International Journal of Multidisciplinary Research And Studies

Available online at https://ijmras.com/index.php/ijmras/article/view/644

Page no. 20/20

INTERNATIONAL JOURNAL OF MULTIDISCIPLINARY RESEARCH AND STUDIES
ISSN: 2640 7272
Volume:06; Issue:11 (2023)
Doi: 10.33826/ijmras/v06i11.1

Development and Assessment of Topical Niosomal Gel of Non-Steroidal Anti-Inflammatory Drug

SUNIL AMLAVDIYA[1*], APURVA PAGARE[2], SUNITA SONARTIA[3], SUNITA PATIDAR[4]

[1]PG Scholar, Swami Vivekanand College of Pharmacy, Indore, [3]Assistant Professor, Swami Vivekanand College of Pharmacy, Indore, [2,4]Associate Professor, Swami Vivekanand College of Pharmacy, Indore.

Corresponding Author, Email ID: samlavdiya95@gmail.com

ABSTRACT

The study aimed to develop and assess a topical Niosomal gel formulation of NSAIDs to enhance drug delivery, improve therapeutic efficacy, and reduce adverse effects. Niosomes, a vesicular carrier system, were used to encapsulate and deliver the NSAID topically, improving drug retention and penetration. The Niosomal gel was characterized for its particle size, zeta potential, drug entrapment efficiency, stability, and rheological properties. The in vitro release kinetics and skin permeation and retention studies were conducted using in vitro and ex vivo models. The results showed that the developed topical Niosomal gel formulation provided controlled drug release, enhanced skin permeation, and improved drug retention compared to conventional gels. These findings suggest the potential utility of Niosomal gel formulations for localized NSAID delivery, offering improved therapeutic outcomes while minimizing systemic side effects.

Keywords: Niosomal Gel Formulation, Enhance Drug Delivery, Improve Therapeutic Efficacy, Vesicular Carrier System, Drug Entrapment Efficiency.

INTRODUCTION

A cutting-edge technology called the Colloidal Drug Delivery System is predicted to completely transform the pharmaceutical and health sciences industries, including drug delivery, diagnosis, and therapy. The development of colloidal drug delivery systems

facilitates the creation of novel formulations that are effective in treating a range of illnesses **(Chein et al, 2005).** Niosomes are drug delivery vehicles where the medicine is enclosed in a vesicle. Niosomes are vesicles created by hydrating a cholesterol and non-ionic surfactant combination**.** In addition to inverse structures that are only present in non-aqueous solvents, these are created by the self-assembly of non-ionic surfactants in aqueous environments as spherical, unilamellar, multilamellar system, and polyhedral structures **(Uchegbu and Florence 1995, Murdan et al,1998).** Niosomes, small, almost microscopic nanoparticles, share structural similarities with liposomes but offer benefits in targeted and transdermal medication administration. Research into these structures may lead to novel drug delivery approaches. **(Lasic et al, 1990).** Drug entrapment in niosomes increases vesicle size due to solute interaction with surfactant head groups, while PEG coated vesicles reduce size increase, influenced by medication's hydrophilic-lipophilic balance**.** Vesicles can either aggressively or passively entrap medication, with passive trapping involving co-dispersion of drug and lipids, and active trapping facilitated by ion gradients, allowing drug trapping after Niosomal carrier formation **(Biswal et al, 2008).** Niosomes are a promising vehicle for drug delivery and being non-ionic it is less toxic and improves the therapeutic index of drug by restricting its action to target cells **(Alamayehu et al, 2010, Madhav et al, 2011).** Niosomes let medications penetrate the skin more deeply and can serve as a local depot for the continuous release of substances that are dermally active. The skin tolerates non-ionic surfactants far better when they are included in Niosomes than when they are used in emulsions **(Jia – Y – Fang et al, 2001).**

MATERIAL AND METHOD

The standard curve for parecoxib is prepared by dissolving potassium dihydrogen phosphate, sodium chloride, and disodium hydrogen phosphate in water. The absorbance and concentration are plotted using a UV-Visible Spectrophotometer. FT-IR studies investigate drug-excipient interactions using a Perkin FT-IR Spectrophotometer. Differential scanning calorimetry uses a Perkin Elmer STA 6000 Thermal Analyzer, calibrated with indium standard.

FORMULATION OF PARECOXIB NIOSOMES

Different ratios of cholesterol to surfactant are used to create Niosomes while maintaining a consistent medication concentration. Formulations are formed using a procedure called thin film hydration. A thin film is created by dissolving cholesterol and non-ionic surfactant in a

solvent mixture and then transferring the mixture to a flask. To obtain a proper dispersion, parecoxib is added to the mixture and vortexed for 45 minutes **(Pratap S. Jadon et al, 2009, Vijay Prakash pandey et al, 2009, Malay K Das et al, 2011, Jong Soo Woo et al, 2009).** The niosomal dispersion is collected and stored at 4ºC for maturation. The empty Niosomes also prepared by the same method without the drug for further evaluation.

Invitro release studies

The study focuses on the in vitro release pattern of Niosomes suspension of Parecoxib using the Himedia dialysis membrane method. The Niosomal preparation is placed in a dialysis bag, which acts as a donor compartment, and a beaker containing 250 ml of buffer phosphate buffered saline pH 7.4. The medium is maintained at 37±1ºC and agitated at 50 rpm speed using a magnetic stirrer. Samples are collected and Analysed spectrophotometrically at 235 nm using a UV-Visible Spectrophotometer. The study also investigates the pharmacokinetics and mechanism of drug release from vesicular systems. The results are fitted with various equations to understand the pharmacokinetics and mechanism of drug release.

FORMULATION OF PARECOXIB NIOSOMAL GEL

The topical gel system is prepared using Carbopol 934, a gelling agent, and Parecoxib Niosomes. The dispersion is hydrated for 4-5 hours, then neutralized with tri ethanolamine to create a translucent gel. The gels are evaluated for drug content, pH, rheological behaviours, particle size, zeta potential, and stability.

EVALUATION OF THE PREPARED PARECOXIB NIOSOMAL GEL

The drug content of Niosomal gel formulations is extracted and diluted with phosphate buffer saline (pH 7.4), followed by filtration and absorbance measurements. The pH of the gel formulations is measured using a pH meter, calibrated before use with buffered solutions at pH 4, 7, and 10. The viscosity of the formulations is determined using a Brookfield DV-111+ Rheometer, and the vesicle sizes of the prepared Niosomal formulation are determined by light scattering based on laser diffraction using the Malvern master-sizer. Zeta potential is measured using a Malvern ZS 90 zeta-sizer and a folded capillary cell. The niosomal gel formulation is characterized for their morphology using transmission electron microscopy (TEM), where a small amount of the gel is placed on a carbon-coated grid and observed under transmission electron microscopy.

In vitro release studies

The study involves in-vitro release of gel formulations into a dialysis bag and a beaker containing 250 ml PBS pH 7.4 at 37 ± 10˚C. Samples are withdrawn at specified intervals and analysed using an UV spectrophotometer. The results are fitted with various pharmacokinetic equations, including zero order, first order, Higuchi's model, Korsmeyer-Peppas, and Hixson-Crowel models. The data is evaluated using equations such as r 2 and k values.

In vivo anti-inflammatory studies

The study compares the anti-inflammatory activity of various formulations of Parecoxib loaded Niosomal gel on albino rats using the carrageen am induced rat paw edema method. The rats were given carrageen am suspension in saline and then applied 0.5 g Niosomal gel formulations and plain gel topically on the edematous paw. The topical activity of the formulations was measured by measuring the increase in hind paw thickness before and after carrageen am administration. The inhibition percentage of the edema formulation was calculated and statistically evaluated. The best formulation of Parecoxib loaded Niosomal gel was subjected to stability studies, where it was stored at different temperatures for 3 months.

RESULT AND DISCUSSION

STANDARD CURVE FOR PARECOXIB

The λmax of Parecoxib was determined by scanning the 10µg/ml of drug solution in phosphate buffer saline (PBS) pH7.4 and it showed the λmax at 235nm. Calibration curve of Parecoxib was plotted by measuring the absorbance of different concentrations of the drug in phosphate buffer saline (PBS) pH 7.4 at 235 nm. The linear correlation co-efficient was obtained for calibration of Parecoxib in phosphate buffer saline (PBS) pH7.4. Parecoxib obeys the beer's law within the concentration range of 1 to 10µg/ml.

PREFORMULATION STUDIES

FT-IR studies

FT-IR infra-red (FT – IR) spectroscopy was carried out separately to check the compatibility between drug, surfactant (Span 20,Span 40,Span 60,Span 80, Tween 60,Tween 80 and Brij-52) cholesterol and physical mixture used for the preparation of Niosomes.

The spectra studied at 4000cm-1 to 400 cm-1. It was found from the spectra that there was no major shifting as well as any loss of functional peaks in the spectra of drug, surfactant,

cholesterol and physical mixture of drug, surfactants and cholesterol, the results indicated that the selected surfactants and cholesterol were found to be compatible with the selected drug **(Gurrapu et al, 2011, Ismail Mouzam et al, 2011, PandeyShivanand et al, 2010).**

Differential scanning calorimetry

DSC is a fast and reliable method to screen drug- excipients interactions as indicated by appearance of a new peak, change in the peak shape and its onset, peak temperature/melting-point and relative peak area or enthalpy. DSC thermograms such as pure drug, span20, span40, span60, span80, tween60, brij52 and cholesterol obtained during the study. Pure Parecoxib showed a sharp endothermic peak at 153º.09ºC.Thermogram of span20, span40, span60, tween60, brij52 exhibits an endothermic peak with onset at 160º,51ºC, 48ºC, 58ºC, 6.33ºC, 172ºC respectively. Tween 80 is reported to show an exothermal peakat -43ºC and endothermal peaks were observed at -14ºC **(Indu Pal Kaur etal, 2011).** Further, DSC thermogram suggests that the formulation components Span 20, Span 40 Span 60, Tween 60, brij-52, cholesterol and the drug Parecoxib do not interact to form any additional chemical entity but remain as mixture.

FORMULATION OF PARECOXIB NIOSOMES

Niosome formulations were formulated by thin film hydration method using different surfactants (Span 20, Span 40, Span 60, Span 80, Tween 60, Tween 80, and Brij 52) and Cholesterol with different ratios as per the formula resulted a stable, uniform dispersion of Niosomal vesicles **(Pratap S. Jadon et al, 2009, Vijay Prakash pandey et al, 2009, Malay K Das et al, 2011, Jong Soo Woo et al, 2009).** The formation of Niosomal vesicle was confirmed by Transmission electron microscopy (TEM).

Drug content

The drug content of the Niosomes was determined after lysing the vesicles with 50% n-propanol and measured at 235 nm in UV-Visible spectrophotometer 1700, Pharma spec, Japan. The drug content was found to be in the range of 97.23% to 99.46%. The results were indicated that the uniform distribution of drug in prepared Niosomal formulations.

Entrapment efficiency

In Niosomal formulations, the impact of surfactant and cholesterol concentration on entrapment efficiency was considerably significant. The ranges of entrapment efficiency of

twenty-eight Niosomal formulations were observed about 71.6% to 96.9%. The highest entrapment efficiency obtained for the formulation prepared with **F12** Span60 (6:1) (300µmol surfactant and 50µmol cholesterol) was found to be 96.9% may be due to surfactant chemical structure (Span series) and having highest phase transition temperature.

The entrapment efficiency of various non-ionic surfactants increases in the order of Span 60 > Span 40>Span 20 > Brij 52 > Span 80>Tween60 >Tween 80.

These results explained that the **Span 60** has higher entrapment efficiency than other Span types and Tween 60, Tween 80 and Brij 52. This can be explained by many facts: a) Span 60 has the highest phase transition temperature**.** (b) The length of alkyl chain of surfactant is a crucial factor in permeability. Long Chain surfactant produces high entrapment. Span 60 has a longer saturated alkyl chain (C16) compared to Span40 and Span20, so it produces Niosomes with higher entrapment efficiency but Span80 has unsaturated alkyl chain (C18) produces less entrapment. c) The longer alkyl chain influences the HLB value of the surfactant mixture which by its turn directly influences the drug entrapment efficiency **(Raja Naresh et al., 1994)**. The lower the HLB of the surfactant the higher will be drug entrapment efficiency **(Guinedi.A.S et al, 2005).**

In vitro Release Studies

The in vitro drug release studies of Parecoxib from Niosomes were carried out by dialysis bag diffusion technique in phosphate buffer saline of pH7.4. Significant changes in release were observed upon changing the type of surfactant used in the bilayer of Parecoxib Niosomes. The experimental studies showed that the rate of drug release depends on the percentage of drug entrapment efficiency. This result was in conformity with the report of **(Arora Rajnish et al, 2010, Ghada Abdelbary et al, 2008).** All Niosomes formulations showed significant slower release than Parecoxib solution (10mg/0.5ml) which showed a release of about 96.6 % within 7 hours. This confirmed that a sink condition for Parecoxib release was accomplished and the dialysis bag used in the dissolution procedure did not limit Parecoxib release.

Effect of surfactants on the release rate of Parecoxib from Niosomes:

From the release studies **F12 (span 60 6:1)** showed slower and prolonged drug release than the other formulations. The comparative release data indicate that, by encapsulation of drug into Niosomes, it is possible to sustain and control the release of drug for longer duration **(Ruckmani et al, 2000).**

Invitro release kinetics

The release constant was calculated from the slope of the appropriate plots and the regression coefficient (r2) were extrapolated by zero order, first order, Higuchi, Korsmeyer- peppas and Hixson- Crowell equations to know the mechanism of drug release from these formulations. In this study, the invitro release profiles of drug from the all formulations could be best expressed by zero order and Higuchi equation, as the plots showed highest linearity (r2=0.977 to =0.998) and (r2=0.896 to=0.978).To confirm the diffusion mechanism, the data were fitted into Korsmeyer- peppas equation. Among the all formulations was found, that the invitro release of F12 – Span60 (6:1) was best explained by higuchi equation, as the plots showed the highest linearity (r2 =0.978), followed by zero order (r2 =0.989) and first order (r2 =0.958). The Korsmeyer-peppas equation indicated good linearity (r2 =0.996). The release exponent n was 0.778 which appears to indicate a coupling of the diffusion and erosion mechanism-so-called anomalous diffusion and may indicate that the drug release is controlled by more than one process. Thus, F12 was selected as the best for Niosomal release of Parecoxib **(Gyanendra Singh et al, 2010).** These results pointed to sustained release characteristics with a higuchi pattern of the drug release, where Niosomes act as reservoir system for continuous delivery of drug. This slow release pattern of entrapped drug may indicate the stability of the Niosomal formulations **(Ismail. A. Attia et al, 2007).**

FORMULATION OF PARECOXIB NIOSOMAL GEL

The selected best niosomal formulation (on the basis of highest (F12Span 60, - 6:1) and lowest (F21 Tween 80, 3:1) entrapment efficiency among the all formulations) was incorporated into suitable gel base (Carbopol 940 as gelling agent 0.9%) to obtain 1% of the drug and plain Parecoxib gel was prepared by incorporating the drug into suitable gel base to obtain same 1% of the drug.

EVALUATION OF THE PREPARED PARECOXIB NIOSOMAL GEL

Drug Content

The drug content was to be 98.7% for FG12 (span60 6:1) and 99.02% for FG21 (Tween 80 3:1) respectively. This indicated that the uniform distribution of drug in prepared gel formulations.

pH measurement

The result of pH measurement showed that all Niosomal gel formulations which were prepared have the pH range in between 6.9 to 7.0 at intervals of 0 , 15 ,30 th day respectively (Patel. R.P et al, 2009).

Rheological Studies

Formulation FG-12 showed better pseudoplastic behaviour compared to FG-21 formulations. The formulation FG-12 selected as best formulation compared to that of FG-21 formulations based on clarity, pH, in vitro release and viscosity.

Particle size

The mean particle diameters of topical Niosomal gel composed of Span 60 and cholesterol in a 6:1(FG12) micro molar ratio were 1368nm. The results reveal that the Niosomes prepared using Span 60 was larger in size and it was reported that surfactants with longer alkyl chains generally gave larger vesicles. This would account for the higher entrapment efficiencies obtained with Span 60 topical Niosomal gel. Similar results were observed in **(Agarwal et al, 2001, Manosroi. A et al, 2003, Sankar et al, 2009)**.

Zeta potential studies

The zeta potential was used to study the surface charge analysis of formulation (FG 12) Surfactant and cholesterol in a 6:1 micro molar ratio was found to be -76mV .

Transmission electron microscopy

Transmission electron microscopy was performed to study vesicle morphology that revealed that Niosomes gel were discrete, and had spherical in shape.

Invitro release studies

The cumulative % drug release at 12 hours was 58.8% for Parecoxib Niosomal gel containing (GF12- Span 60 (6:1), highest entrapment 96.9%). From the results, it was concluded that (GF-12) Parecoxib Niosomal gel showed prolong drug release due to the highest entrapment efficiency when compared to that of F-21 and plain Parecoxib gel.

Invitro release kinetics

The amount of drug release from different Parecoxib Niosomal gel formulations (GF12 and GF21) shows a linear relationship with square root of time. Hence, the drug release rate can

be expressed by higuchi diffusion model (r2=0.979 to 0.944). The high correlation coefficients were obtained for the zero-order drug release kinetics for Parecoxib Niosomal gel was found to be (r2=0.990 to 0.991). The n value obtained from Korsmeyer – peppas equation found to be 0.634 to 1.309 which indicate that the formulation GF12 and GF21 showed drug release by Non-Fickian and case 2 transport diffusion mechanisms. **(Abdul Hasan Sathali et al, 2011).**

In vivo-anti-inflammatory studies

Niosomal topical gel formulation FG 12 (span60 6:1)23.9% showed sustained reduction in the paw thickness for all points of time when compared to that of FG21 (Tween 80 3:1)46.0% and 59.6% for plain gel.

Stability studies

The percentage drug content of was monitored for Parecoxib Niosomal gel formulation (FG12) upon storage at refrigerated temperature 4o±2oC and 25oC±60% RH at accelerated stability chamber for a period of 3 months, the stability studies suggest that the Parecoxib Niosomal gel formulations were comparatively more stable at refrigerated conditions compared to accelerated temperature.

TABLE I CALIBRATION OF PARECOXIB AT 235nm (PBS OF pH 7.4)

S.NO	CONC(µg/ml)	ABSORBANCE AT 235nm (PBS PH 7.4)			AVERAGE ± SD
		TRIAL-1	TRIAL-2	TRIAL-2	
1	1	0.073	0.078	0.082	0.077±0.004
2	2	0.158	0.144	0.166	0.156±0.009
3	3	0.234	0.236	0.233	0.234±0.001
4	4	0.293	0.290	0.292	0.291±0.001
5	5	O.367	0.368	0.370	0.368±0.001
6	6	0.437	0.438	0.440	0.438±0.001
7	7	0.498	0.502	0.504	0.501±0.001
8	8	0.562	0.586	0.581	O.576±0.010
9	9	0.645	0.650	0.657	0.650±0.004
10	10	0.718	0.717	0.721	0.718±0.001

n=3*

TABLE II IR PEAKS OF DRUGS, SURFACTANTS, CHOLESTEROL AND PHYSICAL MIXTURE OF DRUG, SURFACTANTS AND CHOLESTEROL

S. No	Description	Characteristic peaks (cm^{-1}) obtained
1	Parecoxib	3753.57, 3438.85, 3057.58, 2923.70, 2855.50,2368.48, 1599.25, 1497.80, 1431.88 1403.78 ,1299.11, 1144.12, 1085.54 ,1014.26 959.44,840.10, 777.91, 736.14, 636.37, 582.83,543.67, 492.83, 464.80
2	Cholesterol	3402.2,2933.53,2900.74,2867.95,1670.24, 1620.09, 1465.8, 1440.73, 1375. 15,1274.86, 1236.29, 1191.29, 1164.92, 1134.07, 1107.06, 1054.99,1022.2,985.56,956.63,927.7,883.34, 838.98, 800.4,736.76,597.89,501.41.
3	Span 20	3396.41,2923.88,2852.52,1741.6,1461.94,1375.15,1172.64, 1110.92, 1076.21,981.7,923.84,881.41,838.98,773.4,723.26,609. 46.372.24.
4	Span 40	3379.05,2918.1,2850.59,1735.81,1465.8,1382.87,1288.36, 1267.74,1245.93,1224.71,1176.5,1091.63, 1056.92, 979.77,883.34, 811.98, 777.26,721.36.
5	Span 60	3407.98,2918.1,2850.59,1735.81,1467.65,1380.94, 1265.22, 1244, 1220.86, 1176.5,1097.5,1056.92, 885.27,721.33.
6	Span 80	3396.41,2923.88,2854.45,1739.67,1652.88,1461.94,1415.65, 1377.08,1238.21,1174.57,1110.92,881.41,723.26, 609.26, 376.09.
7	Physical mixture of Drug, Span 20 and Cholesterol	3754.33, 3400.44, 2926.88, 2857.09, 2372.15, 1741.85, 1655.67, 1023.89, 458.52
8	Physical mixture of Drug, Span 40 and Cholesterol	3753.76, 3431.95, 2927.29, 2368.35, 1599.38, 1432.03, 1298.98, 1144.00, 1020.32, 839.83, 777.96, 582.93, 543.93, 464.19 ,400
9	Physical mixture of Drug, Span 60 and Cholesterol	3753.84, 3422.05, 2925.65, 2369.42, 1741.78, 1599.75, 1431.83, 1299.50, 1144.57, 1056.22, 839.51, 777.49, 544.10,

10	Physical mixture of Drug, Span 80 and Cholesterol	3753.76, 3401.13, 2926.33, 2372.17, 1655.31, 1459.12, 1023.93, 456.17,400
11	Physical mixture of Drug, Tween 60 and Cholesterol	3404.46, 2924.91, 2367.85, 1738.42, 1655.09, 1459.65, 1108.39, 400
12	Physical mixture of Drug, Tween 80 and Cholesterol	3753.91, 3402.90, 2926.93, 2369.10, 1737.08, 1655.66, 1459.43, 1351.58, 1107.58,400

TABLE invitro CUMULATIVE % DRUG RELEASE PROFILE OF NIOSOME CONTAINING SPAN-60 IN DIFFERENT RATIO

***invitro* RELEASE MEDIUM**	**TIME IN HOURS**	**BATCH CODE (SURFACTANT: CHOLESTEROL)**			
		F9(3:1)	**F10(4:1)**	**F11(5:1)**	**F12(6:1)**
		MEAN±SD	**MEAN±SD**	**MEAN±SD**	**MEAN±SD**
	0.25	2.6±0.20	1.7±0.20	1.1±0.21	0.76±0.12
	0.50	4.5±0.16	3.4±0.16	2.1±0.16	1.6±0.24
	0.75	6.7±0.24	5.5±0.29	3.0±0.09	2.4±0.20
	1	9.0±0.36	7.7±0.45	4.7±0.16	3.3±0.24
	1.5	11.4±0.20	9.5±0.14	6.6±0.12	4.6±0.24
	2	13.9±0.20	11.4±0.21	8.4±0.28	6.4±0.16
	2.5	16.5±0.32	13.6±0.21	10.1±0.44	7.7±0.28
	3	19.3±0.37	16.4±0.24	12.1±0.37	9.7±0.28
	3.5	22.8±0.26	18.3±0.12	14.3±0.16	11.6±0.32
	4	26.1±0.26	20.4±0.36	16.7±0.18	13.6±0.35
	4.5	29.5±0.20	23.3±0.28	18.9±0.26	15.8±0.49
	5	32.7±0.24	26.0±0.26	21.3±0.21	18.1±0.40
	5.5	35.5±0.12	28.9±0.33	24.0±0.16	20.5±0.21

PBS pH 7.4	6	39.2±0.63	31.7±0.20	26.3±0.20	22.7±0.32
	6.5	41.6±0.44	34.5±0.21	28.8±0.32	25.0±0.24
	7	44.3±0.41	37.3±0.33	31.5±0.26	27.2±0.24
	7.5	47.6±0.14	40.2±0.46	33.9±0.98	29.9±0.63
	8	51.1±0.24	43.1±0.41	36.4±0.33	32.5±0.54
	8.5	54.9±0.44	45.8±0.24	39.1±0.26	34.8±0.62
	9	58.2±0.64	49.0±0.16	41.6±0.26	37.6±0.49
	9.5	61.7±0.70	52.3±0.28	44.6±0.36	41.0±0.30
	10	66.0±0.94	55.3±0.20	47.2±0.16	43.7±0.45
	10.5	69.5±1.06	58.9±0.20	50.7±0.20	46.2±0.44
	11	72.9±1.20	62.8±0.31	54.5±0.12	49.5±0.45
	11.5	75.9±1.26	66.2±0.42	57.4±0.97	53.0±0.32
	12	78.5±1.16	69.8±0.21	62.2±0.41	55.3±1.02

n=3*

Table invitro RELEASE KINETICS OF PARECOXIB NIOSOMES CONTAINING SPAN-60 AT DIFFERENT RATIO

FORMULATION CODE	**ZERO ORDER**		**FIRST ORDER**		**HIGUCHI MODEL**		**KORSMEYER - PEPPAS**		**HIXSON-CROWELL**	
SPAN-60	**R^2**	**KO(h-1)**	**R^2**	**K1(h-1)**	**R^2**	**KH h(-1/2)**	**R^2**	**n value**	**R^2**	**KHC (h-1/3)**
F9 (3:1)	0.998	6.426	0.949	-0.051	0.953	26.27	0.992	0.922	0.974	-0.147
F10 (4:1)	0.995	5.581	0.951	-0.039	0.938	22.69	0.986	0.938	0.971	-0.117
F11 (5:1)	0.99	4.984	0.95	-	0.92	20.1	0.994	0.961	0.97	-0.099

	2		5	0.031	9	9			1	
F12 (6:1)	0.989	4.622	0.958	-0.027	0.998	26.23	0.996	0.878	0.971	-0.088

TABLE COMPOSITION OF PARECOXIB PLAIN GEL

SL. NO	INGREDIENTS	FOR 50 G
1.	Carbopol 934	0.9g
2.	Triethanolamine	0.5 ml
3.	Water	50 ml
4.	Drug (PARECOXIB)	500 mg

TABLE COMPOSITION OF PARECOXIB NIOSOMAL GEL

SL. NO	INGREDIENTS	FOR 50 G
1.	Carbopol 934	0.9g
2.	Triethanolamine	0.5 ml
3.	Water	50 ml
4.	Parecoxib Niosomes	25 ml

TABLE X DRUG CONTENT OF PARECOXIB NIOSOMAL GEL

SL. NO	FORMULATION	% DRUG CONTENT
1	FG12(SPAN 60) 6:1	98.70
2	FG21(TWEEN80) 3:1	99.02
3	PLAIN PARECOXIB GEL	98.88

TABLE XII RHEOLOGICAL EVALUATION OF NIOSOMAL GELFORMULATIONS

S.NO	RPM	VISCOSITY IN CPS	
		FG12	FG21
1	0.1	54888	44091

2	0.5	11937	9178
3	1.0	5699	4499
4	5.0	1188	935
5	10.0	666	542
6	20.0	415	325
7	50.0	202	172
8	100	132	114

n=3*

TABLE COMPARISON OF invitro CUMULATIVE % DRUG RELEASE PROFILE OF PLAIN GEL AND NIOSOMEL GEL CONTAINING HIGH ENTRAPMENT AND LOW ENTRAPMENT

invitro **RELEASE MEDIUM**	**TIME IN HOURS**	**BATCH CODE (SURFACTANT: CHOLESTEROL)**		
		FG12 (6:1) :(H.E)	**FG21 (3:1) :(L.E)**	**PLAIN GE; L**
		MEAN±SD	**MEAN±SD**	**MEAN±SD**
PBS pH 7.4	0.25	0.89±0.36	7.0±0.41	9.2±0.16
	0.50	1.58±0.42	8.8±0.28	17.6±0.16
	0.75	2.7±0.51	11.9±0.28	22.9±0.46
	1	3.5±0.65	15.6±0.36	30.4±0.32
	1.5	4.4±0.73	19.5±0.41	36.1±0.28
	2	5.8±0.21	23.4±0.57	41.2±0.73
	2.5	7.1±0.33	26.1±0.72	45.0±0.87
	3	8.9±0.49	29.4±0.86	51.9±0.96
	3.5	12.7±0.51	31.5±0.73	57.1±0.21
	4	14.5±0.21	34.8±0.16	62.5±0.16
	4.5	16.9±0.38	39.4±0.28	69.1±0.71
	5	17.8±0.16	42.6±0.63	76.7±0.71
	5.5	23.7±0.29	45.4±0.45	80.5±0.86
	6	28.5±0.38	47.9±0.41	90.9±0.93
	6.5	30.9±0.45	49.2±0.67	95.1±0.16
	7	32.2±0.21	52.4±0.17	98.8±0.58
	7.5	35.5±0.16	55.8±0.46	

	8	36.7±0.43	59.3±0.71	
	8.5	39.3±0.26	62.8±0.21	
	9	42.2±0.21	66.5±0.48	
	9.5	45.1±0.86	71.2±0.51	
	10	48.4±0.21	76.1±0.49	
	10.5	49.7±0.86	83.1±0.53	
	11	53.1±0.16	88.9±0.51	
	11.5	55.4±0.93	92.1±0.48	
	12	58.8±0.86	95.1±0.37	

n=3*

TABLE XIV invitro RELEASE KINETICS OF PARECOXIB NIOSOMAL GEL CONTAININ FG12, FG21 AND PUREDRUG AT DIFFERENT RATIO

FORMULATION CODE	ZERO ORDER		FIRST ORDER		HIGUCHI MODEL		KORSMEYER - PEPPAS		HIXSON-CROWELL	
	R^2	(h-1) K_O	R^2	K_1(h-1)	R^2	KH h (-1/2)	R^2	n value	R^2	KHC (h-1/3)
FG12(6:1)	0.991	5.080	0.971	-0.031	0.979	20.59	0.992	1.309	0.971	-0.099
FG21(3;1)	0.990	7.035	0.813	-0.813	0.944	28.85	0.979	0.765	0.904	-0.200
PURE DRUG	0.990	12.53	0.794	-0.204	0.980	40.65	0.977	0.634	0.929	-0.428

TABLE XV COMPARISON OF % INHIBITION OF RAT PAW EDEMA USING PLAIN PARECOXIB GEL, NIOSOMAL GEL CONTAINING FG12 AND FG21

S.NO	TIME IN HOUR	STANDARD MEAN±SD	TEST-1 HIGH ENTRAPMENT(FG12) MEAN±SD	TEST-2 LOW ENTRAPMENT(FG21) MEAN±SD

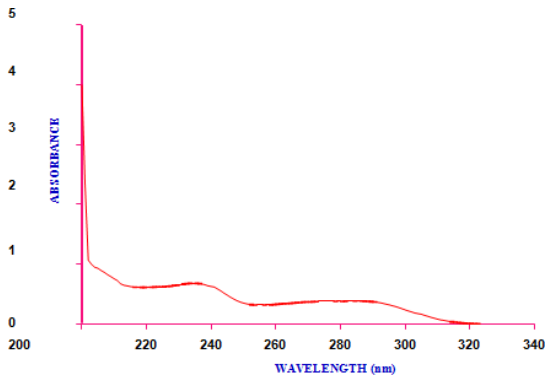
	S			
1	1	28.2±0.72	16.9±0.82	27.7±0.70
2	2	28.9±0.82	19.9±0.98	28.4±0.78
3	3	34.8±0.52	18.1±0.68	31.2±0.70
4	4	39.8±0.50	19.1±0.46	37.3±0.56
5	5	49.0±0.52	19.4±0.69	38.9±0.48
6	6	51.7±0.44	21.2±0.62	44.5±0.32
7	24	59.6±0.30	23.9±0.46	46.0±0.52

n=3*

TABLE STABILITY STUDY ON PARECOXIB CONTENT IN NIOSOMAL FORMULATION (FG12) FOR 3 MONTHS OF STORAGE PERIOD

REFRIGERATOR TEMPERATURE	TIME OF STORAGE IN MONTHS	DRUG CONTENT*
4^0C	0	98.62±0.23
	1	98.57±0.66
	2	98.23±0.25
	3	98.08±0.22

n=3*



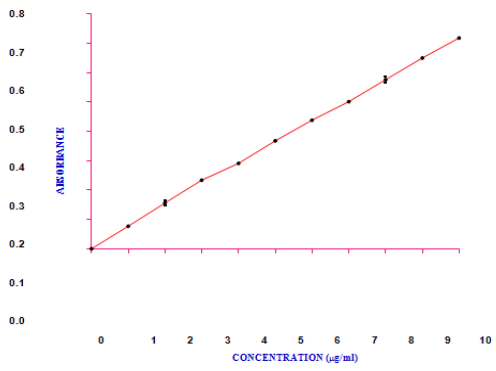
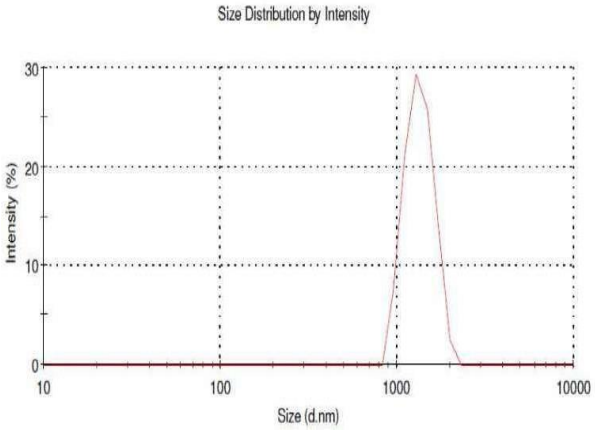
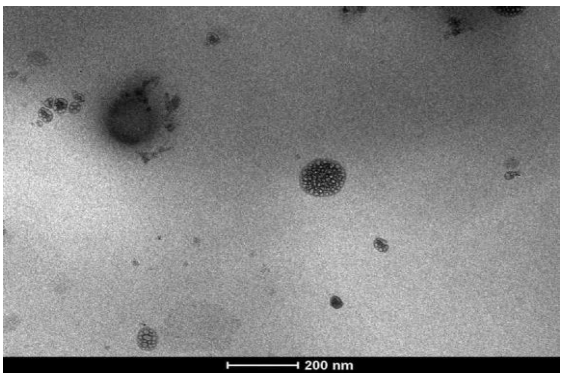


Figure 13: Determination of ƛmax of Parecoxib, Calibration of Parecoxib at Pbs of pH7.4



FG12-(Span 60 6:1)



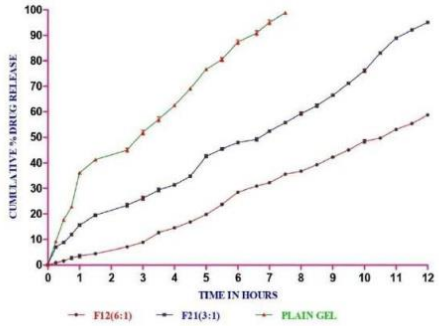


Figure 22 Comparison of *Invitro* Release of Plain Gel, Niosomel Gel with Highest and Lowest Entrapment Efficiency

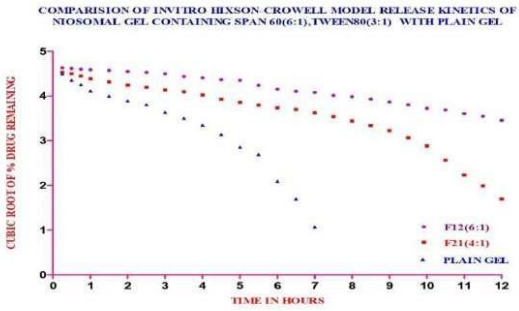
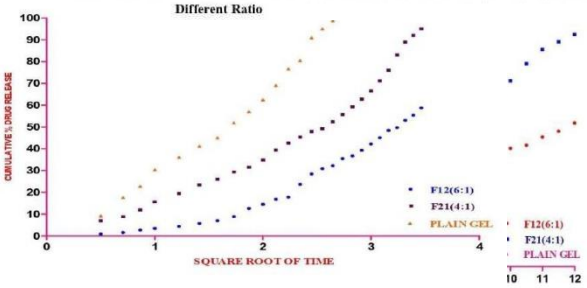
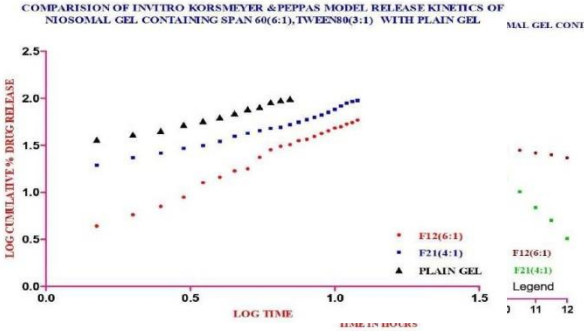
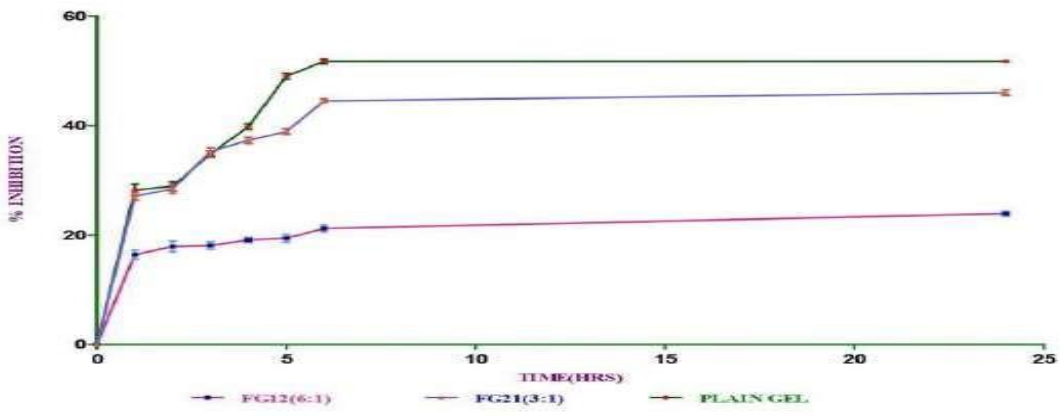


Figure 23 *invitro* Release Kinetics of Niosomal Gel Containing F12 (6:1), F214:1) in Different Ratio







Comparison of percentage inhibition of Rat Hind Paw Edema Method using Parecoxib Gel and Niosomal Gel Containing FG12 and FG21

CONCLUSION

The study prepared Niosomal formulations using cholesterol and non-ionic surfactants, resulting in stable Niosomes with high entrapment efficiency and retention properties. The Niosomal gel showed pseudoplastic behaviour, spherical vesicles, and sustained release of Parecoxib. In vitro and in-vivo anti-inflammatory studies showed prolonged drug release behaviour, suggesting the Niosomal gel could be used as a novel drug delivery carrier for skin targeting of Parecoxib.

REFERENCES

1. Chien, Y.W., (2005). Novel Drug Delivery Systems, 2nd edition, Revised and Expanded, Marcel Dekker, INC, New York, 1.
2. Uchegbu, I. F., & Florence, A. T. (1995). Non-ionic surfactant vesicles (niosomes): physical and pharmaceutical chemistry. Advances in colloid and interface science, 58(1), 1-55.
3. Murdan, S. (1998). Non-ionic surfactant-based organogels: their structures and potential as vaccine adjuvants. University of London, University College London (United Kingdom).
4. Lasic, D. D. (1990). On the thermodynamic stability of liposomes. Journal of colloid and interface science, 140(1), 302-304.
5. Biswal.S., Murthy P.N., (2008). Vesicles of Non-ionic Surfactants (Niosomes) and Drug Delivery Potential. Int. J. Pharm. Sci. & Nanotech. 1(1), 1-8.
6. Alamayehu Tarekejen., Nisha M Joseph., (2010). Niosomes in targeted drug delivery:

Some recent advances. Int. J. Pharm. Sci. & Res. 1(9), 1-8.

7. Madhav NVS., Saini A., (2011).Niosomes: A Novel Drug Delivery System. Int. J. Res.Pharm. & Chem. 1(3), 498-511
8. Jia-You Fang., Ying-Yue Wang., Wen- Ta Chiu., (2001). Effect of liposomes and niosomes on skin permeation of Enoxacin. Int.J.Pharm 219, 61-72.
9. Pratap S.Jadon., Rajesh S.Jadon., Virendra Gajbhiye., (2009). Enhanced oral bioavailability of Griseofulvin via Niosomes. AAPS. Pharm. Sci. Tech. 10(4), 1186-1192.
10. Vijay Prakash pandey., Karthikeyan Deivasigamani.,(2009). Preparation and Characterization of ofloxacin non-ionic surfactant vesicles for ophthalmic use. J.Pharm.Res. 2(8), 1330-1334.
11. Malay K.Das., Narahari N Palei., (2011). Sorbitan ester niosomes for topical delivery of Rofecoxib.Ind.J.Exp.Bio. 49,438-445.
12. Jong Soo Woo., Chul Soon Yong., Jong oh Kim., (2009). Formulation and invitro assessment of Minoxidil niosomes for enhanced skin delivery.Int.J.Pharm. 377, 1-8.
13. Gurrapu., Raju Jukanti., Sharan Reddy Bobbala., (2011). Improved oral delivery of Valsartan from maltodextrin based proniosome powders.Adv.Powder.Tech. 30, 1-8.
14. Ismail A.Attia., Sanna A.El-Gizawy., Medhat A.Fouda.,(2007). Infuence of a Niosomal formulation on oral bioavailability of Acyclovir in Rabbits. AAPS.Pharm.Sci.Tech. 8(4), E1-E7.
15. Pandey Shivanand., (2010). Development and characterization of Cefpodoxime proxetil Niosomes. Int.J.Pharma World. Res. 1(3) 1-11.
16. Indu Pal Kaur., Shilpa Kakkar., (2011). Spanlastics-A novel nanovesicular carrier system for ocular delivery.Int.J.Pharm. 413,202-210.
17. Naresh, R. R., Pillai, G. K., Udupa, N., & Chandrashekar, G. (1994). Anti-inflammatory activity of niosome encapsulated diclofenac sodium in arthritic rats. Indian Journal of Pharmacology, 26(1), 46-48.
18. Guinedi, A. S., Mortada, N. D., Mansour, S., & Hathout, R. M. (2005). Preparation and evaluation of reverse-phase evaporation and multilamellar niosomes as ophthalmic carriers of acetazolamide. International journal of pharmaceutics, 306(1-2), 71-82.

19. Ghada Abdelbary., Nashwa El-gendy.,(2008). Niosomes-Encapsulated Gentamicin for Ophthalmic controlled delivery.AAPS.Pharm.Sci.Tech.2008, 9(3), 740-747.

20. Arora Rajnish., Sharma Ajay.,(2010). Release studies of Ketoprofen niosomes formulation.J.Chem.Pharm.Res.2(1),79-82.

21. Ruckmani, K., Jayakar, B., & Ghosal, S. K. (2000). Nonionic surfactant vesicles (niosomes) of cytarabine hydrochloride for effective treatment of leukemias: encapsulation, storage, and in vitro release. Drug development and industrial pharmacy, 26(2), 217-222.

22. Gyanendra Singh., Harinath Dwivedi., Rakesh Pundir., (2010). Targeted Delivery of Rifampicin by Niosomal Drug Delivery System.J.Pharm.Res. 3(5), 1152-1154.

23. Agarwal.A., Katare.O.P., Vyas.S.P., (2001). Preparation and in-vitro evaluation of Liposomal/Niosomal delivery systems for antipsoriatic drug Dithranol. Int.J.Pharm. 228, 43-52.

24. Manosroi. A., Jantrawut.p., Manosroi.J., (2008). Anti-inflammatory activity of gel containing novel elastic niosomes entrapped with Diclofenac diethylammonium. Int.J.Pharm. 360,156-163.

25. Sankar V., Ruckmani K., (2009). Niosome drug delivery system: Advances and Medical Applications – An overview. Pharmacology online, 2, 926-932.

26. Abdul Ahad., Asgar Ali., Mohamed Aqil., (2011). Formulation and Evaluation of nano transfer somes using experimental design technique for accentuated transdermal delivery of Valsartan.J.Nano.Med. 30, 1-13.