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Formulation and Evaluation of Lawsone Loaded Nanosponge Gel for Topical Delivery

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ABSTRACT

The target of the current report considers producing controlled-release lawsone-loaded nanosponge gel for topical delivery. Lawsone is also known as hennotannic acid, is an active pharmaceutical agent found in the general leaves of the henna plant responsible for an antifungal agent to treat cutaneous candidiasis. The current nanosponge formulation is carried out using ethyl cellulose as polymer, polyvinyl alcohol as co-polymer dichloromethane as a cross-linker & propylene glycol as a permeation enhancer. The formulation was prepared through emulsion solvent diffusion approach as well as the prepared nanosponge gels were evaluated by physical appearance, determination of PH, spreadability, extrudability, skin irritation test, drug content, entrapment efficiency, and *in-vitro* diffusion studies. The physical appearance of the LNS1 & LNS7 formulation was watery and the remaining formulations were found to have smooth, transparent, homogenous with a gel-like consistency. The PH of formulated nanosponge gel formulation was found to be in the range between 4.5-5.5. It was concluded that all the PH values within the range of skin PH. The spreadability values ranging from 7.2-8.5. In the formulations (LNS1 & LNS8) far more than 90% going from contents had been extrudable indicating they need perfect extrudability with the except for LNS1 & LNS7 as 80% of the contents were extrudable. The skin irritation test of lawsone loaded nanosponge gels (LNS1-LSN5) had been strain irritation at a site of application. The drug content ranging from 79-92.2% & entrapment efficiency ranging from 66-80% was obtained. *In-vitro* drug diffusion research had been performed by diffusion apparatus containing 100ml PH 5.0 phosphate buffer maintained at 37 ^{o}C. LNS6 was found to show a drug release of 68.8%. Therefore LNS6 formulation sustained the drug release and was considered as optimized formulation over LNS4-LSN7. The 'n' value of formulation LNS6 was 0.899and suggesting drug was released by Zero-order kinetics.

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INTRODUCTION

The main objective of the current report to provide a controlled release dosage form and target the drug to the specific site. To enhance the solubility containing poorly water-soluble drugs. It's useful to sustain the drug in the body for a prolonged period. Nanosponges will be porous polymeric delivery systems that will be small spherical particles having a big porous surface [1]. Such will be utilized passive focused on consisting of cosmetic agents to the skin so that completing major

benefits given to decrease the compute dose, retention going from dosage stand on the retention consisting of dosage place on the skin, and turning away of systemic absorption. These nanosponges could be properly incorporate on topical systems for prolonged-release as well as skin retentivity therefore reducing the variability in drug absorption, toxicity as well as bettering patient deference by delaying dosing intervals [2]. It can raise the overall irritation of drugs with no lowering their efficacy. For topical administration, they can be effectively incorporated into the topical hydrogel [3]. It also helps to lower body temperature and burning effect. *Lawsonia inermis* contains a red-orange pigment known as lawsone. It is the ancient herb of grace and healing when it disturbs the surface it is active to the skin. Powerful active elements provide chilling as well as astringent action at the side of protection as opposed to fungus and bacteria [4].

MATERIAL & METHODS

Ethylcellulose was once purchased from Himedia laboratories PVT. Ltd. Mumbai; Polyvinyl alcohol & Carbopol 934 became purchased free of charge sample from Loba chemicals, Pvt. Ltd Mumbai, Eudragit E 100, Dichloromethane & Propylene glycol was a gift stratified sample of Sdfine chemicals. Ltd, Mumbai. Triethanolamine, Methylparaben & Propylparaben was purchased from Yarrow chemicals, Hyderabad and other ingredients used were of Analytical grade.

Extraction of Lawsone

The fifty grams of the powdered plant material got through 300 ml containing ethanol, macerated thrice, and filtered. The filtrate was dry in a hot air oven for three days. The dry residue was scrapped and the powder acquired was 4.98 grams [5].

Compatibility studies

FTIR was once conducted to verify the potential of the interaction of chemical bonds between drug and polymer [6].

Nanosponges Preparations

Nanosponges were prepared by using different proportions of ethyl cellulose and polyvinyl alcohol. In this method, two phases are present i.e. dispersed phase consists of ethylcellulose and the drug was dissolved in 20 ml dichloromethane and slowly added to a definite amount of polyvinyl alcohol in 150 ml of the aqueous continuous phase. The reaction mixture was stirred at 1000 rpm for 2 hours. Followed by filtration and dried in an oven at 40 degrees centigrade [7]. It's stored in vacuum desiccators to verify the removal of residual solvent (Table 1).

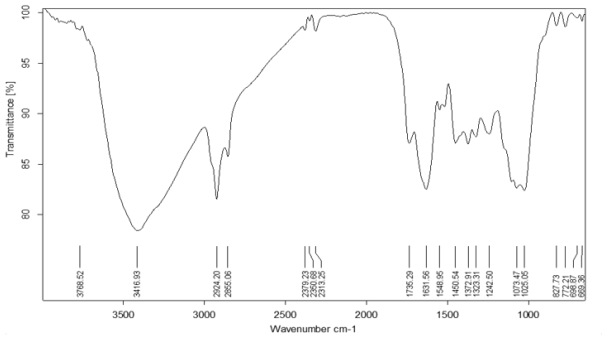

Figure 1: FTIR image of lawsone

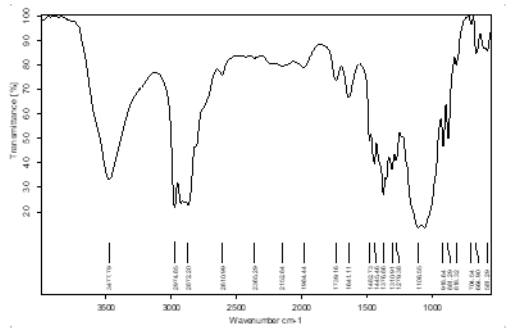

Figure 2: FTIR image of ethyl cellulose

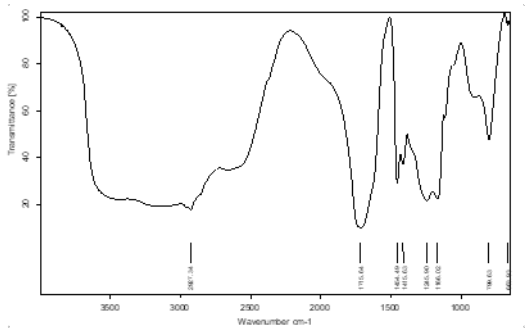

Figure 3: FTIR image of carbopol

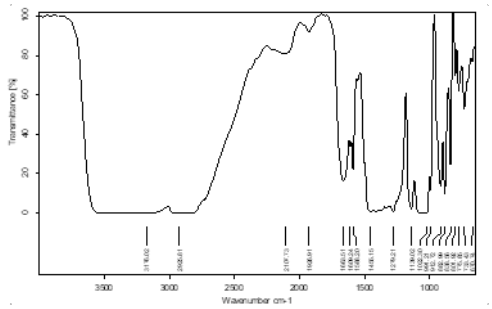

Figure 4: FTIR image of lawsone + all excipients

Formulation of Lawsone Loaded Nanosponge Gel

Weigh accurate quantity of Carbopol 934 soaked in water for 24 hrs for over lasting swelling of the polymer. From the above-prepared gel base, lawsone

Table 1: Composition of lawsone loaded Nanosponges

Excipients	LNS1	LNS2	LNS3	LNS4	LNS5	LNS6	LNS7	LNS8
Lawsone (mg)	100	100	100	100	100	100	100	100
Ethyl cellulose (mg)	0.15	0.2	0.25	0.3	0.15	0.2	0.25	0.3
Dichloromethane (ml)	20	20	20	20	20	20	20	20
Polyvinyl alcohol (%w/v)	0.2	0.2	0.2	0.2	0.3	0.3	0.3	0.3

Table 2: Formulation of Lawsone Loaded Nanosponges Gel

Ingredients	Quantity
Lawsone nanosponges	1% W/W
Carbopol 934	1% W/W
Propylene glycol(ml)	1
Methyl paraben(gm)	0.02
Propyl paraben(gm)	0.01
Triethanolamine	Quantity sufficient

Table 3: FTIR spectrum of Lawsone & Mixture of compounds

FTIR Spectrum	IR absorption bands (cm^{-1})		Bond	Functional group
	Observed peak	Characteristic peak		
Lawsone	3768.52	3000-3700	O-H stretch	Alkenes, aromatic ring
	3416.93	3000-3700	O-H stretch	Alkenes, aromatic ring
	2920.20	2500-3000	C-H stretch	Alkenes, Aromatic ring
	2313.25	2100.2660	C=C stretch	alkynes
	1735.29	1600-1900	C=O stretch	Aldehyde, ketones.
Ethyl cellulose	3416.93	3000-3700	O-Hstrech	Alkenes,aromatic
	2152.84	2100-2660	C=Cstrech	alkynes
	2365.29	2100.2660	C=C stretch	alkynes
	1739.16	1600-1900	C=O stretch	Aldehyde, ketones.
Carbopol	3682.31	3000-3700	O-Hstrech	Alkenes, aromatic
	1715.64	1600-1900	C=O stretch	Aldehyde, ketones.
	1454.40	600-1500	C-Cl stretch	alkanes
	1245.63	600-1500	C-Cl stretch	alkanes
lawsone + all excipients	3176.02	600-1500	O-H stretch	Alkenes, aromatic ring
	2925.81	2500-3000	C-Hstrech	Alkenes, aromatic ring
	2107.73	2100-2660	C=Cstrech	alkynes
	1926.91	2100-2660	C=Cstrech	Alkynes
	1455.15	600-1500	C-Cl stretch	Alkanes

Nanosponge equivalent to 1% w/w were uniformly distributed [8]. Permeation enhancers and preservatives are added and subjected to the homogenizer. During stirring add triethanolamine drop wise to adjust PH (Table 2).

Quality Control Parameters of Nanosponge gels

Physical appearance

The physical appearance of the prepared Nanosponge gel was evaluated by visual perception [9].

Determination of PH

The lawsone loaded nanosponge gel formulation was determined with a digital pH meter [10].

Spreadability

Two sets of glass slides of standard dimensions were taken. The gel was placed over one of the slides. One gram of your formulation belongs in a circle going

Table 4: Evaluation of lawsone loaded nanosponge gel

Formulation Code	Spreadablity (gm cm/sec)	Extra durability	Drug content (%)	Entrapment efficiency (%)	PH	Skin Irritation
LNS1	8.5	Good	79.0	68	5.3	No Irritation
LNS2	7.2	Excellent	83.4	75	5.5	No Irritation
LNS3	7.9	Excellent	90.6	79	5.4	No Irritation
LNS4	8.1	Good	88.1	71	4.9	No Irritation
LNS5	7.2	Excellent	87.7	73	5.5	No Irritation
LNS6	7.5	Excellent	92.2	80	5.4	No Irritation
LNS7	8.3	Good	80.9	66	9.8	No Irritation
LNS8	7.6	Excellent	84.5	72	5.1	No Irritation

Table 5: Lawsone loaded nanosponge gel skin irritation & appearance

Formulation Code	Skin Irritation	Appearance
LNS1	No Irritation	Watery
LNS2	No Irritation	Smooth, Transparent &Homogenous
LNS3	No Irritation	Smooth, Transparent &Homogenous
LNS4	No Irritation	Smooth, Transparent &Homogenous
LNS5	No Irritation	Smooth, Transparent &Homogenous
LNS6	No Irritation	Smooth, Transparent &Homogenous
LNS7	No Irritation	Watery
LNS8	No Irritation	Smooth, Transparent &Homogenous

Table 6: *In-vitro* diffusion data for formulation LNS1- LNS8

Time	% cumulative drug release							
	LNS1	LNS2	LNS3	LNS4	LNS5	LNS6	LNS7	LNS8
0	0	0	0	0	0	0	0	0
0.5	9.7	9.8	9.9	10.4	10.1	10.2	10.7	10.0
1	28.2	14.6	17.5	20.0	23.9	20.4	19.0	16.2
2	36.9	30.8	23.4	34.3	33.2	24.1	27.5	24.3
4	45.5	39.0	35.2	38.3	46.2	39.0	38.1	39.5
6	49.3	55.5	50.8	46.4	51.1	44.6	53.0	40.9
8	56.4	59.6	58.7	50.4	56.7	50.2	57.2	48.7
10	81.0	78.1	73.2	66.6	60.6	68.8	61.5	56.9

from 1cm diameter pre-marked on type a ground glass slide. A weighting consisting of 500g be permitted to rest on the upper glass slide for 5 min upper glass slide for 5min [11]. The spreadability had been calculated from the following formula.

Spread ability = $M \times L/T^{45}$

Extrudability

An unreceptive collapsible tube involving almost 20 grams of the gel used to be pressed firmly at the crimped end and a fix used to be applied to prevent whatever rollback. The cap used to be taken away and also the gel used to be extruded. In the direction of the extruded gel was collected and weighed [12].

Skin irritation test

Test for skin irritation was performed on human volunteers. For each gel, four volunteers were selected and 1.0g of the formulated gel was applied on an area of 2 square inches to the back of the hand. The volunteers were observed as far as lesions or irritation [13].

Drug content

1 gram of the prepared gel was mixed with 10 ml of

Table 7: Release order kinetics for formulation LNS1 to LNS8

Formulation code	Zero-order (R^2)	First-order (R^2)	Higuchi model (R^2)	Korsmeyer-Peppas model	
				(R^2)	n
LNS1	0.9932	0.8951	0.9508	0.9889	0.817
LNS2	0.9642	0.8427	0.9843	0.9932	0.794
LNS3	0.9853	0.8582	0.9587	0.9832	0.768
LNS4	0.9923	0.8763	0.9517	0.9948	0.876
LNS5	0.9865	0.9311	0.9687	0.9985	0.895
LNS6	0.9832	0.7731	0.9623	0.9881	0.899
LNS7	0.9807	0.8851	0.9649	0.9786	0.892
LNS8	0.9869	0.8341	0.9611	0.989	0.793

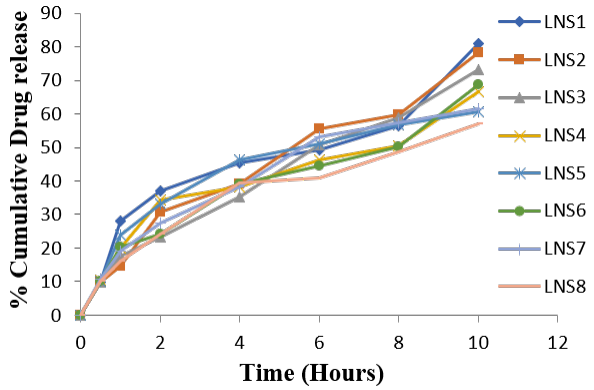

Figure 5: *In-vitro* diffusion data for formulation LNS1- LNS8

suitable solvent obtained mixture was centrifuged for 90mins [14]. The supernatant obtained after 90 mins centrifugation was analyzed spectrophotometrically for total drug content at 234nm.

Entrapment efficiency

For determining entrapment efficiency, nanosponge gel was dissolved in a suitable solvent and subjected to centrifugation [15]. A known amount of the gel equivalent to 10mg of drug was dissolved in 10ml phosphate buffer 5.0. This mixture was centrifuged for 10mins. After centrifugation, the supernatant was collected and diluted accordingly and the drug entrapment was analyzed by UV spectrometric ally at 234nm.

In-vitro diffusion studies

The overall cylindrical glass tube used to be opened up at both the ends.1gm of gel similar to 10mg of lawsone gel was once spread out uniformly apparent the cellophane membrane and used to arrange the only end of the tube [16]. The entire assembly was placed on a thermostatic hot plate with a magnetic stirrer maintained at temperature 37°C, the list has been stirred up with a magnetic bar at 100 rpm for a period of 24 hrs, 2ml of measures have been withdrawn at different time intervals. The respective sample was measured at 234nm by utilizing a UV spectrophotometer.

Release kinetics

To investigate the possible mechanism of drug release from the prepared nanospong gel, the release data were analyzed mathematically according to the following models [17].

Zero-order- Q=Ko t

First-order- Log Q= Log Qo-K1 t/2.303.

Higuchi- Qt = KH t $\frac{1}{2}$.

Korsmeyer - Peppas- Qt/Qα = K tn.

Where,

Q is the amount of drug release at a time (t) and K is the rate constant.

RESULTS AND DISCUSSION

Compatibility studies

All the characteristic peaks of lawsone were present in spectra at their respective wavelength. Thus, indicating compatibility between drug and polymers (Table 3). This indicates that there's no significant change within the chemical integrity of any drug as shown in Figures 1, 2, 3 and 4.

Characterization and evaluation of nanosponge gels

The particular will be tiny sponges having a size of 250nm to 1μm. These are a novel class of hyper cross-linked polymer-based colloidal structure that is formed by reacting polyester (cyclodextrins) with appropriate cross-linking agents result in the production of nanosponges.

It solubilizes poorly water-soluble medicines and gives prolonged discharge as well as improves the bioavailability containing the drug. Nanosponges play a vital role in targeting drug delivery in a controlled manner and suitable for both lipophilic and hydrophilic drugs. Nanosponges are a novel carrier having a wide range of biomedical applications that can offer controlled drug delivery also as drug targeting.

The physical appearance of formulated nanosponge gel has recorded the result of the study reveal that the LNS1& LNS7 formulations were watery were as the remaining formulations i.e, LNS2-LNS8 were found to have smooth, transparent, homogenous with a gel-like consistency (Table 5). The PH of the formulated nanosponge gel was recorded. The result of the study reveals that the PH of the lawsone-loaded nanosponge gel formulation was found to be in the range of 4.8-5.5. It was concluded that all the formulations PH values within the range of skin PH (Table 4).

The spreadability of gel mainly depends on gelling agents (Carbopol). The increasing concentration of gelling agents is always associated with reducing spreadability. The spreadability of nanosponges gel formulation encounters the ultimate in the range between 7.2-8.5. The more spreadability at LNS1& LNS2 & LNS5 exhibited the least value (Table 4).

Among the many gel formulations LNSF1& LNS8, an excess of 90% of the contents were extrudable indicating they need very good Extrudability except for LNS1, LNS4 & LNS7 as 80% of the content (Table 4). The results of the skin irritation test of lawsone loaded nanosponge gels were recorded. The result of the study reveals that all the formulations LNS1-LNS8) were free from irritation at the site of application (Table 4).

The lawsone-loaded nanosponge gel formulation was found ultimately within the range between 7.7-92.2%. It was mainly dependent on polymer concentration. As the polymer concentration increases, drug content also increases. LNS6 formulation exhibited the highest value, whereas LNS1exhibited the least (Table 4).

The Entrapment efficiency was found in the range between 60-80%. The Entrapment efficiency of drug-loaded into the carrier also depends on the polymer used in the formulation F_6 exhibited the highest Entrapment efficiency whereas LNS7 exhibited the least (Table 4).

In-vitro diffusion studies

It was observed that the drug release decreases and the polymer concentration increase and exhibited a sustained effect.

The drug releases all the general formulation was in the range of 9.7 to 10.7. Usually nanosponge gels show 100% release for 8 hours, but here nanosponge gel formulations had shown only 48.7 to 59.6 LNS6 formulation sustained the drug release and was considered optimized over LNS4 & LNS7 (Table 6) (Figure 5).

Release order kinetics

The kinetic models selected were Zero order, First order, Higuchi Matrix, and Korsemayer Peppas. The regression coefficient values for all these models were shown in Table 7.

In all the cases the best-fit model was found to be peppas with 'n' value between 0.768 to 0.895.

The 'n' value of formulation LNS6 was 0.899 and tendering so the drug appears by Zero-order kinetics.

CONCLUSION

Nanosponges are promising nanocarriers in novel drug delivery systems to overcome the problems related to conventional drug delivery systems**.** Nanosponges are the carriers, which carry the drug to the desired site of action and have a vital role in the drug. Targeting improved solubility and facilitate controlled release of the drug molecule**.** All the prepared lawsone-loaded nanosponges gels were evaluated. The physical appearance of most of the formulations was smooth, transparent, homogenous with a gel-like consistency, while a few were watery. The pH of formulated nanosponges gels was found within the range of skin pH. Spreadability and extrudability of lawsone nanosponges gels were recorded and produce good results. The skin irritation tests of lawsone loaded nanosponges gels (LNS1- LNS8) were free from irritation.

The drug content ranging from 79-92.2% and entrapment efficiency ranging from 66-80%. *In-vitro* drug release data of the LNS6 formulation was found to be 68.8%, which was considered as an optimized release. Among the formulations, LNS6 depicts the required characteristics with maximum drug content of 92.2%, entrapment efficiency of 80%, and in vitro diffusion studies. Based on the observations, the LNS6 formulation was considered as an optimized formulation and exhibited a controlled release effect along with minimized side effects. The best fit model encounter to be peppas with 'n' value between 0.768 to 0.895. The 'n' value of formulation LNS6 was 0.899and suggesting that the drug was released by Zero-order kinetics.

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Conflict of interest

The authors declare that they have no conflict of interest in this study.

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