality control tool. A simple, precise and cost-effective UV- visible spectrometry method for the estimation of niosomal gel was developed. The said method was developed using economical percentage of organic phase in aqueous media as solvent. Said validated UV- visible method can be efficiently used for the estimation of Calendulla officinalis and nelumbo nucifera in bulk as well as formulation.
Keywords*: UV- visible spectrometry, Calendulla officinalis, Nelumbo nucifera, validation*

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INTRODUCTION:

The Calendulla officinalis and nelumbo nucifera Plant pharmacological studies have suggested that calendula& nucifera extracts may have anti-viral, anti-genotoxic, and anti-inflammatory properties in vitro. In an in vitro assay, the methanol extract of Calendulla& nucifera exhibited antibacterial activity and both the methanol and the ethanol extracts showed antifungal activities. And both drug used in treatment of eczema disease. The human integumentary system is the most readily accessible organ system and contains the skin, which is the largest human organ serving the purpose of protecting and isolating the internal organs while also being the focus of some novel pharmaceutical dosage forms for drug delivery. Most people will require pharmaceutical intervention for skin diseases and infections at least once in their expected lifetime. Eczema are some of the most common dermatological conditions requiring treatment in patients. [1, 2, 3]

This study aimed to investigate the feasibility of topical delivery of herbal drug -loaded niosomes and incorporation into a gel. Niosomes were developed using an ether injection method by completely dissolving the drug into the organic phase, which was drop wise added to an aqueous phase using magnetic stirring and finally stored separately in glass storage sample containers.[4, 5, 6]

The optimized topical niosomal gel formulation of Calendulla officinalis and nelumbo nucifera were characterized using UV validation method .In spite of therapeutic vitality and extensive utility of calendulla officinalis and nelumbo nucifera, there are limited scientific reports that demonstrate the development and validation of analytical methods for its estimation in bulk and formulation. Therefore, considering the therapeutic importance of the calendulla officinalis and nelumbo nucifera and the need of simple yet precise and robust analytical method for the same, it was envisaged that development of UV-Visible spectrophotometric method for the determination of calendulla officinalis and nelumbo nucifera niosomal gel.[7, 8, 9]

Fig 1: Calendula Officinalis L.

Fig. 2: Nelumbo nucifera

MATERIAL AND METHOD:

❖ Instruments and reagents :

A double beam UV-visible spectrometer (UV-730, Jasco) with spectra manager software were used for the analysis. Quartz cells having 3 cm length with 1 cm path length were used for spectral measurement. Weighing balance (Mettler Toledo) with internal calibration mode was used for the accurate weighing purpose. Calendulla officinalis and nelumbo nucifera purchase from Amruta herbal LTD. Methanol was purchase from Merck. All the chemicals of analytical grade were used for the proposed study. And cholesterol purchase from S.D. Fine chemical Mumbai.

❖ Methods of Preparation of Niosome:

After optimization of ratio of tween 60: soyalecithin : Cholesterol in 5:5:1 ratio then formulation of niosomes were prepared by loading calendula officinalis & nelumbo nucifera drug in various % of calendula officinalis & nelumbo nucifera that is 0.5 %,1.0%,1.5%, 2.0%, 2.5%.it was processing with rotary evaporation method. Then drug loaded niosomes are formulated. Results and batches are reported in table no 1

Table No. 1: Formulation of calendula officinalis & nelumbo nucifera loaded Niosomes.

Batch Code	Tween 60 (mg)	Soyalecithin (mg)	Cholesterol (mg)	Calendula officinalis & nelumbo nucifera(in %)
F1	500	500	100	0.5%
F2	500	500	100	1.0%
F3	500	500	100	1.5%
F4	500	500	100	2.0%
F5	500	500	100	2.5%

Procedure:

- **Analysis of the niosome formulation:**[10]

Niosome solution (1 ml) containing equivalent to 10 mg of both drugs was transferred to 50 ml volumetric flask and excipient extracted with chloroform. Then drug dissolved in methanol. The sample solution was then filtered through Whatman filter paper. This solution was appropriately diluted to get approximate concentration of 20 µg/ml of coumerins and chorogenic acid each, the absorbance of sample solution were measured at 230 nm and 254 nm against blank.

❖ **Validation Of Method By UV Spectrophotometric Method** [11,12, 13, 14,]

- Accuracy
- Precision
- Specificity
- Limit of detection
- Limit of quantification
- Linearity
- Range
- Robustness

1. **Accuracy:** Accuracy is expressed as the nearness of agreement between the values found and values that are already available. It can also be defined as the closeness between the true value and the observed value. It is sometimes called as trueness. And it could be determined byusing at least 9 determinations over a minimum of 3 concentration over the specified range.

2. **Precision:** The exactness of an analytical procedure expressed the nearness of agreement (degree of scatter) between a groups of measurement obtained from different sampling of a uniform sample underneath the prescribed conditions. Precision may be taken into consideration at 3 levels:

a. **Repeatability:** It expresses the exactness below a similar operating condition over a brief intervalof time and also referred as intra assay precision. A minimum of six replicates test preparation of a similar or consistent sample ready at the 100% check.

b. **Intermediate precision:** It expresses the exactness under inside research laboratories, in distinct days, through distinct analyst, on distinct instruments/equipment. Two different analysts each preparing six sample solution, as per specified method.

c. **Reproducibility:** It refers to the precision between different analytical labs. Every research facilityset up an aggregate of six sample solutions, according to analytical technique.

3. **Specificity:** For every stage of development, the analytical technique should demonstrate specificity.The technique should have the power to unequivocally assess the analyte of interest whereas within the presence of all expected parts, which can encompass degradants, excipients/sample matrix, and sample blank peaks.

4. **Limit of Detection:** Lowest quantity of an analyte which may be detected by the chromatographical separation however it is not necessary that this quantity will quantify as a precise value. A blank resolution is injected and peak to peak quantitative noise relation we have to calculate from blank chromatograms. Then, calculate the concentration at the signal to quantitative noise relation is concerning 3:1.

   LOD can be expressed as **LOD=3.3 SD/S**

   Where, SD= standard deviation of response, S= Slope of calibration curve.

5. **Limit of Quantification:** It is characterized by the least quantify of an analyte that can be quantified with exactness and precision. LOQ can be communicated as:

   LOQ=10 SD/S

   Where, SD= standard deviation of response, S= Slope of calibration curve.

6. **Linearity:** Linearity may be characterized as the capacity of an analytical technique to produce outcomes which are directly related to the concentration of an analyte.

7. **Range:** It can be characterized as the interval amongst upper and lower quantities of analyte in the sample. Minimum of the specified range to be 80% to 120% of the test sample for theassay test.

8. **Robustness:** Ruggedness is the degree of measure of reproducibility under different situations such as in different laboratories, different analyst, different machines, environmental conditions, operators etc. All results are reported in below tables.

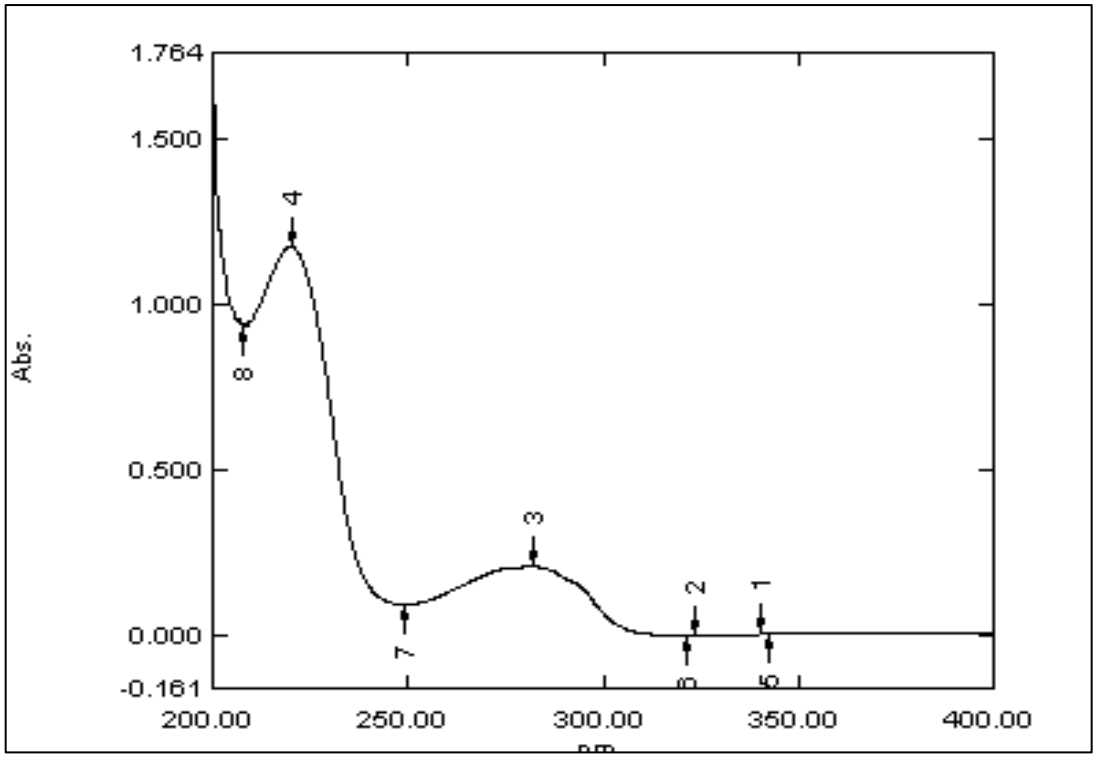
❖ **Results and Discussion :**

A. Selection of solvent: various solvent system used on trial and error basis practically, it was found that niosomal gel is freely soluble in, methanol, Ethanol, PBS. So, methanol and PBS was selected as ideal solvent for spectrophotometric analysis of prepared niosomal gel.

B. Preparation of standard stock solution: Standard stock solution of niosomal gel, was prepared by dissolving 10 mg of niosomal gel in 10 mL of methanol and PBS and to give 1 mg/mL. solution, from above stock solution 1 mL of aliquot was pipette out in a 10 mL volumetric flask and volume was made up to the mark with methanol and pbs(1:1) solution to obtain the final concentration of 100 µg/Ml.

C. Study of Spectra and Selection of Analytical wavelength: The maximum absorption value of pure drug, prepared niosomal gel was found to be 200-400 nm Wavelength. Therefore 220 nm were recorded as λ max of the prepared niosomal gel The Observed λmax value of drug was found to be similar as given in literature. Hence the prepared formulation was considered to be pure. The UV spectrum of prepared niosomal gel was showed in graph.

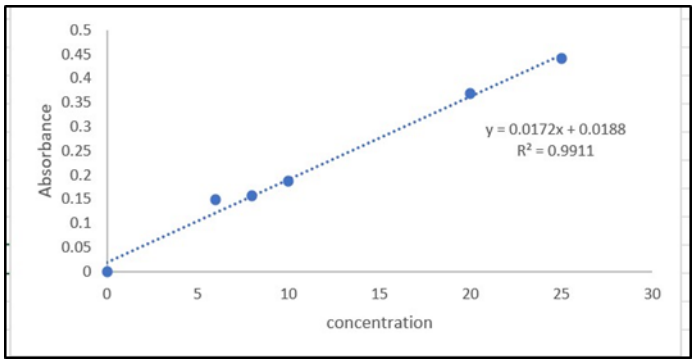
D. Preparation of standard calibration curve: Appropriate aliquots were pipette out from the standard stock solution in to a series of 10 mL volumetric flasks. The volume was made up to the mark with methanol and PBS for each volumetric flask to get series of concentration range of 5 to 100 µg/mL. Absorbance of the above solutions was assured at 220 nm and a calibration curve of absorbance against concentration was plotted. The drug obeys Beers Law in the concentration range of 6 to 25µg/mL. The regression equation and coefficient were determined.



Graph 1: Spectra of niosomal gel formulation

Table no. 2: Standard Calibration curve of prepared Formulation at 220nm.

Sr.no	Concentration in ug/ml	Absorbance
1	6	0.148
2	8	0.157
3	10	0.187
4	25	0.440



Graph 2: Calibration curve of prepared formulation

E. Validation parameter of niosomal gel by UV spectrophotometry

1. Linearity: Linearity curve at 220 nm

Table No 3: data of linearity for niosomal gel at 220 nm

Sr.no	Concentration (ug/ml)	Absorbance
1	6	0.148
2	8	0.157
3	10	0.187
4	20	0.368
5	25	0.440
		Mean =0.2600
		R ^{2}= 0.9954

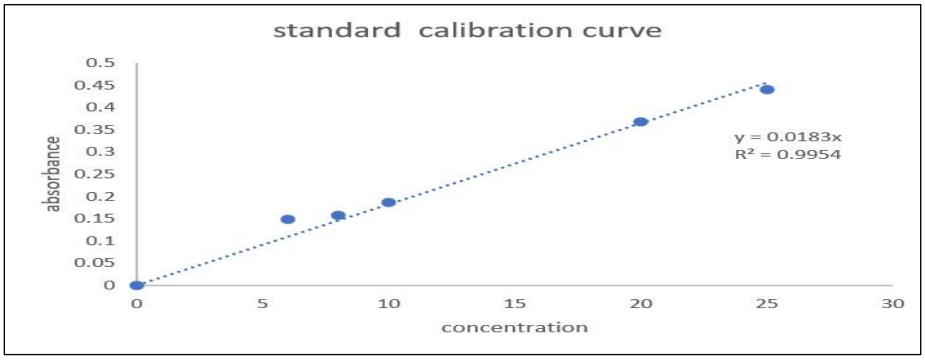


Table no. 4: Determination of accuracy (% recovery)

Sr. no	Formulation	Amount of drug taken(ug/ml)	Amount of drug added(ug/ml)	Amount of drug found (ug/ml)	% recovery Sd
1	Niosomal gel	20 ug/ml	5	26.8	104.32
2		20ug/ml	10	30.96	103.2
3		20ug/ml	15	33.81	96.57

2. Precision:

Table No.5: Intraday precision data of niosomal gel at 220 nm

Sr. No.	Concentration(ug/ml)	Absorbance	Mean	Sd	%Rsd
1	**10**	**0.189**	**0.540**	**0.28311**	**52.44**
2	**20**	**0.367**			
3	**30**	**0.521**			
4	**40**	**0.713**			
5	**50**	**0.911**			
Interday precision of niosomal gel at 220nm					
1	**10**	**0.219**	**0.5394**	**0.295660**	**54.81**
2	**20**	**0.351**			
3	**30**	**0.497**			
4	**40**	**0.645**			
5	**50**	**0.985**			

The precision of niosomal gel with interday and intraday % C.officinalis & N. nucifera were found to be 54.81%and 52.44%.

***3.* Repeatability:**

Table No.6: Repeatability data of niosomal gel at 220 nm

Table No.6: Repeatability data of niosomal gel at 220 nm

Sr. no	Concentration (ug/ml)	Absorbance	Mean
1	**25**	**0.510**	**0.549**
2	**25**	**0.565**	
3	**25**	**0.583**	
4	**25**	**0.572**	

CONCLUSION :

Niosomal gel was estimated using a straightforward, precise, and accurate UV-Visible spectrophotometric approach that was created and validated. By employing methanol and phosphate buffer as solvents, UV-spectroscopy techniques were used to confirm the formulation. It was discovered that the created UV-spectroscopic approach was straightforward, precise, sensitive, accurate, specific, affordable, and quick. By using this technique, the niosomal gel was effectively validated and improved. This approach was discovered to be much specialized. It was discovered that the UV Spectroscopic technique was linear over a larger concentration range. For routine quantitative and qualitative analysis of niosomal gel, the established approach can therefore be used. According to the ICH criteria, this approach was validated. The pharmaceutical business can use the established UV spectroscopic approach for pharmaceutical compositions.

Future Prospects:

Niosomes represent a promising drug delivery molecule. There is alot of scope to encapsulate anti-fungal drugs, anti-cancer drugs, anti-infective drugs, anti-AIDS drugs, anti-inflammatory drugs, anti-viral drugs, etc. in niosomes and to use them as promising drug carriers to achieve better bioavailability and targeting properties and for reducing theand side-effects of the drugs. Niosomal gel as a promising approach for enhancing drug bioavailability. We can also do animal study and bioavailability study. The ionic drug carriers are relatively unsuitable whereas niosomal carriers are safer. Handling and storage of niosome require no special condition.

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