Divalproex Sodium Niosomes: Formulation and Evaluation for the Treatment of Epilepsy

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ABSTRACT

Epilepsy and other seizure disorders may be managed and treated with the use of a medicine known as divalproex sodium, which is a kind of anti-epileptic medication. The study was carried out with the consideration of these three goals in mind. The completion of this research effort resulted in the loading of an anti-epileptic medication into niosomes for the treatment ofepilepsy. These niosomes are able to provide the patient control over the dose that they get. The formulations of niosomes were made better by modifying the area of Tween and Span in the amounts that they occupy, respectively. In order to prepare the formulations, the film hydration method was carried out. After that, the formulation was examined so that its viscosity, morphological properties, and encapsulation efficiency could be figured out. It was found that niosomes made with Tween 80 and Span 60 were capable of entrapping considerable amounts of the drug that they were designed to target. After that, the niosomes were produced by utilising a number of different concentrations. After that, they were optimised at effective concentrations, evaluated for gelation temperature, melting temperature, and heat of enthalpies, and exhibited findings that were to the satisfaction of the researcher. The formulations of the niosomes were tested in vitro, and the results showed that they delivered an appropriate level of medicine delivery. As a consequence of this, we are in a position to arrive at the conclusionthat the niosomes have the potential to be a successful technique for the creation of an anti- epileptic medication.

KEYWORDS: Divalproex Sodium, Niosomes, Epilepsy, Dichloromethane.

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INTRODUCTIO N:

Epilepsy is a set of progressive neurologic illnesses characterized by rapid, brief, and repeated seizures; these seizures are produced by aberrant firing of neurons in the brain. The occurrence and intensity of epileptic seizures may be mitigated by any number of antiepileptic medications now on the market. However, AEDs are unable to reach the brain and maintain an adequate therapeutic concentration in the brain due to the limitations of the blood brain barrier (BBB) as well as other biological variables [1, 2].

Epilepsy comes from the Greek verb epilambanein, which means to seize or attack. Two or more convulsive episodes without provocation characterize the chronic neurological disorder known as epilepsy (World Health Organization, 2001). Clinical signs thought to originate from an "aberrant and inappropriate firing of a group of neurons across the brain," the definition of a seizure states. Involuntary muscular spasms, loss of awareness and even convulsions may

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accompany seizure episodes [3, 4].

Divalproex Sodium is an antiepileptic that also has applications in the treatment of bipolar disorder, migraine, and schizophrenia. It's also taken to keep one's emotions in check. Since only a small percentage of ingested Divalproex Sodium actually reaches the brain, it must be given in large dosages for any noticeable therapeutic impact to manifest. Moreover, because of its long-term nature and the high doses necessary to treat its symptoms, Divalproex Sodium is associated with a wide range of drug interactions as well as health consequences. One of the aims of the current research is to determine the efficacy of low-dose Valproic acid administration. When compared to other anticonvulsants such phenytoin and phenobarbital, Divalproex Sodium has a lower cerebral distribution when taken orally.

In the treatment of mania related to bipolar disorder, epilepsy, including frequent headaches, divalproex sodium, a persistent coordination compound consisting of sodium valproate with valproic acid, is employed. The BCS classification class II medication valproicacid has a low solubility in water. Sodium valproate, a salt version of the drug, is manufactured as a capsule, sustained-release tablet, enteric-coated tablet, solution, and intravenous injectionsto improve its solubility [5-7].

Niosomes are resistant to chemicals, contain minimal toxicity due to their non-ionic nature, and may be seen as low-cost, non-biological alternatives to liposomes for increasing solubility and bioavailability. These may entrap hydrophilic and lipophilic medicines thanks totheir ability to self-assemble into vesicular membranes or an aqueous layer in water.

Microscopic lamellar structures, known as niosomes or non-ionic surfactant vesicles, are generated during hydration of a combination of non-ionic surfactant of the alkyl or dialkyl polyglycerol ether class and cholesterol in aqueous conditions. One or more lipid bilayers encapsulate an aqueous core in niosomes, and niosomes may undergo alteration or modification by including additional excipients like cholesterol into the membrane. Surfactants derived from sucrose esters and polyoxyethylene alkyl ethers are only two examples of the many different substances that have been employed to create niosomes. Niosomes have the potential to be used in a controlled and targeted manner for the delivery of drugs. Other benefits include their chemical stability, minimal toxicity owing to their non-ionic nature, and the absence of any particular handling conditions [4, 8-10].

The oral route of medication delivery is preferred because of its simplicity and convenience. However, when the medication is significantly metabolized by the first pass action in the liver, oral administration is usually not preferred. Since oral administration of drugs does not result in systemic absorption, scientists have looked into other methods, including intravenous fluid, intramuscular, subcutaneous, intranasal, intradermal, etc. administration. Quick onset of the effects of a drug to the brain is requisite during an epileptic attack, and the nasopharyngeal pathway can be regarded as an alternative route to the central nervous system due to its fast absorption and ability to avoid hepatocellular first pass metabolism [11, 12].

This research aimed to develop a niosomal in-situ-nasal gel form of valproic acid to decrease required dosing, boost patient compliance, and provide longer-lasting effects. The formulation was also exposed to a histopathology examination, and the diffusion efficiency was investigated using bovine nasal mucosa. The gelation and gel melting efficiencies of the best-performing formulations were also estimated [5, 13-15].

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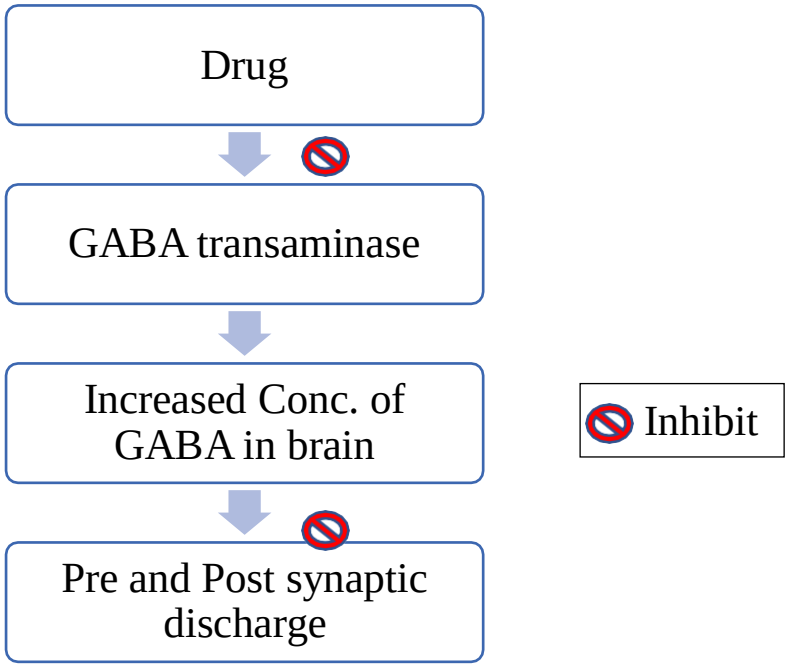

Fig: Mechanism of Divalproex Sodium

MATERIALS AND METHODS:

Drugs and all the surfactants and humectants were gifted by Hema laboratories, Selaqui Dehradun. The solvents were purchased from Fisher Chemicals. All available safety data were included in the analysis, the number of patients who did not complete the study, general tolerance, side-effects and drug interactions.

Preparation of Niosomes Formulation:

Cholesterol and span-60 (surfactant) were dissolved in 10 ml of dichloromethane. In a rotating vacuum evaporator at 40°C for 40 minutes, the organic solvent was evaporated under

vacuum to create a thin layer in the round bottom flask. Thin coating of organic solvent is removed at 50°C after 2 hours. 10 ml of phosphate buffer solution with Divalproex Sodium at60°C hydrated the surfactant film. The suspension was mechanically shaken for 30 minutes. Ultrasonication was used to produce multilamellar niosomes from the solution. It's kept overnight at 4°C [9, 16].

Batch Code	Coded Values		Actual Values	
	Z1	Z2	Z1 (Span-60)	Z2 (Cholesterol)
F1	-1	-1	20	20
F2	-1	0	20	25
F3	-1	+1	20	30
F4	0	-1	30	20

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F5	0	0	30	25
F6	0	+1	30	30
F7	+1	-1	40	20
F8	+1	0	40	25
F9	+1	+1	40	30

Table: Composition of Divalproex Sodium loaded niosomes by 3^2 factorial

***Mean ± SD (n = 3)**

For Z1: 20 mg (-1), 30 mg (0), 40 mg (+1) and for Z2: 20mg (-1), 25mg (0), 30 mg(+1)

Characterization of Prepared Niosomes:

Entrapment Efficiency:

5ml of freshly made formulation was pipetted into a centrifuge tube and put in a centrifuge. 50 minutes were spent centrifuging the niosomal solution. After centrifugation, the supernatant was diluted. Using UV spectroscopy (Shimadzu, Japan), the quantity of free medicine in the supernatant was determined, and the % EE (DVS) was estimated-

$$Drug\ entrapment\ (\%) = \frac{Total\ drug * Free\ drug}{Total\ drug} * 100$$

Where A is the entrapped drug and B is the total drug added.

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Zeta Potential Measurements:

Zeta potential is the nanoparticles' surface charge. Niosomal suspension zeta potentialmeasured. 60s of analysis at 25^{o}C.

Partical size:

Zetasizer (Litesizer 500) measures niosomal vesicle particle size. The zetasizer measures the intensity of dynamically dispersed laser light caused by particle movement. Niosomal vesicle size was measured. 60s of analysis at 25^{o}C [10, 17].

Transmission Electron Microscopy:

Transmission Electron Microscopy (TEM) [Hitachi (H-7500)] at 120 KV was used to evaluate niosomal vesicle shape and surface morphology. Niosomes were diluted and absorbedfor 2 minutes on a carbon-coated grid. The absorbed niosomes were dyed with uranyl acetate and air-dried before viewing.

In vitro release study of niosome:

Franz diffusion cell determined Divalproex Sodium penetration from Niosomes. Cellophane was soaked overnight in pH- 7.4 phosphate buffer solution. Cellophane membraneclamped between donor and receptor compartments in vertical diffusion cell. Effective diffusion area:1cm^{2}. The receptor chamber was filled with 20 ml of pH-7.4 phosphate buffer solution and kept at 37±0.5^{o}C. Cellophane contacted phosphate buffer solution. During the experiment, the assembly was agitated at 400rpm. The donor compartment received 2ml of theformulation. At intervals, 4ml of the sample is removed and replaced with new medium to preserve skin condition. When needed, samples were diluted and filtered using 0.45m paper. All compositions' UV absorbance at 222nm was measured.

Stability studies:

Testing for two months at 40°C and 75% RH was done on a sample stored in a stability chamber. An artificial membrane was used to test water resistance and diffusion along withnonvolatile content and drying time [18-20].

RESULT AND DISCUSSION:

Melting point:

Purified Divalproex Sodium melting point is 127-135°C. This range is found in articlesabout the drug's purity.

UV- Vis Spectrophotometric study:

UV- Vis Spectrophotometric study was conducted in phosphate buffer solution pH 7.4 and a gamut is set between 200-400nm for the examination. λmax was observed in 222nm in phosphate buffer solution 7.4.

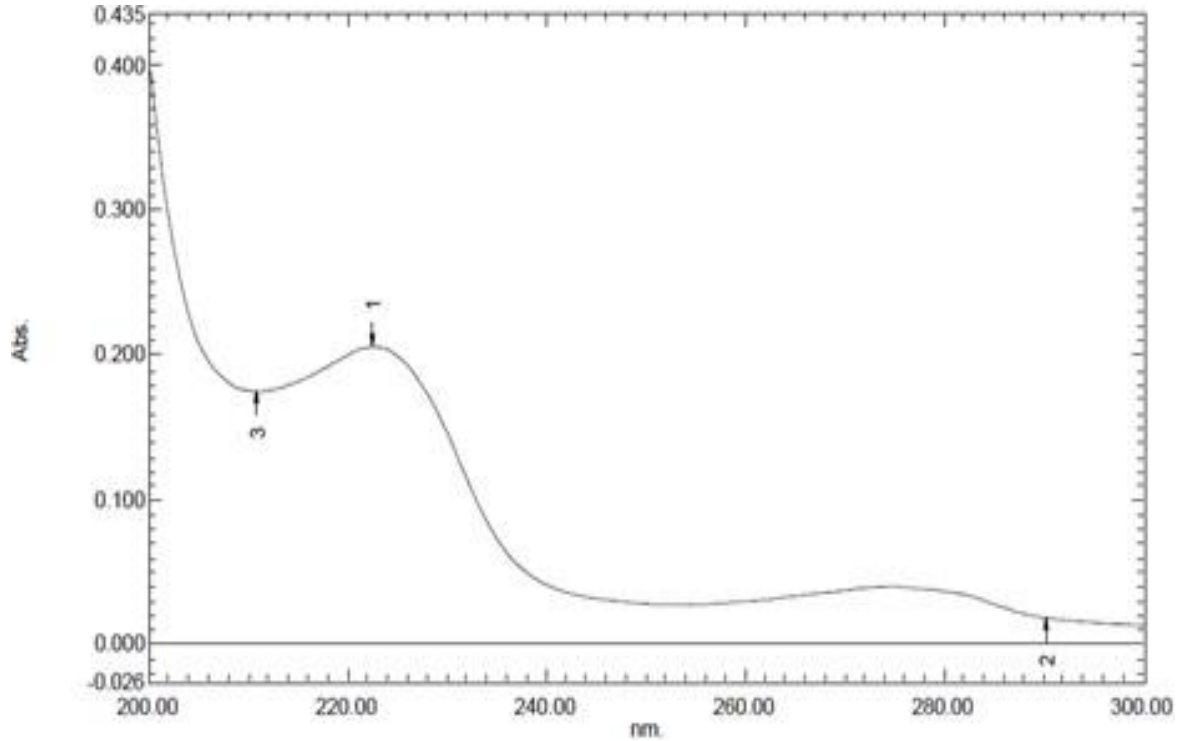

Fig: λ_{max} scan for DVS 222nm in phosphate buffer 7.4.

Table Preparation of calibration curve:

S. No	Concentration (µg/ml)	Absorbance
1.	10	0.205
2.	20	0.424
3.	30	0.598
4.	40	0.816
5.	50	1.028

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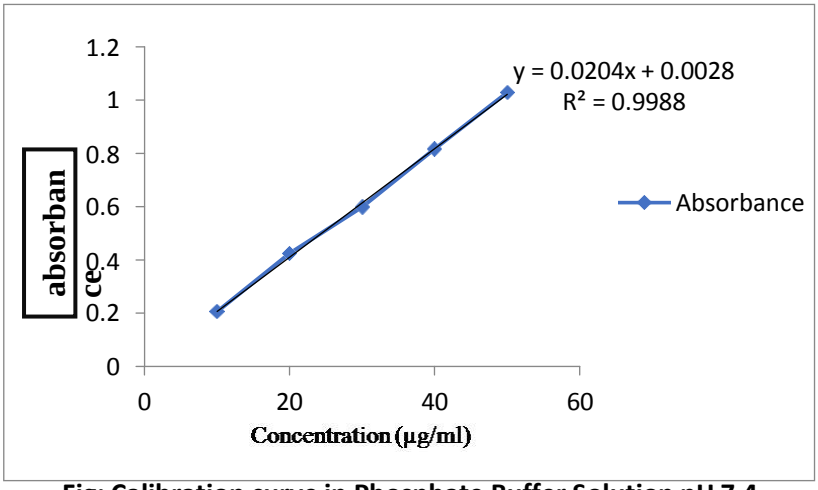

Fig: Calibration curve in Phosphate Buffer Solution pH 7.4

Solubility Study:

DVS was soluble in phosphate buffer (pH- 7.4) and distilled water. In phosphate buffer (pH-7.4) and distilled water, Divalproex Sodium solubility was 1.24 mg/ml.

Partition coefficient:

The partition coefficient of the Divalproex Sodium in n-octanol/water system was estimated to be 2.4 ± 0.14 (n=3).

FTIR spectral analysis:

The FT-IR spectrum of pure Divalproex Sodium sample was recorded by FT-IRspectrum, which was compared with functional group [21-23].

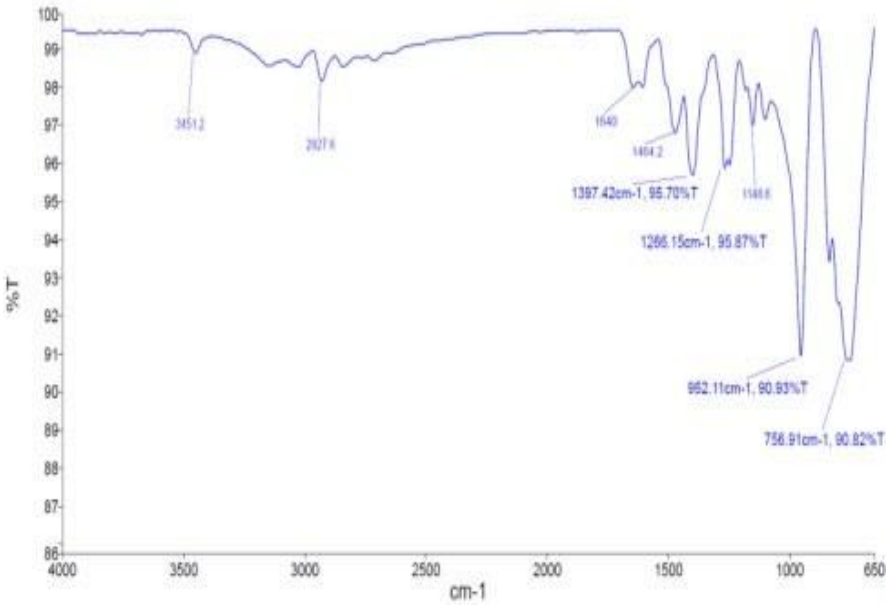

Fig: FT-IR spectra of Divalproex Sodium

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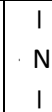
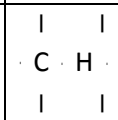
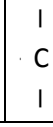
Table IR frequencies of Divalproex Sodium:

S. No.	Functional group	Range(cm^{-1})	Observed Frequency (cm^{-1}
1.		3300-3500	3451.2
2.		600-1500	1266.15
3.	> C = C <	1620-1680	1640
4.	- NO2	1330-1540	1464.2
5.		2850-2960	2927.6

Compatibility study (Drug and Excipients):

The compatibility study of drug and excipients were performed through FT-IR

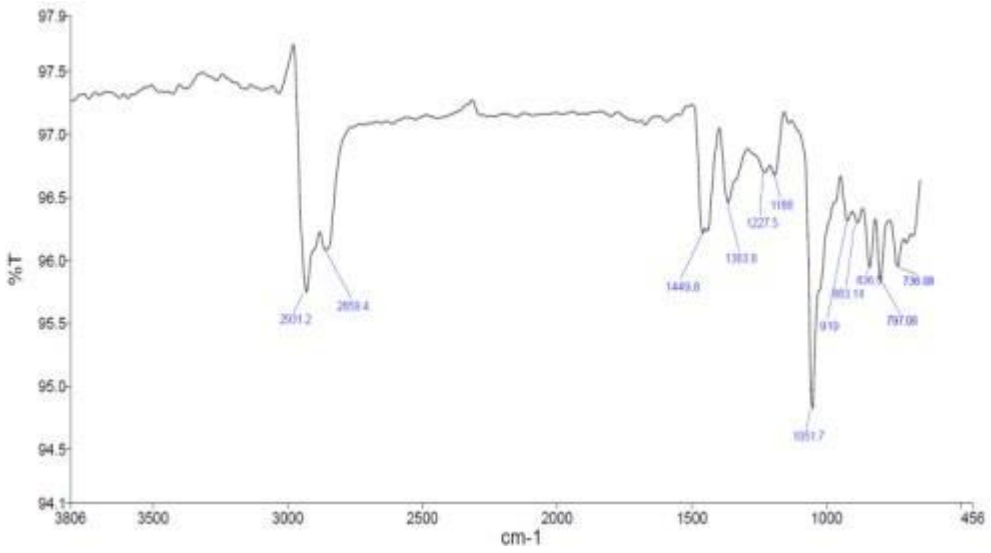


Fig: FT-IR spectra of cholesterol

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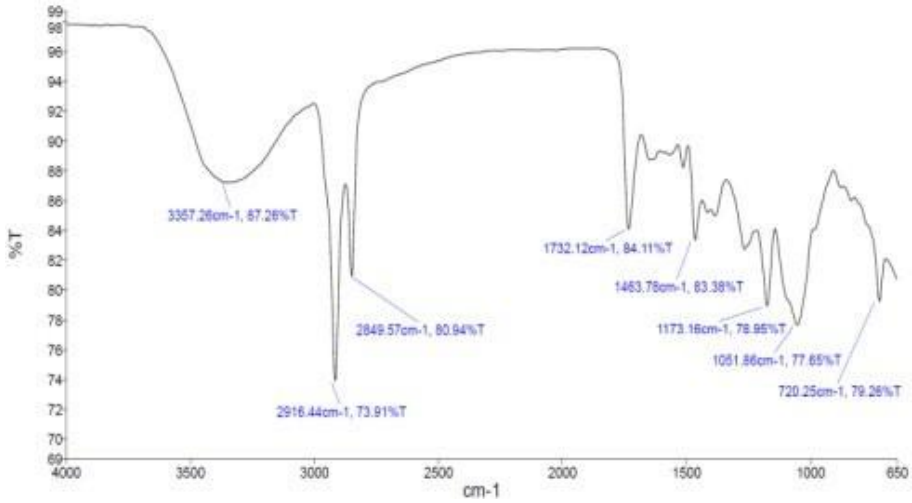

Table IR frequencies of Cholesterol:

S. No.	Functional group	Range(cm^{-1})	Observed Frequency (cm^{-1})
1.	I I · C · H · I I	600-1500	1363.8
2.	I · C · O · I	1000-1300	1227.5
3.	- NO_2	1330-1540	1449.8
4.	I · C · H I	2850-2960	2859.4

Fig: FT-IR spectra of span-60

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Table IR frequencies of span-60:

S. No.	Functional group	Range(cm^{-1})	Observed Frequency (cm^{-1})
1.	C H	600-1500	1173.16
2.	C H	2850-2960	2916.44
3.	O H	3200-3400	3357.26
4.	- NO_2	1330-1540	1463.78
5.	> C = O	1680-1760	1732.12

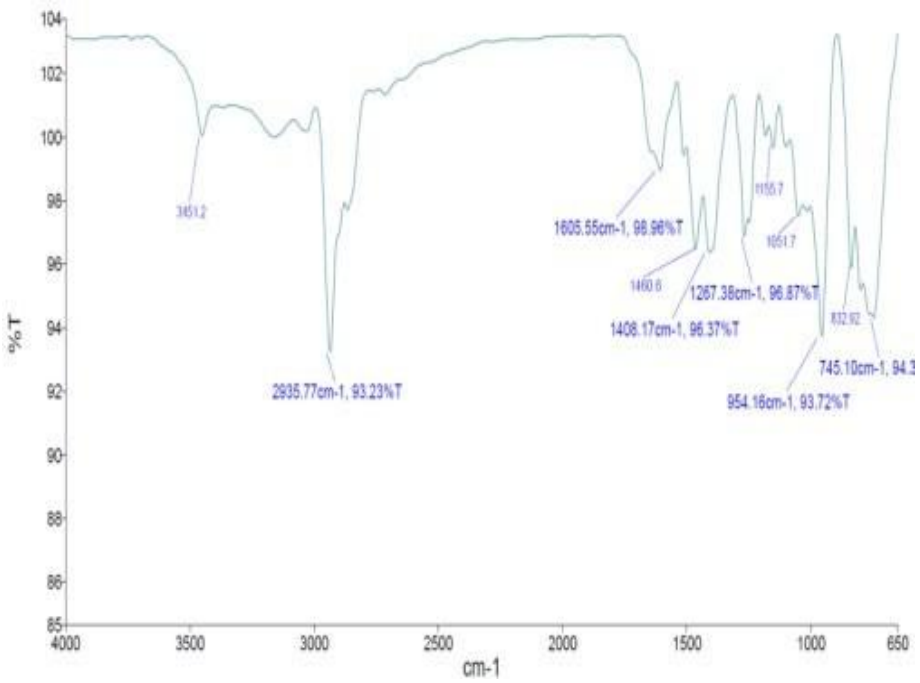

Fig: FT-IR spectra of Divalproex Sodium, cholesterol and span-60

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Table FT-IR frequencies of Divalproex Sodium, cholesterol and span-60:

S. No.	Functional group	Range(cm^{-1})	Observed Frequency (cm^{-1})
1.	C H	600-1500	1267.38
2.	C H	2850-2960	2935.77
3.	N H	3300-3500	3451.2
4.	C O	1000-1300	1155.7
5.	C = C	1500-1600	1591.51

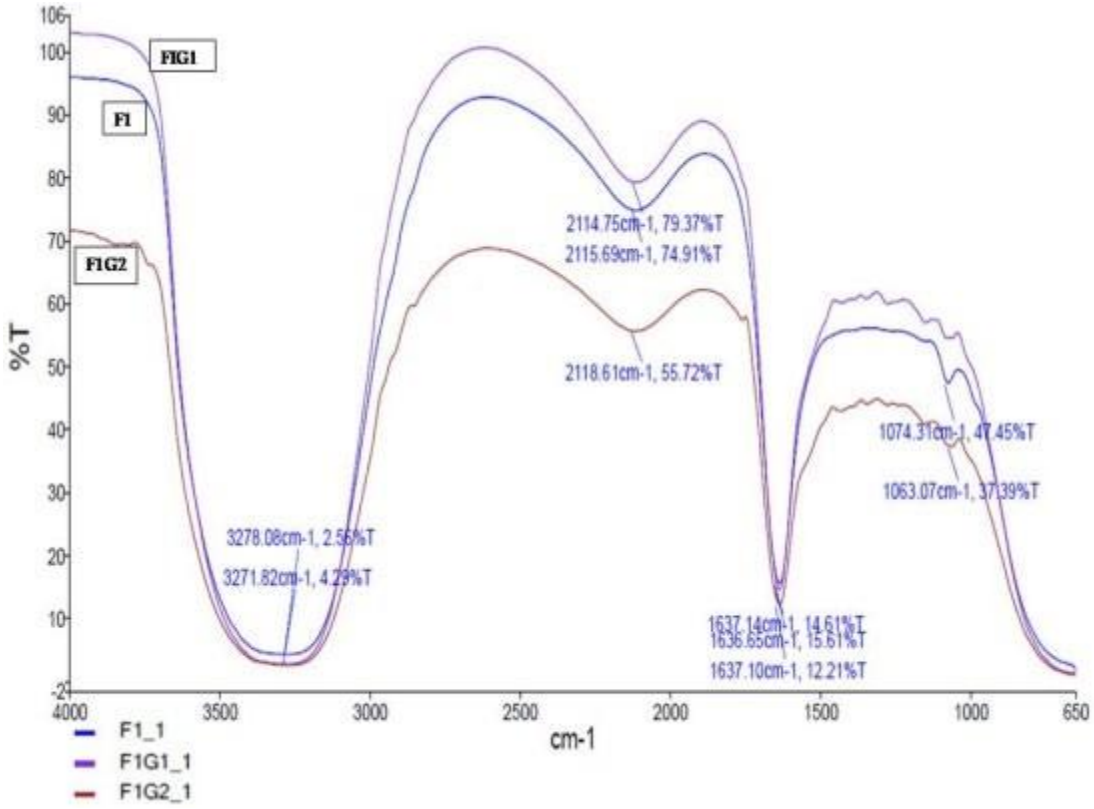

Fig: FT-IR spectra of F1, F2 and F3

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Table FT-IR frequencies of F1, F2 and F3:

S. No.	Functional group	Range(cm^{-1})	Observed Frequency (cm^{-1})
1.	O H	3200-3400	3278
2.	C H	600-1500	1074.31
3.	> C = C <	1620-1680	1637.10

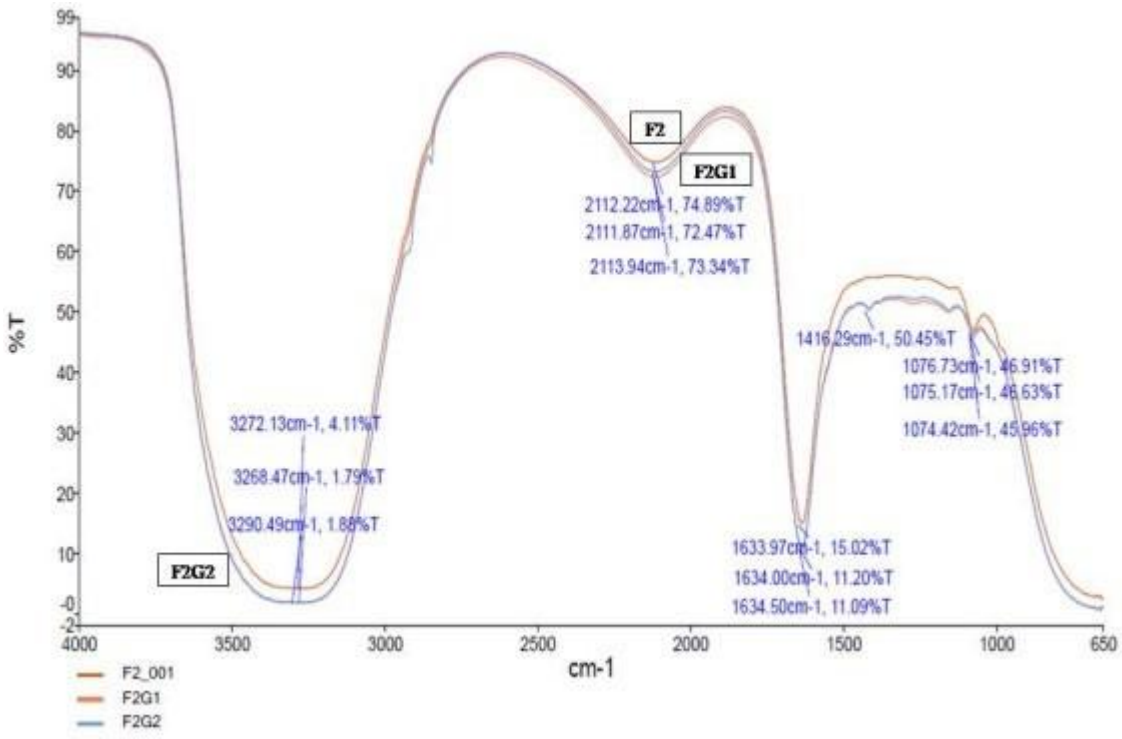

Fig: FT-IR spectra of F4, F5 and F6

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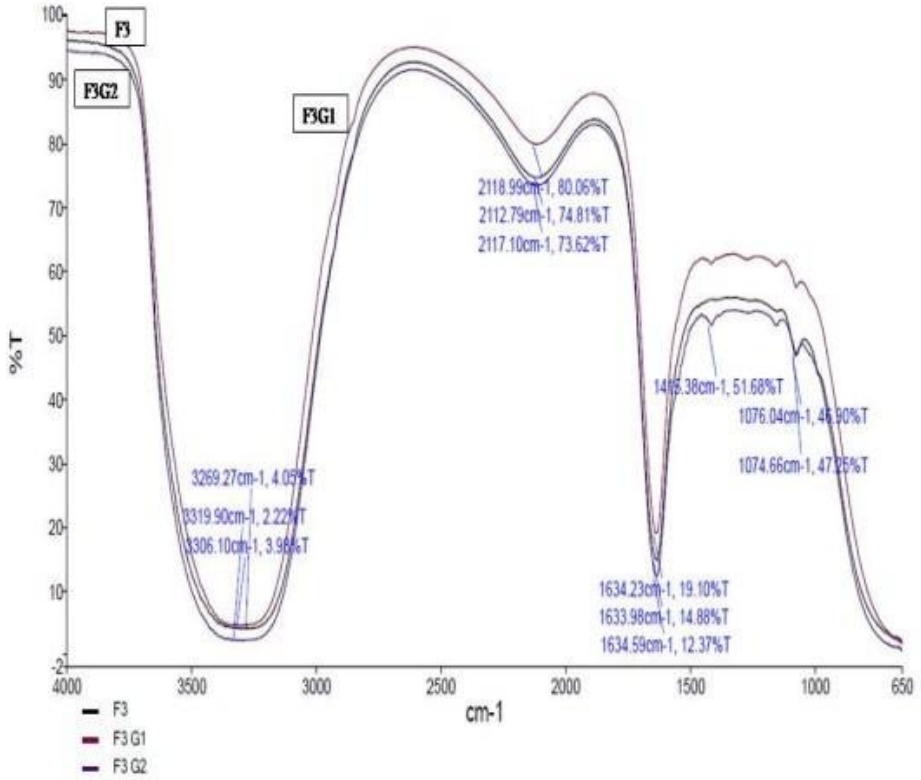

Table IR spectra of F4, F5 and F6:

S. No.	Functional group	Range(cm^{-1})	Observed Frequency (cm^{-1})
1.	O H	3200-3400	3272.13
2.	C H	600-1500	1074.42
3.	> C = C <	1620-1680	1634.00

Fig: FT-IR spectra of F7, F8 and F9

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Table IR spectra of F7, F8 and F9:

S. No.	Functional group	Range(cm^{-1})	Observed Frequency (cm^{-1})
1.	O H	3200-3400	3306.10
2.	C H	600-1500	1074.66
3.	> C = C <	1620-1680	1634.23

Entrapment Efficiency:

Table Entrapment Efficiency of Niosomes:

S. No.	Formulation code	Entrapment Efficiency
1.	F1	83.7
2.	F2	76.2
3.	F3	72.5
4.	F4	78.6
5.	F5	82.2
6.	F6	74.3
7.	F7	80.8

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8.	F8	77.5
9.	F9	79.8

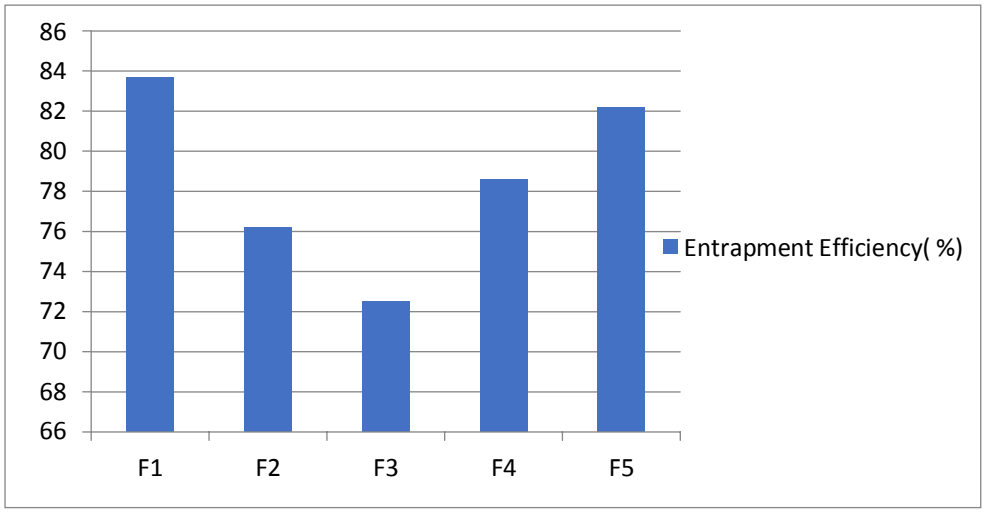

Fig: Graph showing Entrapment efficiency F1-F5

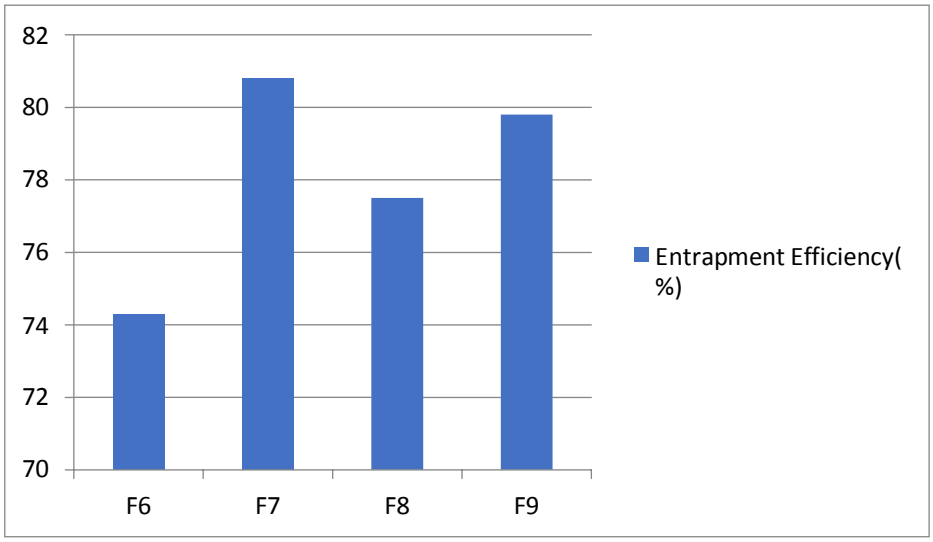

Fig: Graph showing Entrapment efficiency F6-F9

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Zeta potential:

Table Zeta potential (dependable variables):

S. No.	Formulation code	Zeta potential
1.	F1	-22.4 ± o.5 mV
2.	F5	-22.4 ± o.5 mV
3.	F7	-22.6 ± o.5 mV

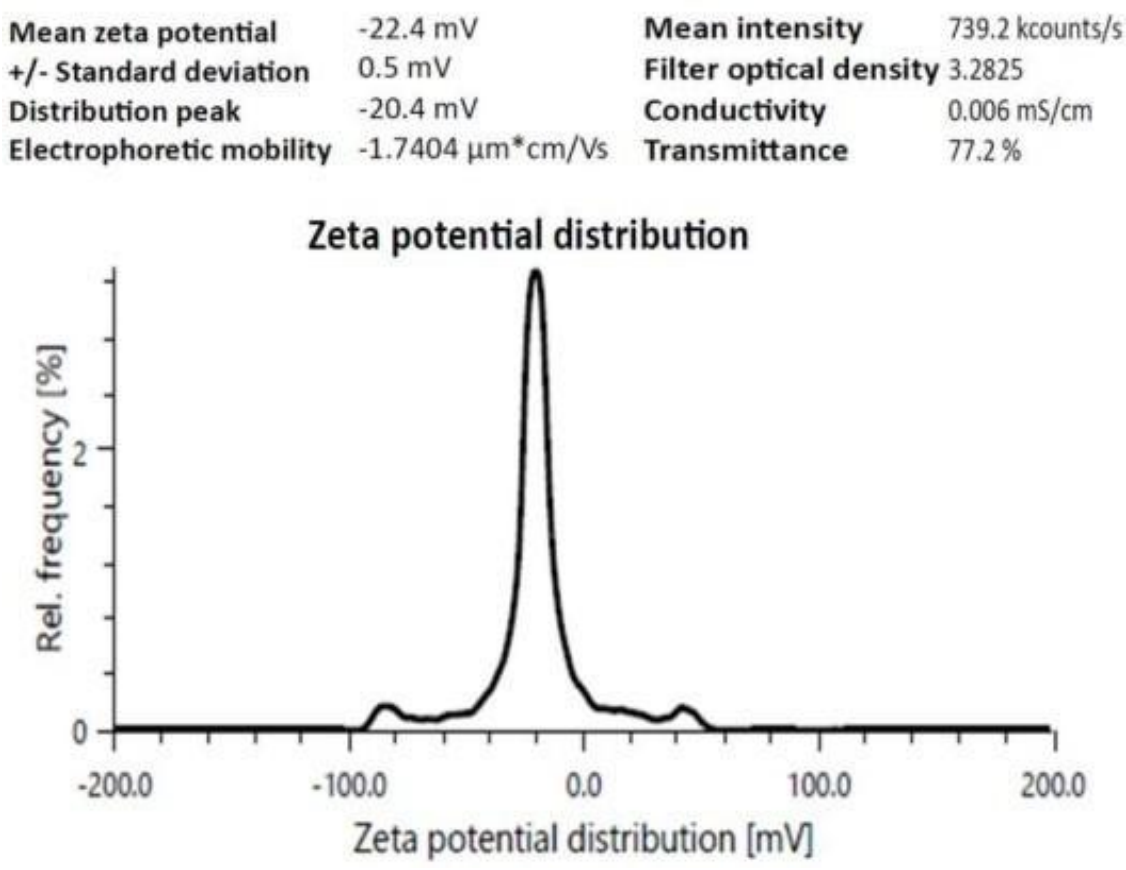

Fig: Zeta Potential F1

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Table Zeta particle size:

S. No.	Formulation code	Particle size
1.	F1	342.9 nm
2.	F5	353.6 nm
3.	F7	334.1 nm

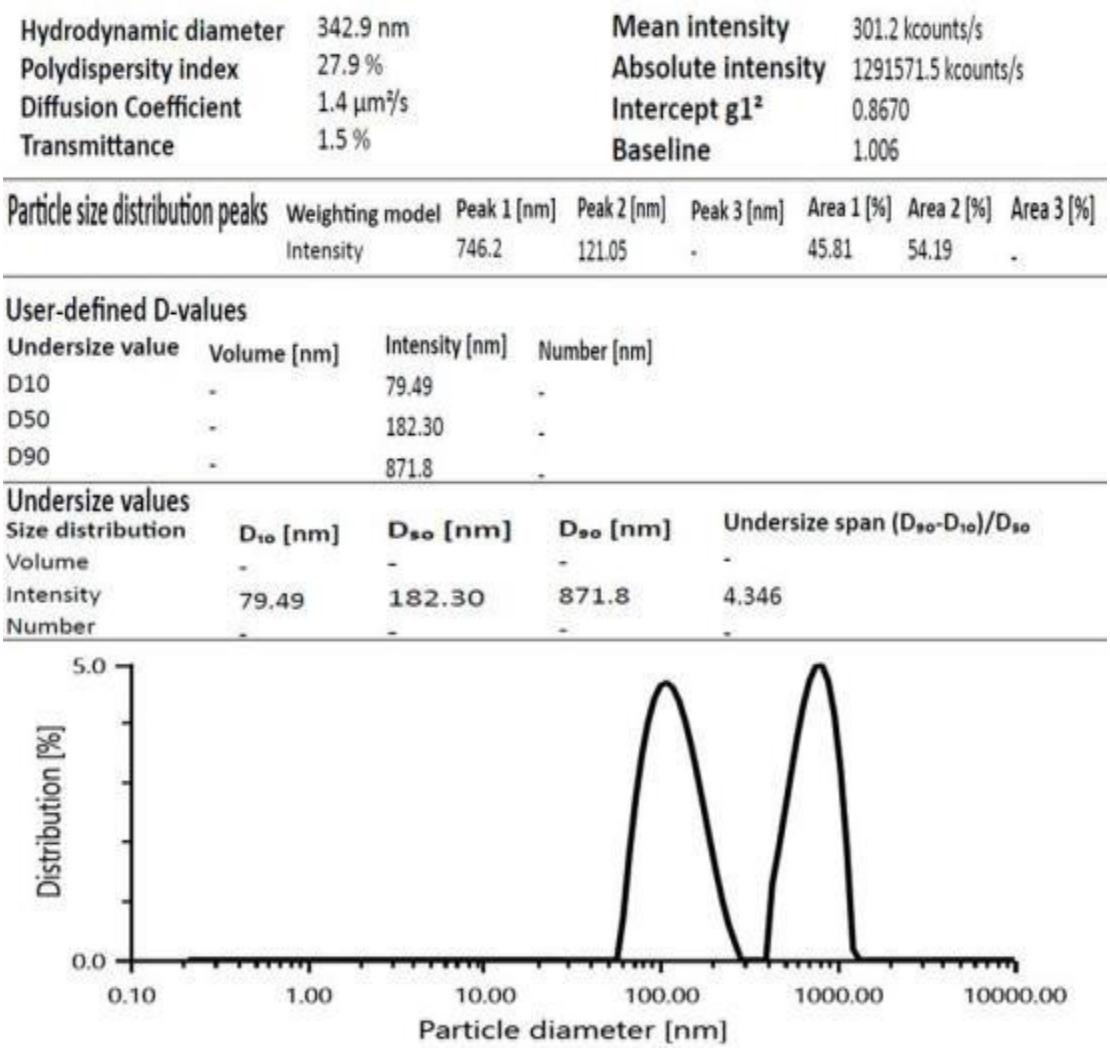

Fig: Particle size F5

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Transmission Electron Microscopy:

Images of optimized Niosomes formulations F1, F5 and F7

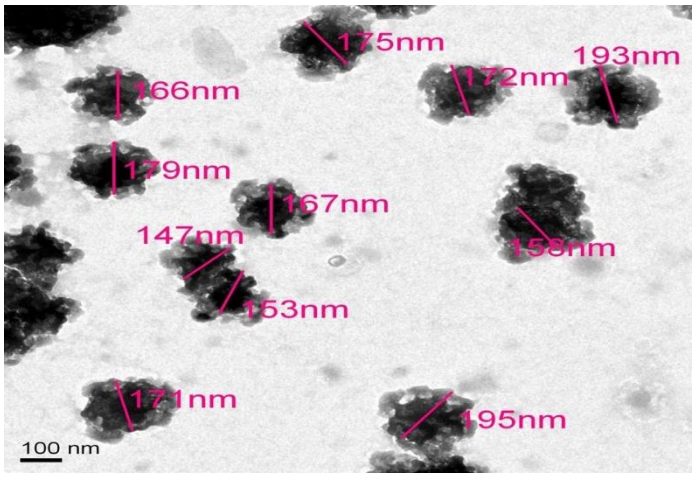

Fig: TEM of F1

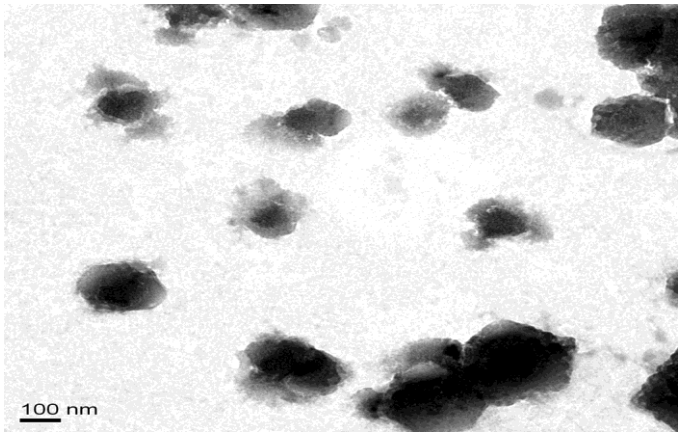

Fig: TEM of F5

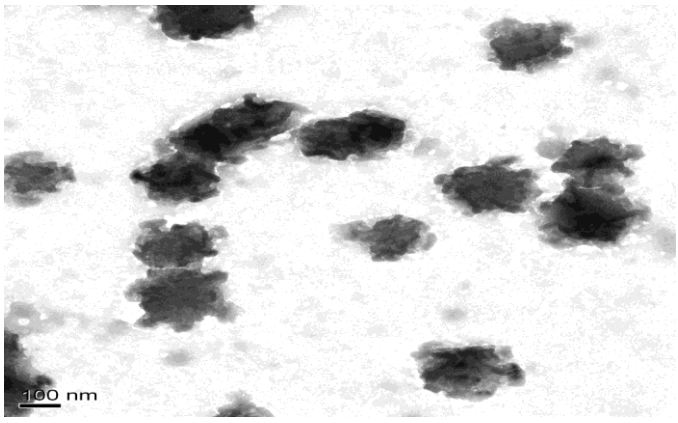

Fig: TEM of F7

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Table *In-vitro* release of Divalproex Sodium loaded niosomes:

Time in (Hrs)	% Drug release								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0.5	7.625	9.375	6.125	7.625	9.375	6.875	10.125	5.125	7.375
1	11.8	14.8	8.3	9.3	12.3	9.725	8.73	8.55	8.55
1.5	13.225	18.225	10.225	10.725	16.225	11.975	13.225	10.725	10.225
2	16.15	24.65	13.15	13.65	20.15	13.65	16.9	13.65	12.9
2.5	20.6	30.1	18.6	18.1	24.35	17.35	22.1	18.1	15.35
3	24.95	34.45	23.45	24.45	29.45	21.95	24.95	21.95	19.45
3.5	30.475	37.975	25.475	27.975	31.475	24.825	30.475	20.475	23.725
4	36.35	44.35	28.85	33.85	36.35	28.85	36.35	28.85	28.85
4.5	42.625	47.625	32.625	40.125	40.125	32.625	42.375	32.625	32.375
5	48.3	54.625	38.3	45.8	45.8	38.3	48.3	38.3	34.05
5.5	54.85	58.85	44.85	49.85	52.35	44.85	57.35	44.85	39.85
6	57.575	62.575	48.075	55.075	57.575	52.575	60.075	47.575	42.575
6.5	63.35	68.35	53.35	60.85	65.35	60.85	65.85	53.35	47.35
7	68.95	73.95	58.95	66.45	71.45	66.45	71.45	59.7	55.2
7.5	74.575	77.575	67.575	70.075	74.95	70.075	74.825	65.075	62.575
8	80.075	79.825	74.575	77.575	80.025	75.075	82.575	72.575	71.325

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Table Kinetic data analysis of in-vitro release data of F1, F5 and F7:

Formulation code	Zero order R^2	First order R^2	Higuchi model R^2	Korsemeyer peppas equation
F1G2	0.999	0.986	0.982	0.997
F5G1	0.998	0.966	0.976	0.993
F7G1	0.992	0.932	0.946	0.984

***In-vitro* release graph:**

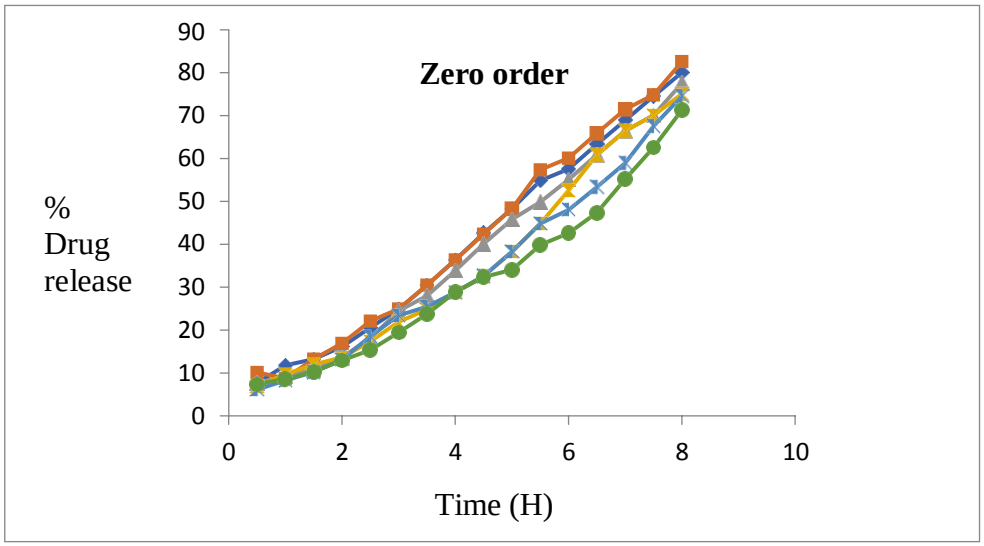

Fig: Zero order plot of F1-F9 Divalproex Sodium loaded niosomes

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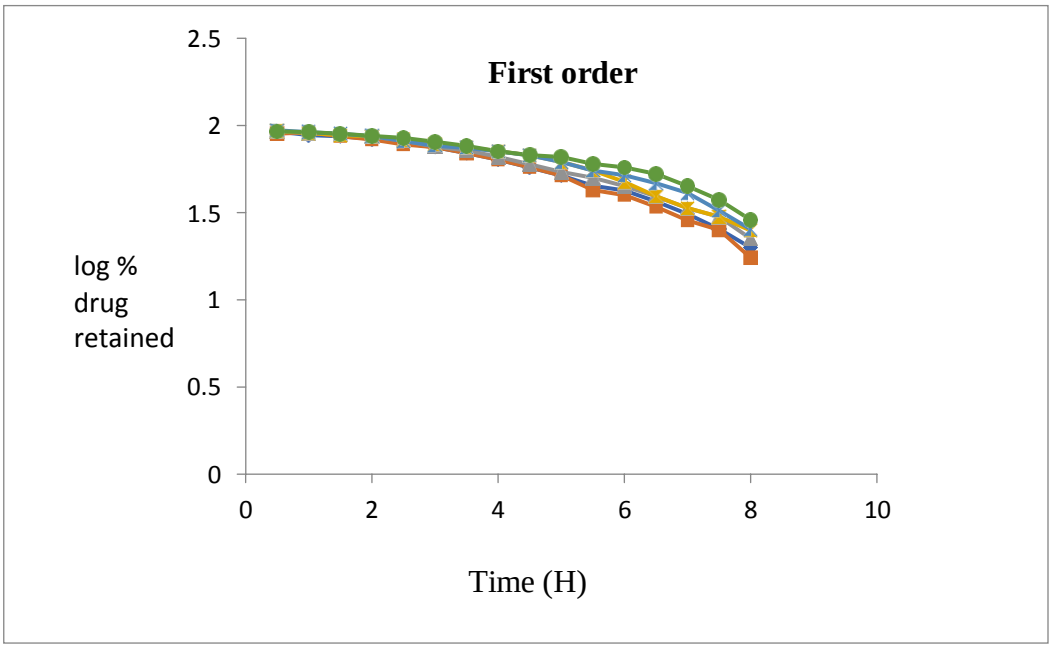

Fig: first order plot of F1-F9 Divalproex Sodium loaded niosomes

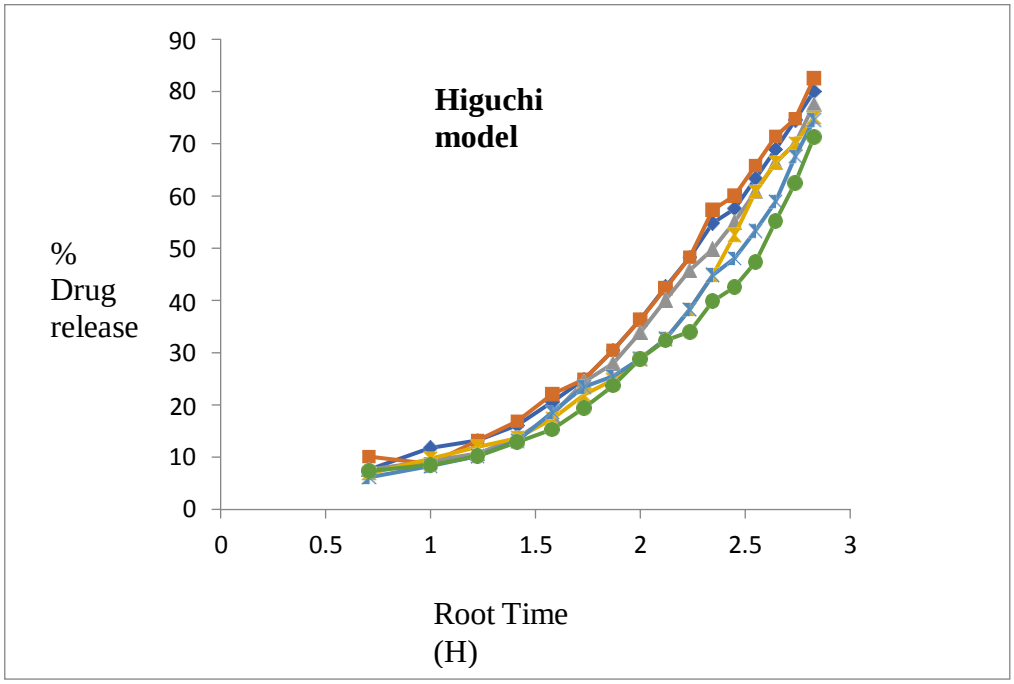

Fig: Higuchi plot of F1-F9 Divalproex Sodium loaded niosomes

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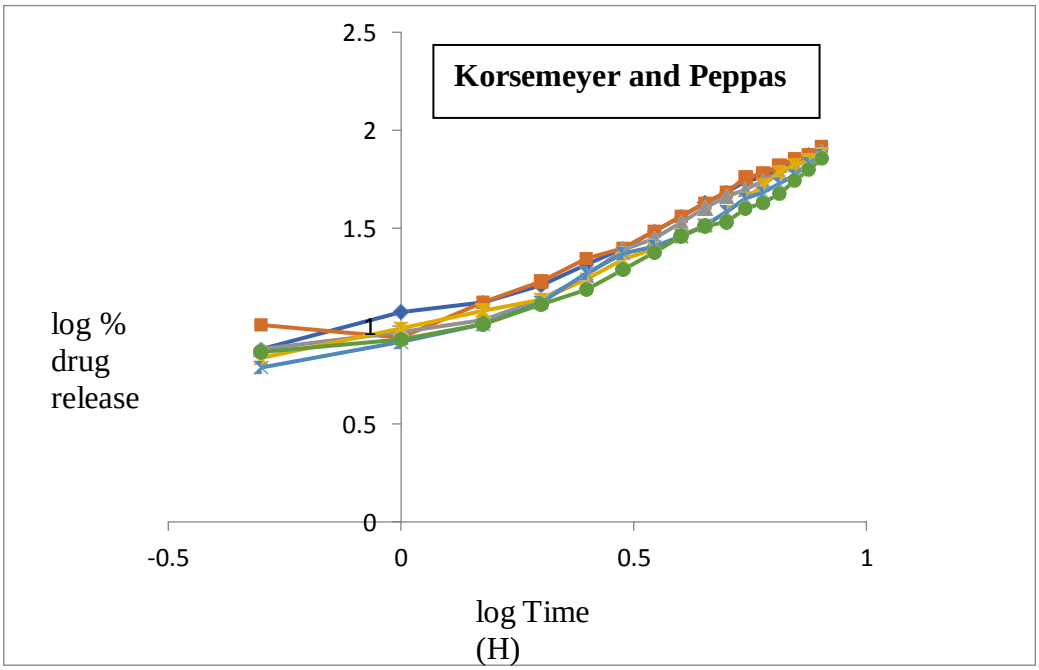

Fig: Korsmeyer and Peppas plot of F1-F9 Divalproex Sodium loaded niosomes

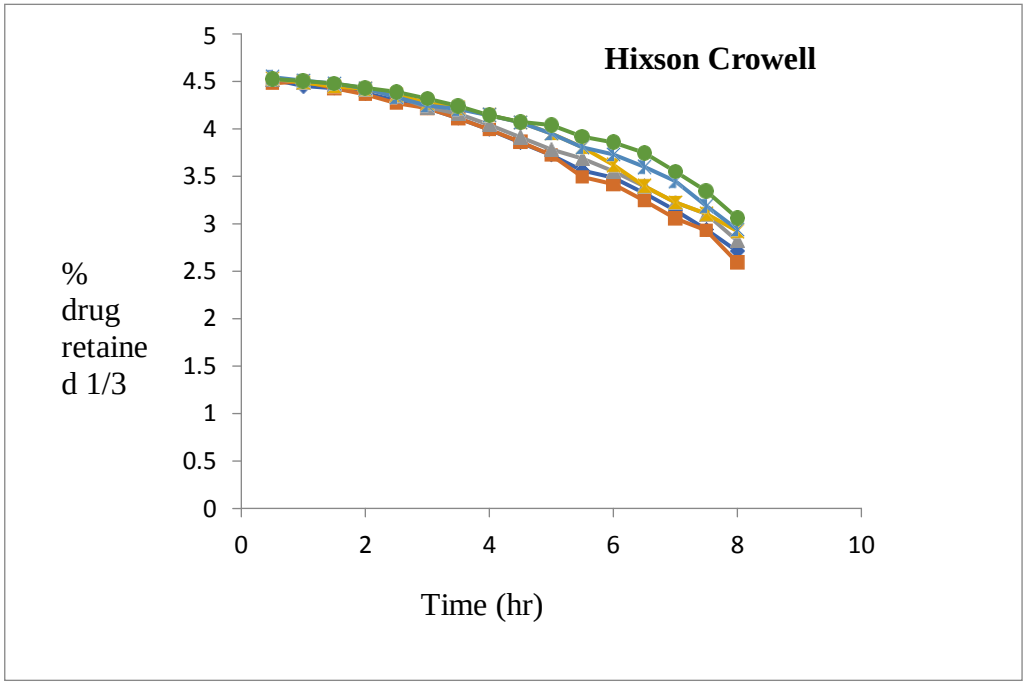

Fig: Hixson Crowell plot of F1-F9 Divalproex Sodium loaded niosomes

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Stability:

Stability characteristics of formulations were conducted in varied relative humidity and temperature variations per ICH recommendations Q1 A (general) to obtain storage conditions.Table, All formulations passed ICH-recommended stability tests [106-108].

Table of stability result:

S. no	Storage conditions	Formulation		
		F1	F5	F7
1.	**Long-term** (25 ± 2) °C and (60 ± 5)% relative humidity	96.1%	93.7%	95.2%
2.	**Intermediate** (30 ± 2) °C and (65 ± 5)% relative humidity	93.5%	93.2%	93.8%
3.	**Accelerated** (40 ± 2) °C and (75 ± 5)% relative humidity	90.3%	91.8%	92.3%
4.	**Refrigerator** 5°C ± 3°C	98.8%	92.2%	96.4%

CONCLUSION:

The current study effort was carried out with the purpose of fabricating intranasal Divalproex Sodium niosomes utilizing surface active ingredients through the use of the thin film hydration process. Cholesterol, Span 60 as the non-ionic surfactant, and dichloromethane were the three components that were utilised in the process of fabricating niosomal vesicles. In order to confirm the results of the compatibility research, an FT-IR analysis was done on the niosomes, niosomal gel, cholesterol, span 60, Divalproex Sodium, and chitosan individually, as well as on the physical combination of these substances. According to the findings of this research, Divalproex Sodium is completely compatible with all of the chemicals that were utilised in the production of the niosomal in-situ gel. In a phosphate buffer with a pH of 7.4, the maximum absorbance of divalproex sodium was measured to be 222 nm. The optimum formulation, F1, had a particle size of 342.9 mm. The TEM pictures of the improved formulation revealed the niosomes vesicles that were produced by

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the formulation. Using the same ratio of the surfactant and cholesterol was used, it was discovered that the %EE was high; however, when the amount of the surfactant was increased, the %EE was observed to drop. The formulation was adjusted to achieve the highest possible entrapment efficiency, which was determined to be 83.7%. In-vitro release was carried out over a period of 8 hours, and the results demonstrate maximal release. After putting the developed formulations through a drug release test for eight hours, the highest amount of drug released was 82.57%. The optimised formulation F1 has a zeta potential value of -22.4Mv, which demonstrates that the system is stable. The ICH recommendations are followed in the course of conducting the stability research. Entrapment efficiency was taken into consideration while choosing the three most effective formulas. During the course of the stability investigation, each of the parameters was carefully preserved in the appropriate manner [24]. The stability studies on all of the formulations yielded positive results, which point to the formulations' capacity to maintain their stability.

PROSPECT

Niosomes have the potential to be used as a treatment for epilepsy in people; however,prior to this happening, further clinical and pharmacokinetic studies must be conducted.

Reference

1. Manford M. Recent advances in epilepsy. Journal of neurology. 2017 Aug;264(8):1811-24.
2. Grabrucker AM, Ruozi B, Belletti D, Pederzoli F, Forni F, Vandelli MA, Tosi G. Nanoparticle transport across the blood brain barrier. Tissue barriers. 2016 Jan 2;4(1):e1153568.
3. Song N, Zhang C, Wang S, Guan Y. Lamotrigine loaded nano-liposomes enhance brain selectivity in vivo. Pakistan Journal of Pharmaceutical Sciences. 2021 May 1;34(3).
4. Mannam AK. *Formulation and Evaluation of Levetiracetam Niosomes for Improved Anti-Convulsant Activity* (Doctoral dissertation, KMCH College of Pharmacy, Coimbatore, Tamil Nadu, India).
5. Vadlamudi HC, Sevukarajan M. Niosomal drug delivery system-a review. Indo American Journal of Pharmaceutical Research. 2012;2(9).
6. Kawtikwar PS, Kulkarni NP, Yadav S, Sakarkar DM. Formulation and evaluation of an anti-epileptic drug-loaded microemulsion for nose to brain delivery. Asian Journal of Pharmaceutics (AJP). 2009;3(2).
7. Bhaskaran S, Lakshmi PK. Comparative evaluation of niosome formulations prepared by different techniques. Acta Pharmaceutica Sciencia. 2009;51(1).
8. Khan R, Irchhaiya R. Niosomes: a potential tool for novel drug delivery. Journal of pharmaceutical investigation. 2016 Jun;46(3):195-204.
9. Khan AR, Yang X, Fu M, Zhai G.

eISSN 1303-5150

Recent progress of drug nanoformulations targeting to brain. Journal of Controlled Release. 2018 Dec 10;291:37-64.

10. Gaillard PJ, Appeldoorn CC, Rip J, Dorland R, van der Pol SM, Kooij G, de Vries HE, Reijerkerk A. Enhanced brain delivery of liposomal methylprednisolone improved therapeutic efficacy in a model of neuroinflammation. Journal of controlled release. 2012 Dec 28;164(3):364-9.
11. Gugleva V, Michailova V, Mihaylova R, Momekov G, Zaharieva MM, Najdenski H, Petrov P, Rangelov S, Forys A, Trzebicka B, Momekova D. Formulation and Evaluation of Hybrid Niosomal In Situ Gel for Intravesical Co-Delivery of Curcumin and Gentamicin Sulfate. Pharmaceutics. 2022 Mar 30;14(4):747.
12. Schmutz M, Olpe HR, Koella WP. Central actions of valproate sodium. Journal of Pharmacy and Pharmacology. 1979 Sep;31(1):413-4.
13. Bhatt P, Kumar V, Goel R, Sharma SK, Kaushik S, Sharma S, et al. Structural modifications and strategies for native starch for applications in advanced drug delivery. Biomed Res Int [Internet]. 2022;2022:1–14. Available from: http://dx.doi.org/10.1155/2022/2188940
14. Shahiwala A, Misra A. Studies in topical application of niosomally entrapped nimesulide. J Pharm Pharm Sci. 2002 Sep 1;5(3):220-5.
15. Sengodan T, Sunil B, Vaishali R, Chandra RJ, Nagar S, Nagar O. Formulation and evaluation of maltodextrin based proniosomes loaded with indomethacin. Int J PharmTech Res. 2009;1(3):517-23.
16. Bhatt P, Singh S, Kumar Sharma S, Rabiu S. Development and characterization of fast dissolving buccal strip of frovatriptan succinate monoydrate for buccal delivery. Int J Pharm Investig [Internet]. 2021;11(1):69–75. Available from: http://dx.doi.org/10.5530/ijpi.2021.1.13
17. Sundaresan P, Sravanthi C, Gowtham T. Evaluation of aceclofenac niosomes prepared by various techniques. Int J Pharm Sci Rev Res. 2012;16(1):75-8.
18. Kumar YP, Kumar KV, Kishore VS. Preparation and evaluation of diclofenac niosomes by various techniques. Res J Pharm Tech. 2013 Oct 1;6(10):1097-101.
19. Al-Snafi AE, Singh S, Bhatt P, Kumar V. A review on prescription and non-prescription appetite suppressants and evidence-based method to treat overweight and obesity. GSC biol pharm sci [Internet]. 2022;19(3):148–55. Available from: http://dx.doi.org/10.30574/gscbps.2022.19.3.0231
20. Patil VB, Tadavi SA, Pawar SP. Formulation of niosomal gel of aceclofenac and it's in- vitro characterization. Indian Journal of Drugs. 2017;5(2):78-87.
21. Popli H, Nair MS. Niosomal delivery of tenoxicam. Indian journal of pharmaceutical sciences. 1996;58(4):163.
22. Pankaj. Anti-cancer cyclodextrin nanocapsules based formulation development for lung

eISSN 1303-5150

chemotherapy. J Pharm Res Int [Internet]. 2021;54–63. Available from: http://dx.doi.org/10.9734/jpri/2020/v32i3931024

23. Kumbhar D, Wavikar P, Vavia P. Niosomal gel of lornoxicam for topical delivery: in vitro assessment and pharmacodynamic activity. AAPS pharmscitech. 2013 Sep;14(3):1072-82.
24. Shilakari Asthana G, Asthana A, Singh D, Sharma PK. Etodolac containing topical niosomal gel: formulation development and evaluation. Journal of drug delivery. 2016;2016.

eISSN 1303-5150