Clinical Images and Case Reports

Received 2 Apl 2024 | Revised 4 Apl 2024 | Accepted 24 Apl 2024 | Published Online 10 May 2024

Published By: Vision Publisher

ISSN 2942-0776

CICR 02 (5), 01-10

Original Article

Encapsulation of suitable drug in proniosomes for improved and effective drug delivery

Sagar Vaishnav, Dr. Praveen Khirwadkar, Dr. Narendra Mandoria, Dr.Kamlesh Dashora, Dr.Darshan Dubey, Dr.Tanu Bhargava

Institute of Pharmacy, Vikram University, Ujjain (M.P.) India

Abstract:- All formulations were prepared for drug content, encapsulation efficiency, stability, dispersion, viscosity, pH & excipient interactions of the drug were examined are the most suitable formulas are containing span 40 and span 60 in equal measure among all species. The pH of the entire composition was about 7.11 to 7.20, indicating that there was no skin irritation. The active medication content ranged from 92 to 98 percent. In terms of drug viscosity, the gel's composition can be categorised as follows: Dt3> Dt2> Dt9> Dt7> Dt4> Gel Market> Dt6> Dt5> Dt1> Dt8. Dt3> Dt2> Dt9> Dt7> Dt4> Gel Market> Dt6> Dt5> Dt1> Dt8. In comparison to the gel on the market, the prevalence of Dt9 formulations, including Amlodipine besylate gel was good. The correlation coefficients (r) values suggested that the distribution profile followed zero-order kinetics. In terms of Amlodipine besylate release levels, the gel's components can be organized in the following order: Dt9>Dt8> Dt10> Dt6> Dt7,> Dt1,> Dt3,> Dt2.> Dt5.> Dt4. From the permeation profile, it was clear that the Dt9 formulation containing span 40 & span 60 (50:50) proniosomal gel showed a drug release up to 12 h. The structure of Dt9 has been found to have better penetration and can be considered a candidate for the development of volume capacity forms. The encapsulation of drug in proniosomal gel formation ranges from 82.16% to 94.24%.

Keywords: proniosomes, pharmaceutical compounds, encapsulation, spreadibility, permeation

Corresponding Author: Sagar Vaishnav†, Institute of Pharmacy, Vikram University, Ujjain (M.P.) India

Supplementary information The online version of this article (https://doi.org/xx.xxx/xxx.xx) contains supplementary material,which is available to autho-rized users.

Introduction:

The development of alternative drug delivery systems, particularly the Transdermal Drug Delivery System utilizing advanced nanocarriers, presents a promising solution to the challenges posed by prolonged oral administration of drugs like NSAIDs. This approach not only addresses safety concerns and improves patient compliance but also demonstrates enhanced efficacy and convenience through controlled and sustained drug release[1,2,3].

Formulation of Proniosome encapsulated gel of Amlodipine besylate

Proniosomal gels are performed in an exceedingly way that separates the coacervation phase. Accurately measured amounts of Amlodipine besylate, non-ionic surfactants, soy lecithin and cholesterol were taken from a glass bottle with a good clean and waterlessness containing ethanol 2.5 ml. The open area of the bottle was covered with a lid to avoid loss of solvent and heated to 65 ± 3 ° C until the surfactant mixture was completely dissolved. Then 1.8 ml of phosphate buffer pH 7.4 (liquid phase) was added to the surface and heated to get an equal scattering. Cooling was then allowed until the dispersion was converted to proniosomal gel. The improved construction was compared to the merchandise on the market. Nine styles of Amlodipine besylate were developed and described as Dt1 to Dt9, respectively[10]. The composition of gels is listed in Table 1.

Evaluation of Proniosome encapsulated gel of Amlodipine besylate

Gel Evaluation Methods

1. PH Measurement: By digital pH meter all nine formulations of transdermal proniosomal gel of dexketoprofen was measured.

2. The Drug Content-In 50 ml of methanol, one gram gel was dissolved. The resulting solution was mass transferred to volume flasks, and purification was performed with phosphate buffer pH 7.4 and analyzed the content of Amlodipine besylate at 260 nm with UV-spectrophotometer.

Rheological Studies

Viscosity: For non-Newtonian fluids like gel we use multiple points of viscometer so here, Brookfield digital viscometer (DV-I + model) was used to measure the viscosity (in cps). Spindle no.90 was rotated at 7 rpm. The composition viscosity was superb which was near 100% torque. Samples were rated at 36 ± 10 C. The reading was obtained 36 seconds after the measurement was performed, at which point the extent was stabilized.

Spreading: Concentrated circles of various radii were drawn on paper, and a glass plate was placed on that. The gel (25.0 gm) is transferred to the middle of the lower plate. A 100 ± 5 gm glass plate was gently located within the gel, and also the distribution width was recorded after 1 minute of each addition.

In-vitro release studies of the proniosomal transdermal gel of Amlodipine besylate for in-vitro release as a receptor, phosphate buffer pH 7.4 was utilized. In the Franz cell distribution, the premade membrane was used. A gel sample was applied to the membrane, which was subsequently placed in the distribution cell between the donor and receiver. A phosphate repository with a pH of 7.4 is found in the receptor component. The temperature of the diffusion medium was thermostatically controlled at 37°C and activated by a magnetic stirrer spinning at 100 rpm. At predefined periods, the material was spectrophotometrically analyzed at 260nm using a phosphate bath pH 7.4 as a solvent.. For drug encapsulation efficiency purposes in an extremely glass tube, a proniosomal gel of Amlodipine besylate (0.2 g) was reconstituted with 10 ml of phosphate buffer of pH 7.4 and centrifuged at 15000 rpm for 90 minutes at 25°C. The free drug absorption inside the resultant solution was measured using a UV spectroscopic technique at 260 nm after the supernatant was collected and diluted with phosphate buffer of pH 7.4.

The following equation was used to calculate the proportion of drug encapsulation.

$$EP (\%) = [(ct - cr)/ct] \times 100$$

(EP) is that the encapsulation proportion, (Ct) is the concentration of total drug and (Cr) is the concentration of the free drug. Trans-mission microscopy (TEM) Morphology and, therefore the structure of the prepared proniosomal gel

was examined using a microscope to transmit high clarity, MAKE: JEOL, MODEL: JEM 2100 plus. A well-developed proniosomal gel (dt9) was tested.

6.3.4. Stability Studies

The construction was maintained at 4°C, 25°C, and 45 °C for 45 days and was tested with the following parameters

1) Physical Stability: The composition of the gel was assessed by visual characteristics such as phase separation and color change, odor, and rheological parameters.

2) Chemical Stability: The medication concentration of the gel formulations was assessed, as well as the separation of liquid exudates.

Results and Discussion

Preformulation Studies:

Organoleptic Properties: Organoleptic properties of the drug were found within limits

TABLE 1: ORGANOLEPTIC PROPERTIES OF THE DRUG

S. no.	Properties	Inference
1	colour	White to off white
2	state	Powder is Crystalline
3	odour	Odourless
4	Taste	Bitter

7.1.2. Determination of λmax: Maximum absorbance of the drug was found at 254 nm, as shown in Fig 9.

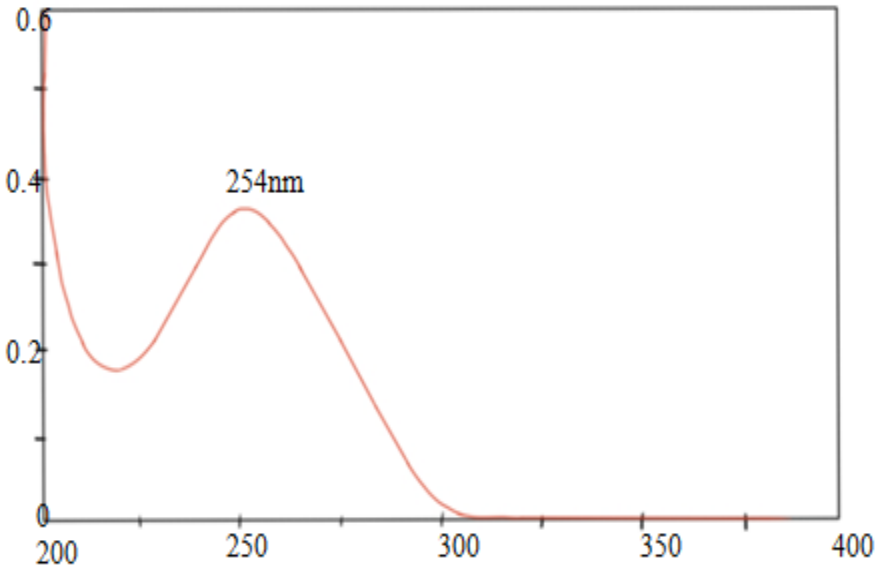


Fig 9: λmax of Amlodipine besylate

Standard Calibration Curve of Amlodipine besylate: Standard calibration curve was constructed

TABLE 2: Amlodipine besylatevs. Absorbance in phosphate buffer pH 7.4

S no.	X (concentration in ug/ml)	Y (Absorbance)
1	0	0
2	2	0.182
3	4	0.32
4	6	0.562
5	8	0.781
6	10	0.920

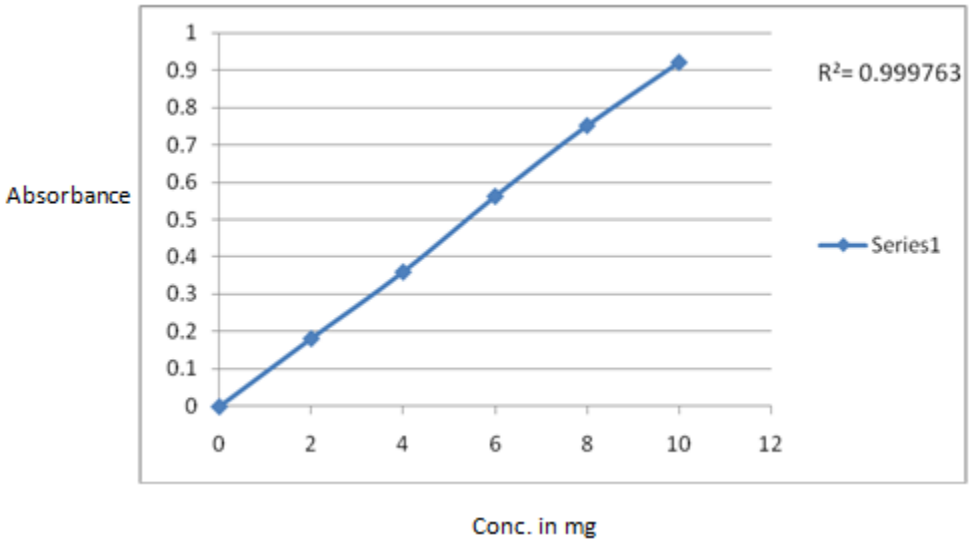


Fig 10: Calibration Curve of Amlodipine besylate

Identification of Pure Drug by Fourier Transform Infrared Spectroscopy

Observed Carbonyl groups between 1770 cm-1 and 1750 cm-1 with strong bands may berecognized to the stretch vibration of the carbonyl groups present in the two monomers. Medium intensity bands between 1300 cm-1 and 1150 cm-1 show asymmetric and symmetric streches C-C(=O)-O, respectively, esters are identified by distinctive bands. “According to the literature, confirmation of dexketoprofen by an strong band at (1536 cm−1), 1020 cm−1), (771 cm−1) ‘at (1571 cm−1), (1020 cm −1), (881 cm−1) & (641cm −1), Vibrations indicate the purity of dexketoprofen we concluded that functional group are represents in this IR that the given drug are pure and identical.

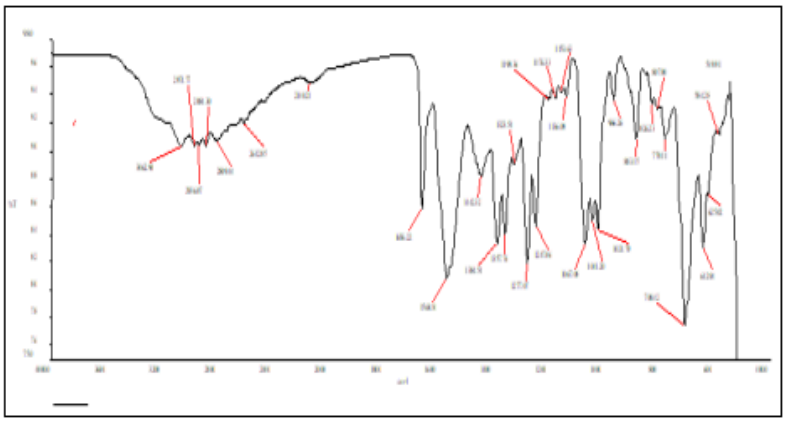


Fig 11: FTIR spectra of pure drug Amlodipine besylate

Drug-Excipient Compatibility Studies

The results of Drug-Excipient Compatibility studies suggest drug and excipients' stability. Amlodipine besylate and all excipients are stable and accepted. A spectrum of Amlodipine besylate and its physical mixtures with excipients are revealed in Fig. 4. The FTIR spectrum analysis revealed a shift in % transmittance, which might be attributed to crystallinity changes, but no removal of any of the pure drug Amlodipine besylate's distinctive peaks in the physical mixing of drug to polymer. This eliminates the possibility of a drug-polymer compound interaction.

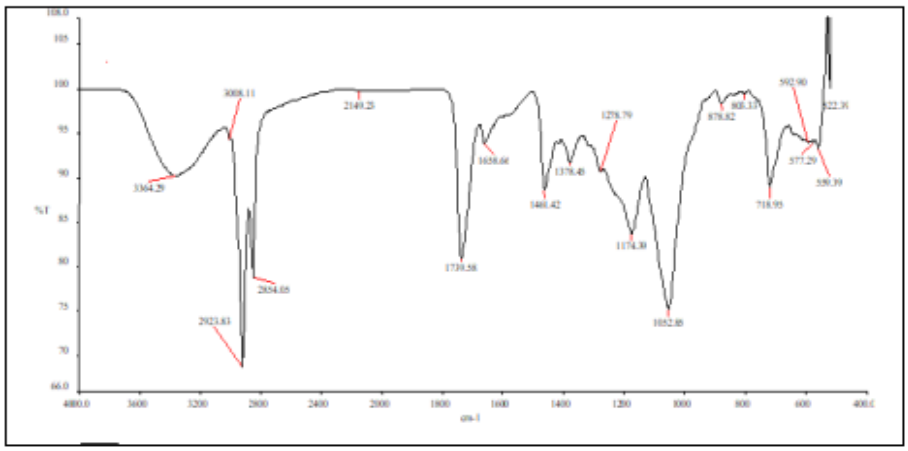


Fig: FTIR spectra of pure drug and excipient

Evaluation of Proniosomal Transdermal Gel:

Gel Evaluation

1. **pH Measurement:** Measurement of pH All formulations had a pH close to that of the skin, as shown in Table 4, indicating that there was no danger of skin irritation and that they were superior to the marketed formulation due to their neutral pH.

TABLE 4: FORMULATION'S pH

S. no.	Formulations	pH
1	Dt1	7.14
2	Dt2	7.11
3	Dt3	7.18
4	Dt4	7.12
5	Dt5	7.16
6	Dt6	7.20
7	Dt7	7.17
8	Dt8	6.90
9	Dt9	7.26
10	Dt10 (Marketed gel)	6.47

2.**Drug Content:** The drug content in each sample was determined by using the standard calibration curve. The percent drug content of all formulations and marketed preparation was shown in Table 5; the drug content values of the formulations were well within the range of 92-97 %.

TABLE 5: DRUG CONTENT OF DIFFERENT FORMULATIONS

S. no.	Formulations	Drug content%
1	Dt1	92.56
2	Dt2	95.06
3	Dt3	94.26
4	Dt4	96.48
5	Dt5	96.68
6	Dt6	94.23
7	Dt7	94.79
8	Dt8	96.36
9	Dt9	97.89
10	Dt10 (Marketed gel)	97.56

Rheological Studies

Non-Newtonian (plastic flow) was seen in all gels. The gel compositions were found to have good spreadability and viscosity.

1.**Viscosity Study:** Table 6 shows Gel formulations can be graded in the following order concerning the viscosity of the drug: Dt3> Dt2> Dt9> Dt7> Dt4> Marketed gel> Dt6> Dt5> Dt1> Dt8.

TABLE 6: VISCOSITY OF DIFFERENT FORMULATIONS

S. no.	Formulations	Viscosity (cps)
1	Dt1	2186
2	Dt2	4598
3	Dt3	4862
4	Dt4	2903
5	Dt5	2396
6	Dt6	2815
7	Dt7	4126
8	Dt8	1989
9	Dt9	4418
10	Dt10(Marketed gel)	2886

2. Spreadability: The spreading area was plotted as a function of the applied mass in the results. Gel weight: 25 gram Compared to the marketed gel, the spreadability of formulations Dt9 and Dt7 containing Amlodipine besylate gel was good.

TABLE 7: SPREADABILITY OF DIFFERENT FORMULATIONS

S. no.	Formulations	Spreadability
1	Dt1	15.97
2	Dt2	23.96
3	Dt3	16.89
4	Dt4	19.07
5	Dt5	23.56
6	Dt6	20.68
7	Dt7	25.52
8	Dt8	21.36
9	Dt9	28.21
10	Dt10(Marketed gel)	22.53

the findings of the in-vitro diffusion research over the egg membrane using different gels. The diffusion profile follows zero-order kinetics, as evidenced by the correlation coefficient values (r). In terms of the rates of release of Amlodipine besylate from the gel formulations, they can be graded in the following order: Dt9>Dt8> Dt10> Dt6> Dt7, > Dt1, > Dt3, > Dt2.> Dt5.> Dt4. Dt9>Dt8> Dt10> Dt6> Dt7, > Dt1, > Dt3, > Dt2.> Dt5.> Dt4. The permeation profile revealed that formulation Dt9, which contained a span 40 and spanned 60 proniosomal gel in a 50:50 ratio, provided the best drug release for up to 12 hours. The Dt9 formulation was shown to have superior penetration and hence might be evaluated as a possibility for topical dosage form development

TABLE 8: STUDY OF IN-VITRO RELEASE IN PBS 7.4 pH

S. no	Time (hrs)	% Drug release									
		Dt1	Dt2	Dt3	Dt4	Dt5	Dt6	Dt7	Dt8	Dt9	Dt10
1	0	0	0	0	0	0	0	0	0	0	0
2	2	19.05	20.96	23.95	17.84	20.56	26.15	15.8	19.33	19.45	21.2
3	4	37.52	36.11	38.55	29.46	37.48	37.08	33.05	32.79	30.45	33.53
4	6	65.62	48.68	45.62	38.91	42.06	47.35	52.23	48.08	51.43	62.31
5	8	72.96	59.92	58.69	47.74	53.42	56.02	60.57	62.44	79.92	74.13
6	10	85.14	89.82	90.2	77.21	88.61	87.09	84.99	87.68	89.87	89.07
7	12	92.46	92.58	93.21	90.56	92.17	93.02	93.16	94.61	94.93	94.77

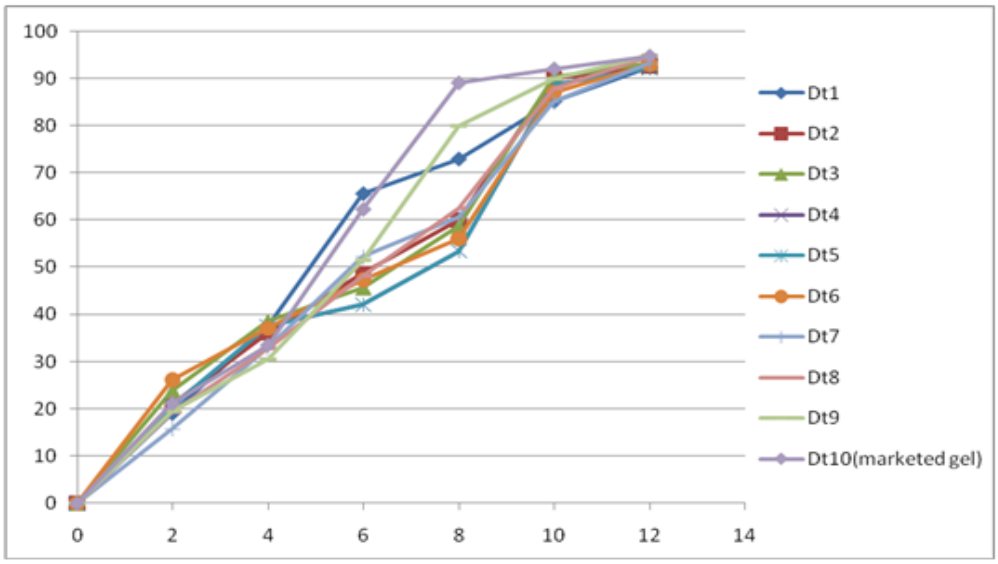


Fig 13: Percent Drug Release

Drug Encapsulation Efficiency Determination:

Proniosomal gel formulations had encapsulation efficiency ranging from 82.10 percent to 94.12 percent. Table 10 shows the drug encapsulation efficiency of nine formulations.

Table 9: encapsulation efficiency of different formulation

S. no.	Formulations	EE%
1	Dt1	82.16
2	Dt2	87.25
3	Dt3	85.35
4	Dt4	81.32
5	Dt5	90.25
6	Dt6	93.86
7	Dt7	82.63
8	Dt8	90.56
9	Dt9	94.24

Transmission Electron Microscopy (TEM)

HRTEM showed that the particles have circular, uniform shapes. The dense, well-distributed pattern observed in Fig. 6 in the electron micrographs of dt9, Transmission reveals the structure of hydrated niosomal vesicles that are well-defined. The niosomes are unilamellar vesicles, spherical, nanosize, with sharp and well-separated limits.

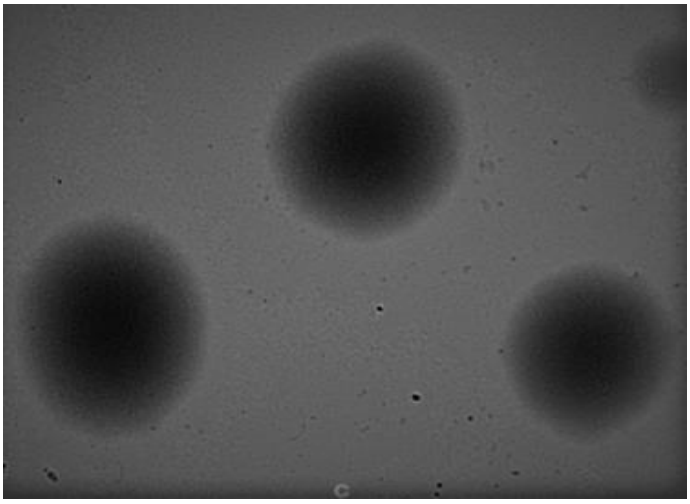
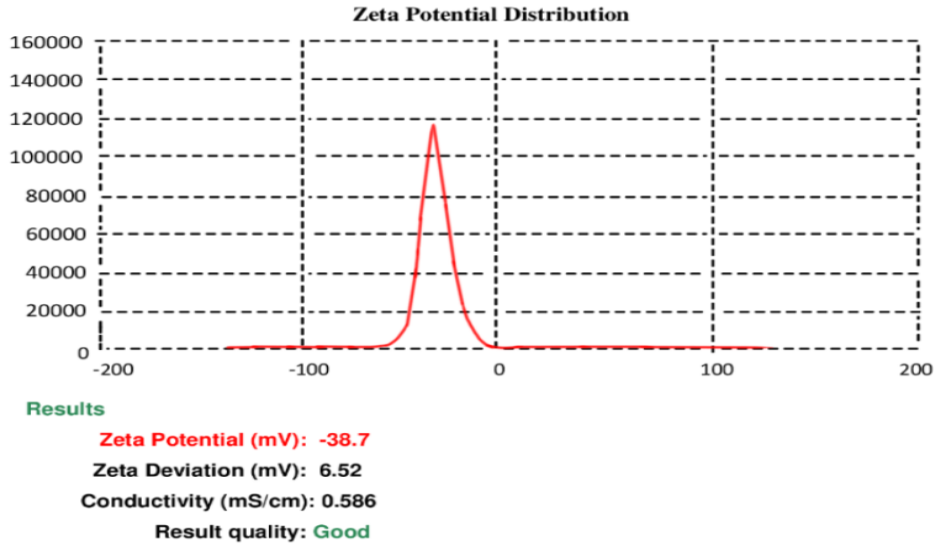


Fig 14: HRTEM Analysis

Particle Size, Zeta Potential &Polydispersibility Index

Analysis of the proniosome-based niosome particle size shows that the SD (nm) particle size is 207.93 nm with a polydispersity index of 0.178. The zeta strength of the prepared



Structure shown in Fig. 8 dt9 obtained within a range of 38.7 shows good stability of proniosomal gel. Zeta Potential

Stability Studies

There was no change in colour, odour, drug content, rheological properties, pH, or phase separation during 45 days at varied temperature conditions (4°C, 25°C, and 45°C) reported in Table 11, as there was no change in colour, odour, drug content, rheological properties, pH, or phase separation. As a result, it's possible to establish that formulation (Dt9) was chemically and physically stable.

Table 10: accelerated stability studies of formulation

S. no.	Parameters	Dt9		
		4°C	25°C	45°C
1	pH	7.18	7.25	7.26
2	Viscosity in cps	4281	4402	4379
3	Phase separation	Not found	Not found	Not found
4	Spreadability	Good	Good	Good
5	% Drug content	97.12	97.20	97.41

Discussion

The Amlodipine besylate transdermal proniosomal gel was formulated, and all formulations were prepared for drug content, encapsulation efficiency, stability, dispersion, viscosity, pH & excipient interactions of the drug were examined are the most suitable formulas are containing span 40 and span 60 in equal measure among all species. The pH of the entire composition was about 7.11 to 7.20, indicating that there was no skin irritation. The active medication content ranged from 92 to 98 percent. In terms of drug viscosity, the gel's composition can be categorised as follows: Dt3> Dt2> Dt9> Dt7> Dt4> Gel Market> Dt6> Dt5> Dt1> Dt8. Dt3> Dt2> Dt9> Dt7> Dt4> Gel Market> Dt6> Dt5> Dt1> Dt8. In comparison to the gel on the market, the prevalence of Dt9 formulations, including Amlodipine besylate gel was good. The correlation coefficients (r) values suggested that the distribution profile followed zero-order kinetics. In terms of Amlodipine besylate release levels, the gel's components can be organized in the following order: Dt9>Dt8> Dt10> Dt6> Dt7,> Dt1,> Dt3,> Dt2.> Dt5.> Dt4. From the permeation profile, it was clear that the Dt9 formulation containing span 40 & span 60 (50:50) proniosomal gel showed a drug release up to 12 h. The structure of Dt9 has been found to have better penetration and can be considered a candidate for the development of volume capacity forms. The encapsulation of drug in proniosomal gel formation ranges from 82.16% to 94.24%

References

1. Kalpesh Chhotalal Ashara, Jalpa S Paun, MM Soniwala, JR Chavda, SV Nathawani, Nitin M Mori, and VISHAL P Mendapara, 'Vesicular Drug Delivery System: A Novel Approach', Mintage J Pharm Med Sci, 3 (2014), 1-14.
2. Shikha Jain, Vikas Jain, and SC Mahajan, 'Lipid Based Vesicular Drug Delivery Systems', Advances in Pharmaceutics, 2014 (2014), 1-12.
3. Konatham Teja Kumar Reddy, and Kumaraswamy Gandla, 'Novel Vesicular Drug Delivery Systems Proniosomes', Pharm Res, 6 (2022), 000272.
4. V Sankar, K Ruckmani, S Durga, and S Jailani, 'Proniosomes as Drug Carriers', Pak J Pharm Sci, 23 (2010), 103-7. 32. Venkata Ramesh Yasam, Satya Lavanya Jakki, Jawahar Natarajan, and Gowthamarajan Kuppusamy, 'A Review on Novel Vesicular Drug Delivery: Proniosomes', Drug delivery, 21 (2014), 243-49.
5. Ibrahim A Alsarra, AA Bosela, SM Ahmed, and GM Mahrous, 'Proniosomes as a Drug Carrier for Transdermal Delivery of Ketorolac', European journal of pharmaceutics and biopharmaceutics, 59 (2005), 485-90.
6. Asmaa Ashraf Nemr, Galal Mohamed El-Mahrouk, and Hany Abdo Badie, 'Development and Evaluation of Proniosomes to Enhance the Transdermal Delivery of Cilostazole and to Ensure the Safety of Its Application', Drug Development and Industrial Pharmacy, 47 (2021), 403-15.
7. Minakshee G Nimbalwar, Wrushali A Panchale, Shivrani W Nimbokar, Bhushan R Gudalwar, Jagdish V Manwar, and Ravindra L Bakal, 'A Brief Review on Principle, Preparation and Properties of Proniosomes: A Provesicular Drug Delivery System', World Journal of Pharmaceutical Sciences (2021), 149-62.
8. Swati Mittal, Amit Chaudhary, Anjali Chaudhary, and Ankit Kumar, 'Proniosomes: The Effective and Efficient Drug-Carrier System', Therapeutic delivery, 11 (2020), 125-37.
9. Hiral Shah, Anroop B Nair, Jigar Shah, Shery Jacob, Praful Bharadia, and Michelyne Haroun, 'Proniosomal Vesicles as an Effective Strategy to Optimize Naproxen Transdermal Delivery', Journal of Drug Delivery Science and Technology, 63 (2021), 102479
10. Bhargava Tanu., Dr. Dashora kamlesh proniosomes- encapsulated dexketoprofen trometamol, formulation, optimization,characterization with improved drug release.international journal of pharmaceutical sciences and research.E-ISSN:0975-8232;2022;Vol.13(9):3658-3667.