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Original Research Article

Formulation and Evaluation of Nanosuspension Containing Carbamazepine

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Abstract:
Carbamazepine (CBZ) is an antiepileptic drug with poor water solubility, which limits its bioavailability and therapeutic effectiveness. Nanosuspensions have emerged as a promising strategy to enhance the solubility and dissolution rate of poorly water-soluble drugs. This study aims to formulate and evaluate a nanosuspension of carbamazepine to improve its solubility and bioavailability. The nanosuspension was prepared using the wet milling technique, and various parameters such as particle size, polydispersity index (PDI), drug content, and in vitro dissolution were evaluated. The optimized nanosuspension exhibited a mean particle size of 120 nm, and PDI of 0.284 to 0.595 indicating good stability. The in vitro dissolution studies demonstrated a significant improvement in the release rate of carbamazepine from the nanosuspension compared to the pure drug. These findings suggest that nanosuspension is an effective approach to enhance the solubility and bioavailability of carbamazepine.
Key Words: Carbamazepine, Nanosuspensions, bioavailability, polydispersity index.

Introduction

Nanosuspensions are submicron colloidal dispersions of nanoparticles stabilized by surfactants, polymers, or a combination of both. They have gained significant attention in the pharmaceutical field for their ability to improve the solubility, bioavailability, and therapeutic efficacy of poorly water-soluble drugs. By reducing the particle size to the nanometer range, the surface area of the drug particles is significantly increased, leading to enhanced dissolution rates and absorption. [1]

Carbamazepine (CBZ) is widely used in the treatment of epilepsy and bipolar disorder. However, its clinical application is hindered by its poor water solubility, leading to low bioavailability and inconsistent therapeutic effects. Various formulation approaches, including solid dispersions, micronization, and complexation, have been explored to overcome these limitations.[2]

The objective of this research was to enhance the techniques used to prepare and analyze

nanosuspensions for medicinal compounds that have low solubility in water. Subsequently, the nanosuspensions were formulated into appropriate pharmaceutical dosage forms, and their effectiveness was evaluated by in vitro testing. [3,4]

Methodology

A nanosuspension of carbamazepine was created using high pressure homogenization. Different polymers, including soya lecithin (F1 & F2), Poloxamer 407 (F3 & F4), Poloxamer 188 (F5 & F6), HPMC (F7 & F8), and Tween-80 (F9 & F10), were used in varying proportions (0.75% and 1.5%) with 1% TPGS as a stabilizer. The selection of the polymers was determined by a thorough examination of existing literature and preformulation investigations. Furthermore, it was noted that the inclusion of TPGS in the nanosuspension system resulted in enhanced stability and significantly increased the saturation solubility and in-vitro dissolution. [5,6]

Evaluation of Nanosuspension

Nanosuspension particle size as well as size distribution

Particle size and shape were determined using an Optical Microscope. Photon Correlation Spectroscopy (PCS) was used to estimate average particle size and the Polydispersity Index (PI), which affects saturation solubility, dissolving velocity, and biological performance. PCS can analyze particle sizes from 3 nm to 3 µm, while Laser Diffractometry (LD) measures sizes from 0.05 to 80 µm, detecting particles up to 2000 µm. Minimizing PI ensures nanosuspension stability. Additionally, Atomic Force Microscopy was used to visualize particle morphology. [7]

Entrapment efficiency/ Vesicle Size Determination:

This approach is appropriate for assessing the entrapment effectiveness of nanosuspensions when a relatively large quantity of the free drug remains in the supernatant afterwards centrifugation. A 10 ml aliquot of the recently generated and cooled nanosuspension was subjected to centrifugation at 10,000 revolutions per minute for duration of 10 minutes using a microcentrifuge. The liquid portion was extracted and the quantity of medicine that had not been absorbed was determined by measuring the absorbance of the liquid at a wavelength of 285 nm using a UV spectrophotometer.

Drug content uniformity

A volume of 10ml from each formulation was dissolved in 10ml of isotonic solution and left overnight. A dose of 10 mg of the medication, which is the same as the amount used in the formulation, was administered. This was then diluted to a concentration of 10µg/ml. The dilutions underwent filtration and were then tested using UV spectroscopy to determine their content homogeneity. This absorbance of all formulations was measured using a UV-Vis spectrophotometer with a one cm cell. The equipment was calibrated to measure at a wavelength of 285 nm. The medication concentration in every formulation has been determined by calculating the absorbance measurements of recognized standard solutions. [8, 9]

Dissolution Method

The dissolution of Carbamazepine was conducted in both acidic and neutral solutions, using a 100 mg equivalent. The dissolving media had a volume of 900 ml and a temperature of 37.0±0.2°C. At predetermined intervals, samples were collected and subjected to filtration. The concentration of the samples was then determined by measuring their ultraviolet absorbance at 285 nm employing a Shimadzu UV-Visible spectrophotometer. [10, 11]

Stability studies

The optimized batch underwent short-term stability experiments for duration of 1 month, following the parameters set by the ICH. The current investigation conducted stability research at a temperature of 40 °C ±2°C and a relative humidity of 75% ± 5%. Additionally, the study also examined the stability of

Carbamazepine at room temp. Over a period of 90 days. [12, 13]

Results and Discussion

Particle Size Analysis & Polydispersity Index Measurement

All the prepared formulations were in the nano size. The prepared nanosuspension shows nano size range from 70.89 to 144.5 and poly dispersity index range from 0.284 to 0.424. It indicates good uniformity in particle size distribution.

Table1: Particle size and poly dispersity index of nanosuspension

S.No	Formulations	Average Particle size (nm)	Poly dispersity index
1.	F1	74.37 ± 0.16	0.327 ± 0.05
2.	F2	80.52 ± 0.13	0.284 ± 0.01
3.	F3	70.89 ±0.21	0.293 ± 0.09
4	F4	95.94 ± 0.16	0.359 ± 0.69
5	F5	100.6 ± 0.28	0.265 ± 0.21
6	F6	106.3 ± 0.21	0.595 ± 0.16
7	F7	129.0 ± 0.13	0.422± 0.26
8	F8	110.7 ± 0.64	0.318 ±0.21
9	F9	133.8 ± 0.15	0.424 ± 0.16
10	F10	144.5 ± 0.13	0.393 ± 0.13

Drug Content and Drug Entrapment Efficiency

The Carbamazepine Nanosuspension that was produced had significant drug content with a limited standard deviation, suggesting little drug loss during the production process. The entrapment effectiveness of Carbamazepine in F2 exhibited a much higher value (94.75 ± 0.62%) in comparison to the other nano formulations.

Table 2: Percentage of drug content & entrapment efficiency of Carbamzipine Nanosuspension.

S.No	Formulations	Drug content	Drug entrapment efficiency (%)
1	F1	95.49±0.63	89.0 ±0.23
2	F2	98.61±0.32	94.75±0.62
3	F3	94.73±0.12	88.26±0.86
4	F4	95.00±0.61	90.12±0.48
5	F5	91.34±0.56	80.45±0.01
6	F6	93.48±0.10	84.0±0.48
7	F7	89.45±0.28	78.56±0.72
8	F8	90.12±0.92	80.43±0.73
9	F9	87.34±0.26	73.69±0.73
10	F10	89.45±0.71	74.37±0.76

In-Vitro Dissolution and Kinetic Studies

In-vitro drug release data from the Carbamazepine nanosuspension were carried out for 12hrs. Based on the above data, soya lecithin with TPGS based Carbamazepine formulation (F2) showed maximum in-vitro release i.e. 99.31 % (in 0.1 N HCl) drug was released at the end of 12 hrs with increasing carrier proportion. The surfactant soya lecithin increased the solubility of the drug by the action of wetting and dispersion. So, the dissolution profile of the complex was found to be improved. It was reported TPGS, a water miscible form of vitamin E, is composed of a hydrophobic vitamin E part and a hydrophilic PEG chain. It exhibits excellent drug delivery

capability based on this special amphiphilic structure. The enhanced release of formulations may be due to the synergistic effect of surfactants.

Table 3: Dissolution profile of Carbamazepine Nanosuspensionin 0.1 N HCl (pH 1.2).

Time in hours	F1	F2	F3	F4	F5	F6	F7	8	F9	F10
0	0.00± 0.0	0.00± 0.0	0.00± 0.0	0.00± 0.0	0.00± 0.0	0.00± 0.0	0.00± 0.0	0.00± 0.0	0.00± 0.0	0.00± 0.0
1	05.80 ±0.01	08.70 ±0.07	05.22 ±0.25	08.12 ±0.43	04.64 ±0.63	06.38 ±0.03	04.06 ±0.16	04.06 ±0.57	03.48 ±0.15	03.48 ±0.32
2	12.78 ±0.32	16.84 ±0.06	11.03 ±0.03	13.94 ±0.34	11.61 ±0.17	13.94 ±0.47	09.87 ±0.63	09.87 ±0.15	08.13 ±0.36	06.97 ±0.26
3	19.76 ±0.41	24.99 ±0.14	18.01 ±0.47	23.25 ±0.15	17.43 ±0.71	21.50 ±0.57	15.69 ±0.26	15.11 ±0.52	12.20 ±0.15	11.62 ±0.45
4	26.17 ±0.04	33.15 ±0.05	24.42 ±0.07	30.82 ±0.03	23.26 ±0.25	28.49 ±0.74	20.93 ±0.42	19.77 ±0.16	17.44 ±0.42	15.12 ±0.18
5	33.16 ±0.06	41.31 ±0.15	30.83 ±0.05	38.40 ±0.06	29.09 ±0.05	36.07 ±0.27	26.18 ±0.36	23.86 ±0.63	22.11 ±0.16	19.78 ±0.18
6	40.17 ±0.06	50.07 ±0.36	38.42 ±0.16	46.57 ±0.15	34.93 ±0.53	43.66 ±0.62	32.02 ±0.43	29.11 ±0.16	26.19 ±0.67	23.28 ±0.16
7	47.18 ±0.11	58.25 ±0.25	44.85 ±0.15	54.75 ±0.09	40.77 ±0.16	50.68 ±0.63	37.86 ±0.25	34.37 ±0.16	30.29 ±0.17	27.37 ±0.21
8	54.78 ±0.35	67.03 ±0.26	51.28 ±0.52	61.78 ±0.15	47.21 ±0.52	58.28 ±0.72	43.13 ±0.15	39.63 ±0.07	34.97 ±0.42	31.47 ±0.15
9	61.23 ±0.06	74.65 ±0.36	57.73 ±0.26	69.80 ±0.17	53.07 ±0.51	65.31 ±0.03	48.40 ±0.36	43.74 ±0.08	39.65 ±0.37	34.99 ±0.52
10	67.68 ±0.06	83.44 ±0.52	63.60 ±0.26	77.61 ±0.26	58.35 ±0.26	72.94 ±0.47	53.68 ±0.26	49.01 ±0.18	43.76 ±0.52	39.09 ±0.18
11	74.73 ±0.07	91.08 ±0.16	70.06 ±0.02	85.82 ±0.42	64.22 ±0.15	79.40 ±0.16	58.96 ±0.52	53.71 ±0.38	47.87 ±0.16	43.2± 0.42
12	81.78 ±0.02	99.31 ±0.52	75.94 ±0.06	93.46 ±0.18	70.10 ±0.53	87.62 ±0.62	64.25 ±0.17	58.42 ±0.17	52.57 ±0.17	46.73 ±0.13

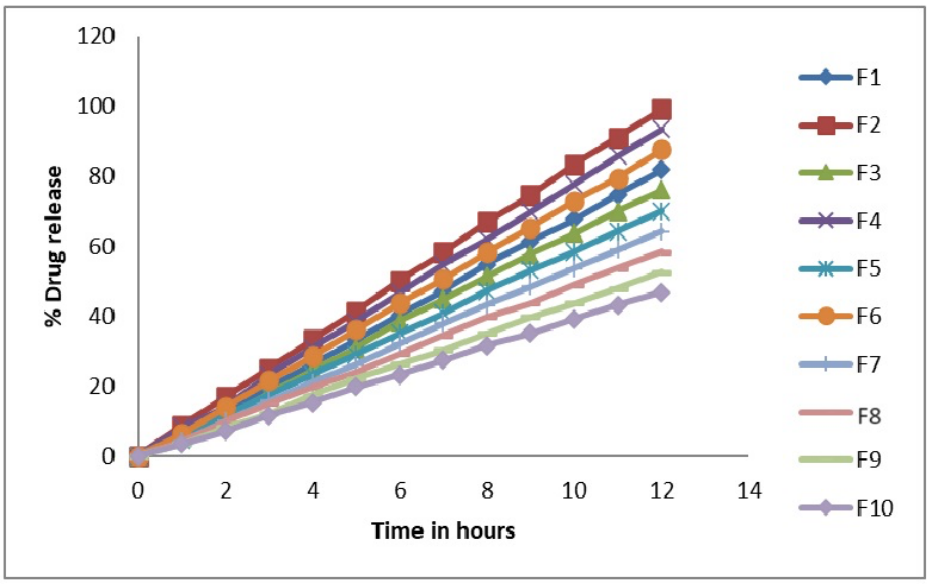

Figure 1: Dissolution Profile Plot of Carbamazepine Nanosuspensionin 0.1 N HCl (pH 1.2).

Stability of Carbamazepine Nanosuspension

Based on physiochemical studies, such as parameters like particle size, PDI, percentage of drug content and in-vitro release studies, Carbamazepine formulation (F2) that prepared from combination of soya lecithin and TPGS selected for an accelerated stability study.

Table 4: Particle size analysis of selected Carbamazepine Nanosuspension (F2) formulation

Formulation	Storage temperature condition	Initial particle size (nm)	Particle size after three months (nm)
F2	Room temperature	80.52 ± 91.96	85.61 ± 95.40
	40^0C		92.02 ± 11.06

Table 5: In-vitro dissolution profile of F2 in stability studies

S.No	TimeinHours	% Drug Release		
		0.1 NHCl (pH1.2)		
		1Month	2Month	3Month
1.	0	0.00± 0.0	0.00±0.00	0.00± 0.0
2.	1	16.30±0.12	12.68±0.31	9.66±0.38
3.	2	24.78±0.52	21.75±0.37	16.92±0.46
4.	3	32.66±0.27	27.82±0.46	23.58±0.57
5.	4	41.50±0.18	32.08±0.32	26.53±0.32
6.	5	49.65±0.01	40.57±0.07	32.09±0.05
7.	6	59.37±0.12	46.05±0.01	39.38±0.08
8.	7	69.10±0.15	53.95±0.14	47.27±0.13
9.	8	80.05±0.05	62.47±0.07	52.76±0.18
10.	9	88.60±0.32	72.20±0.26	60.07±0.21
11.	10	90.51±0.08	77.12±0.18	73.38±0.48
12.	11	93.63±0.13	89.62±0.25	84.29±0.22
13.	12	98.73±0.03	97.17±0.07	96.37±0.05

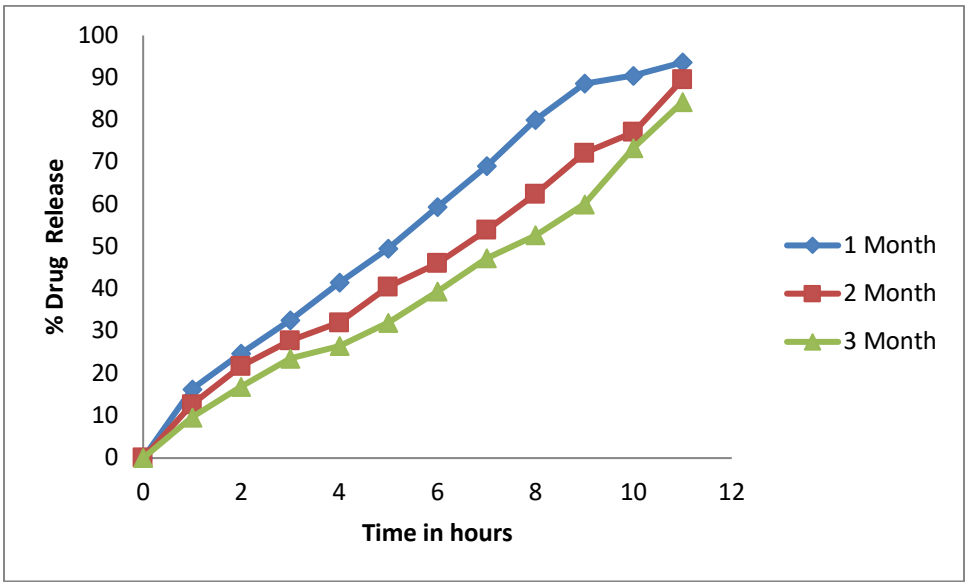

Figure 2: In-vitro dissolution profile plot of F2 in stability studies.

The visual characteristics of the Carbamazepine nanosuspension remained unchanged after being stored at a temperature of 40°C for a period of 3 months. The optimized formulation F2 remained stable at temperatures of 40±2°C and relative humidity of 75±5% for a period of 90 days, without any degradation in its physical properties.

Conclusion

Nanosuspensions represent a versatile and promising approach for enhancing the solubility and bioavailability of poorly water-soluble drugs. The nanosuspensions exhibited uniform particle sizes and limited size distributions, indicating their stability and ability to deliver drugs effectively. Among the formulations tested, Formulation F2 demonstrated the highest drug content and efficacy in trapping the drug. In-vitro dissolution tests revealed that the release of drug from F2 followed zero-order kinetics, ensuring a consistent and controlled release of the drug over a period of 12 hours. Stability experiments conducted under accelerated conditions for 90 days demonstrated that the optimized formulation maintained its physical appearance and drug content without any changes. These findings suggest that the use of Carbamazepine nanosuspensions could enhance therapeutic effectiveness by improving stability, solubility, and controlled release of the drug.

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