



CODEN [USA]: IAJ PBB

ISSN : 2349-7750

**INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES**

SJIF Impact Factor: 7.187

<https://doi.org/10.5281/zenodo.23345645>Available online at: <http://www.iajps.com>

Research Article

**FORMULATION AND EVALUATION OF SOLID LIPID
FORMULATION AND IN VITRO EVALUATION OF
ASENAPINE MALEATE USING NANOPARTICLES****Pravat Ranjan Guru, Kumar Tanmaya Sahoo, Sayed Tashkilur Rashedin, Satya
Ranjan Dalai, Rajat Kumar Kar**Department Of Pharmaceutics, Dadhichi College Of Pharmacy,
Vidya- Vihar, Sundargram, Odisha 754002.**Abstract:**

Asenapine Maleate is an atypical antipsychotic drug used in the management of schizophrenia and bipolar disorder. However, its therapeutic effectiveness is limited by extensive first-pass metabolism and poor oral bioavailability, necessitating the development of an advanced drug delivery system capable of improving drug release and therapeutic efficacy. The present study was undertaken to formulate and evaluate Asenapine Maleate-loaded nanoparticles using different polymers at varying drug-to-polymer ratios to achieve a sustained drug release profile.

Nanoparticle formulations (F1–F9) were prepared using suitable polymers in different concentrations and ratios. Prior to formulation, compatibility studies between the drug and excipients were carried out and confirmed the absence of significant drug–excipient interactions. The prepared formulations were evaluated for pre-compression parameters, including angle of repose, bulk density, tapped density, Carr's index, and Hausner's ratio. The results indicated good flowability and compressibility, with all values falling within the acceptable limits specified by the Indian Pharmacopoeia (IP), ensuring suitability for further processing.

The formulated nanoparticles were subjected to comprehensive post-formulation evaluation, including percentage yield, particle size, zeta potential, drug content, entrapment efficiency, surface morphology, and in vitro drug release studies. All formulations exhibited satisfactory physicochemical properties, with the evaluated parameters remaining within acceptable IP limits. The type and concentration of polymers had a marked influence on nanoparticle characteristics and drug release behaviour. An increase in polymer concentration resulted in enhanced entrapment efficiency and prolonged drug release due to the formation of a denser polymeric matrix.

Among all the formulations, F6 was identified as the optimized formulation because it exhibited the most desirable sustained-release profile. The optimized formulation achieved a cumulative drug release of 99.48% over 12 hours, indicating effective control of drug release while maintaining formulation stability and acceptable pharmaceutical characteristics. The release profile suggested that the selected polymer combination and optimized drug-to-polymer ratio were suitable for sustaining the release of Asenapine Maleate over an extended period.

Keywords: Asenapine Maleate, Nanoparticles

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Please cite this article in press **Pravat Ranjan Guru et al., Formulation And Evaluation Of Solid Lipid
Formulation And In Vitro Evaluation Of Asenapine Maleate Using Nanoparticles.,. Indo Am. J. P. Sci, 2026;
13(10).**

INTRODUCTION:

The development of a wide spectrum of nanoscale technologies is beginning to change the scientific landscape in terms of disease diagnosis, treatment, and prevention. These technological innovations, referred to as nanomedicines by the National Institutes of Health, have the potential to turn molecular discoveries arising from genomics and proteomics into widespread benefit for patients. Nanoparticles can mimic or alter biological processes (e.g., infection, tissue engineering, de novo synthesis, etc.). These devices include, but are not limited to, functionalized carbon nanotubes, nanomachines (e.g., constructed from interchangeable DNA parts and DNA scaffolds), nanofibers, self-assembling polymeric nanoconstructs, nanomembranes, and nano-sized silicon chips for drug, protein, nucleic acid, or peptide delivery and release, and biosensors and laboratory diagnostics.

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Drug delivery systems (DDSs) have been used in past eras to treat numerous ailments. All medicines rely on pharmacologic active metabolites (drugs) to treat diseases.² Some of the drugs are designed as the inactive precursor, but they become active when transformed in the body. Their effectiveness depends on the route of administration. In conventional drug delivery systems (CDDSs), drugs were delivered usually via oral, nasal, inhaled, mucosal, and shot methods.³ The conventionally delivered drugs were absorbed less, distributed randomly, damaged unaffected areas, were excreted early, and took a prolonged time to cure the disease. They were less effective due to many hurdles like their enzymatic degradation or disparity in pH, many mucosal barriers, and off-the-mark effects, and their immediate release enhanced toxicity in blood.⁴

Due to all such reasons, the controlled-release drug delivery system was developed. Such evolution in

the DDS enhances drug effectiveness in many ways.⁵ DDSs have been engineered in recent years to control drug release. Such engineered DDSs used various novel strategies for controlled drug release into the diseased areas. These strategies were erodible material, degradable material, matrix, hydrogel, osmotic pump, and reservoir.⁶ They all provided a medium for the medicines to deliver at the desired sites like tissues, cells, or organs. In these approaches, drugs are often available for many diseases. Such strategies were unsuccessful due to lower distribution, less solubility, higher drug aggregation, less target selection, and poor effects for disease treatment.⁷ Moreover, drug development is the most expensive, intricate, and time-consuming process. The innovative drug findings involved the identification of new chemical entities (NCEs), having the vital distinguishing characteristics of drug capacity and pharmaceutical chemistry. This methodology, however, was confirmed to be less effective in terms of the overall attainment percentage.⁸ As 40% of drug development was botched due to its changeable responses and unpredicted noxiousness in humans. From past decades until now, drug development and its delivery are shifting from the micro to the nano level to prolong life expectancy by revolutionizing drug delivery systems.

Nanomedicine is a relatively new discipline that arises from the intersection between nanotechnology and medicine. It is based on the control of matter at the nanometer scale for applications in the field of human health. The use of materials in this range has been a great advance for the pharmacology by modifying fundamental properties of the drugs such as solubility, diffusivity, half-life in the bloodstream and drug release and distribution profiles. Although the production and use of nano-sized matter dates from hundreds of years, nanomedicine as a modern interdisciplinary science was first established at the end of the last century. Many authors consider the beginning of nanotechnology in the famous lecture of the physicist and Nobel laureate Richard P. Feynman in 1959 for the American Physical Society entitled: "There's Plenty of Room at the Bottom: An Invitation to Enter a New Field of Physics". In it, Feynman presented a futuristic vision of technology that leads towards the atomic scale and towards the final limits established by physical laws. Revolutionary ideas were put forward, such as reducing the integrated circuits of a computer to diameters between 10 and 100 atoms. To understand the scope of his predictions, suffice it to remember that, at the time of presenting these ideas, a computer occupied an entire room if not several. However, the word (or the prefix) nano was not mentioned even once in his presentation, Feynman stuck to describing the miniaturization of machines and its

possible applications. The honor of having coined the term “nano” is awarded to Norio Taniguchi, for his presentation “On the basic concept of nanotechnology” in 1974.

It is important to emphasize that the term nanotechnology applied to the study of nanoparticles simply consists in renaming the study of colloidal dispersions, in which field the contributions of renowned scientists such as Michael Faraday stand out, who in 1857 disseminated the first synthesis of gold nanoparticles and other metals.⁹ In the paper,

Faraday reveals his amazement at the changes in the optical properties of metallic colloidal dispersions. These properties were later explained in 1908 by Gustav Mie who would give a solution to Maxwell's equations for particles with a finite volume. In 1925, Richard Zsigmondy would be awarded the Nobel Prize in Chemistry for his demonstration of the heterogeneous nature of colloidal dispersions.¹⁰ His contributions in methodological terms have become fundamental for the study of modern colloidal chemistry and nanotechnology.

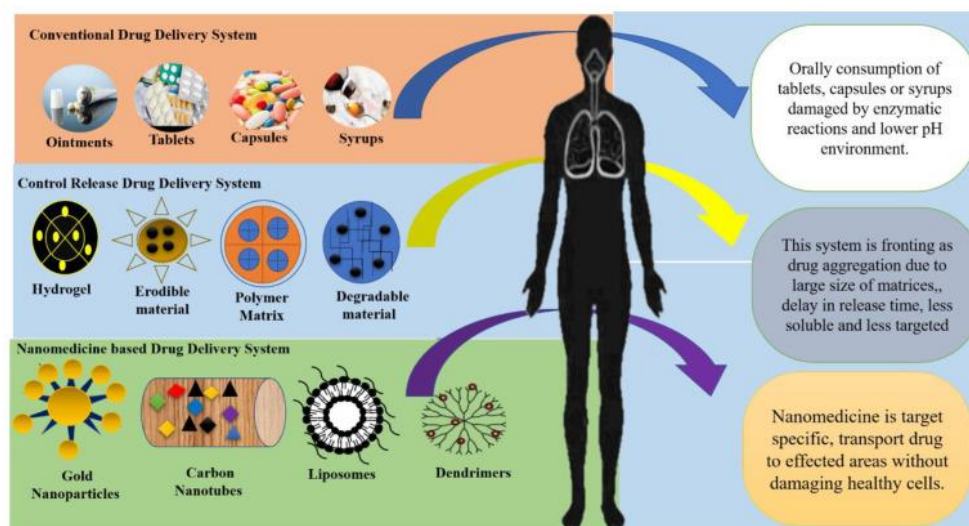


Figure 1.1 Illustration of how traditional medications were administered without the use of nanocarriers and harm was done to healthy organs or cells. In contrast, modern procedures use nanomedicines to transport medications to specific parts of the body.

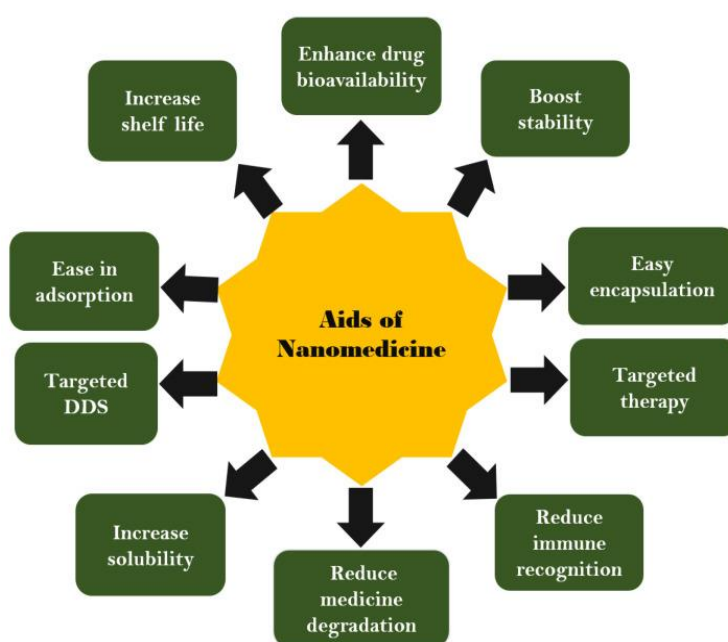


Figure 1.2 Aids of using nanomedicine platform for delivering drugs to the tumor complex.

The field of nanotechnology is one of the fastest-growing areas of scientific research and development, with significant advances being made in a range of applications.

MATERIALS:

Sin	Materials	Manufacturer / Supplier
1.	Asenapine Maleate	Sura Labs, Dilsukhnagar, Hyderabad
2.	Eudragit L 100	Lactel, Durect corporation Birmingham Division
3.	Eudragit RS 100	Eastman company, UK
4.	Poloxamer 188	SRL
5.	Tween 80	Himedia
6.	PVP K 30	Rankem
7.	Acetone	Rankem

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 220 nm 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 Asenapine was prepared in Methanol and subsequent working standards (5, 10, 15, 20 and 25µg/mL) were

prepared by dilution with phosphate buffer of pH-5.5. These solutions were used for the estimation Asenapine 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 Asenapine loaded nanoparticles

Asenapine loaded Nanoparticle was prepared by previously reported emulsification sonication method. Asenapine 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/cm³, 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
Asenapine Maleate (mg)	20	20	20	20	20	20	20	20	20
Eudragit L 100 [mg]	20	40	60	-	-	-	-	-	-
Eudragit RS 100 [mg]	-	-	-	20	40	60	-	-	-
Poloxamer 188 [mg]	-	-	-	-	-	-	20	40	60
Tween 80 [mg]	15	15	15	15	15	15	15	15	15
PVP K 30 [mg]	10	10	10	10	10	10	10	10	10
Acetone [ml]	5	5	5	5	5	5	5	5	5

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:

Asenapine 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 220 nm 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

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

Entrapment Efficiency:

Entrapment Efficiency (EE) of the Asenapine 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 cutoff 100KD (Pall

existence sciences-India) at 5000rpm for 15min at 40c, and therefore the supernatant was separated. The amount of Asenapine inside the supernatant changed into determining the usage of a UV-Visible spectrophotometer (U-1800, Hitachi) at lambda max 220nm after suitable dilution.

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

$$\%EE = \frac{\text{Total drug content} - \text{Free drug}}{\text{Total drug content}} \times 100$$

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°C. 5ml of samples were withdrawn periodically and replaced with fresh buffer. The withdrawn samples were periodically diluted and analysed for drug .

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 220 nm.

b. Calibration curve

Graphs of Asenapine Maleate was taken in 7.4 Phosphate buffer

Table 8.1: Calibration curve data for Asenapine Maleate at 220 nm

Concentrations [µg/mL]	Absorbance
0	0
5	0.114
10	0.232
15	0.341
20	0.462
25	0.568

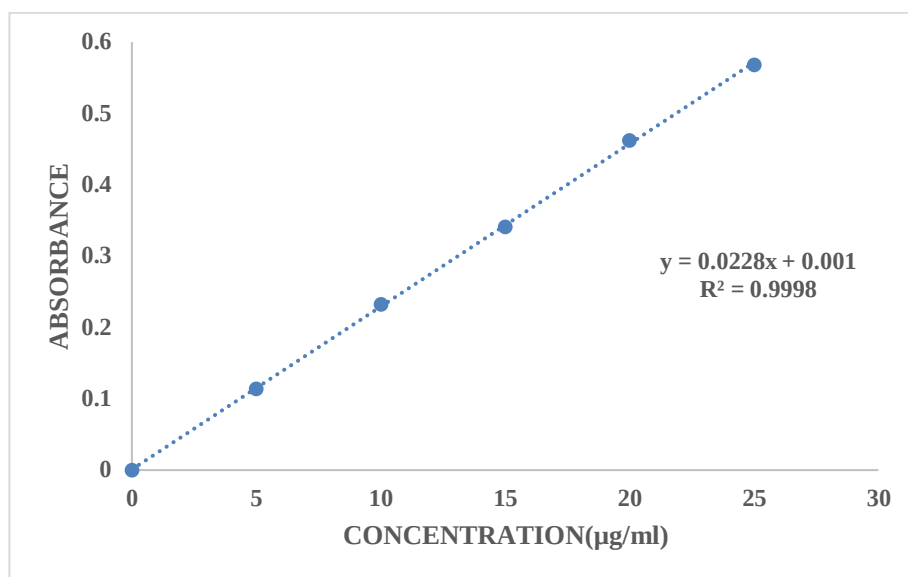


Fig 8.1: Standard graph of Asenapine Maleate in 7.4 Phosphate buffer

Standard graph of Asenapine Maleate 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 Asenapine Maleate showed good

linearity with R^2 of 0.998, which indicates that it obeys “Beer- Lamberts” law.

EVALUATION OF ASENAPINE MALEATE 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	286.12 ± 18	68.14	93.51	63.92	0.668	-26.12 ± 1.8
F2	292.22 ± 19	71.54	95.81	72.29	1.268	-28.22 ± 1.9
F3	305.19 ± 16	75.92	97.65	80.41	1.153	-30.19 ± 1.6
F4	267.22 ± 20	75.20	91.54	76.91	0.868	-27.22 ± 2.0
F5	278.56± 18	79.81	94.82	82.83	0.577	-28.56± 1.8
F6	281.72± 23	86.34	98.84	87.92	0.309	-32.61± 2.3
F7	351.72± 23	73.92	95.14	62.79	0.498	-25.72± 2.3
F8	368.32± 42	77.69	97.14	70.30	0.385	-26.32± 2.2
F9	371.52± 32	83.44	97.82	76.98	0.325	-27.52± 2.4

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 F6 formulation i.e., 0.309 respectively. The Zeta potential range from -25.72 mV to -32.61 mV to all the formulations.

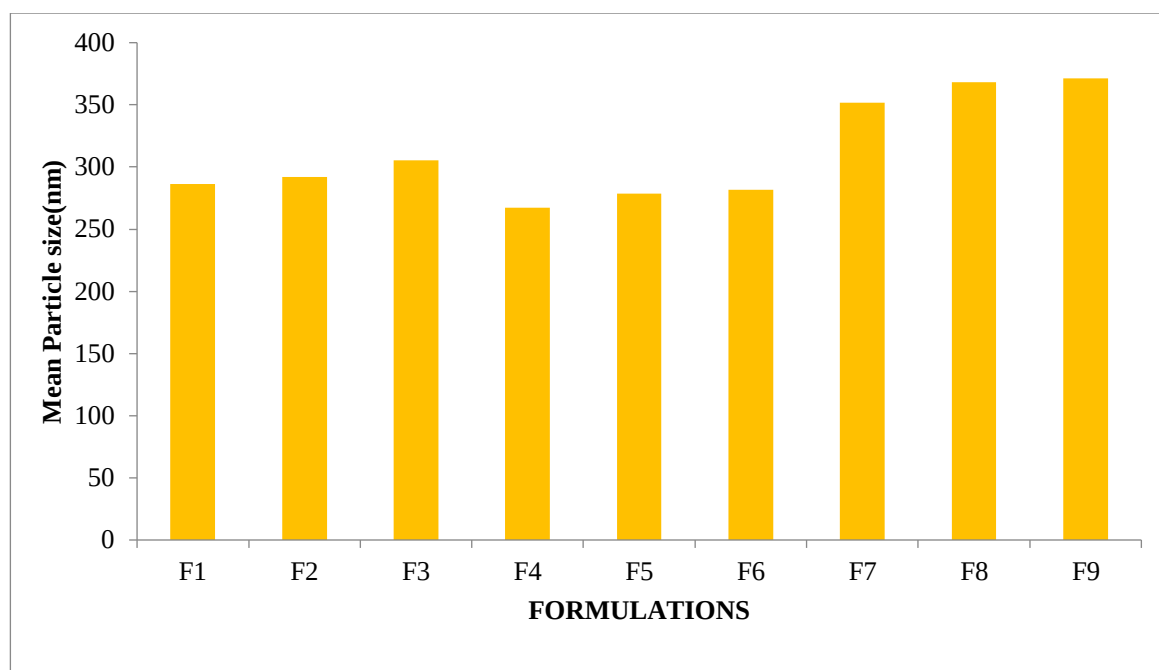


Fig 8.2: Mean Particle size (nm)

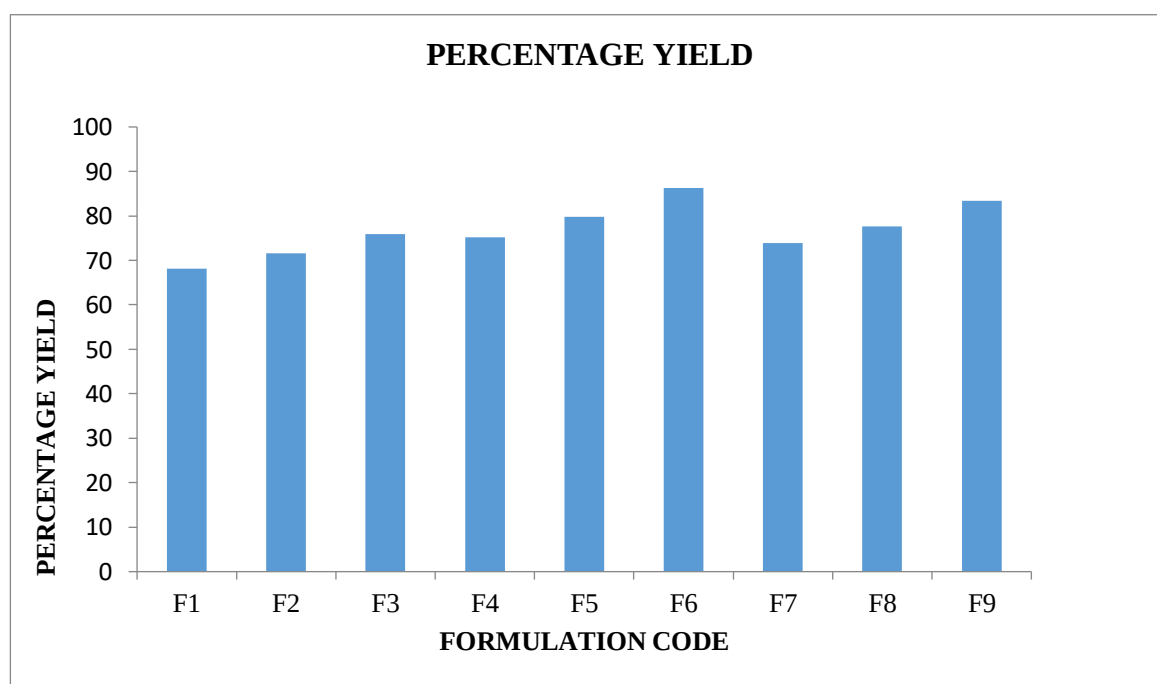


Fig 8.3: %Yield

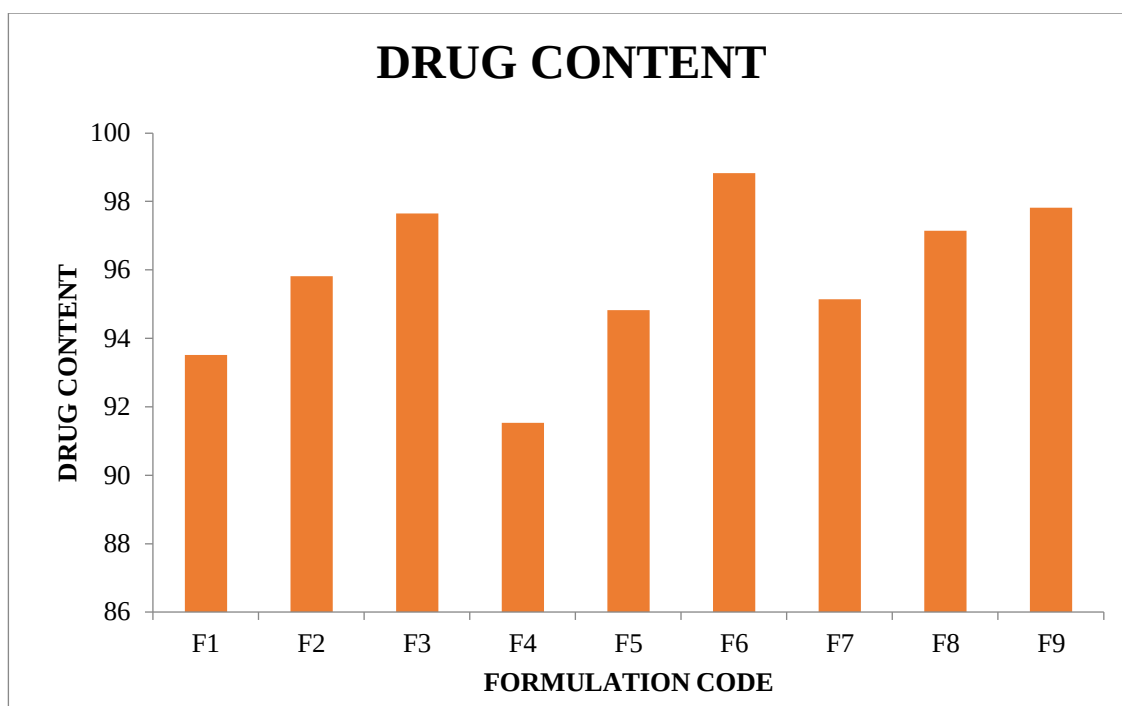


Fig 8.4: Drug content

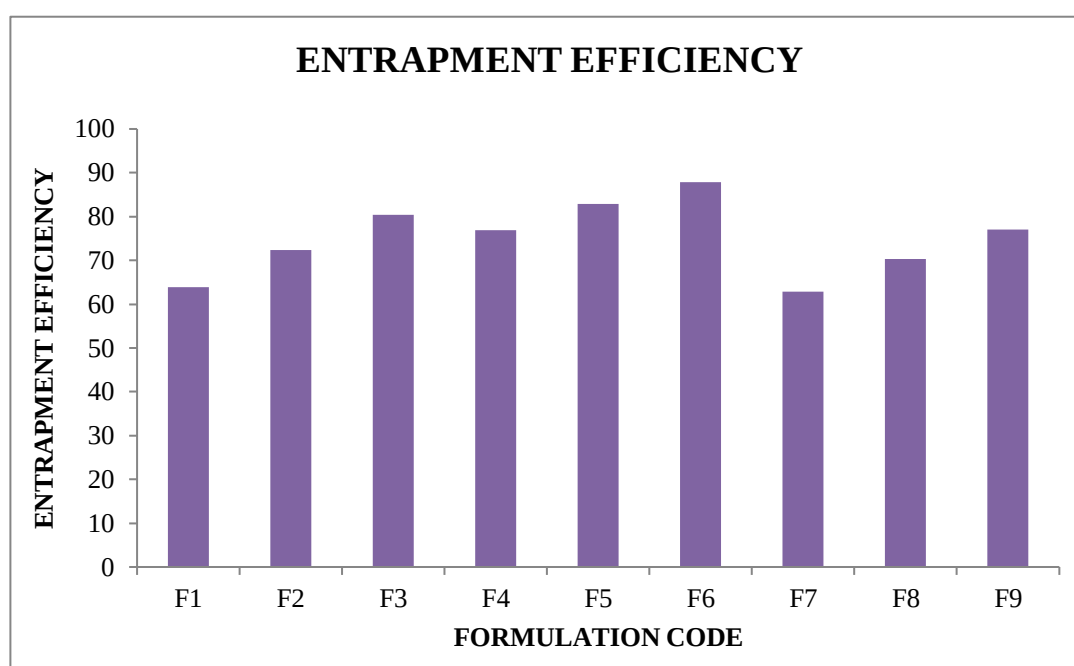


Fig 8.4: Drug encapsulation efficiency

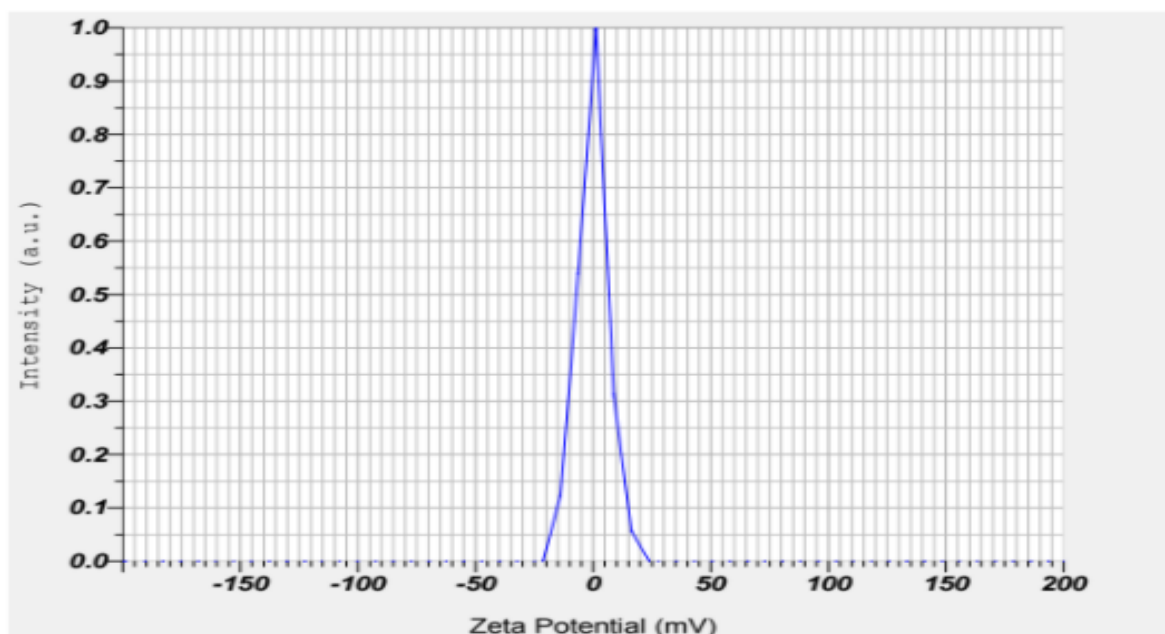
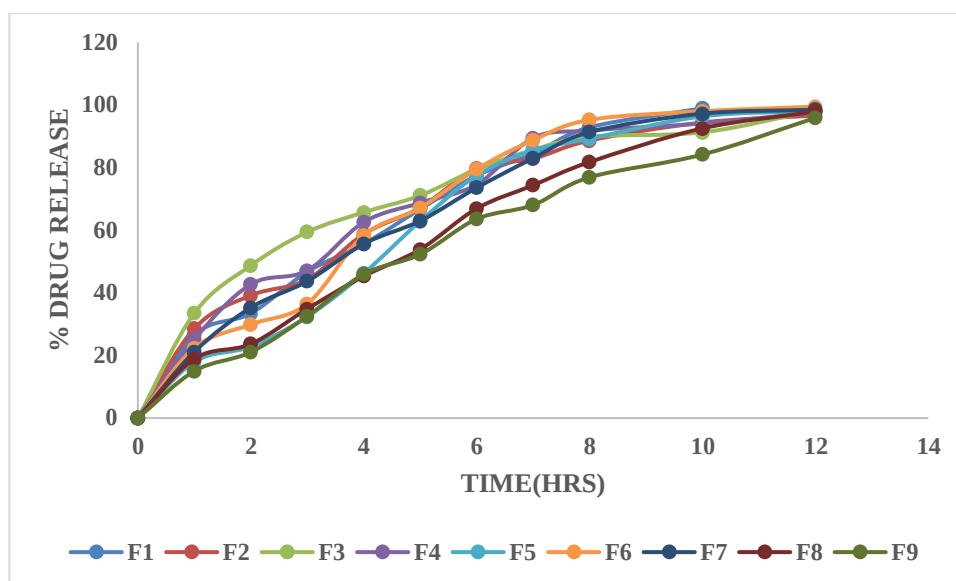


Fig 8.5: Zeta Potential of F6 Formulation

In vitro* Drug release studies:*Table 8.3: *In vitro* Drug release studies of Asenapine Maleate**

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	26.53	28.58	33.52	25.14	17.96	22.37	21.13	18.93	15.02
2	33.45	39.18	48.74	42.73	22.82	29.89	35.27	23.66	21.08
3	46.71	44.27	59.45	47.13	32.42	36.47	43.72	34.88	32.52
4	55.62	58.76	65.72	62.58	46.22	58.35	55.64	45.33	45.97
5	66.73	67.21	71.09	68.76	62.89	67.14	62.99	53.88	52.32
6	77.45	79.75	79.48	74.59	77.47	79.52	73.57	66.91	63.58
7	84.37	82.87	85.67	89.44	85.51	88.77	82.98	74.37	68.05
8	92.88	88.65	89.88	91.86	89.25	95.26	91.34	81.78	76.92
10	98.93	94.42	91.29	94.12	96.38	98.04	97.25	92.54	84.19
12		96.65	98.25	97.65	98.12	99.48	98.51	97.92	95.92



CONCLUSION:

The present study on the formulation and in vitro evaluation of Asenapine Maleate nanoparticles successfully demonstrated that nanoparticles can be effectively prepared using different polymers at varying drug-to-polymer ratios to enhance the physicochemical and pharmaceutical properties of the drug. The selection of suitable polymers and optimization of their concentrations played a significant role in influencing particle size, entrapment efficiency, drug release, and overall formulation performance.

The pre-formulation studies confirmed that Asenapine Maleate was compatible with the selected excipients and polymers, with no significant drug-excipient interactions observed. The pre-compression parameters, including angle of repose, bulk density, tapped density, Carr's index, and Hausner's ratio, indicated satisfactory flow characteristics and compressibility of the nanoparticle blends, making them suitable for further processing. All evaluated parameters were found to be within the acceptable limits prescribed by the Indian Pharmacopoeia (IP).

The prepared nanoparticle formulations were subjected to comprehensive post-formulation evaluation, including particle size analysis, percentage yield, drug content, entrapment efficiency, zeta potential, surface morphology, and in vitro drug release studies. The formulations exhibited acceptable physicochemical characteristics, with all post-compression/post-formulation parameters complying with IP specifications. Among the various polymer combinations and drug-to-polymer ratios evaluated, one optimized formulation demonstrated superior performance by producing nanoparticles with high drug entrapment efficiency, uniform particle size distribution, good stability, and a controlled,

sustained drug release profile compared to the other formulations.

The in vitro drug release studies confirmed that polymer type and concentration significantly influenced the release behaviour of Asenapine Maleate. Increasing the polymer concentration generally resulted in prolonged drug release due to the formation of a denser polymeric matrix, thereby providing sustained release over an extended period. The optimized formulation exhibited the highest cumulative drug release with desirable release kinetics, suggesting improved therapeutic potential and reduced dosing frequency.

Overall, the study concludes that nanoparticle formulation is a promising drug delivery approach for Asenapine Maleate. The optimized polymeric nanoparticle formulation demonstrated satisfactory pharmaceutical characteristics, controlled drug release, and compliance with Indian Pharmacopoeial standards. These findings suggest that nanoparticle-based delivery systems have the potential to improve the bioavailability, therapeutic efficacy, and patient compliance of Asenapine Maleate.

ACKNOWLEDGEMENT:

The Authors are thankful to the Management and Principal, Dadhichi College Of Pharmacy, Vidya-Vihar, Sundargram, Odisha. 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.

REFERENCES:

1. Kreuter J. Encyclopaedia of Pharmaceutical Technology. Marcel Dekker Inc.; New York, USA: 1994a. Nanoparticles; pp. 165–190.

2. Li S., Zhang H., Chen K., Jin M., Vu S.H., Jung S., He N., Zheng Z., Lee M.S. Applicatio of chitosan/alginate nanoparticle in oral drug delivery systems: Prospects and challenges. *Drug Deliv.* 2022;29:1142–1149. doi: 10.1080/10717544.2022.2058646.
3. Tibbitt M.W., Dahlman J.E., Langer R. Emerging frontiers in drug delivery. *J. Am. Chem. Soc.* 2016;138:704–717. doi: 10.1021/jacs.5b09974.
4. Alshammari M.K., Alshehri M.M., Alshehri A.M., Alshlali O.M., Mahzari A.M., Almalki H.H., Kulaybi O.Y., Alghazwani M.K., Kamal M., Imran M. Camptothecin loaded nano-delivery systems in the cancer therapeutic domains: A critical examination of the literature. *J. Drug Deliv. Sci. Technol.* 2022;79:104034. doi: 10.1016/j.jddst.2022.104034.
5. Lai H., Liu S., Yan J., Xing F., Xiao P. Facile Fabrication of Biobased Hydrogel from Natural Resources: L-Cysteine, Itaconic Anhydride, and Chitosan. *ACS Sustain. Chem. Eng.* 2020;8:4941–4947. doi: 10.1021/acssuschemeng.0c00774.
6. Smolensky M.H., Peppas N.A. Chronobiology, drug delivery, and chronotherapeutics. *Adv. Drug Deliv. Rev.* 2018;9–10:828–851.
7. Mak K.K., Pichika M.R. Artificial intelligence in drug development: Present status and future prospects. *Drug Discov. Today.* 2019;24:773–780. doi: 10.1016/j.drudis.2018.11.014.
8. Jain K.K. Drug delivery systems—An overview. *Drug Deliv. Syst.* 2008;437:1–50.
9. Faraday M. Experimental relations of gold (and other metals) to light. *Philos Trans R Soc London.* 1857 Dec;147(0):145-181.
10. Richard Zsigmondy. Properties of colloids. *Nobel Lect.* 1926;1:1.
11. Thi T.T., Suys E.J., Lee J.S., Nguyen D.H., Park K.D., Truong N.P. Lipid-based nanoparticles in the clinic and clinical trials: From cancer nanomedicine to COVID-19 vaccines. *Vaccines.* 2021;9:359. doi: 10.3390/vaccines9040359.
12. Zhang H., Zhang L., Zhong H., Niu S., Ding S., Lv S. Iridium oxide nanoparticles-based theranostic probe for in vivo tumor imaging and synergistic chem/photothermal treatments of cancer cells. *Chem. Eng. J.* 2022;430:132–675. doi: 10.1016/j.cej.2021.132675.
13. Komarova Y.A., Kruse K., Mehta D., Malik A.B. Protein Interactions at Endothelial Junctions and Signaling Mechanisms Regulating Endothelial Permeability. *Circ. Res.* 2017;120:179–206. doi: 10.1161/CIRCRESAHA.116.306534.
14. Sahni J.K., Doggui S., Ali J., Baboota S., Dao L., Ramassamy C. Neurotherapeutic applications of nanoparticles in Alzheimer's disease. *J. Control. Release.* 2012;152:208–231. doi: 10.1016/j.jconrel.2010.11.033.
15. . Wilson B., Samanta M.K., Santhi K., Kumar K.P.S., Paramakrishnan N., Suresh B. Targeted delivery of tacrine into the brain with polysorbate 80-coated poly(n-butylcyanoacrylate) nanoparticles. *Eur. J. Pharm. Biopharm.* 2008;70:75–84. doi: 10.1016/j.ejpb.2008.03.009.
16. . Yusuf M., Khan M., Khan R.A., Ahmed B. Preparation, characterization, in vivo and biochemical evaluation of brain targeted Piperine solid lipid nanoparticles in an experimentally induced Alzheimer's disease model. *J. Drug Target.* 2013;21:300–311. doi: 10.3109/1061186X.2012.747529.
17. Zimmermann E., Müller R.H., Mader K. Influence of different parameters on reconstitution of lyophilized SLN. *Int. J. Pharm.* 2000;196:211–213. doi: 10.1016/S0378-5173(99)00424-X.