ISSN: 2306-6091

International Journal of Pharmaceuticals and Health Care Research (IJPHR)

IJPHR |Vol. 14 | Issue 3 |Jul–Sep2026

www.ijphr.com

DOI : https://doi.org/10.61096/ijphr.v14.iss3.2026.414-428

Formulation and Evaluation of Amantadine Loaded Nanoparticles

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Published on: 10.07.2026
Published by: Futuristic Publications

Abstract: The present study was undertaken to formulate and evaluate amantadine-loaded nanoparticles with the objective of enhancing drug delivery and achieving sustained drug release. Amantadine-loaded nanoparticles were prepared using a suitable formulation technique and optimized to obtain desirable physicochemical characteristics. The prepared formulations were evaluated for precompression parameters including angle of repose, bulk density, tapped density, Carr's index, and Hausner's ratio. All the precompression parameters were found to be within Pharmacopoeial limits, indicating good flow properties and compressibility of the powder blend.

Post-compression evaluation of the formulated nanoparticles showed satisfactory results in terms of particle characteristics, drug content uniformity, and in vitro drug release studies. Among the different formulations, F3 was identified as the optimized formulation as it exhibited superior drug release, achieving 99.24% drug release over a period of 12 hours, demonstrating an effective sustained release profile. The results confirm that the optimized nanoparticle formulation possesses acceptable physicochemical properties and meets the required evaluation standards.

In conclusion, the successful formulation and evaluation of amantadine-loaded nanoparticles indicate that the developed nanoparticulate system is a promising approach for sustained drug delivery. The optimized F3 formulation, with its excellent release characteristics and parameters within Pharmacopoeial limits, may enhance therapeutic efficacy and improve patient compliance.

Key words: Amantadine-loaded nanoparticles

INTRODUCTION

Nanoparticles.[1-5]

1. Nanoparticles are nanometer-sized particles that are nanoscale in three dimensions. They include nanopores, nanotubes, quantum dots, nano shells, dendrimers, liposomes, nanorods, fullerenes, nanospheres, nanowires, nanobelts, nano rings, and nano capsules. The applications of nanoparticles include drug delivery systems, cancer targeting, and dentistry.

2. Nanoparticles are of great scientific interest as they are effectively a bridge between bulk materials and atomic or molecular structures.

3. A bulk material should have constant physical properties regardless of its size, but for the nanoscale this is often not the case. Size-dependent properties are observed such as quantum confinement in

semiconductor particles, surface plasmon resonance in some metal particles, and super paramagnetism in magnetic materials.

4. Nanoparticles exhibit a number of special properties relative to bulk material. Nanoparticles often have unexpected visual properties because they are small enough to confine their electrons and produce quantum effects. For example, gold nanoparticles appear deep red to black in solution.

5. The often very high surface-area-to-volume ratio of nanoparticles provides a tremendous driving force for diffusion, especially at elevated temperatures. Sintering is possible at lower temperatures and over shorter durations than for larger particles.

6. This theoretically does not affect the density of the final product, though flow difficulties and the tendency of nanoparticles to agglomerate do complicate matters. The surface effects of nanoparticles also reduce the incipient melting temperature.

7. Nanoparticles are being applied in various industries, including medicine, due to various properties such as increased resistance to wear and the killing of bacteria, but there are worries due to the unknown consequences to the environment and human health.

8. Nanoparticles are an important and diverse class of materials with applications in all major areas of the economy, including manufacturing, medicine, and energy. The use of engineered nanoparticles in consumer products increases dramatically each year.

9. The Project on Emerging Nanotechnologies reports over 1600 nano-containing consumer products on the market as of October 2013, as compared to 54 products in 2005 (Project on Emerging Nanotechnologies, 2013). The main classes of nanoparticles utilized in products include carbon-based (nanotubes and fullerenes), metal nanoparticles (including gold, silver, iron, and copper nanoparticles), metal oxide nanoparticles (iron oxide, ZnO, TiO2, CeO2, SiO2, among others), and quantum dots (Hornyak et al., 2009).

10. There are endless possibilities for nanoparticle coatings that can be applied to the surface of these particles in order to improve solubility, improve biocompatibility, target interactions with other molecules, or prevent interactions with the nanoparticle’s environment.

11. More complex nanoparticles, such as core-shell nanoparticles for medical applications, are being developed. All of these nanoparticle systems will require analytical characterization.

12. Complete characterization of the material, including the core, coatings, and any other factors affecting nanoparticle use are essential to understanding its potential as a commercial product, evaluating the effects of its release into the environment, or developing it for biological or medical applications.

13. A control of the synthesis of nanomaterials in combination with suitable functionalization techniques of their surface, led to the development of new functionalized nanoparticles which bring possibilities of their potential use in anticancer therapy.

14. Systems and gadgets. The level of nanomaterials is the most advanced currently in terms of both commercial uses and scientific knowledge. Ten years previously, nanoparticles were examined due to their size-dependent chemical and attributes. They are now in the commercial investigation phase.

15. Science and engineering applied to the nanoscale is called nanotechnology. The development and synthesis of materials, devices, and systems at the nanoscale is known as nanotechnology.

16. As much as 1-100 nm. High surface volume ratios are found in nano formulations. The creation of tiny objects, such as electronic devices, catalysts, sensors, etc., is the focus of nanotechnology.

17. One of the most significant and fascinating areas of research in physics, chemistry, biology, medicine, engineering, and technology in recent years is nanomaterials. Design, development, and use of materials at the atomic, molecular, and macromolecular range are represented by nanotechnology. Creation and use of materials at the molecular, macromolecular, and atomic levels.

18. A nanoparticle matrix is used to dissolve, entrap, encapsulate, or bind the medication. Based on nanoparticles, nanospheres or nanocapsules can be produced depending on the preparation technique.

19. Nanoparticles exhibit a range of special qualities that are not present in bulk materials. The most important aspect of nanoparticles is their characteristics, which include their electrical, optical, magnetic, and so forth) are highly dependent upon the dimensions and dispersion of the fragments.

20. Although they have a long history, nanoparticles are thought to be a discovery of modern science. Nanotechnology has been used by ancient humans for thousands of years.

21. However, it's unclear when people started using the benefits of nanoparticles in various domains. One of the most important and basic characteristics of nanoparticles is their optical quality.

For Example:

- The colour of a silver NP is greyish-yellow.
- The colour of a gold NP with a 20 nm size is similar to red wine.
- The nanoparticles of palladium (Pd) and platinum (Pt) are black in colour

For centuries, the nanoscale range has been used in the study of biological systems and the manufacture of numerous materials, including colloidal dispersions, metallic quantum dots, and catalysts.

Au Nanoparticles, for instance, are known to be used by the Chinese as an inorganic colour to add the colour red to their porcelain ceramics about a millennium ago. Utilization Of colloidal gold has been around for a while, but a thorough investigation into the production and First publication of colloidal gold's qualities occurred in the middle of the 19 the century.

Intractable the gold dispersion that Faraday created in 1857 was steady. Nearly a century passed before being demolished in the course of World War II.

Another example of colloidal gold usage is in medicine. Arthritis was and is still treated with colloidal gold. As a result of their complexity, nanoparticles are made up of three layers: the surface layer, which can be functionalized by a wide range of small molecules, metal ions, surfactants, and polymers. The outer shell layer, a substance that differs from the core in every way chemically, and the core, which is basically the middle section.

Classification of Nanoparticles.[6,7]

In general, there are three types of nanoparticles: organic, inorganic, and carbon-based.

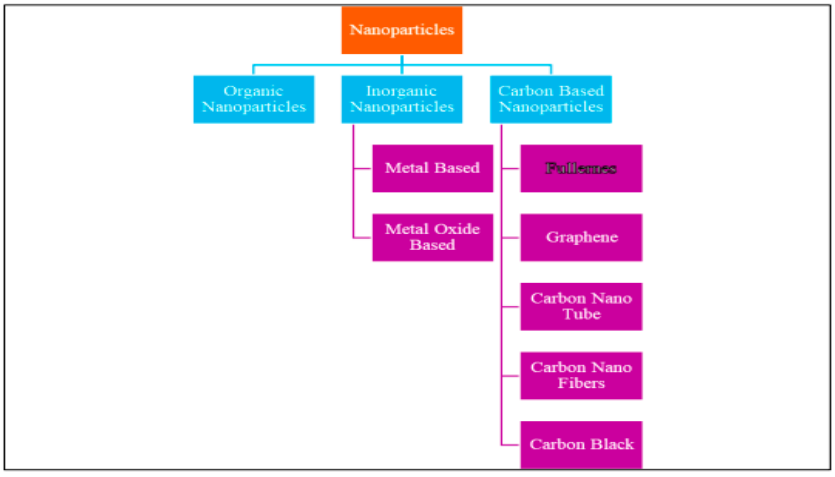

Fig 1.1: Classification of Nanoparticles

Organic nanoparticles

Ferritin, liposomes, dendrimers, and other organic nanoparticles or polymers are well-known examples. Thesenanoparticles are non-toxic and biodegradable, yet some, like micelles and liposomes, have a hollow core and are Susceptible to electromagnetic and thermal radiation, including heat.

The increasing production of nanoparticles in several areas has a discernible impact on the environment and living organisms, hence affecting their health and overall well-being. Nanoparticles are a double-edged sword, and their drawbacks must be mitigated by taking safeguards. This study examines how nanoparticles affect the environment by directly interacting with human tissue, which may be toxic and cause health problems.

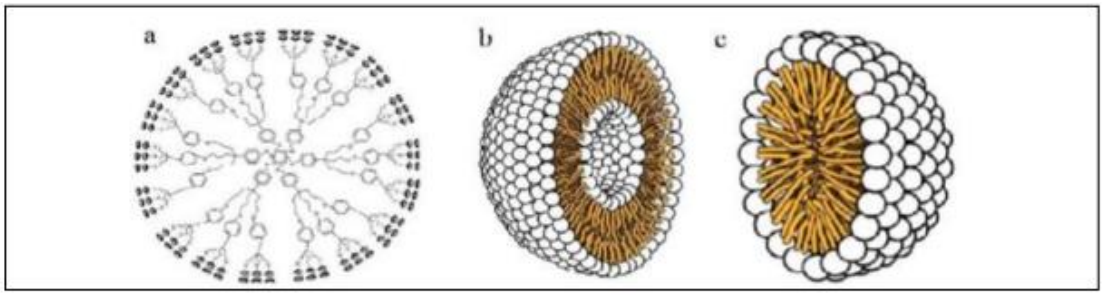

Fig 1.2: Organic nanoparticles: a) Dendrimers, b) Liposomes and c) micelles

Inorganic nanoparticles.[8]

Non-carbon-based particles are known as inorganic nanoparticles. Inorganic nanoparticles are often defined as those based on metal and metal oxides.

Metal nanoparticles

Metallica nanoparticles are manufactured from metals by either constructive or destructive processes. The pure metal nanoparticles are produced using the metal precursors. Because of the plasma on resonance characteristics, the metal nanoparticles have special optoelectrical capabilities. The shape, facet, and size of metal nanoparticles govern their production.

All metal's nanoparticles are produced. Among the most well-known metal nanoparticles are those of aluminium, gold, iron, lead, silver, cobalt, zinc, and copper. The small size (10–100 nm), surface properties (surface area to volume ratio, surface charge, pore size, surface charge density), shapes (spherical, rod, hexagonal, tetra-gonial, cylindrical, and irregular), colour, and environmental factors (sunlight, moisture, air, and heat) all contributed to the unique properties of nanoparticles.

Metal Oxides Based Nanoparticles

Metal oxides-based NPs are NPs made from metals that can be transformed into their corresponding Oxides. When compared to their metal equivalents, nanoparticles based on metal oxides exhibit remarkable features.

Examples of metal oxide-based nanoparticles (NPs) include magnetite and iron oxide (Fe2O3). (Fe3O4), silicon dioxide (SiO2), titanium, aluminium oxide (Al2O3), and cerium oxide (CeO2) Titanium dioxide (TiO2), zinc oxide (ZnO) (M. B. Sathayandaran, R. Balachandranath, Genji in 2013.Subbiah doss, G., Kannaiyan, S. K., and Srinivasulu, Y. These NPs rely on metal oxides discovered to be more responsive and effective.

Carbon based nanoparticles[9-10]

There are two main categories of carbon-based NPs: fullerenes and carbon nanotubes (CNTs). Fullerenes contain nanomaterials composed of globular hollow cages, such as allotropic forms of carbon. They've shown remarkable interest in business.

Because of their excellent strength, structure, electron affinity, electrical conductivity, and adaptability. These materials have sp2 hybridized carbon units organized in both pentagonal and hexagonal configurations. Figure 4 displays the well-known fullerenes C60 and C70, which have diameters of 7.114 and 7.648 nm, respectively.

CNTs are elongated, 1- 2 nm-diameter tubular structures. Considering their diameter these can be categorized as semiconducting or metallic based on their telicity. These appear to be rolling graphite sheets on top of one another. One type of carbon nanotube is single-walled (SWNT). The rolled sheets might be single-walled (DWNTs) or multi-walled (MWNTs).

Usually, they are created via deposition using an electric arc or laser. Carbon precursors that evaporated from graphite and were deposited on metal, especially atomic carbons Fragments.

The synthesis of them by chemical vapour deposition (CVD) has been introduced recently. Due to These components' distinct mechanical, chemical, and physical characteristics make them useful for Fillers effective gas adsorbents for cleaning up the atmosphere and serving as a support material for numerous Catalysts, both organic and inorganic.

C60 is one of the most well-known and often used fullerenes, Buckminster fullerene. It has the shape of a soccer ball due to the cage-like arrangement of its 60 carbon atoms, each of which has three bonds. Twelve pentagons and twenty hexagons are utilized in the C60 structure. Two well-established characteristics of this structure are resonance stabilization and icosahedral symmetry.[11]

It is used in material science because of its unique combination of physicochemical characteristics. Recently, a wide range of applications in nanoscience and nanotechnology have made extensive use of C60-based nanostructures, such as nanorods, nanotubes, and nanosheets. Because of its versatility, C60 can be employed in a variety of ways to accelerate the reactions of a broad spectrum of chemicals.

It can be included into systems to enhance particular behaviours due to its special characteristics. Through covalent, endohedral, and supramolecular transformations, C60 can be subjected to molecular manipulation and the creation of polymeric material for use in environmental applications.[12]

7. METHODOLOGY

Analytical Method Development

Determination of absorption maxima: Absorption maxima are the wavelength at which maximum absorption takes place. For accurate analytical work, it is important to determine the absorption maxima of the substance under study.

Procedure: For the preparation of calibration curve stock solution was prepared by dissolving 100 mg of accurately weighed drug in 100ml of Methanol (1mg/ml). Further 1ml of the stock solution was pipette out into a 100 ml volumetric flask and volume was made up with phosphate buffer (5.5pH). From this stock solution pipette out 1ml and dilute to 10 ml with phosphate buffer and subject for UV scanning in the range of 200-400 nm using double beam UV spectrophotometer. The absorption maxima were obtained at 433nm with a characteristic peak.

Preparation of calibration curve: It is soluble in Methanol; hence Methanol was used for solubilizing the drug. Stock solution (1 mg/mL) of Amantadine was prepared in Methanol and subsequent working standards (10, 20, 30, 40and 50 µg/mL) were prepared by dilution with phosphate buffer of pH-5.5. These solutions were used for the estimation Amantadine by UV method. The whole procedure was repeated three times and average peak area was calculated. Calibration plot was drawn between concentrations and peak area. Calibration equation and R^2 value are reported.

Preparation of nanoparticles

Preparation of Amantadine loaded nanoparticles

Amantadine loaded Nanoparticle was prepared by previously reported emulsification sonication method. Amantadine was dissolved in organic solvent (20 ml, methanol and DCM 30ml). Polymers in different concentrations were dissolved in water. The organic phase was added drop wise into the polymeric solution for emulsification. Then the dispersion was sonicated (20 min) with the application of ultra-probe sonication (60 W/cm^3, Hielscher, Ultra-sonics, Germany). The formulation was stirred at 1500 rpm for 6 h using a magnetic stirrer to evaporate the organic solvent. The prepared NPs were centrifuged at 15,000 rpm for 20 min at 25 °C (Remi, Mumbai, India). NPs were separated and lyophilized using cryoprotectant (Mannitol 0.2%) and stored for further evaluation.

Table: Composition of nanoparticles formulations (F1 to F9)

Excipients	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Amantadine (grm)	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Carbopol 934P(grm)	1	1.5	2	-	-	-	-	-	-
HPMC K4M (grm)	-	-	-	1	1.5	2	-	-	-

Sodium CMC (grm)	-	-	-	-	-	-	1	1.5	2
Span 60 (ml)	0.2	0.4	0.6	0.8	-	-	-	-	-
Dichloromethane (ml)	-	-	-	-	-	0.2	0.4	0.6	0.8
Methanol (ml)	10	10	10	10	10	10	10	10	10
Distilled water (ml)	qs	qs	qs	qs	qs	qs	qs	qs	qs

Characterization of nanoparticles:

Particle Sizes, PDI, Zeta Potential:

The mean particle length and polydispersity index (PDI), that's a degree of the distribution of nanoparticles population, was decided the usage of dynamic light scattering (Delta Nano C, Beckman counter), and Zeta capability becomes anticipated on the premise of electrophoretic mobility under an electric powered field, the use of zeta Sizer Nano ZS (Malvern Instruments, UK). Samples had been diluted with the distilled water before measurement and measure at a hard and fast angle of 1650c for the particle size and poly dispersity index (PDI) analysis. For the Zeta ability measurement, Samples have been diluted as 1; 40 ratio with filtered water (v/v) before analysis. Average particle size, PDI, and zeta potential have been then measured in triplicate.

Drug content:

Amantadine content in solid lipid nanoparticles was assayed by an UV-visible spectrophotometer. Nanoparticles (100mg) were dissolved in 10ml methanol by shaking the mixture for 5 mins. One ml of the resultant solution was taken and diluted to 10ml with methanol. Then, aliquots were withdrawn and absorbance was recorded at 433nm using UV-visible spectrophotometer (Lab India 3200).

Yield of nanoparticles:

After complete drying the nanoparticles powders were collected and weighed accurately. The yield of nanoparticles was calculated using the formula

$$Percentage\ yield = \frac{Total\ weight\ of\ nanoparticles}{\text{Total weight of drug } + \text{weight of added materials}} \times 100$$

Entrapment Efficiency:

Entrapment Efficiency (EE) of the Amantadine loaded changed into determined by measuring the awareness of uninterrupted drug in an aqueous medium by centrifugation method. The nanoparticles had been centrifuged during a high-space cooling Centrifuge (C-24. Remi) the usage of nano step centrifuge tubes with ultra-filter out having a relative molecular mass cut-off 100KD (Pall existence sciences-India) at 5000rpm for 15min at 4oc, and therefore the supernatant was separated. The amount of Amantadine inside the supernatant changed into determining the usage of a UV-Visible spectrophotometer (U-1800, Hitachi) at lambda max 215nm after suitable dilution.

The percent entrapment efficiency (%) changed into calculated by means of the usage of the subsequent formula:

$$\%EE = \frac{\text{Total drug content-Free drug x100}}{\text{Total drug content}}$$

Percent amount of drug release from semi permeable membrane

Franz diffusion cell was used for the in vitro drug release studies. Semi permeable membrane was placed between donar and receptor chamber of diffusion cell. Receptor chamber was filled with freshly prepared 30ml 5.5 PH phosphate buffer. SLN gel equivalent to 1gm was placed on semi permeable membrane. The Franz diffusion cell was placed over magnetic stirrer (REMI 1ML) with 500rpm and temperature was maintained at 37 ± 1^0C. 5ml of samples were withdrawn periodically and replaced with fresh buffer. The withdrawn samples were periodically diluted and analysed for drug content using UV visible spectrophotometer (Lab India 3200) at 433nm.

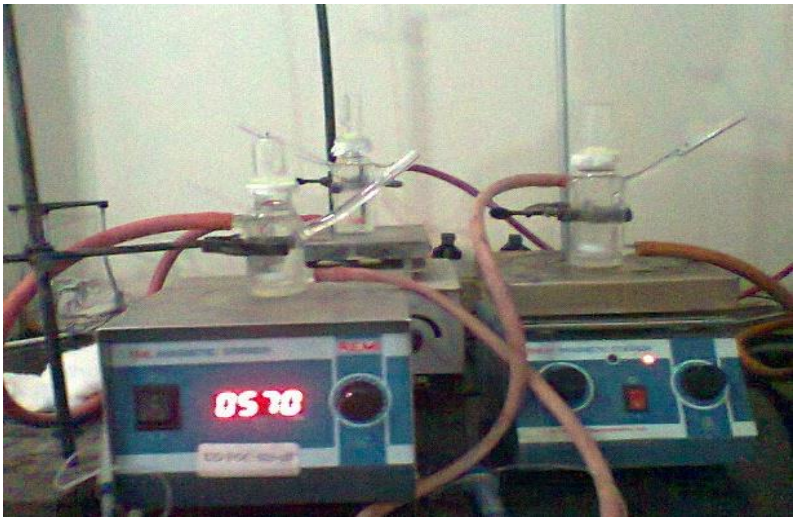

Fig: Drug release from semi permeable membrane

Powder X-ray Diffraction (PXRD) Studies

The prepared mixtures were also analyzed using X-ray powder diffractometer (PXRD) which confirms the formation of the new solid phases. The difference in the 2 theta lines confirms the formation of the new solid phases as no two solids have same 2 theta lines, thus revealing the formation of new solid phases. It also reveals the information about the crystal structure, chemical composition, and physical properties of the material and also helps in structural characterization. This technique detects changes in the crystal lattice and is therefore powerful tool forestudying polymorphism, pharmaceutical salts, and crystal line phases. Spectra of PXRD were taken on a sample stage Spinner PW3064. The samples were exposed to nickel filtrate Cukœ radiations (40 KV, 30 mA) and were scanned from 10° to 40°, 2Θ at astep size of 0.045° and step time of 0.5.

In Vitro Release Studies

Drug release was determined by dialysis method; two ml of each formulation (test and control) were poured into dialysis bags and put into 25 ml phosphate buffer (pH 6.8) and stirred (100 rpm, room temperature). At predetermined time intervals, 2 ml of phosphate buffer was taken and then substituted by fresh phosphate buffer. Finally, the amounts of released Simvastatin in phosphate buffer were measured by spectrophotometer at 433nm. Aliquots withdrawn were assayed at each time interval for the drug released at λ max of 433nm using UV-Visible spectrophotometer by keeping phosphate buffer pH 6.8 as blank and the amount of released drug was estimated by the standard curve.

Fourier Transform Infrared (FTIR) spectroscopy:

The formulations were subjected to FTIR studies to find out the possible interaction between the drug and the excipients during the time of preparation. FT IR analysis of the pure drug and optimized formulation were carried out using an FT IR spectrophotometer (Bruker FT-IR - GERMANY).

Differential Scanning Calorimetry:

The possibility of any interaction between the drug and the Excipients during preparation of SLN was assessed by carrying out thermal analysis of optimized formulation using DSC. DSC analysis was performed using Hitachi DSC 7020, on 5 to 15 mg samples. Samples were heated in sealed aluminium pan at a rate of 10°C/min conducted over a temperature range of 30 to 350°C under a nitrogen flow of 50 mL/min.

SEM (Scanning Electron microscope) studies

The surface morphology of the layered sample was examined by using SEM (Hitachi, Japan). The small amount of powder was manually dispersed onto a carbon tab (double adhesive carbon coated tape) adhered to an aluminium stub. These sample stubs were coated with a thin layer (30Å) of gold by employing POLARON-E 3000 sputter coater. The samples were examined by SEM and photographed under various magnifications with direct data capture of the images onto a computer

RESULTS AND DISCUSSION:

Preparation of Standard Graph:

a. Determination of absorption maxima

The standard curve is based on the spectrophotometry. The maximum absorption was observed at 433 nm.

b. Calibration curve

Graphs of Amantadine was taken in 7.4 Phosphate buffer

Table 8.1: Calibration curve data for Amantadine at 433 nm

Concentrations [µg/mL]	Absorbance
0	0
10	0.114
20	0.216
30	0.317
40	0.422
50	0.531

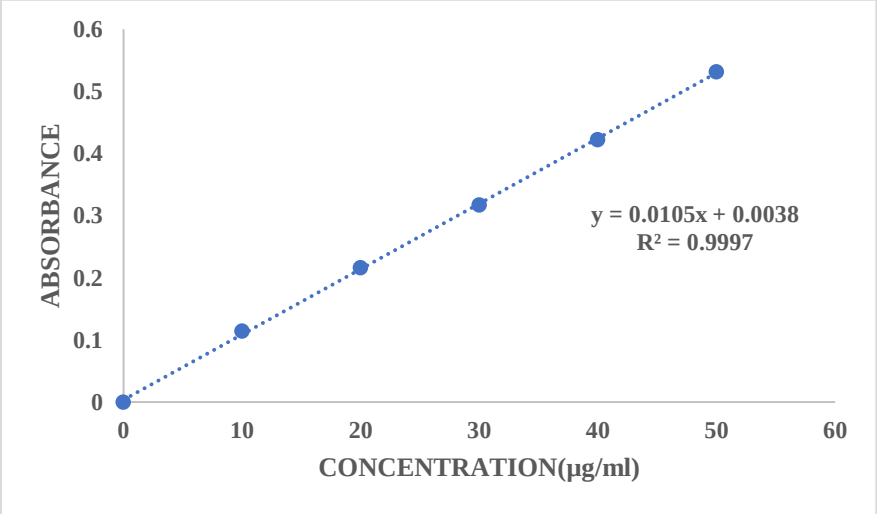

Fig 8.1: Standard graph of Amantadine in 7.4 Phosphate buffer

Standard graph of Amantadine was plotted as per the procedure in experimental method and its linearity is shown in Table 8.1 and Fig 8.1. The standard graph of Amantadine showed good linearity with R^2 of 0.997, which indicates that it obeys “Beer- Lamberts” law.

EVALUATION OFAMANTADINE LOADED NANOPARTICLES:

Table 8.2: Evaluation of Nanoparticles

Batch No	Mean Particle size(nm)	%Yield	Drug Content	Drug encapsulation efficiency	PDI	Zeta Potential (mV)
F1	1314.3	97.15	97.12	86.72	0.782	-34.23
F2	992.4	91.08	99.34	88.93	1.283	-39.92
F3	912.3	93.39	98.86	92.41	1.246	-37.63
F4	523.8	95.94	99.49	95.28	0.257	-47.36
F5	817.5	81.29	97.73	83.54	0.371	-31.66
F6	792.3	88.48	99.66	89.88	0.436	-35.94
F7	668.1	91.38	98.58	92.65	0.782	-38.68
F8	624.5	92.82	98.82	91.22	0.487	-43.22
F9	587.3	93.94	99.48	94.39	0.568	-41.91

Percentage yield of formulations F1 to F9 by varying drug was determined and is presented in Table. Highest drug content, Highest Entrapment efficiency observed for F6 formulation.

PDI observed in the F3 formulation i.e., 1.246 respectively. The Zeta potential range from 31.66mV to -47.36mV to all the formulations.

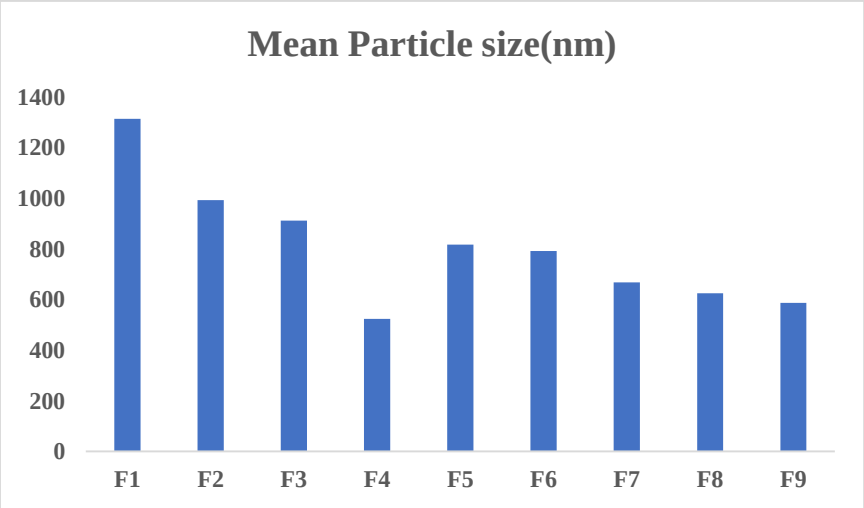

Fig 8.2: Mean Particle size (nm)

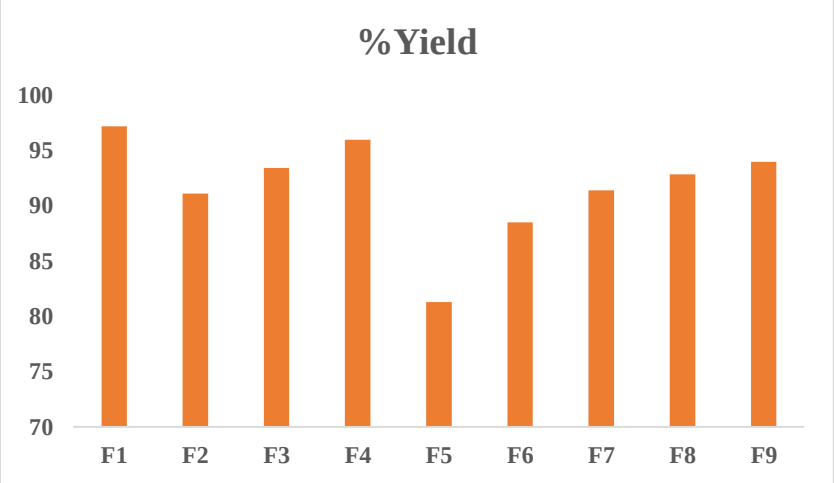

Fig 8.3: %Yield

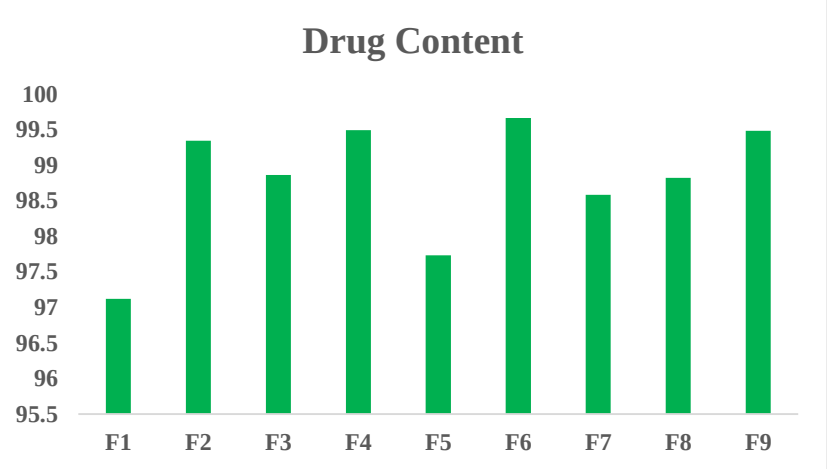

Fig 8.4: Drug content

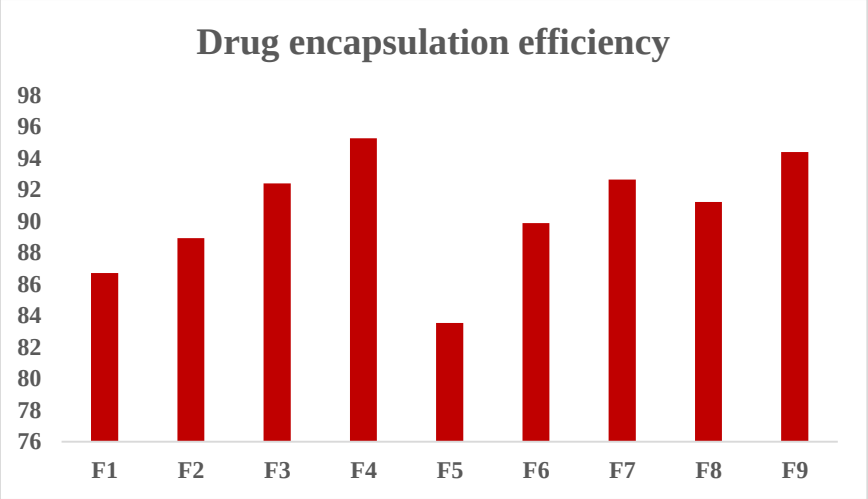

Fig 8.4: Drug encapsulation efficiency

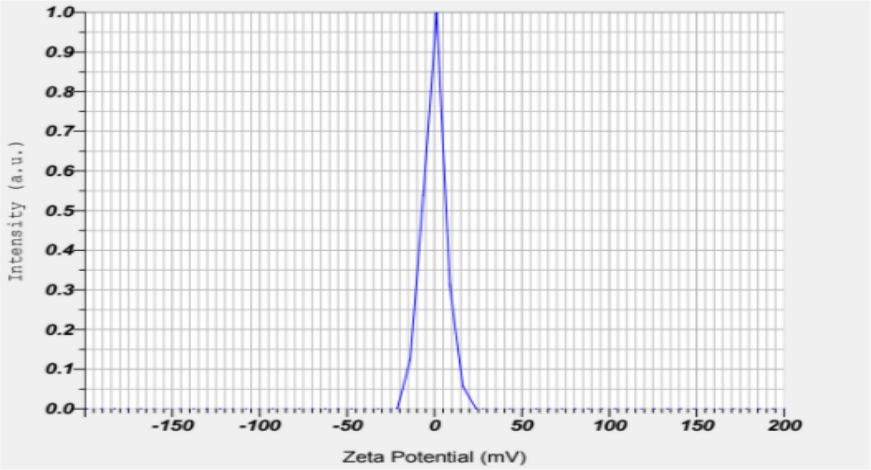

Fig 8.5: Zeta Potential of F6 Formulation

In vitro Drug release studies:

Table 8.3: *In vitro* Drug release studies of Amantadine

TIME (hr)	CUMULATIVE PERCENT OF DRUG RELEASED								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	18.62	22.62	25.07	24.52	19.28	23.15	24.22	18.25	25.66
2	22.08	28.55	29.18	31.22	25.57	27.54	26.68	31.68	29.38
3	29.53	35.95	36.55	38.58	31.66	32.63	28.05	34.54	32.49
4	32.27	42.24	44.56	46.26	48.79	39.77	33.88	43.08	39.57
5	37.79	49.29	48.79	51.49	57.25	46.19	48.64	51.55	45.85
6	46.55	52.73	54.53	55.62	69.07	59.92	54.49	55.28	51.96
7	51.22	58.51	61.24	59.86	71.83	62.88	62.88	59.64	54.68
8	54.49	62.33	65.91	63.14	74.49	66.29	68.73	63.32	58.13
9	59.66	68.46	72.37	68.89	78.97	77.96	76.59	66.28	62.57
10	63.53	74.45	78.66	75.79	82.33	79.66	81.62	71.75	67.26
11	69.11	81.64	85.89	78.55	88.04	82.79	86.47	78.63	74.57
12	76.64	85.53	99.24	83.49	91.38	96.33	97.24	88.42	79.35

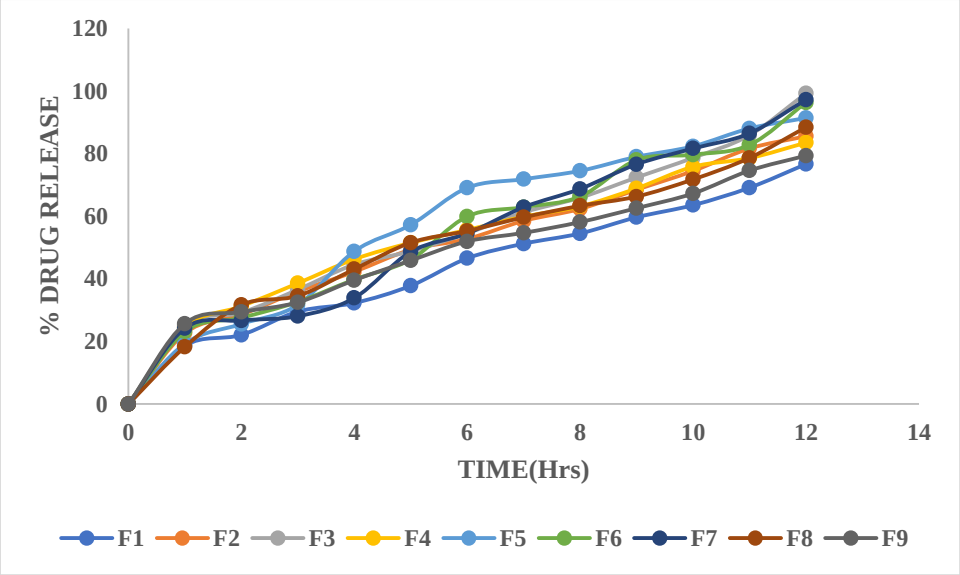

Fig 8.6: Dissolution study of Amantadine Nanoparticles

Hence based on dissolution data of 9 formulations, F3 **Carbopol p934 (1:3) (2grm)** formulation showed better release (99.24%) up to 12 hours. So F3 formulation is optimized formulation.

Application of Release Rate Kinetics to Dissolution Data

Data of *in vitro* release studies of formulations which were showing better drug release were fit into different equations to explain the release kinetics of drug release from Nanoparticles. The data was fitted into various kinetic models such as zero, first order kinetics; Higuchi and Kors Meyer Peppas mechanisms and the results were shown in below table it follows the zero-order kinetics.

Table 8.5: Release kinetics data for optimized formulation (F3)

CUMULATIVE (%) RELEASE Q	TIME (T)	ROOT (T)	%) REL	LOG (T	LOG (%) REMAIN	RELEASE RATE (CUMULATIVE % RELEASE / t)	1/CUM% RELEASE	PEPPAS log Q/100	% Drug Remaining	Q01/3	Qt1/3	Q01/3-Qt1/3
0	0	0	0	0	0	0	0	0	0	0	0	0
25.07	1	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	0.000
29.18	2	1.414	1.465	0.301	1.850	14.590	0.0343	-0.535	70.82	4.642	4.137	0.504
36.55	3	1.732	1.563	0.477	1.802	12.183	0.0274	-0.437	63.45	4.642	3.989	0.653
44.56	4	2.000	1.649	0.602	1.744	11.140	0.0224	-0.351	55.44	4.642	3.813	0.829
48.79	5	2.236	1.688	0.699	1.709	9.758	0.0205	-0.312	51.21	4.642	3.714	0.928
54.53	6	2.449	1.737	0.778	1.658	9.088	0.0183	-0.263	45.47	4.642	3.569	1.072
61.24	7	2.646	1.787	0.845	0.423	8.749	0.0163	-0.213	38.76	4.642	3.384	1.257
65.91	8	2.828	1.819	0.903	0.452	8.239	0.0152	-0.181	34.09	4.642	3.242	1.399
72.37	9	3.000	1.860	0.954	0.477	8.041	0.0138	-0.140	27.63	4.642	3.023	1.618
78.66	10	3.162	1.896	1.000	0.500	7.866	0.0127	-0.104	21.34	4.642	2.774	1.868
85.89	11	3.317	1.934	1.041	0.521	7.808	0.0116	-0.066	14.11	4.642	2.416	2.225
99.24	12	3.464	1.997	1.079	0.540	8.270	0.0101	-0.003	0.76	4.642	0.913	3.729

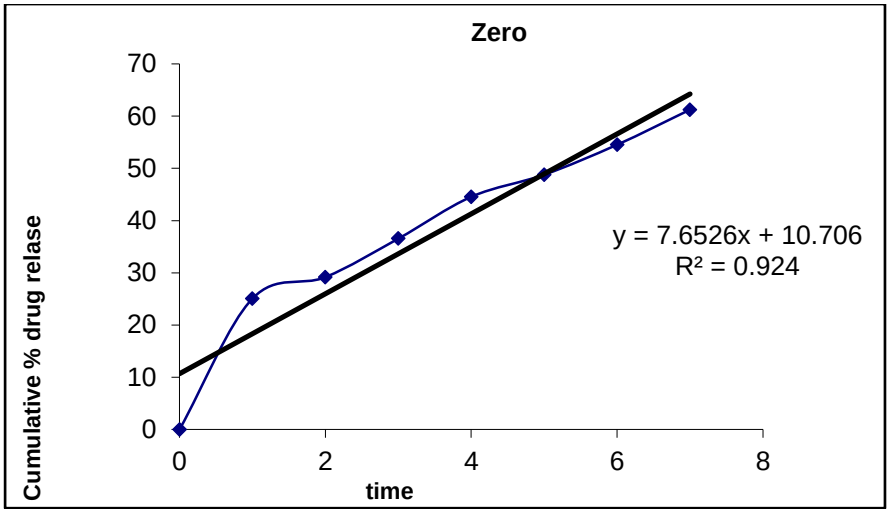

Fig 8.8: Graph of zero order kinetics

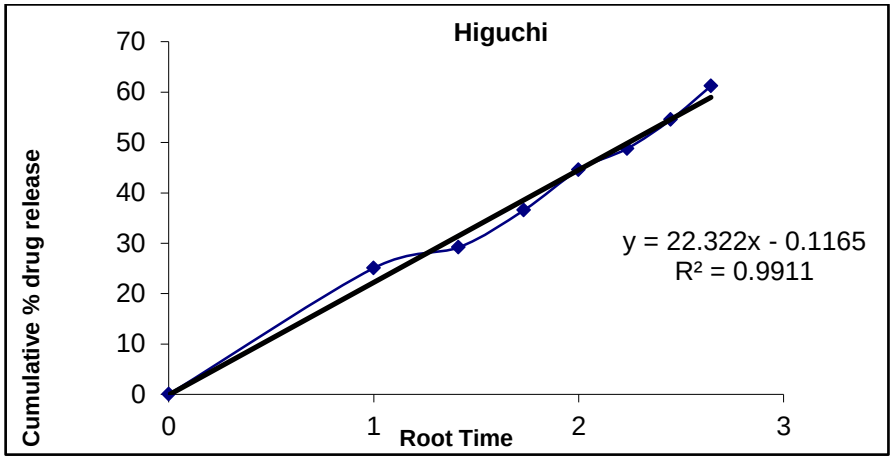

Fig 8.9: Graph of Higuchi release kinetics

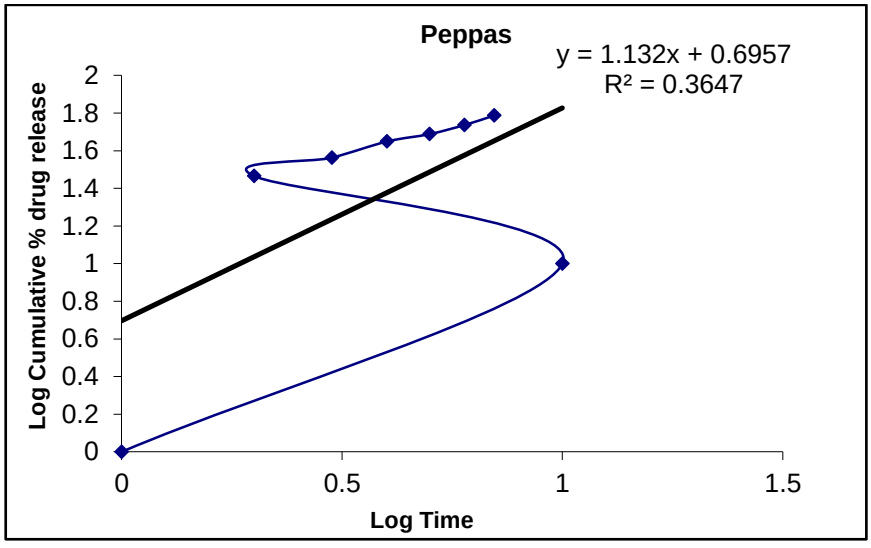

Fig 8.10: Graph of Peppas release kinetics

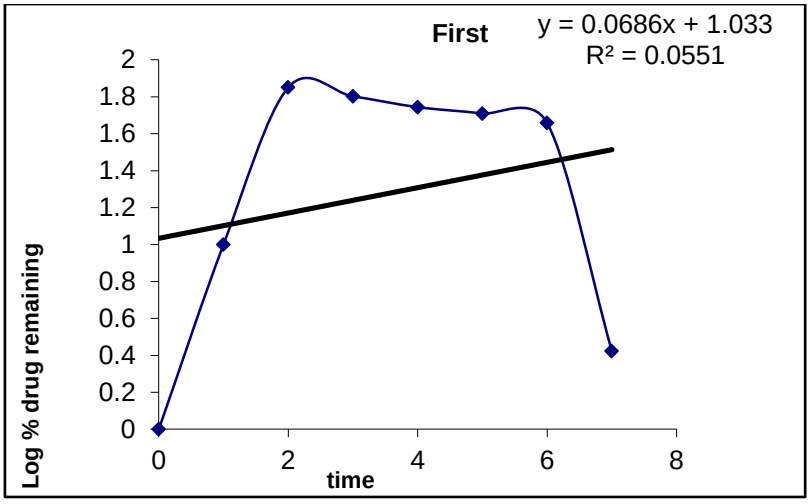

Fig 8.11: Graph of first order release kinetics

Based on the data above results the optimized formulation followed **first order** release kinetics.

Drug – Excipient compatibility studies

Fourier Transform-Infrared Spectroscopy:

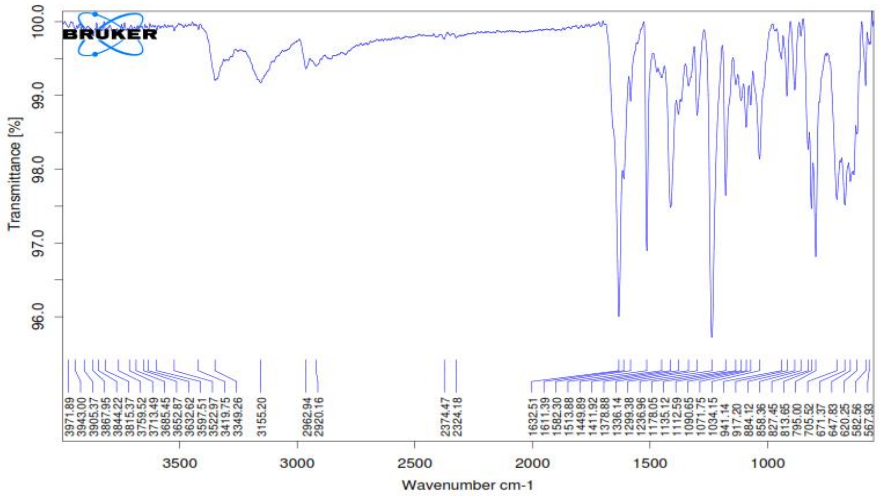

Fig 8.12: FT-TR Spectrum of Amantadine pure drug.

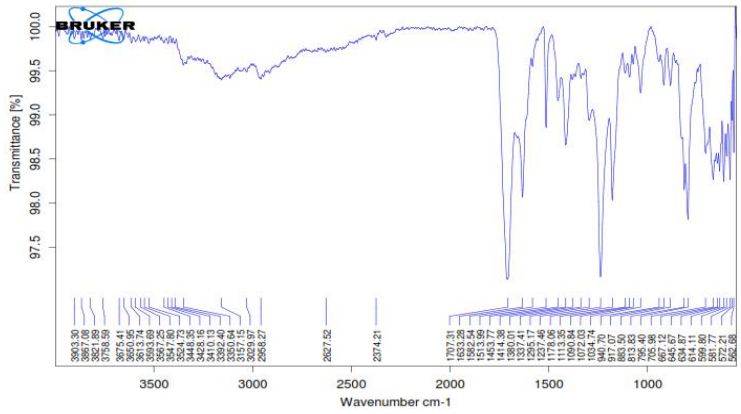

Fig 8.13: FT-IR Spectrum of Optimized Formulation

There is no incompatibility of pure drug and excipients. There is no disappearance of peaks of pure drug and in optimized formulation.

SEM

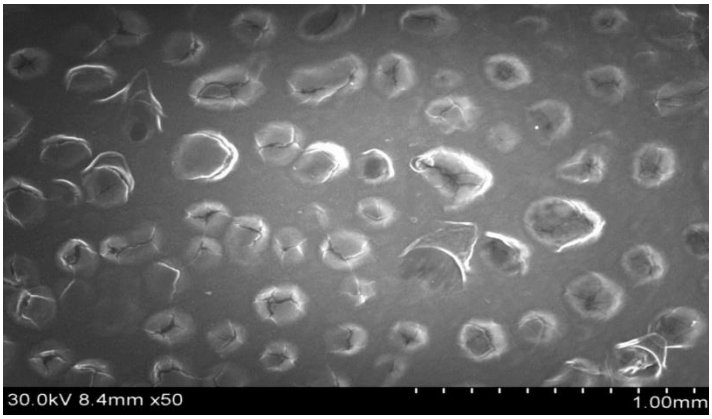

Fig 8.14: SEM graph of optimized formulation

SEM studies showed that the Amantadine - loaded nanoparticles had a spherical shape with a smooth surface as shown in Figure.

XRD

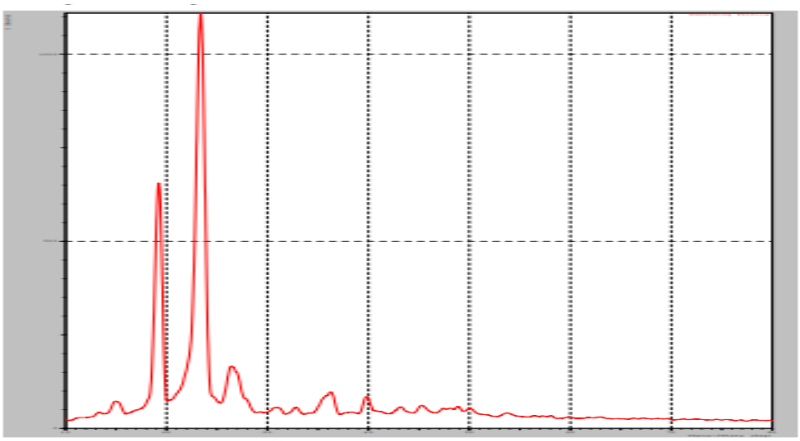

Fig 8.15: Amantadine F3 optimized formulation

9. CONCLUSION

In this study, amantadine-loaded nanoparticles were successfully formulated and evaluated with the objective of improving the drug's delivery and therapeutic performance. The prepared nanoparticle formulation demonstrated desirable physicochemical characteristics, including appropriate particle size, good encapsulation efficiency, and satisfactory stability. Evaluation studies confirmed that the nanoparticles provided a controlled and sustained drug release profile compared to the conventional formulation.

Overall, the results indicate that nanoparticle-based delivery of amantadine is a promising approach for enhancing bioavailability and optimizing drug release. The developed formulation may contribute to improved therapeutic efficacy and patient compliance.

ACKNOWLEDGEMENT

The Authors are thankful to the Management and Principal, Brilliant Grammar School Educational Society's Group of Institutions (Engineering and Pharmacy), Abdullapur (V), Abdullapurmet (M), Rangareddy (D), Hyderabad., for extending support to carry out the research work. Finally, the authors express their gratitude to the Sura Pharma Labs, Dilsukhnagar, Hyderabad, for providing research equipment and facilities.

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