Type of Manuscript: *Research*

Formulation and Evaluation of Niosomal gel containing Desonide with Curcumin for the treatment of Inflammation.

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ABSTRACT:

Olive oil is obtained by pressing whole olives, which are the fruit of the Olea europaea plant; on the other hand, almond oil is derived from almonds. Because of their capacity to shield enclosed pharmaceuticals, lower drug dosage amounts, target drug delivery, lengthen residence times, and increase penetration, antibacterial Niosomal vesicles were selected for the dispersion of olive and almond oils in this study. A modified thin-film hydration method was used to make niosome-containing olive and almond oils, and carbopol 934 was added as a gelling agent to create a smooth niosomal gel formulation for sustained-release delivery of ellagic acid using natural penetration enhancer as olive oil or almond oil. The goal of the current study was to create niosomal gel for acne therapy. Then, niosome fusion with skin lipids and drug release at the deep layers of the skin may cause the medication's release and transdermal absorption.different locations along the penetration path. The development of a gel formulation incorporating niosomes loaded with gallic acid can be helpful in improving cutaneous infections, as evidenced by its persistent action. The best formulation batch, batch G9, was found to exhibit improved stability, longer residence times, and more sustained release.

Keywords : Ellagic acid, Niosome, Olive oil, Almond oil, Span 40, Span 60, Carbopol 934.

INTRODUCTION:

Skin infections are prevalent and frequently present challenges for medical professionals in terms of treatment because of growing worries about drug-resistant bacterial, viral, and fungal strains. [1]This is primarily because they are linked to a variety of illnesses, from mild infections of the skin and soft tissues to potentially fatal conditions like meningitis and systemic sepsis.[2]Niosomes are one of the most promising drug delivery systems because of their bilayer structure, which is produced by cholesterol and non-ionic surfactants self-associating in an aqueous phase.[3] They're either Adsorbed on the skin's surface, they either penetrate the stratum corneum and function as drug reservoirs or they create a large thermodynamic activity gradient at the interface, which facilitates medication absorption.[4-5]

The French chemist and chemist Henri Braconnot made the initial discovery of ellagic acid (EA) in 1831. He called it "acide ellagique," a play on the term"galle," which is read backwards [6]. But the Early in the 20th century, divi-divi (Caesalpinia coriaria (Jacq.) Willd.), oak bark, valonea, pomegranate (Punica granatum L.), myrobalan, and algarrobilla (Prosopishumilis Hook.)[7] were among the plants used to prepare this substance, whose presence in plants was not well understood[8]. Ellagic acid is a polyphenolic chemical found in berries and fruits that has a variety of preventative and therapeutic uses. Its anti-inflammatory, anti-aging, antibacterial, antioxidant, and anti-cancer properties have all been demonstrated.[9]Traditionally, it has been utilised for therapeutic and cosmetic purposes. as a means of treating skin cancer, hyperpigmentation, and numerous other skin conditions. The potent antioxidant potential of ellagic acid is responsible for many of its medicinal effects.[10]

This study aimed to develop and assess a niosomal gel containing ellagic acid. A modified thin-film hydration technique was used to create niosomal formulations that included natural penetration enhancers like almond or olive oil. Based on stability studies, in-vitro features,

entrapment efficiency, and the formulation of niosomal gel, which was further investigated, the optimal niosomal batch was chosen.

Literature survey revealed that essential oils as olive, almond or mustard oil act as good natural penetration enhancer for drug in trasndermal gel formulation. So in the present research study it is decided to formulate control Release niosomal topical gel for transdermal delivery of Ellagic acid using natural penetration enhancer as olive oil or almond oil.

MATERIAL AND METHODS:

Materials:

Organix mantra, located in New Delhi, India, produced olive and almond oils. S.D. Fine Chem Limited, Mumbai, Maharashtra, India, was the manufacturer of cholesterol. India's Loba Chemi, located in Mumbai, Maharashtra, produced Span 40 Span 60 Carbopol 934 Glycerol Tri ethanolamine Chloroform.

METHODOLOGY:[11-16]

Formulation of Ellagic Acid Niosomes:

Thin film hydration (TFH) :

The thin film hydration method was used to create niosomes with minor adjustments. In different ratios, cholesterol and surfactants were dissolved in an organic solvent, and 1% v/v Ellagic acids were incorporated into this resolution. The organic solvent was extracted under vacuum at 60°C using a rotary evaporator until a thin layer developed. More hoover was used to get rid of any organic solvents that might still be present. This film was hydrated with 6 mL of phosphate buffered saline (pH: 7.4), or PBS for 60 minutes at 50°C. The resultant niosomal suspension was subjected to three rounds of sonication at 50 Hz for three minutes each, separated by a five-minute interval. For congealing and future research, the niosomal suspension was stored in a refrigerator at a low temperature of 4–8°C. The formulation of different batches is displayed in Table 1

Table 1: Formulation of Ellagic Acid Niosomes

Sr.No	Formulation Code	Surfactant		Weight Taken (gm)			
		Span 40	Span 60	Ellagic Acid	Cholesterol	Chloroform	PBS (Ph 7.4)
1.	EA 1	1	-	1	1	10	6
2.	EA 2	1	-	1	2	10	6
3.	EA 3	2	-	1	1	10	6
4.	EA 4	-	1	1	1	10	6
5.	EA 5	-	1	1	2	10	6
6.	EA 6	-	2	1	1	10	6
7.	EA 7	1	1	1	1	10	6
8.	EA 8	2	1	1	2	10	6
9.	EA 9	1	2	1	2	10	6

FORMULATION OF ELLAGIC ACID NIOSOMAL GEL :

Carbopol 934 and filtered water were put in a beaker and allowed to soak for twenty-four hours. For this to happen, an appropriate quantity of niosomal batch [N9]. containing 1% almond oil and 1% olive oil was mixed with water, then carbopol 934 (pH: 6.5) was added to neutralise it. Glycerine was added gradually as a moistening agent, stirring gently, until a homogenous gel was formed.

Table 2: Composition of different niosomal gels formulation.

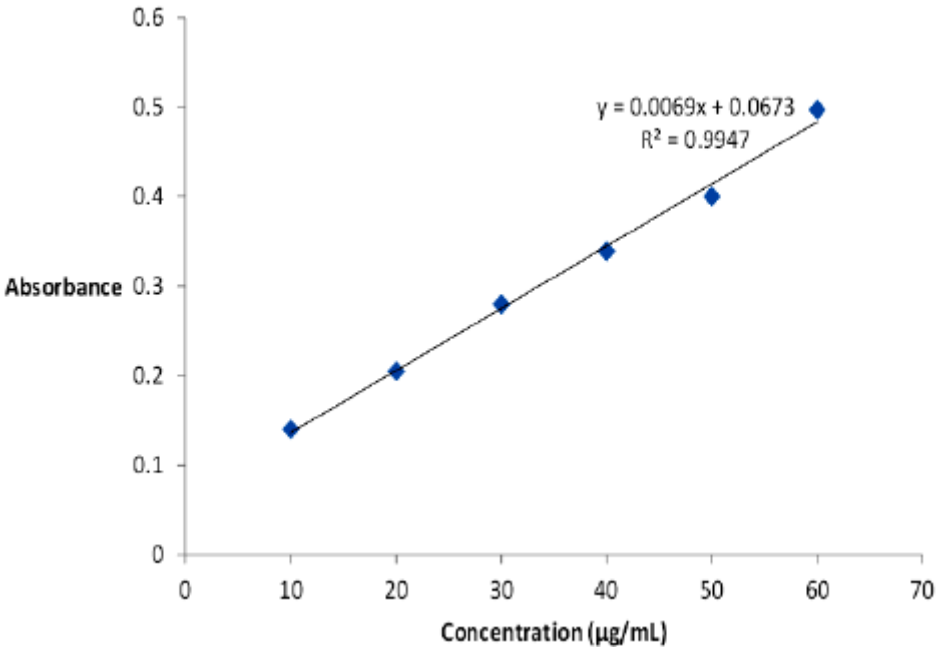
Sr. No	Ingredient	F1	F2	F3	F4	F5
1.	Ellagic Acid Niosomes (mg)	100	100	100	100	100
2.	Carbopol 934 (gm)	0.5	1	1.5	2	2.5

3.	Olive Oil (ml)	7.5	7.5	7.5	7.5	7.5
4.	Almond Oil (ml)	7.5	7.5	7.5	7.5	7.5
5.	Glycerine	50	50	50	50	50
6.	Water	q.s.	q.s.	q.s.	q.s.	q.s.

EXPERIMENTAL AND RESULTS:

Table 3: Callibration Curve of Ellagic Acid.

Sr.No	Concentration (µg/ml)	Absorbance
1.	**10**	**0.156**
2.	**20**	**0.302**
3.	**30**	**0.450**
4.	**40**	**0.612**
5.	**50**	**0.748**



Evaluation of Niosomes:

Vesicle size determination:

Vesicle size was determined using the particle size analyzer.

Entrapment efficiency:

Surface morphology was determined by TEM, for TEM a drop of the sample was placed on a carbon-coated copper grid and after 15 min it was negatively stained with 1% aqueous solution of phosphotungustic acid.

Table 4: Evaluation of niosomes for vehicle size and entrapment efficiency.

Sr.No	Formulation	Vehicle Size (nm)	Entrapment Efficiency %
1.	EA 1	228.53 ±3.40	62.62 ±0.24
2.	EA 2	232.45 ±5.53	80.75 ±0.65
3.	EA 3	270.65 ± 6.70	75.98 ±0.45
4.	EA 4	245.76 ±5.90	71.87 ±0.67
5.	EA 5	284.558 ±7.40	66.98 ±0.55
6.	EA 6	293.985 ±9.47	60.28 ±0.34
7.	EA 7	297.957 ±9.59	64.78 ±0.28
8.	EA 8	310.94 ±7.89	76.34 ±0.45
9.	EA 9	314.85 ±6.98	62.98 ±0.56

Optical microscopy:

Optical microscopy was conducted on the drug sample using a digital microscope (Motic DMWB1-223ASC, Hyderabad). A tiny quantity of the niosomal sample solution was disseminated, and niosomal batches were examined under an optical microscope to examine the vesicles' shape and lamellar characteristics on the glass slide. Various magnification lenses were used to capture the images on this slide.

Particle size and zeta potential determinations:

Zeta Potential/ Particle Sizer NICOMP 380 ZLS, PSS-NICOMP particle sizing systems, Santa Barbara, CA, outfitted with a 5-mW laser, was used to measure the vesicle characteristics, particle size diameter, and zeta potential at room temperature. The niosomal mixtures were diluted with saltwater buffered with phosphate, pH 7.4, for the measurement of particle size and Zeta potential, respectively.

Table 5: Average zeta potential of Ellagic Acid Niosomes.

Sr.No	Formulation	Surface Charge	Avg. Zeta Potential (mv)
1.	**EA 1**	Neutral	-0.12
2.	**EA 2**	Negative	-4.30
3.	**EA 3**	Positive	+4.98
4.	**EA 4**	Neutral	-0.80
5.	**EA 5**	Negative	-7.80
6.	**EA 6**	Positive	+10.97
7.	**EA 7**	Neutral	-0.39
8.	**EA 8**	Negative	-5.7
9.	**EA 9**	Positive	+8.9

Differential scanning calorimetry:

Pellets of niosomal was lyophilized. The medication powder and individual components, Span 60, Span 40, cholesterol, and DCP, as well as differential scanning calorimetry (DSC) thermograms, were examined. The temperature range covered by the heating rate, which was 5˚C/min, was 30–250˚C.

Fourier transform infrared spectroscopy (FTIR):

The infrared spectra of the olive oil and almond oil niosomal batches were measured using an FTIR Spectrophotometer (FT-IR Bruker-Alpha, Apexan Analytical Techniques, Vadodara). After that, these samples were put in a sample holder, and scans with a 2 cm-1 resolution were obtained between 5000 and 500 cm-1.

Drug content:

One millilitre of niosomal buffer solution was mixed with two millilitres of ethanol to assess the amount of drug present. Distilled water was used to make up the remaining volume. The niosomes decompose when ethanol is added. enabling the drug to completely dissolve in a liquid. The target concentration was then achieved by diluting each of these solutions with distilled water. Utilising a UV-visible spectrophotometer (Shimadzo UV visible 1800, Gumtree India Analytical, Nashik), absorbance was measured at 265 nm for olive oil and 275 nm for almond oil.

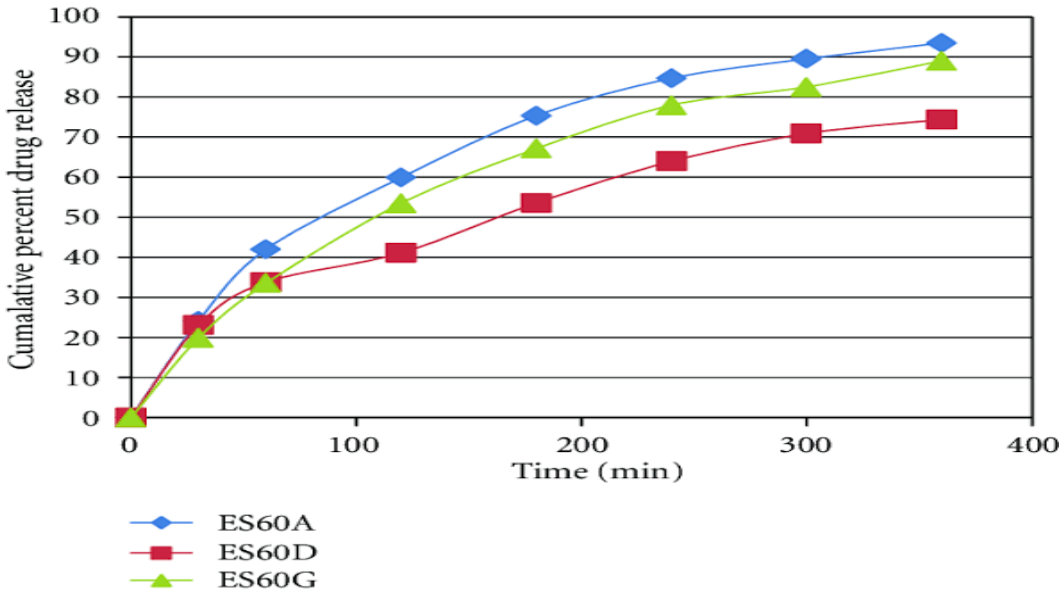
Table 6: Drug Content of Niosomes.

Sr. No	Code	Drug Content %
1.	**EA 1**	97.66±0.32
2.	**EA 2**	92.65±0.34
3.	**EA 3**	94.67±0.56
4.	**EA 4**	98.23±0.89
5.	**EA 5**	95.78±0.65
6.	**EA 6**	96.45±0.23
7.	**EA 7**	97.83±0.34
8.	**EA 8**	99.56±0.43
9.	**EA 9**	96.67±0.52

In vitro drug release of Niosomes:

In an in vitro investigation, a dialysis bag served as the donor compartment. Following two millilitres of the formulation's centrifugation, niosomes containing For the release study, the drug that had been entrapped was re-suspended in 1 millilitre of pH 7.4 PBS. The dialysis membrane was soaked in warm water for ten minutes. Then, one end was sealed, the niosome mixture was pipetted into the bag, and the bag was closed to stop leaks. 100 ml of pH 7.4 PBS was added to the dialysis bag and allowed it to sit at 37°C ± 2°C. The medium that acted as the receptor compartment was stirred at 100 revolutions per minute. The absorbance of olive and almond oils

at 275 and 265 nm was measured using PBS as a blank, and 5 ml samples were taken out of the medium every hour and replaced with fresh buffer. The mean was the outcome. three runs' worth of values.



EVALUATION OF ELLAGIC ACID NIOSOMAL GEL:

Determination of pH:

A digital pH metre was used to weigh 50 gm of gel formulation and transfer it into a 10 millilitre beaker. pH level of the The recommended range for topical gel formulation when treating skin infections is 3–9.

Spreadability:

To measure spreadability, a modified version of the recommended apparatus was employed. The spreadability was assessed using the slip and drag method features of the gel

Viscosity:

A Brook Field viscometer model DV-II was used to measure the viscosity of gels. A helipath stand and a T-Bar spindle were utilised to Get precise measurements while measuring the viscosity.

Drug content:

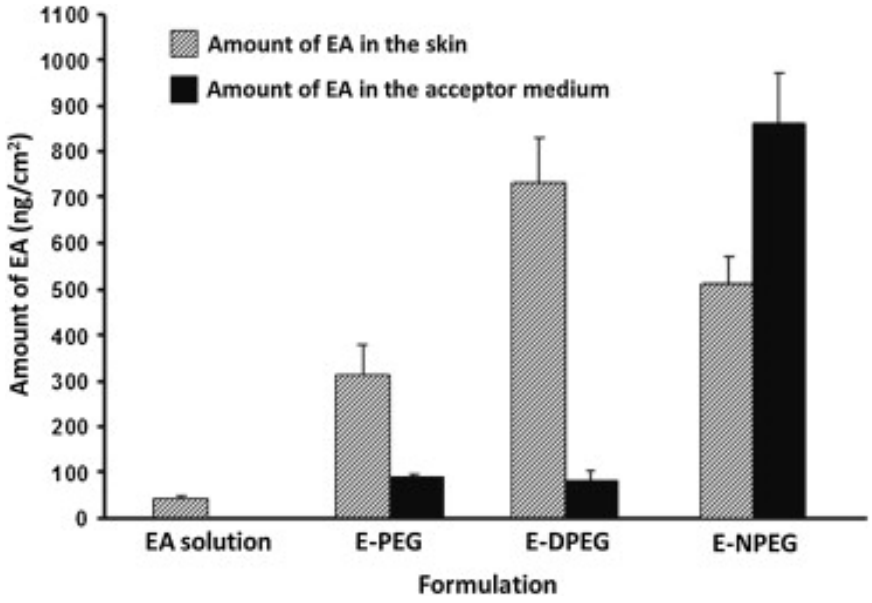
The produced gel weighed one gramme, and 100 millilitres of ethyl alcohol were added. Following appropriate dilutions, aliquots with varying concentrations were created.the absorbance was measured at 265 nm after filtering the stock solution. Using a linear regression analysis of the calibration curve, the drug content was determined.

Table 7: Results of Ellagic Acid Niosomal gel formulation.

Sr.No	Code	Drug Content %	P^H	Spreadability (Gm.cm/sec.)	Viscosity(cps)
1.	**F1**	98.23±0.025	7.0±0.021	22.65±0.067	6789±43
2.	**F2**	99.45±0.0.23	7.2±0.069	23.56±0.056	6897±32
3.	**F3**	98.65±0.014	7.3±0.045	24.09±0.034	7678±45
4.	**F4**	99.67±0.0.17	7.4±0.034	25.89±0.069	7598±76
5.	**F5**	96.45±0.021	7.4±0.067	21.98±0.046	7890±56

In-vitro permeation studies of gels:

In vitro permeation tests were performed utilising cellulose membrane as a semi-permeable membrane to compare the permeability of polymeric gels and niosomal gels and Franz diffusion cell. It positioned the gel formulation in between the lower (receptor) and the donor-side compartment.



Stability studies:

Stability tests were conducted on the best niosomal formulations, tracking changes in drug content, entrapment efficiency, and physical properties as a function of temperature. In two Every fifteen days, ml samples were extracted from niosomal dispersions maintained at 2-8 °C and at room temperature (30±2 °C), resulting in a total of forty-five ml. Spectrophotometry was used to examine the samples at 262 nm following the dissolution of the vesicles in 50% ethyl alcohol. Stability studies for optimized formulations were carried out at 28 ± 0.5ºC for a period of four weeks. There was no significant variation found in physical appearance, average particle size and % drug content of the niosomes gel.

Table 8: Stability studies of Ellagic Acid niosomal gel Formulation at different temperature.

Temperature of Storage				
Time of Storage in Days	**Drug Content % 4-8 ºC**	**Entrapment Efficiency % 4-8 ºC**	**Drug Content % 25ºC ± 2**	**Entrapment Efficiency % 25ºC ± 2**
0	54.50	35.0	54.48	35.0

15	54.32	34.8	54.30	34.3
30	53.26	34.2	53.10	34.1
45	53.22	33.6	52.20	32.4
60	53.10	33.1	51.26	31.3

Conclusion:

One of the most common skin conditions is thought to be acne. Stopping scarring and reducing the length of the illness are the primary objectives of acne treatment. The primary method of treatment is the application of topical treatments, even for minor cases of acne. Multilamellar vesicles called niosomes effectively transport active substances into the skin's layers or systemic circulation. They improve the active substance's skin penetration in topical medication administration systems. This study addresses the need for an efficient and well-tolerated anti-acne treatment by demonstrating the successful creation of a niosomal gel formulation for sustained-release delivery of ellagic acid using natural penetration enhancer as olive oil or almond oil. It was found that encasing ellagic acid in niosomes with a high entrapment effectiveness was feasible using the thin film hydration process. Because this discovery opens the door to the development of safer and more effective treatments, acne sufferers will live better lives as a result.

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