FORMULATION DEVELOPMENT AND *INVITRO* EVALUATION OF STIRIPENTOL NANOSUSPENSION BY SOLVENT EVAPORATION METHOD

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Abstract:
The stiripentol nanosuspension formulation was developed via emulsification solvent evaporation employing Soluplus, Vitamin E, Sodium Lauryl Sulphate, Poly Vinyl Alcohol, Methanol, and adequate water as excipients. Formulations SF_1-SF_{16} entrapped 80.28±1.28% to 98.46±1.67%. The Zeta potential for optimized Formulation SF_4 was -4.49 mv, which was acceptable. The Optimized SF_4 nanosuspension particle size was 110.4 nm. From invitro testing, Formulation SF_4 released the most drug in 60 minutes at 99.49±1.43, but the other formulations did not. Zero-order, first-order, and equation models mentioned Nanosuspension drug release. Based on regression values, Formulation SF_4 optimized follows first-order kinetics.

Keywords: Nanosuspensions, solvent evaporation, particle size analysis, Zeta Potential.

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Introduction

The term "nanotechnology" refers to the science and engineering that go into the design, synthesis, characterization, and application of materials and devices whose smallest functional organization, in at least one dimension, is on the nanometer scale, which is equal to one billionth of a meter. Nanotechnology can be defined as the science and engineering that goes into developing these materials and devices. Consideration of individual molecules and interacting groups of molecules in relation to the bulk macroscopic properties of the material or device becomes important at these scales because it has control over the fundamental molecular structure, which allows control over the macroscopic chemical and physical properties. [1].

It is structurally distinct from other antiepileptic medications due to the fact that stiripentol consists of an aromatic allylic alcohol substance. Stiripentol is used to treat epileptic seizures. Due to the drug's powerful inhibiting effect on hepatic cytochrome P450 (CYP) enzymes, the clinical development and subsequent marketing of stiripentol were first held up [2].

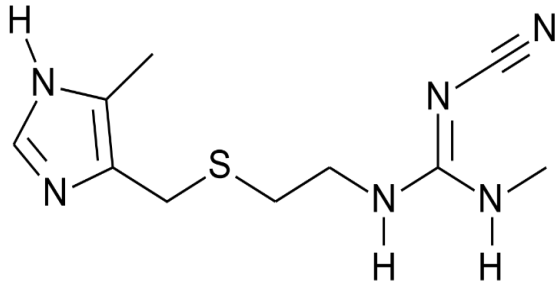

Figure 1: Structure of Stiripentol

Materials and methods:

Stiripentol API was procured from the Xenon Pharma Pvt Ltd, Soluplus , Vitamin E (TPGS), Sodium Lauryl Sulfate, Poly Vinyl Alcohol purchased Lobachemie Pvt Ltd Mumbai, Methanol, Purified Water purchased from Narmada chemicals. The instruments were ised in the project like Electronic Weighing Balance maker Shimadzu Corporation Tokyo, Japan, UV-Vis Spectrophoto meter (T60) maker of PG Instrument, FTIR Spectrophotometer maker of Shimadzu Corporation Tokyo, Japan , Dissolution Apparatus maker from LAB India Magnetic stirrer maker from Remi industries, Kerala.

Methodology: [3-10]

Pre-formulation characterization

In the pre-formulation characterization the physicochemical parameter of the drug substance are characterized with the goal of designing a drug delivery system.

Spectroscopic study:

Identification of pure drug:

Determination of melting point

The capillary glass method was utilized in order to figure out the drug's melting point. In order to ascertain the temperature at which the substance melts, a small amount of the drug was placed in a capillary tube that had one end blocked off. Following the placement of the capillary tube within the thermionic melting point equipment, the temperature at which the medication melted was recorded. values of the melting point that were observed in comparison to those that were reported

Solubility determination of Stiripentol

Qualitatively determined Stiripentol solubility. 10mg drug in 10ml solvents (aqueous/non-aqueous) in a conical flask. Drug solubility was determined using 0.1N HCL, 7.4 pH buffer, 6.8 pH buffer, ethanol, and methanol. Undissolved particles and clarity were checked after shaking.

Determination of λmax by UV - Spectrophotometer

The Stiripentol absorbs most at its peak wavelength. Drug max cannot be altered simply. A clean 10ml volumetric flask contained 10mg Stiripentol dissolved in dichloromethane. Stock solution-I with 1000µg/ml concentration was produced up to 10ml. Pipette 1ml from stock solution-I into a 10ml volumetric flask. Stock solution-II was produced up to 10ml with 0.1N HCL buffer to 100µg/ml. In 10ml volumetric flask, 1ml was pipetted from stock solution-II. 10µg/ml was achieved by adding 0.1N HCL buffer to 10ml. To find the absorption maximum (-max), a UV-Visible twin beam spectrophotometer scanned this solution at 200-400nm. Scan the chemical at 200–400nm to determine its max.

Construction of Calibration curve in 0.1N HCL Buffer

Dissolving precisely weighed 10mg of Stiripentol in 10ml of 0.1N HCL Buffer produced a 1000µg/ml stock solution. Take 1ml and dilute to 10ml with the solvent (100µg/ml). The aforementioned solution was diluted to 2–12µg/ml using 0.2, 0.4, 0.6, 0.8, 1 and 1.2ml volumes. This solution's spectra was recorded against the blank (0.1N HCL) at 301nm using UV; Visible Spectrophotometer.

Method of Preparation of Nanosuspension [11-14].

Preparation of Stiripentol Nanosuspension by Emulsification solvent evaporation method:

The Emulsification Solvent Evaporation Method was used to create the nanosuspension. At ambient temperature (organic phase), stiripentol was dissolved in an organic solvent. The next step is emulsification into stabilizer (PVA) and co-surfactant (SLS) water at room temperature. Organic solvents were added by inserting the needle of a syringe straight into the water-based stabiliser, and the mixture was then agitated on a magnetic stirrer for 2 hours at 40 degrees Celsius so as to permit the volatile solvent to evaporate.

Note: 0.1% SLS prepared &1.5ml added for each formulation

0.1% PVA prepared &1.5ml added for each formulation

2% Soluplus prepared &1ml added in NF4 formulation

Table 1 : Composition of Nanosuspension of Stiripentol (SF1-SF6)

Formulation Code	SF_1	SF_2	SF_3	SF_4	SF_5	SF_6	SF_7	SF_8
Stiripentol (mg)	250	250	250	**250**	250	250	250	250
Soluplus (mg)	62.5	125	187.5	**250**	--	--	--	--
Vitamin E TPGS(mg)	--	--	--	**--**	62.5	125	187.5	250
SLS (mg)	2.5	2.5	2.5	**2.5**	2.5	2.5	2.5	2.5
PVA (mg)	7.5	7.5	7.5	**7.5**	7.5	7.5	7.5	7.5
Methanol (ml)	5	5	5	**5**	5	5	5	5
Purified water(ml)	5	5	5	**5**	5	5	5	5
Total volume(ml)	5	5	5	**5**	5	5	5	5
Drug: solubilizer ratio	1:0.25	1:0.5	1:0.75	**1:1**	1:0.25	1:0.5	1:0.75	1:1

Effect of SLS concentration:

Ingredients	SF_9	SF_4	SF_{10}
Stiripentol (mg)	250	**250**	250
Soluplus(mg)	250	**250**	250
SLS(mg)	1.25	**2.5**	3.75
PVA (mg)	7.5	**7.5**	7.5
Methanol (ml)	5	**5**	5
Purified water(ml)	5	**5**	5
Total volume (ml)	5	**5**	5
Stirring RPM	1000	**1000**	1000
Sonication time (mins)	13	**13**	13

Table 3: Effect of SLS concentration

Effect of PVA concentration:

Ingredients	SF_{11}	SF_4	SF_{12}
Stiripentol (mg)	250	**250**	250
Soluplus (mg)	250	**250**	250
SLS (mg)	2.5	**2.5**	2.5
PVA (mg)	3.75	**7.5**	11.25
Methanol (ml)	5	**5**	5
Purified water(ml)	5	**5**	5
Total volume (ml)	5	**5**	5
Stirring RPM	1000	**1000**	1000
Sonication time	13	**13**	13

Table 4 Effect of PVA concentration

Process optimization trials:

Ingredients	SF_{13}	SF_4	SF_{14}
Stiripentol (mg)	250	**250**	250
Soluplus (mg)	250	**250**	250
SLS (mg)	2.5	**2.5**	2.5
PVA (mg)	7.5	**7.5**	7.5
Methanol (ml)	5	**5**	5
Purified water(ml)	5	**5**	5
Total volume (ml)	5	**5**	5
Stirring RPM	800	**1000**	1200
Sonication time (mins)	13	**13**	13

Table5: Effect of stirring RPM

Effect of sonication time:

TABLE 6 Effect of sonication time

Ingredients	SF_{15}	SF_4	SF_{16}
Stiripentol (mg)	250	**250**	250
Soluplus (mg)	250	**250**	250
SLS (mg)	2.5	**2.5**	2.5
PVA (mg)	7.5	**7.5**	7.5
Methanol (ml)	5	**5**	5
Purified water(ml)	5	**5**	5
Total volume (ml)	5	**5**	5
Stirring RPM	1000	**1000**	1000
Sonication time (mins)	10	**13**	15

Evaluation parameters of Nanosuspension Stiripentol [14-20]

The Nano suspension was evaluated for various parameters:

1. Entrapment efficiency
2. Particles size analysis
3. Zeta potential
4. Scanning electron microscopy.
5. In-vitro drug release studies

1. Entrapment Efficiency:

The free concentration of medication in the supernatant after centrifugation can be calculated by measuring the entrapment efficiency. The entrapment efficiency was calculated by centrifuging 10 ml of the freshly produced nanosuspension at 1000 rpm for 10 minutes. The absorbance of the supernatant solution was measured at 301 nm using a UV-Visible spectrophotometer to determine the amount of medication that had not been integrated.

This drug entrapment efficiency (in percentage) equation was developed.

$$\% \textbf{ of Drug entrapment} = \frac{\textbf{Mass of drug in Nanosuspensions}}{\textbf{Mass of drug used in formulation}} * \textbf{100}$$

2. Particle Size analysis:

The Motic digital microscope was used to measure the particle size of the prepared nanosuspension batches. The micrometre measurements of each batch's particles were kept. Phosphate buffer solution (0.1N HCL) was used to dilute the formulations to the proper concentration. Three separate measurements were taken, with the average used for analysis.

3. Zeta potential:

Zeta potential (ZP) is a physical property that controls electrostatic interactions in particle dispersions and is essential in understanding the stability of colloidal dispersions . It is identified as the difference in potential between the particle and its ionic atmosphere surrounding the medium and is measured in the plane of shear. A ZP value of ± 30 mV is generally chosen to deduce particle stability, with an absolute value greater than 30 mV designated a stable condition, whereas a low zeta potential value of less than 30 mV indicates a condition toward aggregation, instability, flocculation, or coagulation.

4. Scanning electron microscopy.

Scanning electron microscope (SEM) is one of the most widely used instrumental methods for the examination and analysis of micro- and nanoparticle imaging characterization of solid objects. One of the reasons that SEM is preferred for particle size analysis is due to its resolution of 10 nm, that is, 100 Å. Advanced versions of these instruments can achieve a resolution of about 2.5 nm (25 Å) (Goldstein, 2012). This instrument may also be used in conjunction with other related techniques of energy-dispersive X-ray microanalysis (EDX, EDS, EDAX), for the determination of the composition or orientation of individual crystals or features. Generally, tungsten filament lamps or a field emission gun is used as a source for the electron generation. The field emission gun requires ultrahigh vacuum conditions (10−10 to 10−11 Torr) to keep the tip free from contaminants and oxide. So The morphological features of prepared Nano suspensions are observed by scanning electron microscopy at different magnifications.

***In-vitro* drug release studies:**

Dissolution Parameters

Medium	: 900ml, 0.1N HCL
Apparatus	: Paddle (USP-II)
RPM	: 50
Temperature	: 37^{o} C±0.5
Time Points	: 5,10,15,20, 30, 45 & 60 minutes.

Procedure:

The dialysis membrane diffusion technique was used. One millilitre of the nanosuspension was placed in the dialysis membrane (Mw cutoff 12,000–14,000 Hi-media), fixed in a Franz diffusion cell with the receptor volume of 20 ml. The entire system was kept at 37 °C with continuous magnetic stirring. Sample of 1 ml was withdrawn from the receptor compartment at predetermined time intervals and replaced by fresh medium. The amount of drug dissolved was determined using UV spectrophotometer at 301nm

Modelling of Dissolution Profile

Model dependent methods are based on different mathematical functions, which describe the dissolution profile. Once a suitable function has been selected, the dissolution profiles are evaluated depending on the derived model parameters. To compare dissolution profiles between two drug products model dependent (curve fitting), statistical analysis and model independent methods can be used.

Kinetic studies

♦ **Zero order model:**

The pharmaceutical dosage forms following these profiles release the same amount of drug by unit of time and it is the ideal method of drug release in order to achieve a pharmacological prolonged action. The following relation can, in a simple way, express this model:

$$Qt = Q0 + K0t$$

Where,

Qt is the amount of drug dissolved in time t,

Q0 is the initial amount of drug in the solution and

K0 is the zero order release constant.

To study the release kinetics, data obtained from in vitro drug release studies were plotted as cumulative amount of drug released versus time

♦ **First order model:**

The application of this model to drug dissolution studies was first proposed by Gibaldi and Feldman (1967) and later by Wagner (1969). This model has been also used to describe absorption and/or elimination of some drugs, although it is difficult to conceptualise this mechanism in a theoretical basis [67].

$$\log Qt = \log Q0 + (K1/2.303)$$

Where,

Qt is the amount of drug released in time t,

Q0 is the initial amount of drug in the solution and

K1 is the first order release constant.

The data obtained are plotted as log cumulative percentage of drug remaining vs. time which would yield a straight line with a slope of-K/2.303

♦ **Higuchi model:**

This is the first mathematical model that describes drug release from a matrix system, proposed by Higuchi in 1961. This model is based on different hypothesis that [69] Initial drug concentration in the matrix is much higher than drug solubility.

$$f\,t = Q = KH\,\sqrt{t}$$

Where,

KH is the Higuchi dissolution constant.

Higuchi describes drug release as a diffusion process based in the Fick's law, square root time dependent. The data obtained were plotted as cumulative percentage drug release versus square root of time.[70,71,72]

♦ **Korsemeyer- peppas model:**

Korsemeyer et al. (1983) derived a simple relationship which described drug release from a

polymeric system equation Then, if the diffusion is the main drug release mechanism, a graphic representing the drug amount released, in the referred conditions, versus the square root of time should originate a straight line. Under some experimental situations the release mechanism deviates from the Ficks equation, following an anomalous behavior (non-Fickian)**.** In these cases a more generic equation can be used:

$$\mathbf{Mt/M\infty = a}t^{\mathbf{n}}$$

'n' value is used to characterize different release for cylindrical shaped matrices; and it is describe in table 5.7. For the case of cylindrical tablets, $0.45 \leq n$ corresponds to a Fickian diffusion mechanism, $0.45 < n < 0.89$ to non-Fickian transport, $n = 0.89$ to Case II (relaxational) transport, and $n > 0.89$ to super case II transport

Results and Discussions

Determination of melting point:

The melting point of found to be in range of 73-74°C which was determined by capillary B method.

Saturation Solubility:

Saturation solubility was carried out at 25^0C using Methanol, Ethanol, 0.1N HCL, 6.8 phosphate buffer, and 7.4pH buffer. 0.1N HCL buffer is used as dissolution medium, based upon the solubility studies on organic solvents ethanol has more solubility than others so ethanol was used in the nanosuspension formulation.

Table.7 Solubility data

Solvent	Solubility(µg/ml)
Ethanol	23.06±1.25
Methanol	20.67±1.38
0.1N HCL	21.72±1.97
pH 6.8 phosphate buffer	18.99±1.04
pH 7.4 phosphate buffer	16.27±1.32

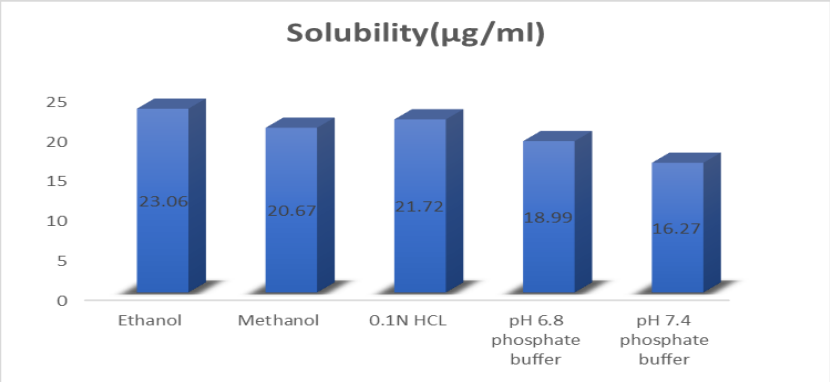

Figure 2 Solubility studies of Stiripentol

Determination of absorption maximum (λmax):

Determination of Stiripentol λ-max was done in 0.1N HCL buffer medium for accurate quantitative assessment of drug dissolution rate. The λmax Was found to be 301 nm.

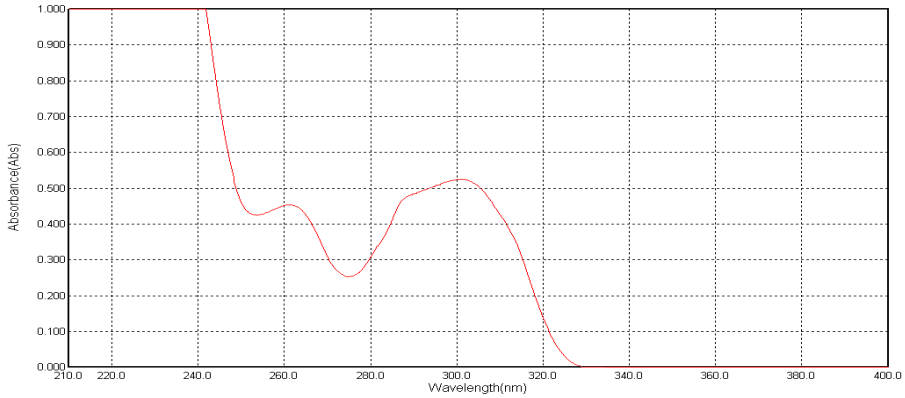

Figure 3 UV spectrum of Stiripentol

Construction of Calibration curve in 0.1N HCL Buffer:

The linearity was found to be in the range of 2-12µg/ml in acetone,0.1N HCL. The regression value was closer to 1 indicating the method obeyed Beer-lamberts' law. The linearity curve and values were tabulated and linear equation was fond to be y= 0.0521+0.0002

Concentration (µg/ml)	Absorbance
0	0
2	0.099±1.18
4	0.212±1.06
6	0.321±1.35
8	0.415±1.72
10	0.518±1.39
12	0.626±1.51

Table. 8 Standard graph of Stiripentol in 0.1N HCL

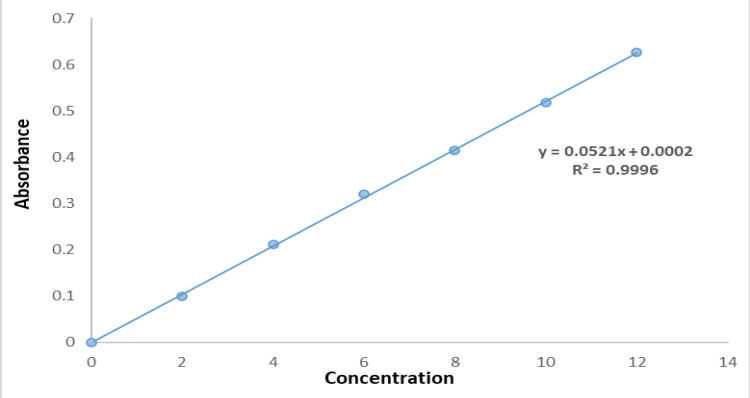

Figure.4 : Standard calibration curve of Stiripentol in 0.1N HCL

Drug excipient compatibility:

Drug and excipient compatibility was confirmed by comparing spectra of FT-IR analysis of pure drug with that of various excipients used in the formulation. The results shows that there are no interactions between the pure drug (Stiripentol) and optimized formulation (Stiripentol + excipients) which indicates there are no physical changes.

Entrapment efficiency: -The entrapment efficiency of the Formulated Nano Suspensions was found in the range of 80.28±1.28%-98.46±1.67% respectively.

Formulation code	Entrapment efficiency
SF_1	91.78±1.24
SF_2	90.38±1.48
SF_3	92.91±1.06
SF_4	98.46±1.67
SF_5	95.38±1.98
SF_6	83.97±1.76
SF_7	81.64±1.35
SF_8	82.71±1.24
SF_9	80.28±1.28
SF_{10}	85.58±1.36
SF_{11}	93.63±1.29
SF_{12}	89.85±1.78
SF_{13}	94.70±1.89
SF_{14}	95.36±1.68
SF_{15}	89.25±1.89
SF_{16}	94.14±1.30

Table. 9 Entrapment efficiency of formulated Nano Suspensions

Particle size analysis:

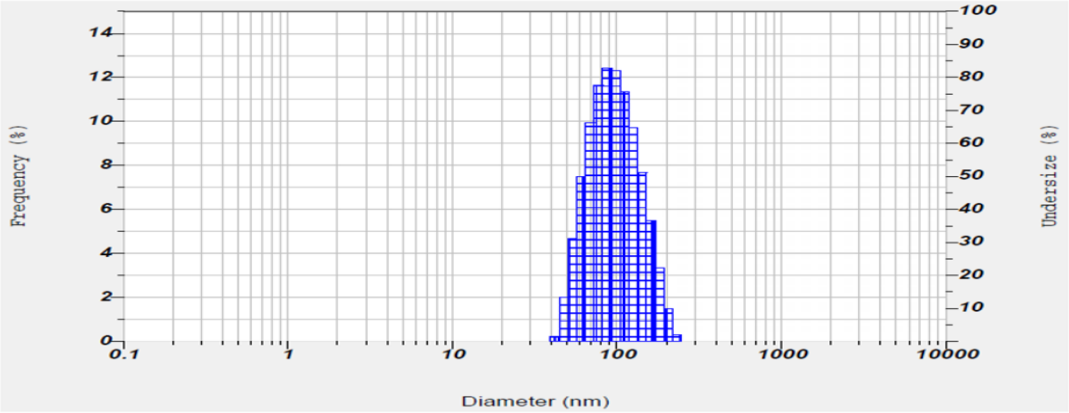

Figure. 5. Particle Size Analysis of Optimized Formulation

Zeta potential:

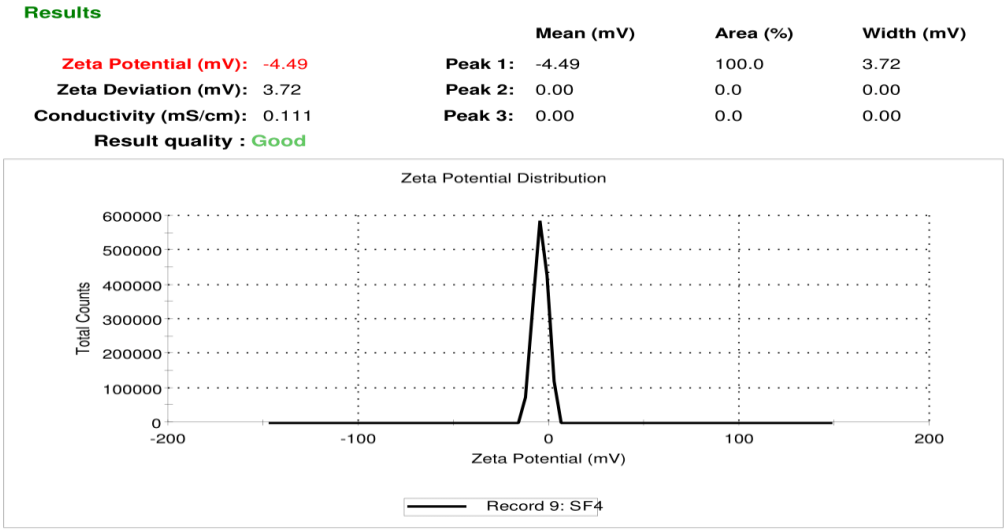

Figure 6 Zeta potential value for the optimized formulation

Scanning electron microscopy:

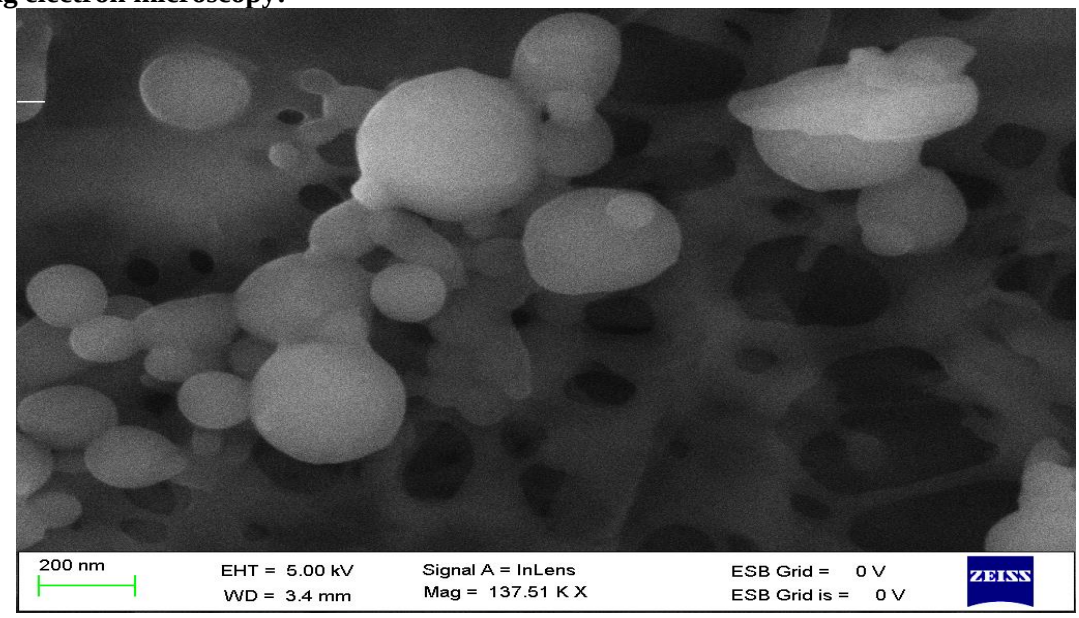

Figure 7 Scanning Electron Microscopy of Optimized Formulation

Dissolution Studies for The Stiripentol nanosuspension formulation $SF_1 – SF_{16}$

Time(mins)	SF1	SF2	SF3	SF4	SF5	SF6	SF7	SF8
0	0	0	0	**0**	0	0	0	0
5	15.87±1.21	28.74±1.21	32.12±1.74	**55.87±1.11**	16.79±1.74	25.11±1.16	35.17±1.21	44.14±1.32
10	31.28±1.40	37.81±1.14	44.12±1.25	**72.42±1.14**	23.12±1.21	42.87±1.25	50.32±1.12	59.25±1.28
15	42.95±1.29	42.21±1.10	53.74±1.41	**79.34±1.12**	37.98±1.32	51.21±1.14	55.96±1.18	65.78±1.36
20	46.35±1.15	53.32±1.21	62.20±1.21	**87.29±1.24**	46.11±1.24	58.31±1.34	67.34±1.86	76.98±1.18
30	54.74±1.57	67.17±1.12	75.19±1.12	**96.83±1.35**	58.82±1.34	72.75±1.24	75.85±1.79	82.74±1.65
45	68.84±1.21	80.25±1.24	85.03±1.14	**98.78±1.74**	69.19±1.66	76.31±1.66	79.24±1.21	88.14±1.14
60	79.98±1.14	89.74±1.15	92.12±1.11	**99.49±1.43**	80.82±1.34	92.36±1.14	88.78±1.32	93.25±1.38

Table. 10. *In-vitro* drug release data of Stiripentol Nano suspension formulation SF_1 to SF_8

Time (mins)	SF9	SF10	SF11	SF12	SF13	SF14	SF15	SF16
0	0	0	0	0	0	0	0	0
5	20.14±1.14	26.58±1.18	38.56±0.99	42.12±1.16	21.12±1.25	34.74±1.25	44.36±1.04	52.21±1.36
10	32.21±1.24	35.78±1.14	46.71±1.12	54.23±1.24	34.12±1.16	43.67±1.32	52.67±1.15	64.14±1.15
15	34.85±1.26	48.25±1.28	57.25±1.99	62.41±1.24	49.14±1.25	57.39±1.25	66.32±1.98	79.96±1.28
20	43.95±1.19	56.98±1.24	63.84±1.24	77.21±1.25	54.21±1.28	69.12±1.35	75.69±1.24	84.69±1.26
30	60.28±1.19	65.14±1.14	78.93±1.24	84.32±1.25	71.45±1.24	76.36±1.25	82.34±1.32	89.34±1.35
45	76.98±1.21	88.28±1.22	89.21±1.25	92.74±1.37	79.74±1.32	85.34±1.36	88.24±1.15	95.98±1.26
60	92.78±1.24	93.14±1.14	94.17±1.35	97.12±1.18	94.12±1.22	97.47±1.18	94.78±1.22	98.84±1.24

Table. 11. In-*vitro* drug release data of Stiripentol Nano suspension formulation SF_9 to SF_{16}

***In-vitro* drug release data of Stiripentol Nano suspension Effect of SLS concentration**

Time (mins)	SF9	SF4	SF10
0	0	**0**	0
5	18.24±1.24	**53.64±1.26**	28.36±1.78
10	29.36±1.34	**69.53±1.11**	39.64±1.24
15	38.41±1.46	**77.61±1.11**	47.31±1.78
20	46.27±1.59	**86.49±1.64**	56.32±1.24
30	59.67±1.69	**98.65±1.32**	64.89±1.64
45	78.34±1.71	**98.66±1.89**	83.14±1.32
60	90.25±1.24	**98.99±1.99**	91.24±1.24

Table 12 In-*vitro* drug release data of Stiripentol Nano suspension Effect of SLS concentration

***In-vitro* drug release data of Stiripentol Nano suspension Effect of PVA concentration:**

Time (mins)	SF11	SF4	SF12
0	0	0	0
5	38.14±0.99	53.64±1.26	45.24±1.86
10	46.28±1.12	69.53±1.11	59.67±1.24
15	57.34±1.99	77.61±1.11	68.24±1.34
20	63.17±1.24	86.49±1.64	78.61±1.25
30	78.98±1.24	98.65±1.32	85.31±1.35
45	89.75±1.25	98.66±1.89	91.34±1.34
60	94.24±1.35	98.99±1.99	96.78±1.38

Table13 *In-vitro* drug release data of Stiripentol Nano suspension Effect of PVA concentration:

***In–vitro* drug release data of Stiripentol Nano suspension Effect of stirring time**

Time (mins)	SF_{13}	SF_4	SF_{14}
0	0	0	0
5	20.41±1.45	53.64±1.26	38.74±1.66
10	36.82±1.56	69.53±1.11	45.67±1.32
15	49.36±1.35	77.61±1.11	58.39±1.24
20	57.24±1.78	86.49±1.64	67.12±1.38
30	69.35±1.24	98.65±1.32	75.36±1.25
45	78.24±1.32	98.66±1.89	84.34±1.36
60	93.75±1.12	98.99±1.99	98.47±1.78

Table 14 *In-vitro* drug release data of Stiripentol Nano suspension Effect of stirring time

***In-vitro* drug release data of Stiripentol Nano suspension Effect of sonication time:**

Time (mins)	SF15	SF4	SF16
0	0	**0**	0
5	48.36±2.04	**53.64±1.26**	54.21±1.36
10	54.67±2.15	**69.53±1.11**	67.14±1.45
15	67.32±1.98	**77.61±1.11**	78.96±1.48
20	78.69±1.24	**86.49±1.64**	82.69±1.56
30	81.34±1.32	**98.65±1.32**	88.34±1.75
45	89.24±1.85	**98.66±1.89**	93.98±1.86
60	92.78±1.62	**98.99±1.99**	98.34±1.24

Table 15 *In-vitro* drug release data of Stiripentol Nano suspension effect of sonication time

Dissolution data of formulations by comparison with various parameters

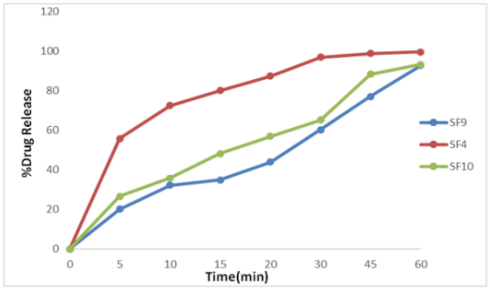

Figure. 8. Effect of SLS concentration on % Drug release

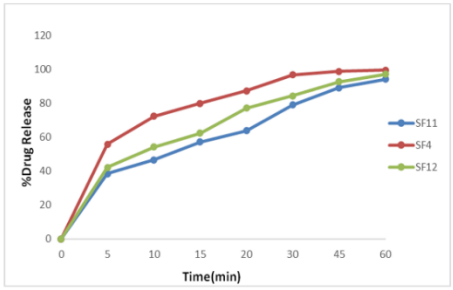

Figure. 9 . Effect of PVA concentration on % Drug release

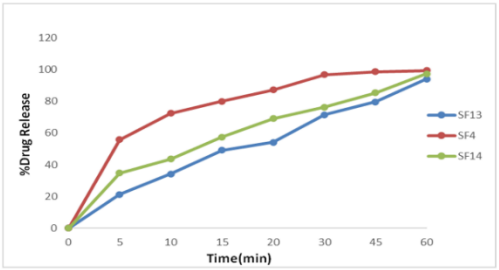

Figure. 10 Effect of stirring time on % Drug release

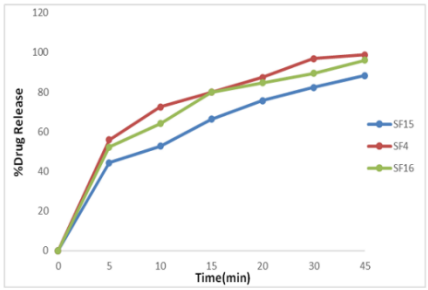

Figure. 11 Effect of sonication time on % Drug release

Kinetic studies for best formulation SF_4

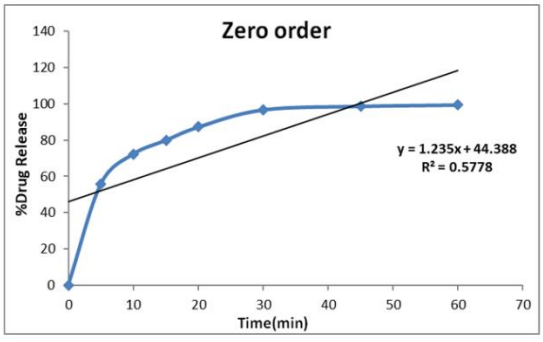

Figure. 12. Zero order release profile of formulation

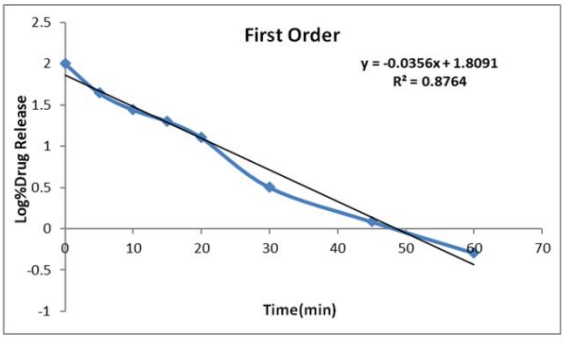

Figure. 13 First order release profile of formulation

Order of kinetics	Zero order	First order
Regression	0.577	0.876

Table 16 Kinetic data of the formulation

The drug release from the Nanosuspension was explained by using mathematical model equations such as zero order, first order, and equation methods. Based on the regression values it was

concluded that the optimized formulation SF_4 follows first order kinetics, indicating concentration dependent drug release.

Discussion

In present investigation Nanosuspensions of Stiripentol was prepared by Solvent Evaporation method. The Nano suspensions are novel promising target and controlled released dosage form which is gaining importance because of ease of manufacturing and diversified applications. The present trend of pharmaceutical research lies in the usage of biodegradable polymer because of its availability and low toxicity. Nanosuspension containing drug was prepared by emulsification solvent evaporation method by using combinations of Soluplus, Vitamin E, Sodium Lauryl Sulfate, Poly Vinyl Alcohol, Methanol and quantity sufficient water). Estimation of Stiripentol was carried out spectrophotometrically at 301nm.The Nanosuspension were evaluated for parameters such as drug content uniformity, scanning electron microscopy, particle size analysis, zeta potential, in-vitro release, drug excipient interactions (GTIR). The stability data was also subjected to statistical analysis.

The melting point of Stiripentol was Found to be in range of 73-74°C which was determined by capillary method.

Saturation solubility was carried out at 25^0C using 0.1N HCL, 6.8 phosphate buffer, 7.4 pH buffer, methanol & ethanol.

From the drug excipient compatibility studies, we observe that there are no interactions between the pure drug (Stiripentol) and optimized Formulation (Stiripentol+ excipients) which indicates there are no physical changes.

The entrapment efficacy of Formulations SF_1-SF_{16} was Found to be In Range of 80.28±1.28%-98.46±1.67%.

Zeta potential value for the optimized Formulation (SF_4) was Found to -4.49 mv which was Found to be within the acceptable limits. Average particle size of nanosuspension of optimized Formulations (SF_4) was Found to be 110.4 nm.

From the invitro studies we can say that Formulation SF_4 shows best drug release of 99.49±1.43 within 60 minutes whereas all the other Formulations didn't release the drug.

The drug release from the Nanosuspension was explained by the using mathematical model equations such as zero order, first order, and equation methods. Based on the regression values it was concluded that the optimized Formulation SF_4 follows first order kinetics.

Conclusion

Based on the results the formulation SF_4 shows the suitable drug release compare with the other formulations.

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