

Improvement and evaluation of a unique natural gel formula of curcumin for wound restoration pastime

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Abstract

Curcuminoids are one of the main active ingredients in the roots or rhizomes of Safran from India. Its miles observed that the roots have medicinal price, Safran from India. Its miles determined that the roots have beneficial for the medicinal drugs. Chemically, Curcuminoids are (1E, 6E)-1, 7-bis (4-hydroxy- three-methoxyphenyl) -1, 6- heptadiene- 3, 5-dione has a high metabolism and negative pores and skin permeation and is poorly soluble in water. With this background, the present observes pursues to improve pores and skin permeation by way of utilizing the polymers Gelucire®44/14 and carbopol 940. In this work, the capability of novel gels, particularly gel-middle Gelucire®44/14, to beautify Curcuminoids delivery to wound websites, decorate recovery price, and decrease scar formation was evaluated. Curcuminoids - Gelucire®44/14 gels have organized the use of an easy approach and evaluated concerning size, entrapment efficiency (% EE), and in vitro launch. The formation of novel gel Curcuminoids and Gelucire®44/14 became confirmed the use of toes-IR and DSC-TG evaluation. They have a look at also aimed to comprise the unconventional gel into the gel base and evaluate whether or not the topical novel gel training finished higher in phrases of wound restoration compared to unprocessed Curcuminoids. It became the simplest device showing marked improvement at days 18–21, and the performance of the novel gel turned into evaluated and handled on excision wounds inflicted on rat skin in the subsequent 12–15 days. The institution of animals handled with the Carbopol 940 gel base couldn't heal the wound, as the mean percent contraction of the wound was discovered to be the lowest. The organizations dealt with the obvious Curcuminoids gel and Curcuminoids - Gelucire®44/14 topical novel gel showed drastically ($P < 0.05$) higher wound contraction. There's no good-sized difference in the epithelization length among the groups handled with Curcuminoids undeniable and the Curcuminoids -Gelucire®44/14 novel gel.

Keywords: Curcumin; Curcumin-Gelucire®44/14 novel gel; Penetration; Gelucire®44/14; Carbopol 940; Wound recovery; ORS without dextrose; many others

1. Introduction

Curcumin is one of the main energetic components of the roots or rhizomes of *Curcuma longa*. The roots are determined to be medicinally treasured. Curcumin (I) is chemically 1, 7-bis-(four-hydroxyl-three methoxyphenyl)-hepta-1, 6- diene-three, five-Dione, and has very low bioavailability because of its negative solubility in water. Curcumin forms the first-rate constituent of roots or rhizomes of *Curcuma longa* L. And has already been notably evaluated for investigation with the aid of numerous researchers across the globe for its ability healing benefits. [1-2].

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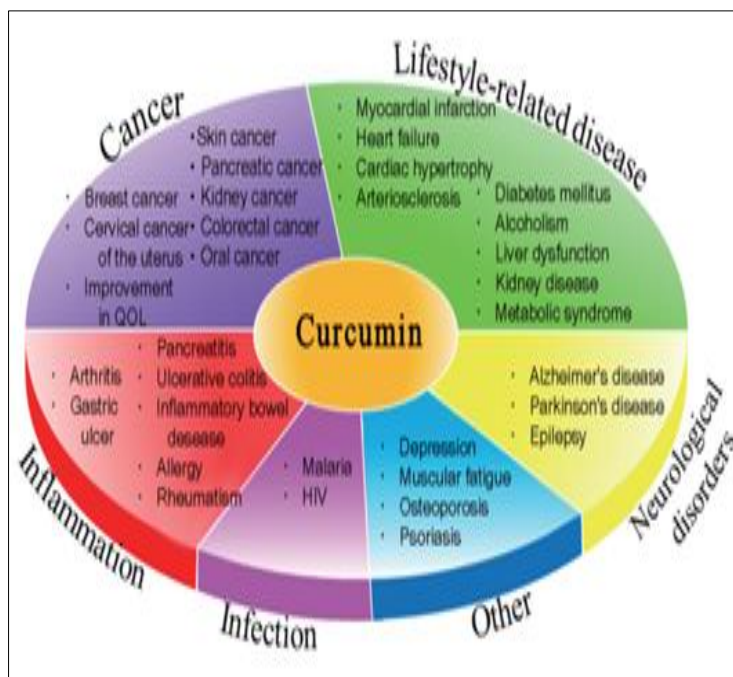


Figure 1 Potential therapeutic effect of curcumin

2. Material and methods

2.1. Materials

A present sample of curcumin changed into received from Dr. D.V. Agavekar owner of "BAPS lifestyles sciences". India provider of herbal plant extract in Thane, Mumbai. Gelucire®44/14 (Lauroyl Polyoxylglycerides) present pattern changed into procured from Gattefosc Corp., (Bombay university of Pharmacy, Kalina, Mumbai, India). Different principal ingredients viz. Carbopol 940 (LOBA Chemie Pvt. Ltd. Mumbai), ORS without dextrose (Qualikems quality Chem Pvt. Ltd, Nandesari, Vadodara, and Gujarat) were procured from the assets referred to and all the solvents and chemicals of A.R. Grades have been applied within the study.

2.2. Preparation and optimization of curcumin-Gelucire®44/14 topical novel gel: [3-23]

The aqueous gel base of 2.5 % w/v of Carbopol 940 was utilized for the instruction of gel containing curcumin-Gelucire®44/14 topical novel gel (equivalent to zero.2% w/w of Curcumin). The amount of the components used for the optimization of the novel gel formula is given in table -01 composition of numerous curcumin gel formulations (For 10 gm of gel).

Table 1 Composition of curcumin-Gelucire®44/14 topical novel gel formulations

Sr. no.	Curcumin topical novel gel formulation	F1	F2	F3
1.	Carbopol 940	0.25 g	0.25 g	0.25 g
2.	Curcumin	500 mg	500 mg	500 mg
3.	Gelucire®44/14	500 mg	1500 mg	1000 mg
4.	Propylene glycol	100 mg	500 mg	500 mg
5.	ORS Without Dextrose	700 mg	700 mg	700 mg
6.	Distilled water	Q.S.	Q.S.	Q.S.

2.3. Preparation of curcumin-Gelucire®44/14 topical novel gel: [9-23]

- Soaked the weighed quantity of Carbopol 940 (LOBA Chemie Pvt. Ltd. Mumbai) in water 10 ml for half-hour for topical novel gel formation.
- Weighed the specified portions of curcumin and Gelucire®44/14 and dissolved them in propylene glycol (LOBA Chemie Pvt. Ltd. Mumbai,) at 40°C with thorough blending.
- The suspension / topical novel gel acquired in step 1 and a couple of have been mixed with non-stop stirring followed by way of the addition of ORS without dextrose (Qualikems high-quality Chem Pvt. Ltd, Nandesari, Vadodara, and Gujarat) without dextrose for offering thickness to the gel. Finally, a sufficient amount of distilled water was introduced to make 10 gm of the gel formulation.

2.4. Fourier Transforms Infrared Spectroscopy

FTIR spectra were recorded for the KBr pellets containing the samples. The spectra had been recorded within the range of 4000 to 400 cm^{-1} , and the characteristic peaks had been recognized and compared. Dedication of wound restoration stages in Rats: The experimental protocols for this have a look at where accredited through the Institutional Animal Ethics Committee (IEAC) for Animal Use with protocol quantity SVBCP/IAEC/PG/13-14/53. Wholesome male Wistar rats with a median body weight of 210 ± 30 g had been housed in polycarbonate cages with 4 animals in each cage under preferred room temperature ($25 \pm 0.5^\circ\text{C}$) and humidity (30 %) and a 12-h light/darkish cycle. Water and meals had been given ad libitum. The animals were divided into three organizations viz. Simple curcumin-Gelucire®44/14 novel gel, with 4 animals in every organization.

2.5. In-vivo evaluation of curcumin-Gelucire®44/14 topical novel gel wound recovery activity

The curcumin novel gel containing curcumin-Gelucire®44/14 topical novel gel was evaluated for wound restoration activity with the use of the excision wound model in rats. The pastime changed into completed on experimental animal's viz. Wistar rats of both intercourses. The curcumin novel gel containing curcumin-Gelucire®44/14 topical novel gel became evaluated by means of treating the excision wounds [24] inflicted in rats, accompanied with the aid of recording % method contraction and the variety of days required to heal the wounds. The effects have been compared with the gel containing simple Curcumin in equal portions.

2.6. Animals

The Wistar albino rats of either intercourse weighing 210 – 220 g were housed underneath trendy situations of temperature and humidity ($25 \pm 0.5^\circ\text{C}$) and 12h light /dark cycle) had been utilized for the studies. The animals have been fed standard pellet food regimen and water ad lithium. The animals were divided into three foremost agencies with six animals in each group viz. Manipulate, fashionable Curcumin topical novel gel without Gelucire®44/14, and curcumin topical novel gel with Gelucire®44/14. The control institution become dealt with the Carbopol 940 topical novel gels without Curcumin, popular corporations had been treated with the curcumin topical novel gel without the Gelucire®44/14 polymer and the check organization changed into handled with the curcumin topical novel gel with curcumin-Gelucire®44/14 novel gel.

2.6.1. Infliction of Wounds

The rats were anesthetized with ether and a complete thickness round wound (vicinity of approximately 2.5 cm^2) turned into made on shaved return of the anesthetized rats (Fig. 10 to 13). The wounding day become taken into consideration as day 0. The injuries were dealt with topical Envisioned from the calibration curve for Curcumin. [25-31]

Data Analysis: All outcomes are supplied as mean \pm S.D. and analyzed the use of one-way analysis of variance (ANOVA) or student t-test. The distinction among the suggestions was tested by the use of the Dunnet check and values of $P < 0.05$ had been taken into consideration as statistically big. Microsoft excels 2007 and graph pad instantaneous three versions were used for the statistical evaluation. The corrections to be finished inside the references are highlighted in a yellow shade.

3. Results

Curcumin is one of the fundamental energetic components of the roots or rhizomes of *Curcuma longa*. The roots are observed to be medicinally valuable. Curcumin is chemically 1, 7-bis-(four-hydroxyl-three-methoxyphenyl)-hepta-1, 6-diene-3, five Dione, and is poorly soluble in water, as a result, there may be a very low concentration of curcumin is received in serum drug. The present takes a look at the worried formation of curcumin and Gelucire®44/14 topical

novel gel, with the purpose of boom the solubility of curcumin in water and as a consequence decorating the bioavailability of curcumin. The HPLC Agilent 1100 collection and the FT-IR spectrum were also recorded for the Curcumin pattern and it changed in comparison with the pronounced spectrum (Fig-03 and 04). The effects supplied in table 03; suggest that the peaks coincide with the reported information. For this reason, the identity of the curcumin sample is showed. [32]

The Curcumin and Gelucire®44/14 topical novel gel application. The overall performance of the topical novel gel turned into evaluated on excision wounds inflicted in rat pores and skin. The results obtained at various ranges of the observation are defined in this paper.

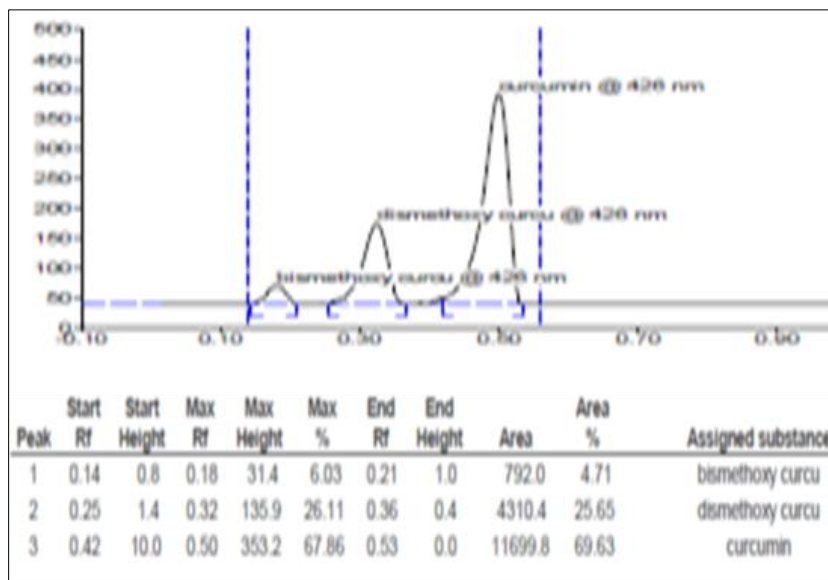


Figure 2 HPLC Agilent 1100 series plain Curcumin of the Spot Corresponding To RF 0.42 (Curcumin)

The present study involved the formation of novel gel curcumin-Gelucire®44/14, in order to increase the solubility of curcumin in water and thus enhance the bioavailability of curcumin. The novel gel for topical application. The performance of the novel gel was evaluated on excision wounds inflicted on rat skin.

The results of wound healing activity by excision wound model are presented in Tables 04, 05 and fig-10, 11, 12, and 13 indicating the mean % wound contraction due to treatment of various formulations on days 3, 5, 7, 9, 11, 13, and 15 days.

The group of animals treated with the gel base could not heal the wound as the mean % contraction of the wound was found to be the lowest. Groups treated with the gel containing the plain curcumin and the curcumin-Gelucire®44/14 novel gel indicated significantly ($P < 0.05$) higher contraction of the wound area.[19-30] There is no significant difference in the epithelization period of the groups treated with curcumin plain and the curcumin-Gelucire®44/14 topical novel gel.

Entrapment performance became determined with the aid of estimating the quantity of curcumin-Gelucire®44/14 topical novel gel. 1gm dissolved in 25 ml methanol. The answer becomes filtered and diluted certainly to get the absorbance at UV –seen spectrophotometer at 426 nm in the range of the calibration curve for fashionable curcumin and the quantity of curcumin changed into extrapolated from the calibration curve. The entrapment efficiency turned into calculated from the following components: The entrapment performance change into calculated from the following method:

$$\% \text{ drug loading (DL)} = \text{Weight curcumin in novel gel} / \text{weight of novel gel} * 100$$

$$\% \text{ theoretical loading (TL)} = \text{Weight of curcumin added} / \text{Weight of curcumin added} + \text{Weight of Polymer added} * 100$$

$$\% \text{ entrapment efficiency (EE)} = \% \text{ Drug Loading} / \% \text{ Theoretical Loading} * 100.$$

The curcumin-Gelucire®44/14 topical novel gel formula yielding the most entrapments of curcumin become applied for characterization. The topical novel gel formulation turned into characterized by using recording HPLC AGILENT 1100 collection, FT-IR spectra, and Differential Scanning Calorimetry (DSC) and Thermogravimetry evaluation (TGA).

3.1. Characterization of the curcumin-Gelucire®44/14 topical novel gel formulation

The curcumin-Gelucire®44/14 topical novel gel formula yielding the most entrapments of curcumin become applied for characterization. The topical novel gel formulation turned into characterized by using recording HPLC AGILENT 1100 collection, FT-IR spectra, and Differential Scanning Calorimetry (DSC) and Thermogravimetry evaluation (TGA).

3.2. Stability testing

The stability of the optimized curcumin-Gelucire®44/14 topical novel gel system changed into evaluated by way of DSC (Differential Scanning Calorimetry), TGA (Thermo gravimetric evaluation), and FT-IR studies after one month of storage at room temperature (25°C)/ 60% RH, and (40°C), 75% RH.

3.3. Thermal Analyses

DSC curves had been received using a DSC 6000 (Pyris collection 6000) for method F2, the topical novel gel of curcumin and Gelucire®44/14, by means of at once setting the weighed pattern aluminum pans and the pans had been sealed. The analysis become carried out from 30 to 320°C in inert surroundings (N₂ flow 50 ml/min) with a heating rate of 10°C/min. TG curves have obtained the usage of 5-mg samples beneath N₂ flux from 30 to 320°C the usage of a TGA-50 (Pyris collection 6000). The temperature of the degree turned multiplied from room to 90°C at a 3°C/min rate with stops for five min at 30, 60, and 90°C.

Packages of gel system until the injuries had been the software of gel components till the wounds were absolutely healed. The wounds have been monitored and the location of the wound became measured with the aid of tracing the wound on a transparent sheet on alternative days 1, 3, 5, 7, 9, 11, 13, and 15 days or until complete epithelization. The outcomes are presented in Tables 04 and 05.

3.4. Preparations of formulations for application to excision wounds

Curcumin-Gelucire®44/14 topical novel gels had been integrated into novel gel components base IP and the subsequent formulations had been prepared.

Table 2 F1- composition of control novel gel formulation, F-2 composition of curcumin topical novel gel without Gelucire®44/14, and F3- composition of curcumin topical novel gel with Gelucire®44/14

Sr. no.	Ingredient	F1(A)	F2(B)	F3(C)
		Quantity (% w/w)		
1.	Standard Curcumin	0.0 g	0.5 g	0.5 g
2.	Carbopol 940	0.1 g	0.1 g	0.1 g
3.	ORS without dextrose	0.7 g	0.7 g	0.7 g
4.	Gelucire 44/14	1.6 g	0.0 g	1.6 g
5.	Propylene glycol	0.0001 ml	0.0001 ml	0.0001 ml
6.	Water quantity sufficient	Up to 10 g	Up to 10 g	Up to 10 g



Figure 3 Distinctive formulations

3.5. Stability studies of curcumin-Gelucire®44/14 topical novel gels formulation containing curcumin and Gelucire®44/14

Stability has a look at curcumin-Gelucire®44/14 topical novel gels formulations for 1 month at distinct temperatures forty, 25^o C /RH 60%, and 40^o C /RH 75% Samples of the formulations stored at various situations of temperature and humidity have been taken out at weekly periods and the concentration of curcumin in these had been determined the use of UV-seen spectrophotometer. The samples had been dissolved in water and definitely diluted to examine absorbance in opposition to the water blank at 426 nm.

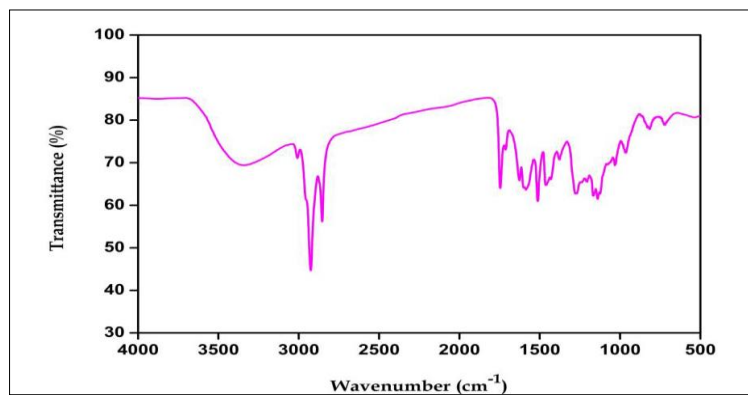


Figure 4 FT-IR Spectrum of Reference Standard of Curcumin. [13-23]

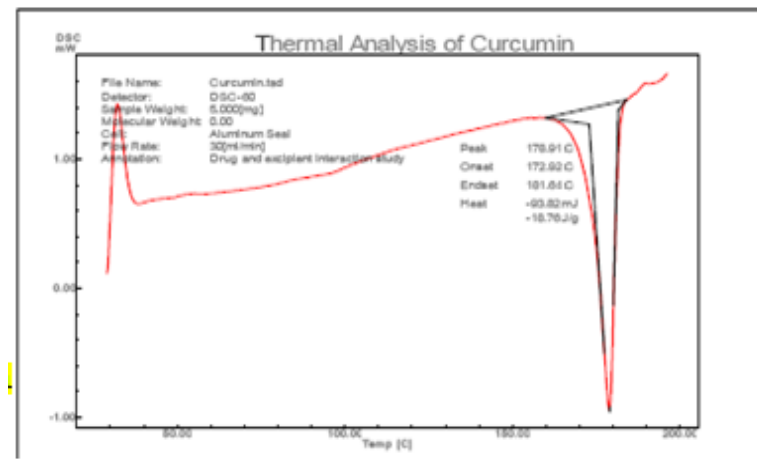


Figure 5 DSC analysis of curcumin.[33]

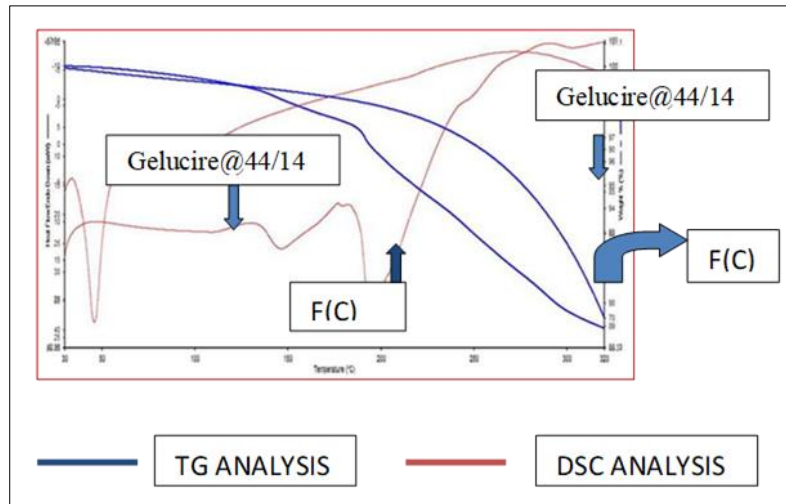


Figure 6 DSC and TG Analysis of curcumin and Gelucire®44/14

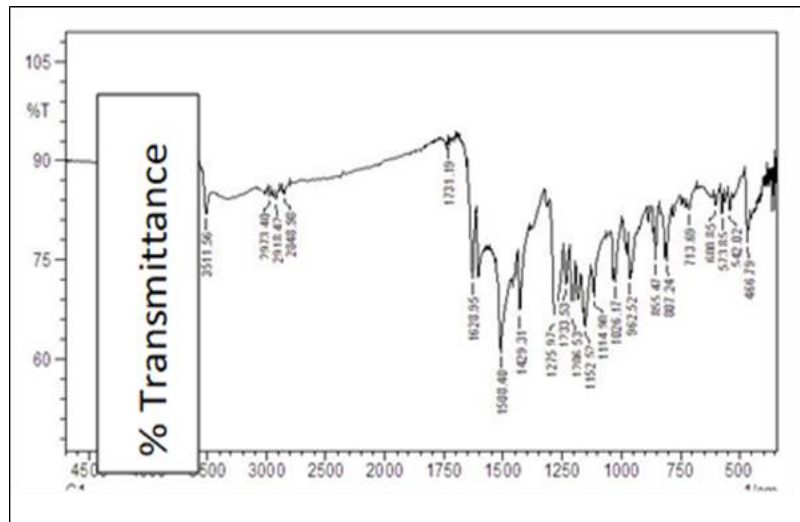


Figure 7 FT-IR Spectrum of Plain curcumin

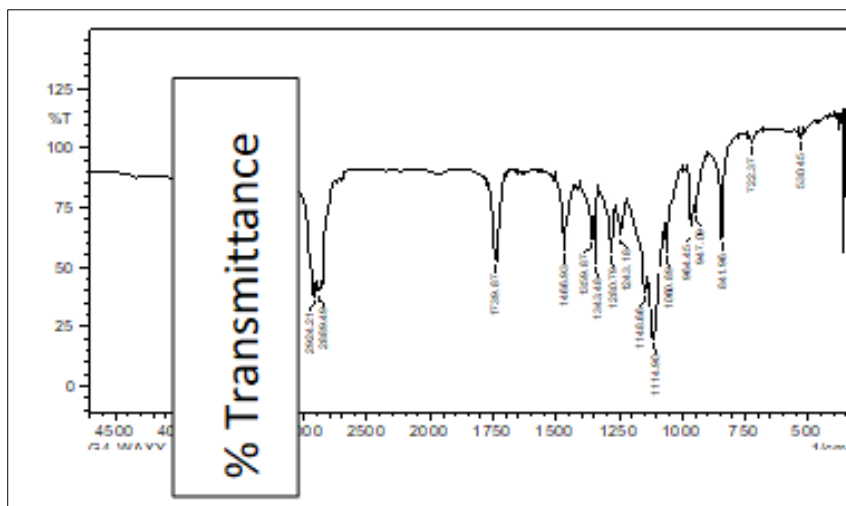


Figure 8 FT-IR Spectrum of Plain Gelucire®44/14

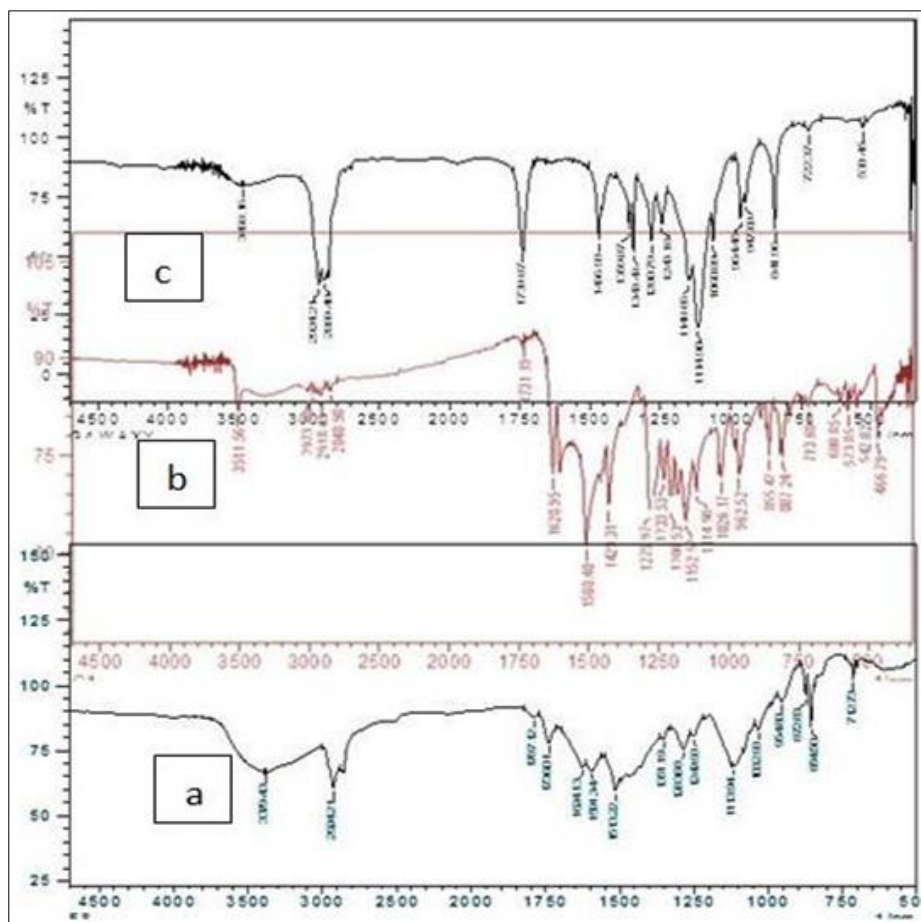


Figure 9 FT-IR Spectrum of Curcumin-Gelucire®44/14 topical novel gel different formulation F (A), F (B), and F (C)

Table 3 FT-IR spectrum for data recording:

Frequency cm-1 Standard curcumin	Frequency cm-1 Sample of curcumin	Possible groups assignment
3341	3340	Free hydroxyl-group of phenol (Ar-OH). (broad)
719, 815 and 962 cm-1	713,807 & 962	-C-H bending of alkenes
1745	1731	- vibration of the carbonyl bond (C=O))
shoulder at 1712	-	-Keto-enol tautomerism of curcumin
1463 and 1378	1430,1350	vibration mode of C-O elongation of the alcohol and phenol
-	1601,1508,1429	Vibration stretching of double bonds (C=C) aromatic

Table 4 Compatibility has a look at curcumin and excipients for use for topical novel gel formulations: effect on the arrival of the mixture:

Day 1: observations						
In	TOC /RH (%)	I/AA	TOC /RH (%)	I/AA	TOC /RH (%)	I/AA
DPC	4	NI	25/65	NI	40/75	NI
DPC+G+C	4	NI	25/65	NI	40/75	I
Day 7: observations						
DPC	4	NI	25/65	NI	40/75	NI
DPC+G+C	4	NI	25/65	NI	40/75	I
Day 21: observations						
DPC	4	NI	25/65	NI	40/75	NI
DPC+G+C	4	NI	25/65	NI	40/75	I
Day 30: observations						
DPC	4	NI	25/65	NI	40/75	NI
DPC+G+C	4	NI	25/65	NI	40/75	I

Table 5 Compatibility looks at curcumin and excipients to be used for topical novel gel formulations: effect at the attention of curcumin in the combos:

Day 1: observations						
In	TOC /RH (%)	I/AA	TOC /RH (%)	I/AA	TOC /RH (%)	I/AA
DPC	4	5.7 ± 0.37	25/65	5.2 ± 0.03	40/75	4.5 ± 0.10
DPC+G+C	4	5.53 ± 0.30	25/65	5.08 ± 0.05	40/75	5.87 ± 0.61
Day 7: observations						
DPC	4	4.86 ± 0.09	25/65	6.31 ± 0.15	40/75	4.47 ± 0.09
DPC+G+C	4	5.33 ± 0.7	25/65	5.01 ± 0.07	40/75	5.73 ± 0.51
Day 21: observations						
DPC	4	5.4 ± 0.17	25/65	5.5 ± 0.15	40/75	4.2* ± 0.09
DPC+G+C	4	5.07 ± 0.2	25/65	4.98 ± 0.3	40/75	5.70 ± 0.49
Day 30: observations						
DPC	4	5.44 ± 0.08	25/65	5.90 ± 0.49	40/75	4.25* ± 0.18
DPC+G+C	4	5.00 ± 0.71	25/65	4.90 ± 0.63	40/75	5.50 ± 0.48

(In- Ingredients, T-Temperature, NI - No Interaction, I - Interactions, G - Gelucire®44/14, DPC- Drug Plain Curcumin, DPC+G+C - Drug Plain Curcumin + Gelucire®44/14 + Carbopol 940, I/AA- Interaction/alteration in appearance.)

The outcomes presented in table-04 and 05 suggest that there is no giant trade within the concentration of curcumin in the combination of gel ingredients at 25° C/RH 65 and 40°C. However at 40°C /RH 75 the good sized (P<0.05) trade inside the attention of the curcumin is discovered at the end of 15 days. [34]

3.6. *In vivo* evaluation of wound healing activity of curcumin novel gel: [3-23]

The results of wound restoration interest through the excision wound model are supplied in Tables 04, 05 and fig-10, eleven, 12, and 13 indicating the implied % wound contraction due to treatment of diverse formulations on days 3, 5, 7, 9, 11, 13, and 15 days.

The organization of animals treated with the gel base couldn't heal the wound as the implied % contraction of the wound became determined to be the bottom. Organizations treated with the gel containing the obvious curcumin and the curcumin–Gelucire 44/14 novel gel indicated significantly ($P < 0.05$) better contraction of the wound place.[19-33] there may be no sizable distinction in the epithelization length of the corporations treated with curcumin simple and the curcumin-Gelucire®44/14 topical novel gel.[25-31]



*: $P < 0.05$ Group C compared with Group B

Figure 10 Effect of topical application of different curcumin–Gelucire®44/14 topical novel gel

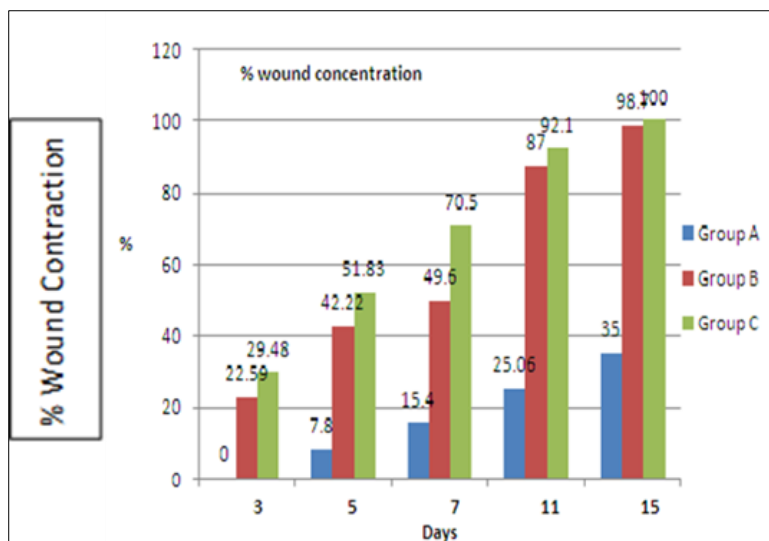


Figure 11 Effect of topical application of different formulation of curcumin on mean contractions of wound area of excised wound in rats. Group A: plain Carbopol 940 gel without curcumin, Group B = Plain Curcumin, Group C = curcumin–Gelucire®44/14 topical novel gel

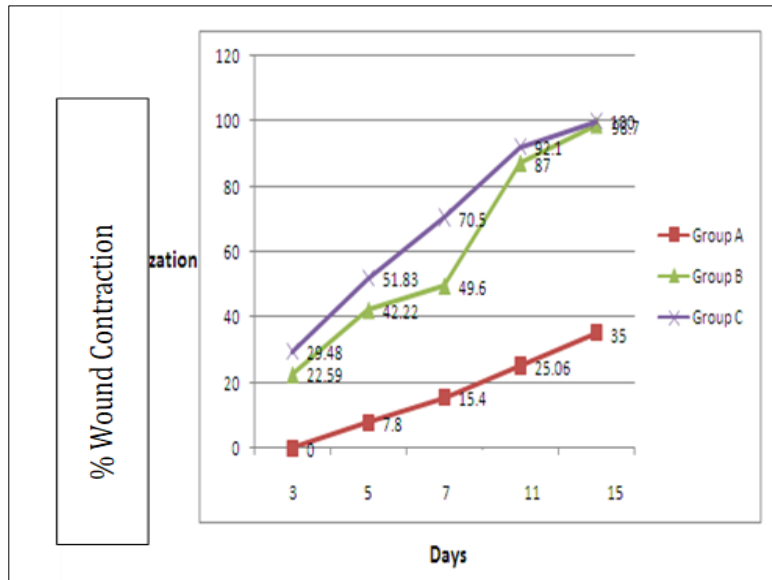


Figure 12 Effect of topical application of different formulations of curcumin on the mean contraction of wound area of excised wound in rats. Group A= plain Carbopol 940 gel without curcumin, Group B= Plain Curcumin, Group C= Curcumin–Gelucire®44/14 topical novel gel

Curcumin–Gelucire®44/14 topical novel gel formulations to the excision wounds on fifteenth day. Group A = plain Carbopol 940 gel without curcumin, Group B = Plain Curcumin, Group C = Curcumin–Gelucire®44/14 topical novel gel.

Table 6 Effect of topical application of different formulation of Curcumin on period of epithelization of excised wound in rats:

Groups	% Wound contraction Mean ± SEM				
	Day 3	Day 5	Day 7	Day 11	Day 15
Group A	0.00 ± 0.00	7.80 ± 0.80	15.4 ± 0.84	25.06 ± 1.36	35.0 ± 1.78
Group B	22.59 ± 0.56	42.22 ± 0.50	49.6 ± 0.67	87.0 ± 0.83	98.7 ± 0.75
Group C	29.48 ± 1.10	51.83 ± 0.77*	70.5 ± 1.12*	92.1 ± 0.44*	100 ± 0.44

Table 7 Effect of topical application of different formulation of Curcumin on period of epithelization of excised wound in rats:

Groups	Animals						P. E. (in days)
	01	02	03	04	05	06	
Group A	21	24	30	25	25	28	25.5 ± 1.11
Group B	16	16	17	17	16	16	16.33 ± 0.32
Group C	15	15	15	14	15	15	14.83 ± 0.13

Group A=plain Carbopol 940 gel without curcumin, **Group B** = Plain Curcumin, **Group C** = Curcumin–Gelucire®44/14 topical novel gel, N=6, **P. E.** = Period of epithelization, etc.

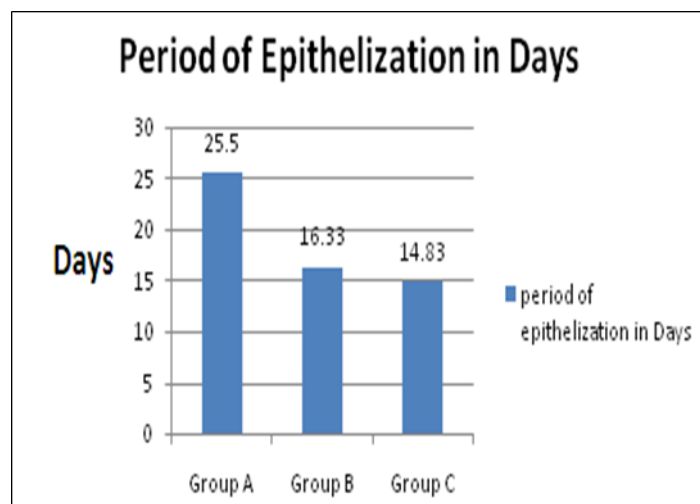


Figure 13 Effect of topical application of different formulations of curcumin on the period of epithelization of the excised wound in rats. Group A= plain Carbopol 940 gel without curcumin, Group B = Plain Curcumin, Group C= curcumin–Gelucire®44/14 topical novel gel. N = 6 Wister albino rats.

3.7. Stability Studies of Curcumin-Gelucire®44/14 Topical Novel Gel Formulation:

Three different formulations, viz., F1, F2, and F3, were prepared by incorporating curcumin-Gelucire®44/14 topical novel gel in various proportions, and these were stored at 4 °C, 25 °C with RH 65%, and 40 °C with RH 75 %.[30-34] Curcumin content was determined by withdrawing samples at weekly intervals. The results are presented in table 08 and Figs. 14–16.

Table 8 Stability Study of Curcumin-Gelucire®44/14 Topical Novel Gel Formulation:

F	T°C/ RH	%	Conc.(mg) Mean ± S.D	T°C/ RH	%	Conc.(mg)Mean± S.D	T°C/ RH	%	Conc.(mg) Mean± S.D
Day 1 : observations									
F1	4		1.28 ± 0.57	25/65		1.68 ± 0.91	40/75		1.27 ± 0.24
F2	4		1.6 ± 0.15	25/65		1.7 ± 0.28	40/75		1.42 ± 0.74
F3	4		1.56 ± 0.83	25/65		1.30 ± 0.90	40/75		1.02 ± 1.35
Day 7: observations									
F1	4		1.24 ± 0.38	25/65		1.65 ± 0.91	40/75		1.24 ± 1.25
F2	4		1.60 ± 1.27	25/65		1.68 ± 0.70	40/75		1.37 ± 0.87
F3	4		1.73 ± 0.49	25/65		1.32 ± 0.89	40/75		1.03 ± 1.01
Day 15: observations									
F1	4		1.2 ± 1.82	25/65		1.4 ± 1.24	40/75		1.2 ± 1.19
F2	4		1.54 ± 1.73	25/65		1.65 ± 0.23	40/75		1.33 ± 0.44
F3	4		1.56 ± 0.14	25/65		1.33 ± 0.712	40/75		1.02 ± 1.32
Day 30: observations									
F1	4		1.18 ± 0.81	25/65		1.2 ± 0.31	40/75		1.1 ± 2.11
F2	4		1.53 ± 0.89	25/65		1.52 ± 0.67	40/75		1.27 ± 0.29
F3	4		1.46 ± 0.41	25/65		1.06 ± 0.34	40/75		1.01 ± 0.92

F-formulation, T-temperature, RH-relative humidity, Conc.-concentration etc Mean ± S.D, N=3

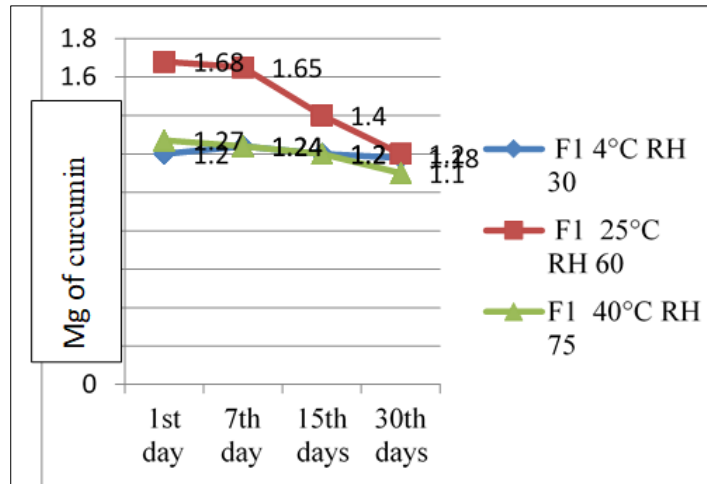


Figure 14 Stability study of F1 formulation containing carbopol 940 topical novel gel

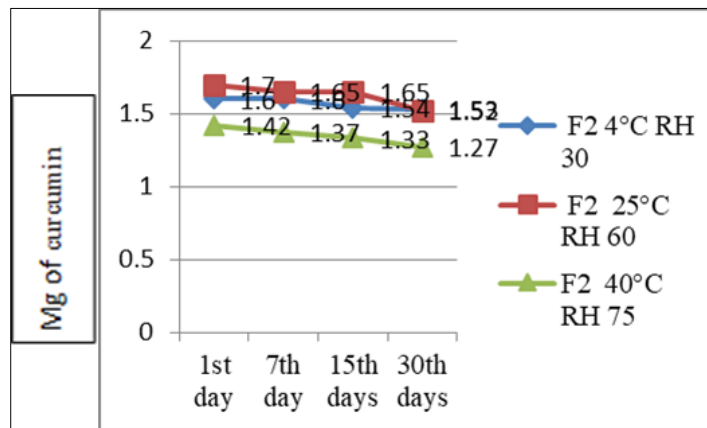


Figure 15 Stability study of F2 formulation containing Curcumin and Carbopol 940 topical novel gel without Gelucire@44/14

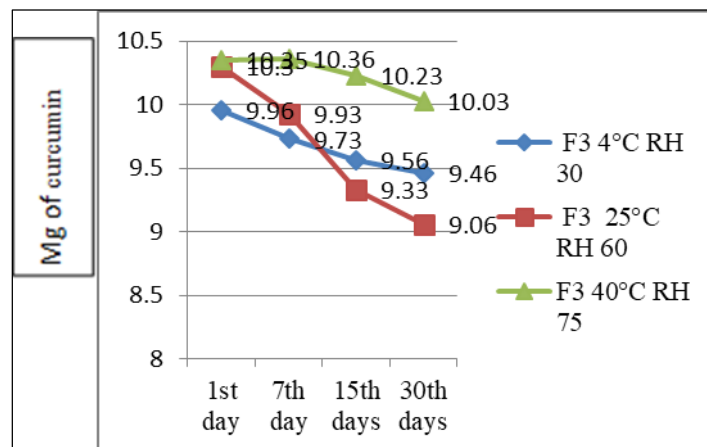


Figure 16 Stability study of F3 formulation containing Curcumin and Carbopol 940 topical novel gel with Gelucire@44/14

The stability studies presented in Table 06 and Figs 14, 15, and 16 reporting the concentration of curcumin in gel show that the formulation F3 is stable at 4 °C and 25 °C / RH 65, with no significant change in curcumin concentration after

one month. °C according to Paradkar *et al.* [27] and 176.8 °C according to Xie *et al.* [26] Fig. 4. Shows the thermoanalytical profile of curcumin.

Gelucire®44/14 and the formulation F3, which contains curcumin, form a novel topical gel formulation. The first peak, corresponding to curcumin melting in the topical novel gel, appeared at a lower temperature, while the second peak appeared at a higher temperature of about 190 °C. These data suggest that curcumin is partially dissolved in the topical novel gel at a molecular level, which may be caused by previous melting of Gelucire®44/14 at 46.4 °C and consequent curcumin solubilization in the formulation ingredients. Both curcumin and Gelucire®44/14 have non-polar characters, which favors their interaction through intermolecular van der Waals forces. Additional energy is supplied to the process by heating, favouring these interactions between the drug and carrier and causing the solubilization of the curcumin in the melted Gelucire®44/14.

The physical or chemical nature of a thermal event can be confirmed using thermogravimetric analysis.

FT-IR is a very sensitive methodology, and most chemical changes can be detected by this method. The broad peak at 3329 cm⁻¹ in the FT-IR spectra for a topical novel gel suggests hydrogen bond interactions between the gel. The results of FT-IR, DSC, and TGA are found to correlate with those of Figs. 05 and 06. Gelucire®44/14 is a nonionic, water-dispersible, self-emulsifying surfactant that has been shown to improve drug solubility (lauroyl macrogol-32 glycerides EP and lauroyl polyoxyl-32 glycerides NF). ability of drugs [27]. The results clearly show that the curcumin content of Gelucire®44/14 increases significantly after the formation of the topical novel gel in the ratio of 1:3 curcumin to Gelucire®44/14. The remarkable solubility enhancement for curcumin with Gelucire®44/14 topical novel gel, associated with the findings of DSC, and FT-IR, suggests that the process of curcumin with Gelucire®44/14 topical novel gel preparation was able to create a molecular dispersion of the drug within the topical novel gel, which was potentiated by hydrogen bonding.

The stability studies presented in Table 06 and Figs 14, 15, and 16 reporting the concentration of curcumin in gel show that the formulation F3 is stable at 4°C and 25°C / RH 65, with no significant change in curcumin concentration after one month. The stability of the formulations was affected at temperatures of 40 °C (RH 75), probably due to melting of the Gelucire®44/14.

4. Discussion

Curcumin is one of the most popular and useful therapeutic agents obtained from the roots and rhizomes of *Curcuma longa*. The molecule has numerous therapeutic properties such as antioxidant, anti-inflammatory, anti-cancer, antibacterial, wound healing, antiviral, hepatoprotective, neuroprotective, and so on. Many attempts have been made to improve solubility through the preparation of gels or complexes with agents like Carbopol 940, PVP, cellulose acetate, mannitol, etc. In the current study, a novel gel of curcumin and Gelucire® 44/14 is prepared, followed by the preparation and evaluation of a topical preparation, in an attempt to improve the skin penetration of curcumin on the skin.

The results obtained in the study are discussed in this paper. The physicochemical tests and spectral studies were performed to confirm the identity of the materials, viz., curcumin and Gelucire®44/14. Following confirmation of identity, the process for preparing novel gel was optimized by varying the proportions of curcumin and Gelucire®44/14 while maintaining the amount of curcumin constant. The proportion yielding the highest concentration of curcumin upon skin penetration was considered to be the optimum one.

A drug excipients compatibility study is an important aspect of the development of any novel gel formulation. The physical mixture of curcumin, Gelucire®44/14, along with the excipients of novel wound healing gel formulations, viz., sodium bicarbonate and calcium carbonate, were stored under different conditions, viz., 4 °C and 25 °C, (RH 65%), sodium bicarbonate and calcium carbonate, were stored under different conditions, viz., 4 °C and 25 °C, (RH 65%), and 40 °C (RH 75%) and calcium carbonate, were stored under different conditions, viz., 4 °C and 25 °C, (RH 65%), and 40 °C (RH 75%), and the physical mixture was analysed for alterations in appearance and curcumin content. The physical mixtures stored at 40 °C (75 % RH) were found to be liquefied due to the low melting nature of Gelucire®44/14, and the concentration of curcumin was found to be 5.24 mg/mL.

The formation of novel gel in the curcumin and Gelucire®44/14 topical novel gel formulation was characterised by FT-IR and thermal studies, viz., DSC and TG. The DSC curves provide information on thermal events characterised by a change in enthalpy in a range of temperatures, such as melting and crystallization, and they can indicate physical or

chemical interactions between components of the formulation. The melting point of curcumin depends on its relative crystallinity and has been reported to be 180°C

Wound healing is a complex process characterised by homeostasis, re-epithelialization, granulation tissue formation, remodeling of the extracellular matrix, and scar formation. Any agent accelerating any of the above processes is a promoter of the wound healing process.[12] Curcuma powder, also known as turmeric powder, is a well-known remedy for healing wounds. [14] To investigate the effect of curcumin with Gelucire®44/14 topical novel gel on wound healing compared to plain curcumin, a topical novel gel preparation containing curcumin with Gelucire®44/14 topical novel gel was incorporated into a Carbopol 940 novel gel base. The wound healing activity was evaluated using an excision wound model in rats, as was the rate of healing. The excision wound model was designed to stimulate commonly encountered excision wounds in clinical practice.

The results presented in Tables 04, 05, and Figs. 10, 11, 12, and 13 for the effect of application of gels containing topical novel gel of curcumin and Gelucire® 44/14 and gel containing plain curcumin on the mean percent wound contraction on day 7 indicate that there is a significant ($P < 0.05$) difference in mean percent wound contraction on day 8. The three stages of wound healing are as follows: homeostasis lasts 1-4 days, granulation lasts 4-8 days, and remodeling tissue formation takes place in the third stage. The results indicate that there is no significant difference in the period of epithelization. This may be due to the increased amount of solubilized curcumin due to the formation of the novel gel.

5. Conclusion

In the present study, attempts have been made to improve the skin penetration of a novel topical gel in order to enhance the wound healing of curcumin. The approach of preparing novel gel with Gelucire®44/14 was utilised to increase the skin penetration and wound healing of curcumin in novel gel. From the present study, the following conclusions can be drawn:

- The topical novel gel preparation, viz., gel, was prepared by incorporating the novel gel of curcumin and Gelucire®44/14 in Carbopol 940 base (5% W/W) and evaluated for its wound healing potential. The study found that applying the gel caused a significant contraction of the wound on days 5 and 7 when compared to the gel containing equivalent amounts of plain curcumin. Although there was no significant difference in the epithelization period between gel with plain curcumin and gel with a topical novel gel of curcumin and Gelucire® 44/14, the compliance of the gel with the novel gel was found to be better
- The formulations were found to be stable at 25 °C and 65% RH but unstable at 40 °C and 75% RH.

The current study suggests that more detailed research is needed to develop better topical gel formulations of curcumin with improved skin penetration and wound healing.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors hereby declare that there is no conflict of interest.

Statement of ethical approval

Prior to in-vivo activity we sanctioned protocol for Animal Use with protocol No. SVBCP/IAEC/PG/13-14/53. Activity was performed under the supervision of research guide Dr. Chhaya H. Gadgoli

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