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Preparation and Characterization of Curcumin based Nanogel for Topical Anti-inflamatory Activity

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Abstract

Although there are challenging systems for both local and systemic effects of drugs, transdermal medication administration holds promise. For transdermal medication administration, the duration of a drug formulation's stay in the skin is crucial. Creating a nanogel with smaller particles was the main goal of the current study in order to increase the bioavailability of the anti-inflammatory medication. With the help of an emulsion-solvent diffusion approach and the addition of a gelling agent to create nanogel, curcuminnanosize dispersion is being created in this work. The particle size ranges from 100 to 400 nm, which is a characteristic of the formulation of an anti-inflammatory and anti-arthritic medication called curcumin.According to the results, a glycerol:water (20:80) co-solvent system was chosen because it has a higher permeability coefficient than alcohol:water co-solvent when creating curcuminnanogels using various polymers.

In a franz diffusion cell, permeation over a cellophane membrane was carried out using 0.9% w/v sodium chloride as the receptor fluid (1.74 cm2). Eudragit polymer-based curcumin gels have demonstrated higher permeability coefficients. The study's findings indicate that when compared to nanogels made with HPMC and methyl cellulose, those made with carbopol and a permeation enhancer showed superior flow augmentation. It has been determined that curcuminnanogels with carbopol 940 as a gelling agent and Eudragit S-100 as a permeation enhancer have demonstrated superior flow augmentation.

Key words: Curcumin, Nanogel, Eudragit S-100, Glycerol, Carbopol-940, Cellophane membrane.

Introduction

Transdermal delivery of drug is promising but challenging system is available for local as well as systemic effect of drug. The entry of drug through the stratum corneum may follow the intercellular, transcellular or appendageal route. The intercellular route is the more common pathway of the drug permeation through the skin[1].The term Nanogel can be defined as a minute molecule created via corporeally or bio chemically reticule copolymerize structure increased as a resolvent. The word Nanogel was established with defined cross-linked bifunctional networks ionic and nonpolar polymer birth of polynucleosomes and poly glycol (PEG)[2].

Nanogel can be termed as dispersion of hydrogel by physical and chemical cross-linking polymer at nanoscale size. Nanogel exhibit properties between those of solids and liquids.

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It consist of small amount of solid components entangled with polymers dispersed in large volume of liquid in which solids form 3D network forming the nanoscale size leading to high surface area providing biconjugation of active targeting sites. Nanogels combine the advantage of hydrogels inherting the property of nanoscale size. Nanogel network provide high specific form can host and protect drug molecules. The release of the drug molecules can be incorporated by providing high-affinity functional groups. Nanogels are able to carry encapsulated drug molecules to targeted tissues or cell structures without premature leakage of the drug into the blood stream or other tissues. Nanogel has been the form having size ranging from 20-200 nm. In oral drug delivery, nanogels have been used to protect unstable peptides from harsh manufacturing and physiological environments and to enhance the drug absorption at specific sites[3]

Nanogels are incised complement of hydrogels associate with the ownership of crystalize with the collide like as a resurface – volume ratio, microhetrogeneous structure and sizes small Called as "nanoscaler polymer networks", "gel nanoparticles," "nanoscale hydrogels", etc., nanogels are balanced, fluffy, and inflamed in excellent solvents. Nanogel are common, model extreme affirmation that devote to the airing against as a drug delivery system. They combine curious thermogenic stability, inflated quantity of solubilization, almost less viscosity, and capacity of endure vicarious sterilization techniques[4] .Nanogel may seduce drugs and living molecules. They can be vastly employed in protein and gene delivery. Nanogelspossoes a hydrofoils nature, check good encapsulate property of quadraphonic drugs. Nanogels add an advance greedy drug delivery for less soluble drugs. They do not increase the solubility and strength but increment event of the biological uptake for the free drug[5].They are approximately high affection to aqueous solutions, a dominant stability, dormancy in the fundamental circulation as well as the internal fluent, and a usefulness for molecular adding in bulk, they are studied auspicious carrier for delivery and essential uptake of proterons peptides and more biological compounds[6].

Turmeric

Turmeric is a spice; they are a more interesting for the both medicating/precise world as well as the palatable world. Turmeric is mismates herbaceous persistent plant (*Curcuma longa*) of the Zingiberaceae family[7].The medicative effects of turmeric and the source of curcumin, also avoved for millennium of years. So, the ability to determine the exact mechanism of action and to determine the bioactive components are a time to time investigate[8].Curcumin (1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione), is a diferuloylmethane. The main natural polyphenol found in the derivative of *Curcuma longa* (turmeric) and is a Curcuma supplement[9]. *Curcuma longa* has been traditionally used in an Asian country as a medical herb due to its antioxidant, anti-inflammatory[10],antimutagenic, antimicrobial[11-12and] anticancer properties[13-14]. Curcuminoids dose is a 12,000 mg/day of 95% concentration of three curcuminoids are as follows - curcumin, bisdemethoxycurcumin, and desmethoxycurcumin[15]

Curcumin (Curcuma Longa)

Curcumin (diferuloylmethane) is the ingredients in the spice of turmeric. Curcumin (CUR), a ingredient of a Curcuma longa (Family – Zingiberaceaae), chemically known as diferuloylmethane is announced to occupy con-oxidating16anti-inflammatory17anticarcinogenic18and hypocholesterolemia properties19So, the novel formulations developed using curcumin include liposomes20solid lipid nanoparticles21transdermal film22microspheres**,** nano emulsion23The capability of curcumin is a poorly consume by the Gastrointestinal tract. Low levels of curcumin are detected in blood and tissues following curcumin ingestion24-25Principal of Curcumin is diagnosed in primordial 1900 over Lampe and Milobadzka. Its structure and biological analysis revealed about 2.5% - 6%. Turmeric comprehend by pure Curcumin.

Characteristic	Cur – I	Cur – II	Cur – III
Chemical Name	Dicinnamoyl Methane	4-OH Cinnamoyl Methane	Bis – 4 -OH Cinnamoyl Methane
Common Name	Cur	DemethoxyCur	Bisdemethoxycurcumin
Colour	Bright orange yellow	Bright orange yellow	Bright orange yellow
Amount present (%)	77	17	3
Molecular Mass (g/mol)	368.4	338.0	308.1
Melting Point (°C)	183.0 – 186.0	172.5-174.5	224.5
Neutral Solvent(water)	Poorly soluble	Poorly soluble	Poorly soluble
Solubility in Organic Solvents	Soluble	Soluble	Soluble
Solubility in Hexane or Ether	Insoluble	Insoluble	Insoluble
Excitation/Emission	420/530 nm	420/530 nm	420/530 nm
Excitation/Emission	536-560 nm	Unknown	Unknown

Table 1 - The chemical and biophysical properties of curcuminoids[26]

Material and Methods

Drug and Eudragit S-100 was purchased from Evonik industries, Mumbai. Carbopol 940 and Glycerol was gift sample from LobaChemiePvt. Ltd., Mumbai. Tween 80 was purchased from S.D. Fine chemical Ltd., Mumbai. Triethanolamine was purchased from Spectrochem, Mumbai.

Preparation of Curcumin Nanogel

Accurately weighed quantity of Drug, Eudragit S-100 (polymer), and Tween-80 as stabilizer are dissolved in glycerol while stirring. Prepared aqueous phase containing Carbopol-940 dissolved in water with continuous stirring and heat. These drug containing phase is sonicated on Ultra sonic bath sonicator. The drug phase is added drop by drop into the aqueous phase during homogenization to form emulsion. The emulsion converted into nanodroplets by homogenizer which formed O/W emulsion. Homogenization was continued for one hour. Triethanolamine added to form the gel with continuous stirring to nanogel. Batch A, B, C was prepared at highest rpm 5000 with alteration in composition.

Evaluation parameters

Appearance

The prepared gel bases were inspected visually for clarity, colour and presence of any particles.

Homogeneity

All developed gels were tested for homogeneity by visual inspection after the gels have been set in the container. They were tested for their appearance and presence of any aggregates.

PH measurement

The pH measurement was carried out by using calibrated digital type pH meter by dipping the glass electrode and the reference electrode completely into gel system so as to cover the electrodes.

U. V. Spectroscopy

A(0.75mL), B(0.4mL), C(0.25mL), weighed accurately and transferred into a 50mL, volumetric flask and made up to the mark with ethyl acetate.

HPLC

A(2.5ml), B(1.25mL), C (0,833) amount of sample was dissolved in 50mL of reagent alcohol by sonication. The sample was further diluted 1:25 in reagent ethyl acetate.

FTIR

The spectra were recorded in the wave number range 400 – 4000cm using a diffused reflectance accessory (DRA) and the background spectrum was that of KBr.

Zeta Potential

The zeta potential was measured by using Zetasizer Nanoseries -ZS90 (Mallvern, UK). the size measured wavelength is 633nm and a scattering angle of 90.

Stability Studies

The stability study of the curcumin placed nanogel was evaluate after storage at 2-8 C room temperature and 45 C for 3 months. the resting drug, pH and colour of the samples were resolute as a function of storage time[27].

Measurement of particle size of formulation

The mean size of the selected nanogels were determined by using Malvern Mastersizer 2000 MS. The mean particle size was recorded.

Spreadability

Spreadibility is determined by apparatus suggested by Mutimer. It consist of wooden block, which is provided by a pulley at one end. By this method, spreadibility is measured on the basis of “Slip” and “Drag”. A ground glass slide is fixed on this block. A sample of 0.1 g of nanogel under study is placed on this ground slide. The gel is fixed on the beach formula was pressed between two slides and a 1 kg weight is placed on the top of two slides and left for about 5 min to expel air and to provide a uniform film of the nanogel between two slides. Excess of the gel is scrapped from edges. The top plate is then subjected to pull the weight. With help of string attaches to the hook and the time required by top slide to cover the distance is noted. A shorter interval indicate better spreadibility, spreadability was calculated by using the formula,

$$S=M.L/T$$

Where, S=spreadability, L=Length of glass slide, M=weight tied to upper slide, T=Time taken to separate the slides.

Rheological Measurement

The rheological measurement is executed by the Brookfield Rheometer . All measurement performed by the room temperature 25± 1C. Rheological properties of the formulated nanogels calculated at 30 rpm and viscosity are measured in cP.

Percentage of Drug Entrapment

The amount of the drug cover into the gel. Normally the percentage of drug defined as bound to the gel analogues and the total amount of the drug. this parameter required for the separation of free drug for the gel formulation. Analysis of free drug and entangle drug fraction and calculate the entrapment efficacy. Entrapment efficacy was estimated by using following formula-

Percent encapsulated = $\frac{\text{(Total curcumin) – (free curcumin)}}{\text{(Total curcumin)}} * 100$

Results and Discussion

UV spectroscopy

After studying the UV spectra of curcumin, it was found that drug shows absorbances at 418 nm but maximum absorbance was at ~425 nm when solution is prepared in distilled water. So, 425 nm was considered as λmax. UV spectra curcumin is shown in Figure 1.

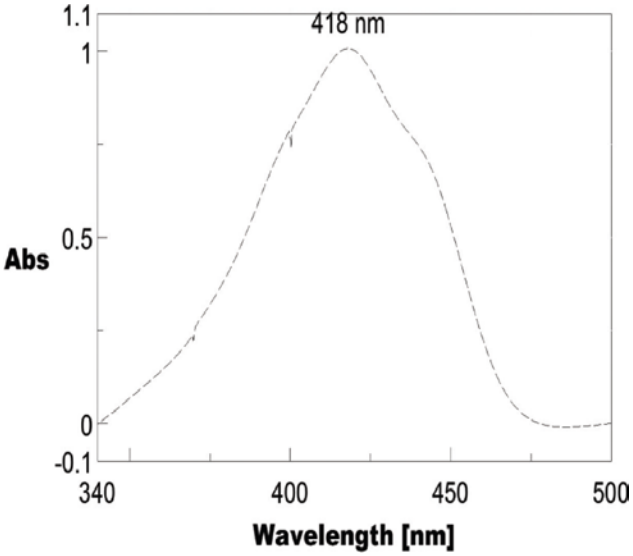

Fig. 1: UV spectrum of curcumin

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Linearity

As per ICH Q2 (R1) guidelines, linearity of an analytical procedure is its ability (within a given range) to obtain test results which are directly proportional to the concentration (amount) of analyte in the sample. Results of linearity are shown in Table 2 and Figure 2.

Concentration of curcumin (µg/mL)	Absorbance (λmax) at 418 nm (Mean±SD) (n=3)	%RSD
1	0.2636±0.0011	0.4172
2	0.4724±0.0023	0.4868
3	0.6641±0.0082	1.2347
4	0.8742±0.0035	0.4003
5	1.0671±0.0014	0.1311

Table 2: Linearity and range of the proposed UV method

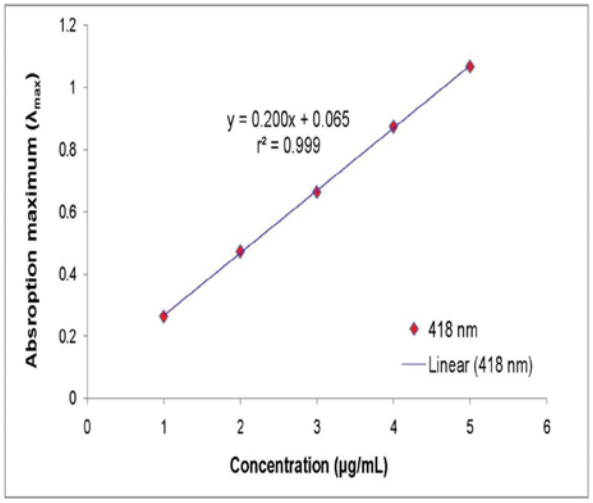

Fig. 2: Linearity and range of the proposed UV method.

HPLC

Annexure 1 (Test solution 1% rep.1 and rep.2)
(Test solution 2% rep. 1 and rep.2)
(Test solution 3% rep. 1 and rep. 2)
Discussion – According to this data are as follows; Table:3

NAME	ASYMMETRY
T1% REP1 (CURCUMIN)	1.15
(DESMETHOXYCURCUMIN)	1.14
(BIS-DEMETHOXYCURCUMIN)	1.12
REP 2 (CURCUMIN)	1.12
(DESMETHOXYCURCUMIN)	1.13
(BIS-DEMETHOXYCURCUMIN)	1.19
T2% REP1 (CURCUMIN)	1.10
(DESMETHOXYCURCUMIN)	1.12
BIS-DEMETHOXYCURCUMIN)	1.09
REP 2 (CURCUMIN)	1.09
(DESMETHOXYCURCUMIN)	1.11
(BIS-DEMETHOXYCURCUMIN)	1.01
T3% REP1 (CURCUMIN)	1.07
(DESMETHOXYCURCUMIN)	1.08
(BIS-DEMETHOXYCURCUMIN)	1.14
REP2 (CURCUMIN)	1.15
(DESMETHOXUCURCUMIN)	1.13
(BIS-DEMETHOXYCURCUMIN)	1.15

All asymmetry is as compared with the standard solution and reference standard are as follows.

FTIR

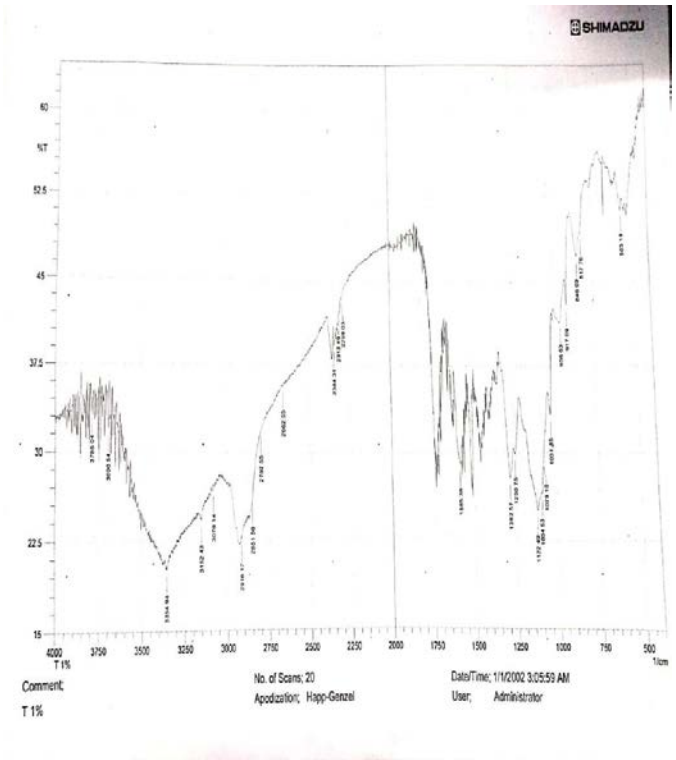

Fig.3. FTIR spectra of test sample 1%

Interpretation –

2797.55 – 2916.17 Correspond to Aliphatic group
3079.14 Correspond to Aromatic group
1031.85 Correspond to Oxygen group
1031.850 – 1282.57 Correspond to Florine
563.18 Correspond to Bromine.

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According to the 1% spectral analysis there was some aliphatic chain, aromatic chain, and some bromine, flourine was present.

Zeta Potential

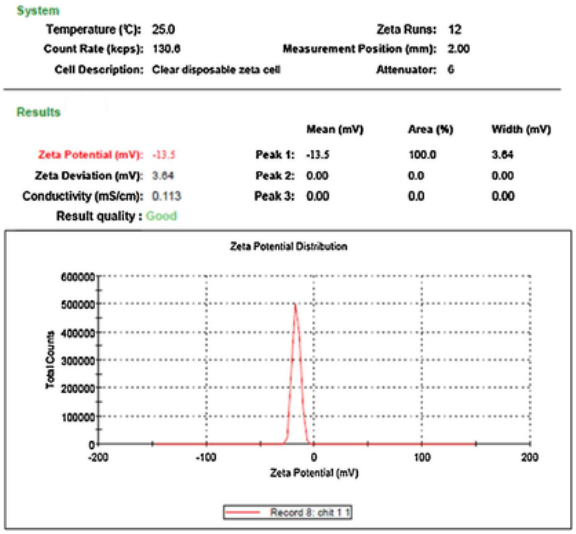

Fig. 4: Malvern Zeta potential graph for potential detection of curcumin loaded test sample 1%.

Particle size

NANOPHOX (NX0088), Auto correlation

A

x_{10} = 287.68 nm x_{50} = 305.53 nm x_{90} x_{16}= 294.68 nm x_{84}=314.76 nm x_{99} = 318.84 nm S_V = 19.75 m²/cm³

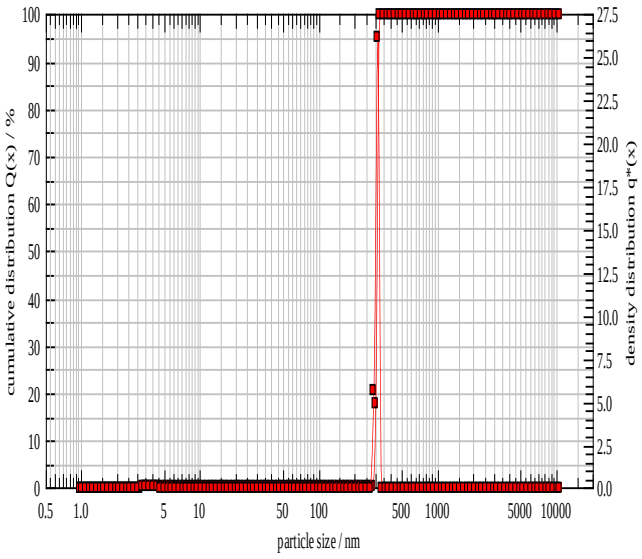

Fig. 5. Malvern Zeta sizer graph for size detection of curcumin loaded test sample 1%.

Stability studies

DURATION TIME	TEST SAMPLE (T1% T2%, T3%)	COLOUR AND pH
15 DAYS	NO CHANGE	NO CHANGE
1 MONTH	NO CHANGE	NO CHANGE
3 MONTH	NO CHANGE	NO CHANGE

Table 4: Stability studies of the curcumin

The duration of stability study of the sample, there was no changes in a concentration, solubility, stability, pH and color.

Spreadbility

S = M*L/T

Test Sample	Spread-ability (g.cm/s)
T1%	20.01
T2%	18.44
T3%	10.09

Table 5: Spreadability of curcumin loaded nanogel

According to this data spreadability is also as to variation with the test sample 1%, 2%, 3% so as to compared with the reference standard.

Viscocity

SAMPLE (30RPM)	ETA	TAU
T1%	122.782	221.007
T2%	97.418	174.025
T3%	96.425	177.566

Table 6: viscosity of curcumin nano gel

The viscosity is as found as the above as follows.

% of Drug entrapment

S. No.	SAMPLE	DRUG ENTRAPMENT (%)	DRUG UNENTRAPMENT (%)
T1 %	500mg	99.9%	.1%

Table 7: Drug entrapment of curcumin loaded nanogel

Conclusion

Curcumin nano gel formulation was successfully created, and it functions as an efficient and superior carrier for transdermal/topical preparation. The homogenicity, particle size, pH, drug content, in vitro drug release, skin irritancy test, spreadability, extrudability, and viscosity of the created nanogel were all optimised.When administered via the dermal route, the drawbacks of oral administration are avoided, and the therapy's single dose plasma levels are maintained. The rapid initial release rate from each formulation may have been caused by incomplete gel formation in the earlier time period, while the release slowed down in the latter time period following complete gel formation. The release profiles showed an inflection point, which suggested gel formation on the diffusion membrane in the donor compartment of the diffusion cell. Drug release slowed down as gel formation transformed the formulation into the gel phase.The results showed that the formed gels had the ability to retain the duration. The production of the formulation is also proved to be better and cost effective in comparison with oral dosage forms.

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