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FORMULATION AND EVALUATION OF MELPHALAN LOADED NIOSOMEFOR CANCER TREATMENT

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ABSTRACT
Niosomes presents a structure similar to liposomes and hence they can they can represent alternative vesicular system with representative to liposomes. Niosomes thought to be better candidate for drug delivery as compared with liposome due to various factor like cost, stability and etc. Entrapment efficiency for different niosomal formulations were calculated and it was found that the F1 formulation had the highest entrapment of 97.12 % and the lowest entrapment of 88.06 % was found from formulation F3. The Zeta potential of the formulation F2 had the highest value of -14.4 and the formulation F1 had lowest value of -0.29. No charge inducing agents were added to these formulations and thus the potential value is low. In-vitro drug release data was studied by using dialysis method for all the prepared niosomal formulations and from this study, it was found that formulation F1 had the maximum percentage release of 96.10 % at the end of the 24th hour. The drug release kinetics for all the prepared niosomal formulations were studied by computational modelling method from this study it was found that F1 formulation followed Hixon with R2 values 0.9877, F2 formulation followed Higuchi with R2 values 0.9553 and F3 formulation followed First order with R2 values 0.9723 respectively.

KEYWORDS: Formulation, Evaluation, Melphalan, Niosome, Cancer Treatment.

INTRODUCTION
The concept of targeted drug delivery is designed for attempting to concentrate the drug in the tissues of interest while reducing the relative concentration of the medication in the remaining tissues. As a result, drug is localised on the targeted site. Hence, surrounding tissues are not affected by the drug. In addition, loss of drug does not happen due to localisation of drug, leading to get maximum efficacy of the medication. Different carriers have been used for targeting of drug, such as immunoglobulin, serum proteins, synthetic polymers, liposome, microspheres, erythrocytes and niosomes.[1] Niosomes are one of the best among these carriers. The self-assembly of non-ionic surfactants into vesicles was first reported in the 70s by researchers in the cosmetic industry. Niosomes (non-ionic surfactant vesicles) obtained on hydration are microscopic lamellar structures formed upon combining non-ionic surfactant of the alkyl or dialkyl polyglycerol ether class with cholesterol.[2] The non-ionic surfactants form a closed bilayer vesicle in aqueous media based on its amphiphilic nature using some energy for instance heat, physical agitation to form this structure. In the bilayer structure, hydrophobic parts are oriented away from the aqueous solvent, whereas the hydrophilic heads remain in contact with the aqueous solvent. The properties of the vesicles can be changed by varying the composition of the vesicles, size, lamellarity, tapped volume, surface charge and concentration. Various forces act inside the vesicle, eg, van der Waals forces among surfactant molecules, repulsive forces emerging from the electrostatic interactions among charged groups of surfactant molecules, entropic repulsive forces of the head groups of surfactants, short-acting repulsive forces, etc. These forces are responsible for maintaining the vesicular structure of niosomes. But, the stability of niosomes are affected by type of surfactant, nature of encapsulated drug, storage temperature, detergents, use of membrane spanning lipids, the interfacial polymerisation of surfactant monomers *in situ*, inclusion of charged molecule. Due to presence of hydrophilic, amphiphilic and lipophilic moieties in the structure, these can accommodate drug molecules with a wide range of solubility.[3] These may act as a depot, releasing the drug in a controlled manner. The therapeutic performance of the drug molecules can also be improved by delayed clearance from the circulation, protecting the drug from biological environment and restricting effects to target cells.[4] Noisome made of alpha, omega-hexadecyl-bis-(1-aza-18-crown-6) (Bola-surfactant)-Span 80-cholesterol (2:3:1 molar ratio) is named as Bola-Surfactant containing noisome.[5] The surfactants used in

niosome preparation should be biodegradable, biocompatible and non-immunogenic. A dry product known as proniosomes may be hydrated immediately before use to yield aqueous niosome dispersions. The problems of niosomes such as aggregation, fusion and leaking, and provide additional convenience in transportation, distribution, storage, and dosing.[6] Niosomes behave *in vivo* like liposomes, prolonging the circulation of entrapped drug and altering its organ distribution and metabolic stability.[7] As with liposomes, the properties of niosomes depend on the composition of the bilayer as well as method of their production. It is reported that the intercalation of cholesterol in the bilayers decreases the entrapment volume during formulation, and thus entrapment efficiency.[8] However, differences in characteristics exist between liposomes and niosomes, especially since niosomes are prepared from uncharged single-chain surfactant and cholesterol, whereas liposomes are prepared from double-chain phospholipids (neutral or charged). The concentration of cholesterol in liposomes is much more than that in niosomes. As a result, drug entrapment efficiency of liposomes becomes lesser than niosomes. Besides, liposomes are expensive, and its ingredients, such as phospholipids, are chemically unstable because of their predisposition to oxidative degradation; moreover, these require special storage and handling and purity of natural phospholipids is variable. Niosomal drug delivery is potentially applicable to many pharmacological agents for their action against various diseases. It can also be used as vehicle for poorly absorbable drugs to design the novel drug delivery system. It enhances the bioavailability by crossing the anatomical barrier of gastrointestinal tract via transcytosis of M cells of Peyer's patches in the intestinal lymphatic tissues.[9] The niosomal vesicles are taken up by reticulo-endothelial system. Such localised drug accumulation is used in treatment of diseases, such as leishmaniasis, in which parasites invade cells of liver and spleen.[10,11] Some non-reticulo-endothelial systems like immunoglobulins also recognise lipid surface of this delivery system.[2–8,10–12] Encapsulation of various anti-neoplastic agents in this carrier vesicle has minimised drug-induced toxic side effects while maintaining, or in some instances, increasing the anti-tumour efficacy.[13] Doxorubicin, the anthracycline antibiotic with broad-spectrum anti-tumour activity, shows a dose-dependent irreversible cardio-toxic effect.[14,15] Niosomal delivery of this drug to mice bearing S-180 tumour increased their life span and decreased the rate of proliferation of sarcoma. Intravenous administration of methotrexate entrapped in niosomes to S-180 tumour bearing mice resulted in total regression of tumour and also higher plasma level and slower elimination. It has good control over the release rate of drug, particularly for treating brain malignant cancer.[16] Niosomes have been used for studying the nature of the immune response provoked by antigens.[17] Niosomes can be used as a carrier for haemoglobin.[18,19] Vesicles are permeable to oxygen and haemoglobin dissociation curve can be modified similarly to non-encapsulated haemoglobin. Slow penetration of drug through skin is the major drawback of transdermal route of delivery.[20]

Melphalan attaches alkyl groups to the N-7 position of guanine and N-3 position of adenine, leading to the formation of monoadducts, and DNA fragmenting when repair enzymes attempt to correct the error. It can also cause DNA cross-linking from the N-7 position of one guanine to the N-7 position of another, preventing DNA strands from separating for synthesis or transcription. Finally, melphalan can induce a number of different mutations. The aim of the present study was to formulate melphalan loaded niosome which are used for cancer treatment. According to the 2020 statistics 2,261,419 new people were affected by breast cancer. So, I would like to contribute towards breast cancer patients via my research work. At present liposomal cancer drugs are available in the market, but they are of very high cost and there will be a problem in affordability for poor patients. So, we wanted to develop new niosomal drugs for breast cancer patients as they are comparatively low cost than available formulations in the market.

MATERIALS

Materials used

Table 1: List of Materials Used in Experiment.

S.No	Chemicals	Source
1	Melphalan hydrochloride	SHILPA MEDICARE LIMITED
2	Tween 60	NICE Chemicals
3	Tween 80	NICE Chemicals
4	Span 60	LOBA chemie
5	Span 80	LOBA chemie
6	Cholesterol	s.d.fine-CHEM LTd
7	Methanol	s.d.fine-CHEM LTd

METHODOLOGY

Construction of standard curve

Preparation of stock solution of melphalan hydrochloride

A 10mg melphalan hydrochloride was accurately weighed and transferred into a 100 mL standard flask. It was dissolved in 50 mL methanol and make up to 100 mL with Phosphate buffer saline pH 6.4.5mL of this solution was transferred into a 50 mL standard flask and make up to volume with Phosphate buffer saline pH 6.4. The final

stock solution was containing 10 µg/mL of melphalan.

Selection of analytical wavelength

The stock solution was scanned over the UV wavelength range between 400 nm to 200 nm. The λ max of melphalan hydrochloride was found and further analysis was performed based on the selected analytical wavelength mentioned in Fig 3.

Standard Graph of Melphalan Hydrochloride

The prepared stock solution was further diluted to get the different concentrations to determine the linearity range. Linearity was obtained in the concentration between 2-10 µg/mL. The standard sample was analysed at 260.5 nm. The absorbance of the various concentration is as mentioned in Table9 and Fig 4.

Compatibility study (FT-IR analysis)

KBr method, 300 mg of KBr and 3 mg melphalan HCL (and with polymers) placed in mortar 60 sec grind with pestle then placed into the hydraulic laboratory press, Press in vacuo at 15,000 pounds for 6 mins. The prepared pellet was analysed by using Shimadzu FTIR-8400S, then from FTIR graph, functional groups were interpreted and shown in Fig 5,6 and Tab 10.

Synthesis of Niosomes

3 different Niosomal formulations such as F1, F2 and F3 containing melphalan hydrochloride were synthesised by ultrasonication method.in this study,10 mg of melphalan hydrochloride added to 20mL phosphate buffer saline 7.4 pH at 50mL beaker and were mixed by magnetic stirrer (REMI 1MLH) at 250 RPM. After the drug was solubilized in phosphate buffer, then added the required amount of surfactant and cholesterol, according to Table 7. This mixture was sonicated by probe sonicator (LABSONIC ULTRASONIC HOMOGENIZER) for 25 min and maintained the probe temperature at 50^{o}C until to get a niosomal suspension (pulse mode range - 50sec sonication and 10sec pause).

Table 2: Composition of melphalan niosomal suspension.

Formulation code	Drug (mg)	Surfactant (mg)	Cholesterol (mg)
F1	10	10	10
F2	10	20	10
F3	10	30	10

Characterization of niosomes

Transmission Electron Microscopy

Niosome imaging was done under confocal microscope with Laser excitations of 100 and 3000 nm. Finally, the imaging process was done under confocal microscope and its process under the imageJsoftware.

Measurement of Particle size

The particle size of 3 different noisomal formulation was measured by particle size analyzer (Malvern version 7.13). For the measurement, 100 µl of the formulation was diluted with an appropriate volume of ethanol and phosphate buffer solution pH 7.4 in 2:8 Ratio and the vesicle diameter of all formulations were determined.

ζ-potential

A 1ml of each niosomal formulation was diluted to 10ml with water, 5 mL of this diluted samplewas transferred to a cuvette and the zeta potential was measured at Malvern Zeta-sizer.

pH

The pH of all 3 noisomal formulation ware measured by using digital pH meter and their valueswere recorded.

Entrapment Efficiency

A 20 mL of each noisomal formulations were centrifuged at 4500-5000 rpm in a 20 mL centrifuge tube for 30 mins and the supernatant solution was discarded and 20 mL phosphate buffer saline 7.4 was added in a centrifuge tube containing niosomal formulation and this procedure was repeated for 3 times. The resultant Purified niosomal formulations was diluted with 1:10 (v/v) (niosomal formulation: methanol) and placed in a bath sonicator for 10 mins. The quantification of the cargo molecules was analysis by JASCO V-530 UV 1600 UV-visible spectrophotometer at 261 nm. The amount of entrapped drug and drug loading capacity calculated from the equation.

$$Entrapment\ Efficiency(EE) = \frac{amount\ of\ drug\ entrapped}{total\ amount\ added} \times 100$$

***In-vitro* release studies**

In-vitro release of 3 different formulations were investigated using dialysis method. This method was carried out by using Himedia dialysis membrane 50 with the molecular weight cut-off range from 12000-14000 Daltons which has the capacity of holding 1.61 mL/cm. The dialysis bag (donor compartment) was soaked in warm water for 30 mins for removal of glycerol and then thread was usedto close the dialysis bag on both sides to prevent the leakage of formulation during drug release study.

The purified each niosomal suspension was placed in the 12 cm dialysis bag and closed with thread. Dialysis bag was placed in 250 mL of phosphate buffer saline pH 7.4 (receptor compartment). The medium was stirred by magnetic stirrer at 50-150 rpm in 37 ^{o}C. at each one-hour interval and 3 mLof sample was withdrawn and makeup to 10 mL with phosphate buffer saline 7.4 pH and replaced the same volume of fresh medium to maintain the sink conditions. determined the absorbance at 261 nm wavelength by using JASCO V-530 UV 1600 UV-visible spectrophotometer.

Following steps are used to find out the percentage drug release

Step 1

$$concentration = \frac{absorbance}{slope}$$

Step 2

$$concentration \times dilution\ factor$$

$$dilution\ factor = \frac{initial\ volume + final\ volume}{initial\ volume}$$

Step 3

$$in\ 250mL = \frac{concentration \times receptor\ volume}{1000mL}$$

Step 4

$$cumulative\ drug\ release = in\ 250mL + cumulative\ drug\ release$$

1st one cumulative value only exceptional

Step 5

$$\%drug\ release = \frac{cumulative\ drug\ release}{amount\ of\ drug\ taken} \times 100$$

***In-vitro* Release Kinetics**

Drug release kinetics of 3 different melphalan loaded niosomal formulations were calculated by using a software Microsoft Office Excel Add – In. The *In-vitro* drug permeation data of obtained formulation was fitted to zero order kinetics (cumulative amount of drug released versus time), first order kinetics (log cumulative percentage of drug remaining versus time), Higuchi model (cumulative percentage drug release versus log time) to assess the kinetic modeling of drug release and the model with higher correlation coefficient (i.e higher R^2) was considered to be best fit model.

RESULT AND DISCUSSION

Selection of analytical wavelength

The prepared stock solution was further diluted and scanned for λ_{max} and it was found to be maximum absorption 260.5 nm (λ_{max}) as shown in Fig 3.

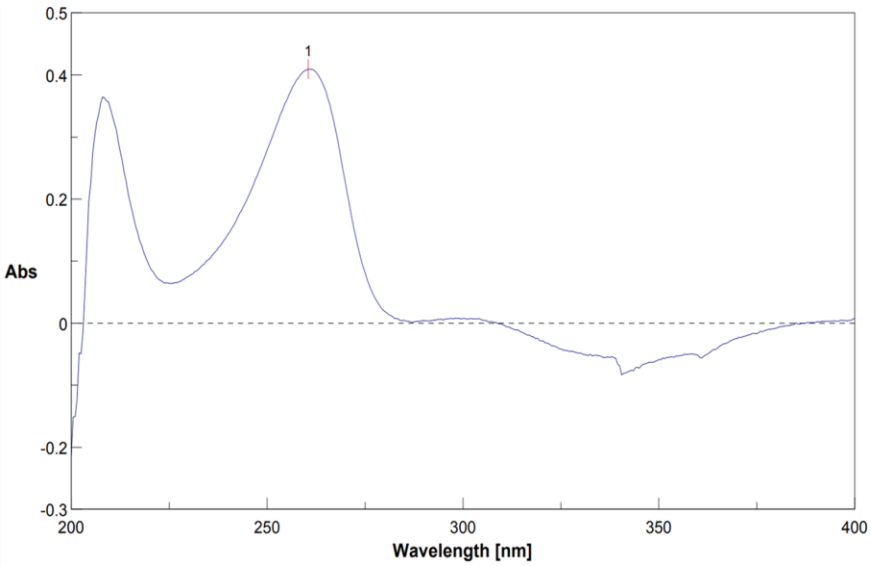

Fig. 1: Spectra of Melphalan Measured Using Uv Spectrophotometer.

Table 3: Analytical Wavelength of Melphalan.

S.No	Wavelength	Absorbance
1	260.5	0.40977

Construction of standard curve

Table 4: Melphalan concentration for calibration graph.

S.No	Concentration (µg/mL)	Absorbance (260.5nm)
1	2	0.149
2	4	0.2857
3	6	0.4301
4	8	0.5588
5	10	0.6918

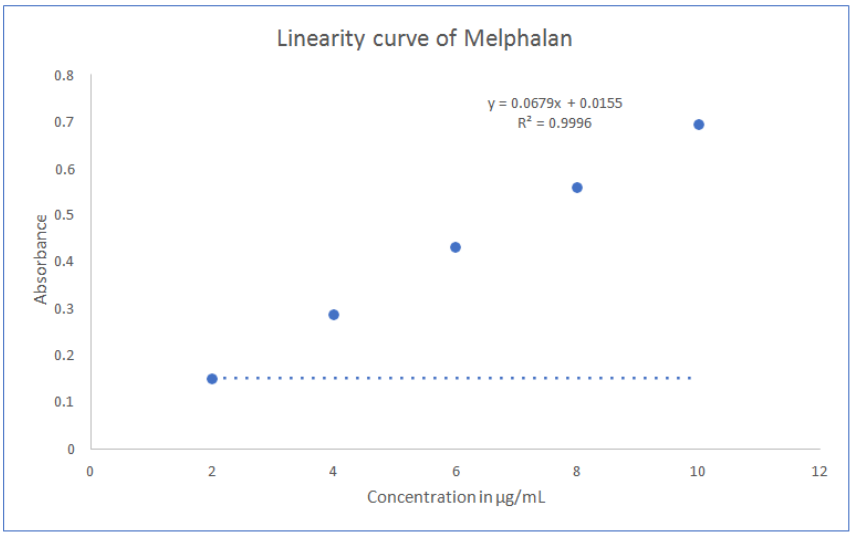

Fig 2: Standard graph of melphalan.

Straight light equation y = 0.0679x+0.0155
Correlation coefficient r^2 = 0.9996

Infrared spectral analysis

The compatibility between the melphan and span 60 was evaluated by using the FT-IR matchingapproach.

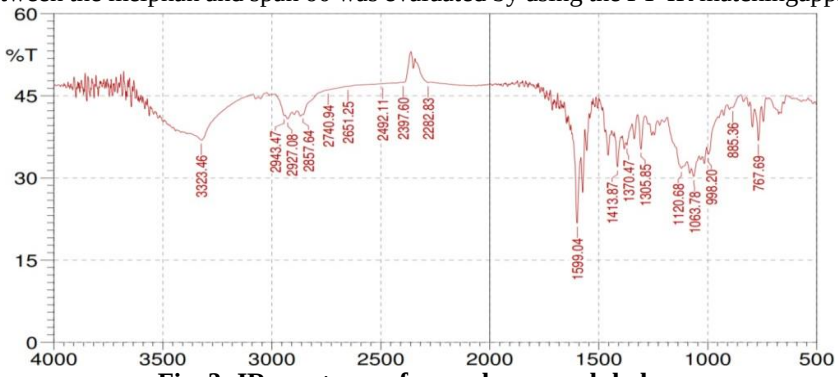

Fig. 3: IR spectrum of pure drug – melphalan.

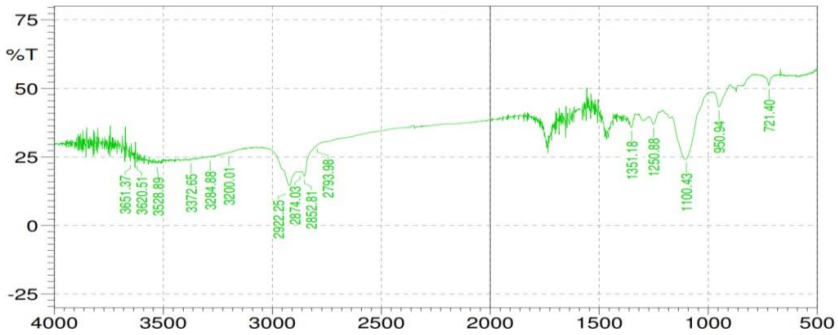

Fig. 4: IR spectrum of melphalan with span 60.

Table 5: FT-IR Spectral analysis.

Peak assignment functional group	Frequency range (cm^{-1})	Wave number (cm^{-1})	
		Spectrum position of IRin pure melphalan (cm^{-1})	Spectrum position of drug and span 60 (cm^{-1})
C=C (stretcharomatic)	1450-1700	1599	-
Tertiary amine	No peak will beseen	No peak	No peak
-C=O-OH	2800-3400	3323	3284
-sp^2 C-H	700-900	885	-
-sp^3 C-H (bend)	2700-3400	1370	1351

FT-IR studies revealed that there is no appearance of a new peak and disappearance of existing peaks, which indicated that there is no interaction between the drug and span 60.

pH

The pH values of all the prepared formulations ranged from 7.25 to 7.45. which probablywould not produce any irritation to the body.

Table 6: pH value for niosomal formulations.

Formulation code	pH
F1	7.26
F2	7.36
F3	7.41

Transmitted electron microscope

The surface morphology of the 3 different prepared niosomal formulations were observed by transmission electron microscope (TEM). TEM photographs were given in the Fig 7.

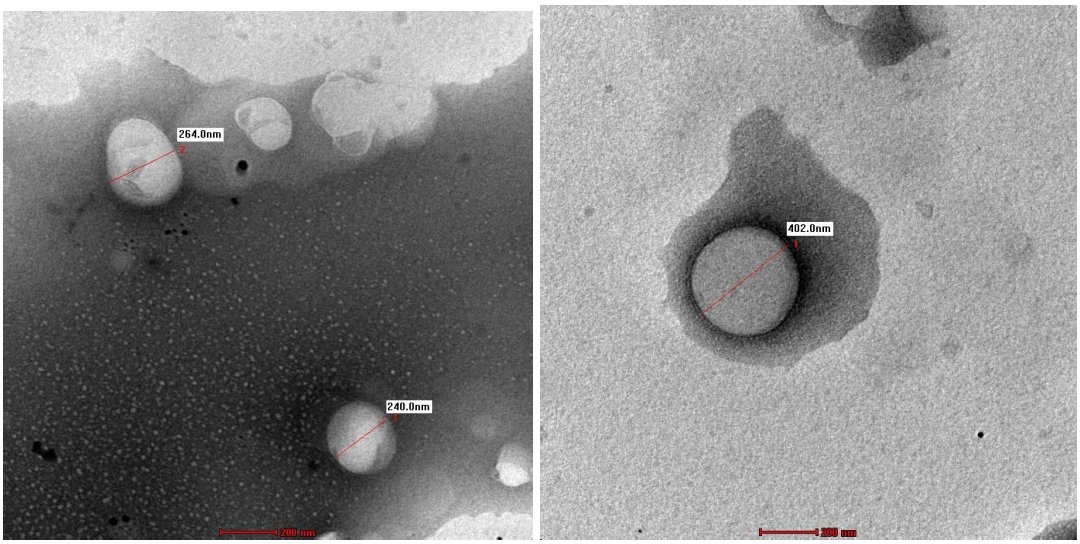

Fig 5: Transmission electron microscopy of niosomal formulation (F1).

Particle size distribution

The size distribution reports were shown in Fig.8,9 and 10. The size distributions along the meandiameter of the niosomes were measured by Dynamic Light Scattering Particle Size Analyzer (Malverninstruments). Particles of all formulations were in nanosize having a smooth spherical surface. Form formulations F1, F2 and F3 the average particle size was found to be. 278 nm, 684 nm and 2650 nm respectively. As the surfactant concentration increased there was an increase in particle size. The particle size of niosomes composed of span 60 and cholesterol formulation F1 in a 1:1 equimolar ratio was 278 nm, which was the least when compared to other formulations.

The particle size data showed that niosomes produced were of nanosize and had a high polydispersity index which indicates relatively broad particle size distribution for F1 and F3 preparations. F2 which has indicated narrow particle size distribution. The polydispersity index (PI) offormulations F1, F2 and F3 was found to be 1.000PI, 0.253PI and 1.000PI respectively.

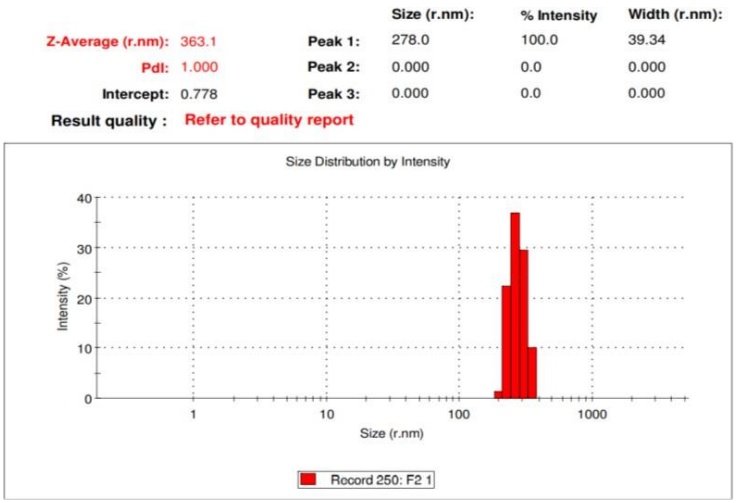

Fig. 6: Particle size distribution of Formulation F1.

		Size (r.nm):	% Intensity	Width (r.nm):
Z-Average (r.nm): 634.0	Peak 1:	684.2	100.0	93.81
PdI: 0.253	Peak 2:	0.000	0.0	0.000
Intercept: 0.809	Peak 3:	0.000	0.0	0.000
Result quality : Refer to quality report				

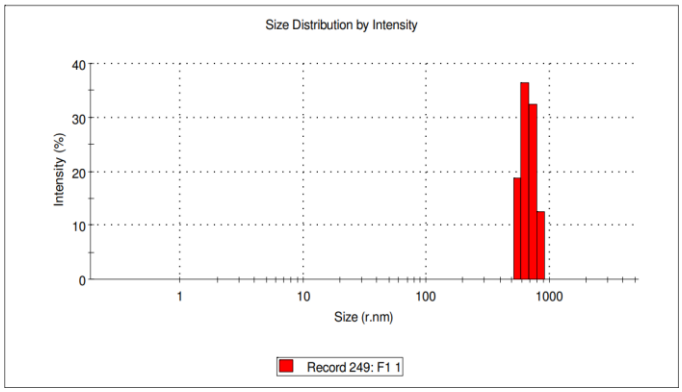

Fig. 7: Particle size distribution of Formulation F2.

		Size (r.nm):	% Intensity	Width (r.nm):
Z-Average (r.nm): 4041	Peak 1:	2650	100.0	179.9
PdI: 1.000	Peak 2:	0.000	0.0	0.000
Intercept: 0.718	Peak 3:	0.000	0.0	0.000
Result quality : Refer to quality report				

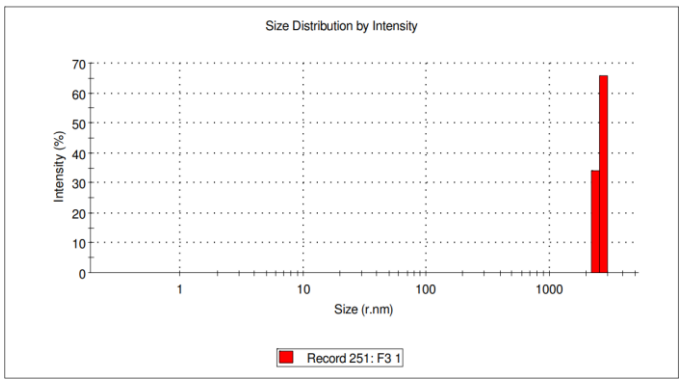

Fig. 8: Particle size distribution of Formulation F3.

Zeta potential

The stability study of the all prepared niosomal formulations were evaluated by measuring the vesicle surface charge (zeta potential) of the niosomes by the zeta meter. The zeta potential reports wereshown in Fig.11,12 and 13. The Zeta potential of all formulated niosomes was in the range of −0.279 to - 4.4 mV which indicates the charge of a particle is neutral & negative.

		Mean (mV)	Area (%)	Width (mV)
Zeta Potential (mV): -0.279	Peak 1:	-0.279	100.0	5.01
Zeta Deviation (mV): 5.01	Peak 2:	0.00	0.0	0.00
Conductivity (mS/cm): 0.722	Peak 3:	0.00	0.0	0.00
Result quality : Good				

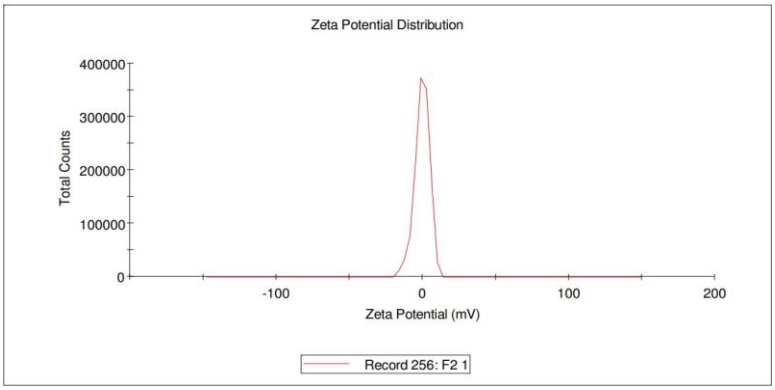

Fig. 9: Zeta potential of Formulation F1.

		Mean (mV)	Area (%)	Width (mV)
Zeta Potential (mV): -14.4	Peak 1:	-14.4	100.0	5.24
Zeta Deviation (mV): 5.24	Peak 2:	0.00	0.0	0.00
Conductivity (mS/cm): 1.68	Peak 3:	0.00	0.0	0.00
Result quality : Good				

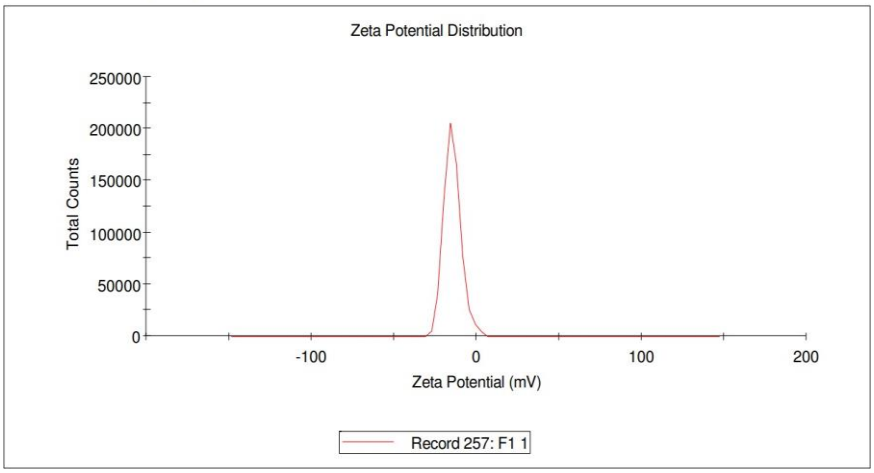

Fig. 10: Zeta potential of Formulation F2.

		Mean (mV)	Area (%)	Width (mV)
Zeta Potential (mV): -13.0	Peak 1:	-7.64	38.0	13.6
Zeta Deviation (mV): 42.1	Peak 2:	31.5	30.4	11.1
Conductivity (mS/cm): 2.97	Peak 3:	-77.5	14.9	9.04
Result quality : See result quality report				

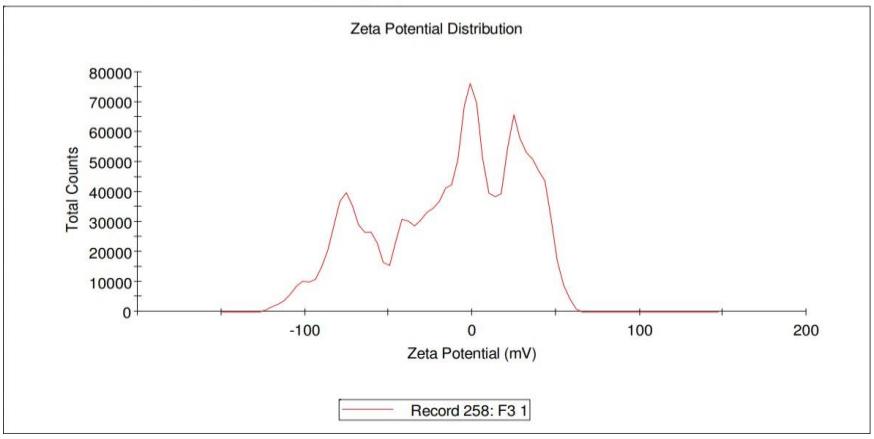

Fig. 11: Zeta potential of Formulation F3.

Entrapment efficiency

All prepared niosomal formulation were tested for percentage entrapment efficiency. The result of percentage entrapment efficiency indicates maximum entrapment has been achieved when niosomal formulation prepared by using span60. The result is shown in the table 12. the percentage entrapment efficiency for 3 different niosomal formulations were found to be 97.12, 95.02 and 88.06% respectively.

Table 7: Percentage entrapment efficiency of niosomes.

Formulation code	Percentage entrapment efficiency (%)
F1	97.12
F2	95.02
F3	88.06

***In-vitro* drug release**

The initial cumulative percentage drug release for F1 formulation was 2.5% at 45 mins and increase up to 70.90% by the end of the 8th hour. The total release percentage by the end of 24 hrs wasfound to be 96.10 %.

Table 8: Drug release data for niosomal formulation F1.

Time (hrs)	concentration	concentration × dilution factor	concentration × receptor volume/1000 mL	cumulative drug release(mg)	percentage drug release (%)
0.45	0.3033	1.0008	0.2502	0.2502	2.5
2	1.0073	3.3240	0.831	1.0812	10.81
4	2.2415	7.3969	1.8492	2.9304	29.30
6	2.4830	8.1939	2.0484	4.9788	49.78
8	2.5596	8.4466	2.1116	7.0904	70.90
24	3.0544	10.0795	2.5198	9.6102	96.10

The initial cumulative percentage drug release for F2 formulation was 3.09 % at 45 mins and increase up to 44.17 % by the end of the 8th hour. The total release percentage by the end of 24 hrs wasfound to be 59.59 %.

Table 9: Drug release data for niosomal formulation F2.

Time (hrs)	Concentration	concentration × dilution factor	concentration × receptor volume/1000 mL	cumulative drug release (mg)	percentage drug release (%)
0.45	0.3755	1.2391	0.3097	0.3097	3.09
2	0.6111	2.0166	0.5041	0.8138	8.13
4	1.3091	4.2963	1.0740	1.8878	18.87
6	1.3195	4.3543	1.0885	2.9763	29.76
8	1.7466	5.7637	1.4409	4.4172	44.17
24	1.8689	6.1673	1.5418	5.9590	59.59

The initial cumulative percentage drug release for F3 formulation was 2.4 % at 45 mins and increase up to 45.55 % by the end of the 8th hour. The total release percentage by the end of 24 hrs wasfound to be 64.71 %.

Table 10: Drug release data for niosomal formulation F3.

Time(hrs)	concentration	concentration × dilution factor	concentration × receptor volume/1000 mL	cumulative drug release (mg)	percentagedrug release (%)
0.45	0.2945	0.9718	0.2429	0.2429	2.4
2	0.9351	3.0858	0.7714	1.0143	10.14
4	1.1620	3.8346	0.9586	1.9729	19.72
6	1.4904	4.9183	1.2295	3.2024	32.02
8	1.6406	5.4139	1.3534	4.5558	45.55
24	2.3225	7.6642	1.9160	6.4714	64.71

The cumulative percentage release of the different niosomal formulation (F1,F2 and F3) is shownin the Fig 14. The formulation F1 had shown the highest drug release of 95 % drug at 24 hrs. The formulation F2 and F3 had shown a similar rate of drug release of about 60 %. In all the formulations, 40-75 % of the drug was released within 10 hrs followed by 70-95 % and followed by next 24 hrs.

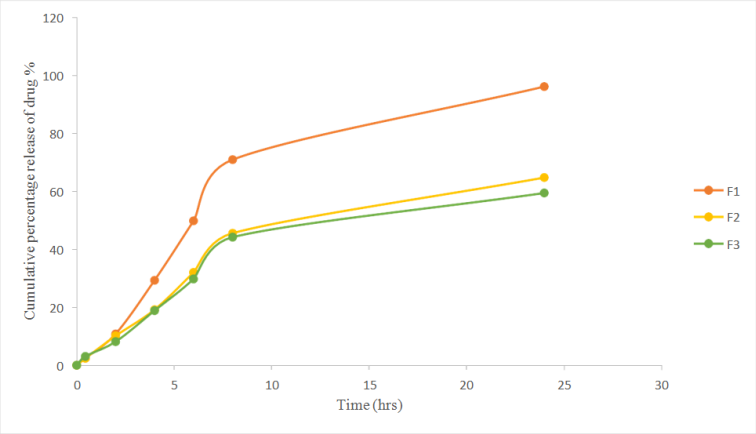

Fig 12: Comparative cumulative percentage release of different niosomal formulations.

Drug release kinetics

Various models such as Zero-order kinetics (percentage amount of drug release versus time), First-order kinetics (log percentage of drug remaining to release versus time), Higuchi (percentage amount of drug unreleased versus square root of time) and Korsermeyer-Peppas (log percentage of drugreleased versus log time) were applied to assess the kinetics of drug release from prepared niosome suspensions. The most suited model for drug release was predicted based on regression coefficient i.e. nearer the value of regression towards 1, greater the suitability of the best-fitted release mechanism. In the table, the kinetic parameter for 3 different melphalan loaded niosomal formulations were presented. As clearly indicated in the Table 16, the in-vitro release profile of drugs from all the formulations could be best expressed by Hixson, First order and Higuchi matrix diffusion type Fig 15,16 and 17.

Table Drug release kinetics.

Formulation code	R^2 value				
	Zero order	First order	Higuchi	Korsemeyer-Peppas	Hixson
F1	0.8949	0.9866	0.9496	0.6343	0.9877
F2	0.8986	0.9512	0.9553	0.6493	0.9359
F3	0.9151	0.9723	0.9642	0.6506	0.9570

Formulation F1 follows Hixson drug release kinetics with R2= 0.9877

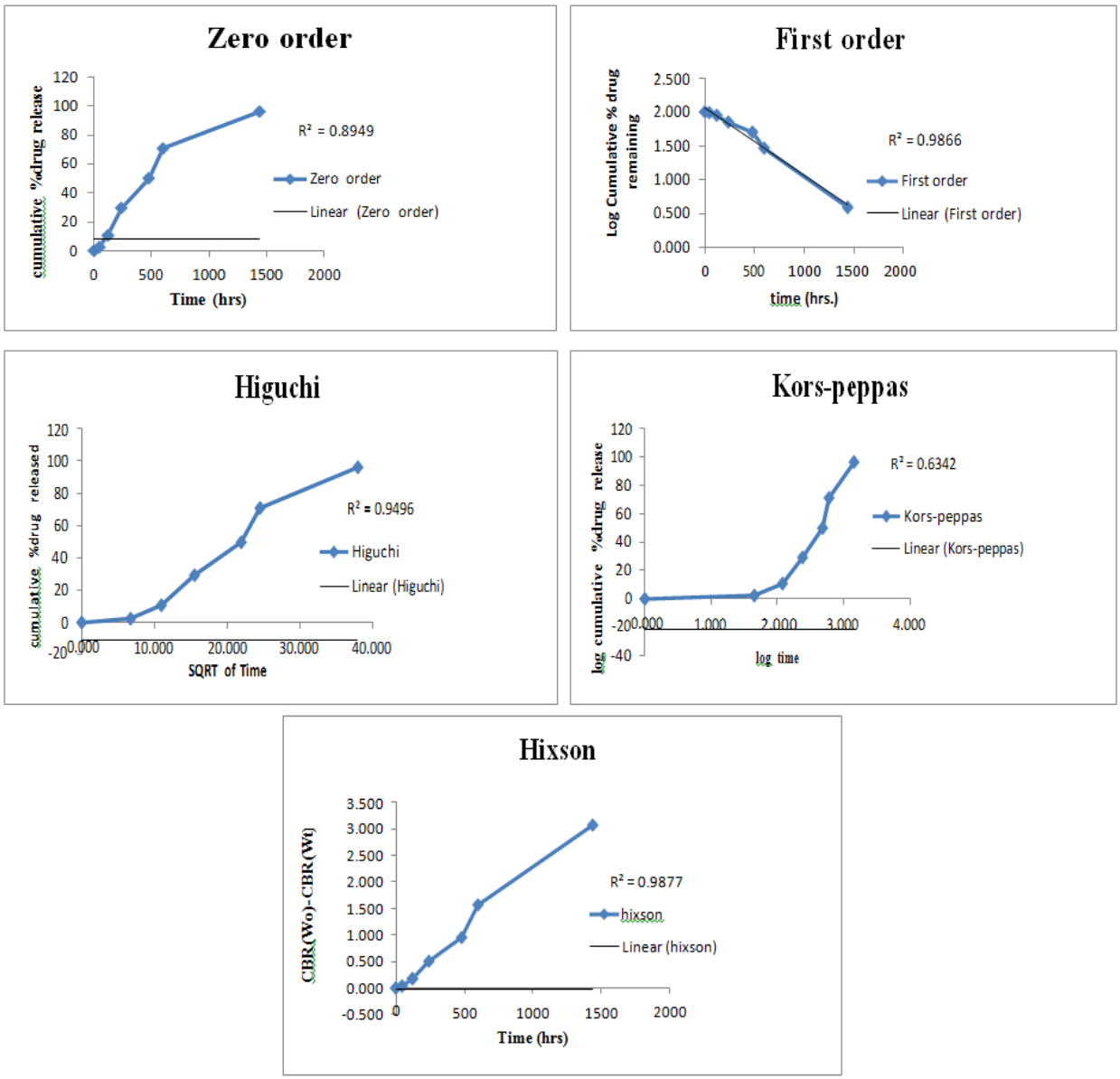

Fig. 13: Drug release rate kinetics of melphalan loaded niosome F1.

Formulation F2 follows Higuchi drug release kinetics with R^2= 0.9553

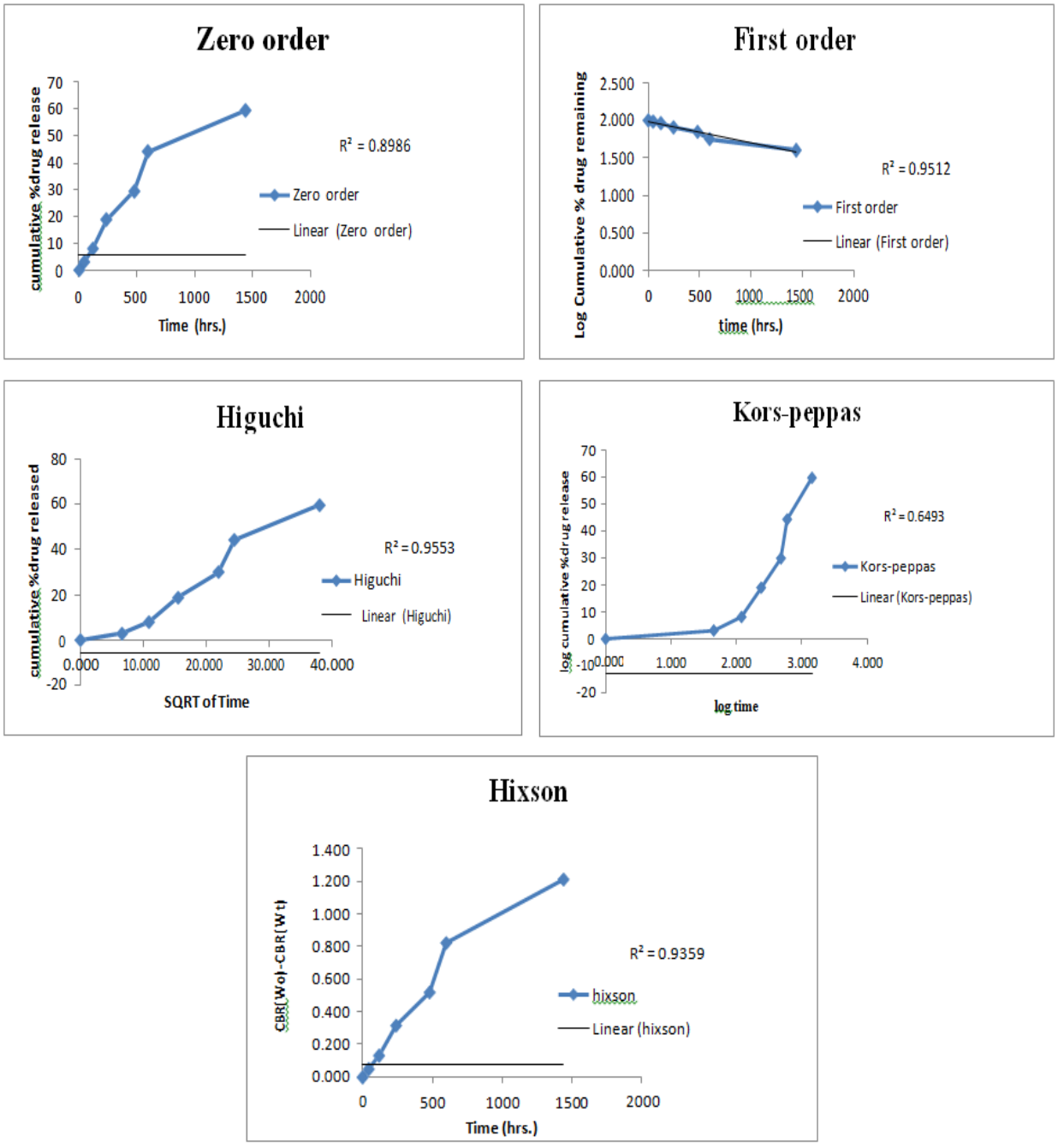

Fig. 14: Drug release rate kinetics of melphalan loaded niosome F2.

Formulation F3 follows First order drug release kinetics with R^2= 0.9723

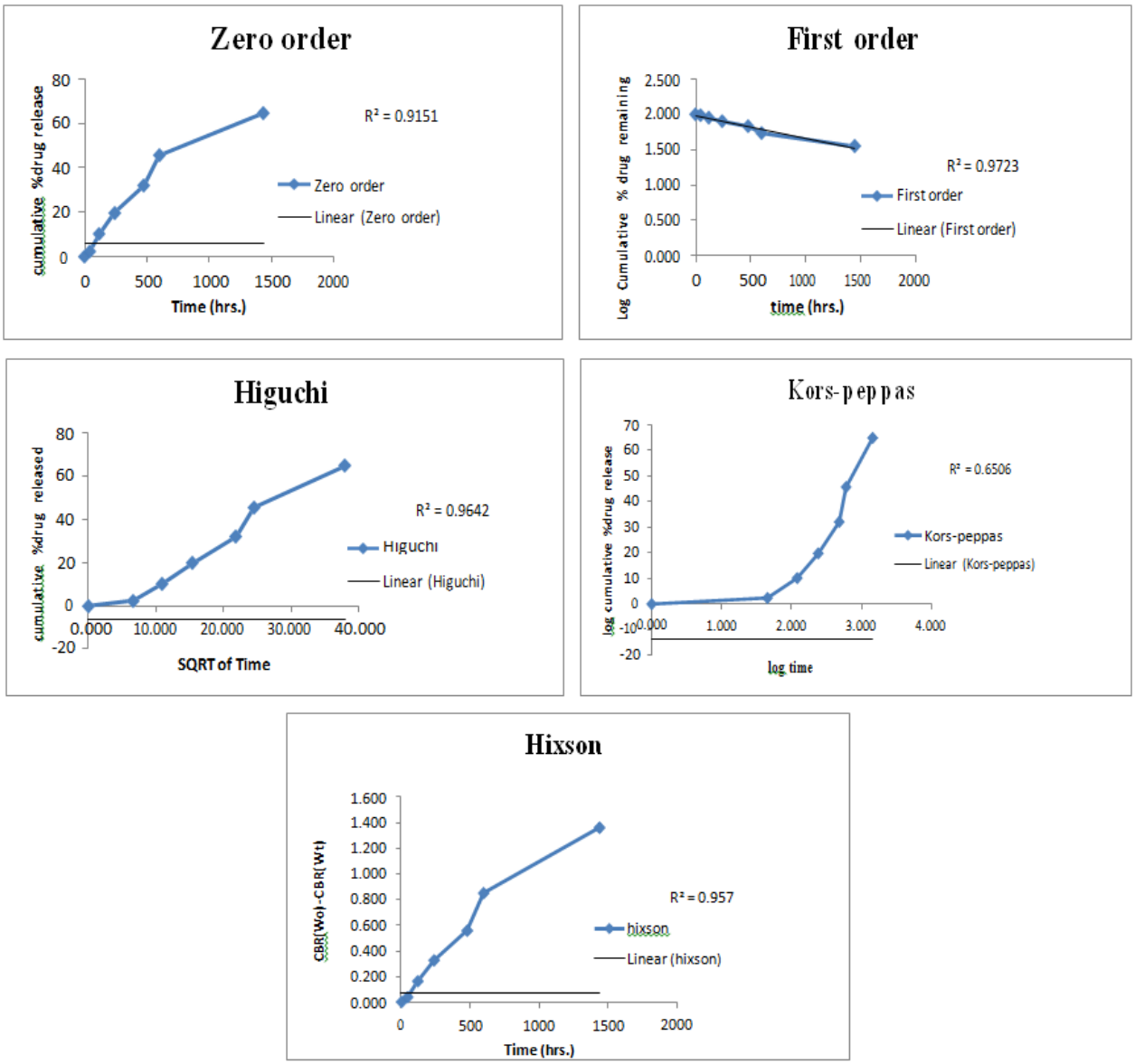

Fig. 15: Drug Release Rate Kinetics of Melphalan Loaded Niosome F3.

SUMMARY AND CONCLUSION

The concept of incorporating the drug into liposomes or niosomes is for better targeting the drug at appropriate tissue destination. It is widely accepted by the researchers and academicians. Niosomes represent as promising drug delivery system.

Niosomes presents a structure similar to liposomes and hence they can they can represent alternative vesicular system with representative to liposomes. Niosomes thought to be better candidate for drug delivery as compared with liposome due to various factor like cost, stability and etc.

Melphalan is an anti-neoplastic drug in the class of alkylating agent used to treat various forms of cancer. The main disadvantage of using melphalan as an anti-cancer drug is as it commonly affects normal cells. There is a correlation between the conventional drug delivery system and cell damage. so, the Targeted drug delivery system may modify this correlation by controlling the cell damage by using novel carriers. The novel delivery system of melphalan is to decrease the normal cell death and also increase the cell death of cancer cells. In this work we prepared different niosomal formulations containing melphalan, span 60 and cholesterol by using probe sonication method.

Chemical compatibility study confirmed that there is no interaction between melphalan (drug) and span60 & cholesterol (excipients) before the formulation. The pH of all prepared formulations was found to be excellent. Particle size was much affected by the drug and polymer ratio. The surface morphology and shape of the different formulated noisome were observed from a transmitted electron microscope. They are spherical and entrapped numerous drug particles and can be assigned for better targeting.

Entrapment efficiency for different niosomal

formulations were calculated and it was found thatthe F1 formulation had the highest entrapment of 97.12 % and the lowest entrapment of 88.06 % was found from formulation F3.

The Zeta potential of the formulation F2 had the highest value of -14.4 and the formulation F1 had lowest value of -0.29. No charge inducing agents were added to these formulations and thus the potential value is low.

In-vitro drug release data was studied by using dialysis method for all the prepared niosomal formulations and from this study, it was found that formulation F1 had the maximum percentage releaseof 96.10 % at the end of the 24^{th} hour.

The drug release kinetics for all the prepared niosomal formulations were studied by computational modelling method from this study it was found that F1 formulation followed Hixon with R^2 values 0.9877, F2 formulation followed Higuchi with R^2 values 0.9553 and F3 formulation followed First order with R^2 values 0.9723 respectively.

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