

Solubility enhancement of Carvedilol Polymeric Nanoparticles by Nanoprecipitation Technique

Ms. Mallika Tamminana^{1*}, and B.V.V. Ravikumar²

^{1,2}Ph.D. Research Scholar, Pharmacy, Biju Patnaik University of Technology, Rourkela, Roland Institute of Pharmaceutical Sciences, Berhampur-760010, Odisha, India

^{1*}mallikatamminana@gmail.com

Received: 4th Sep, 2025; Revised: 24th Oct 2025; Accepted: 6th Nov, 2025; Available Online: 1st December, 2025

ABSTRACT

Carvedilol is an anticancer drug which is used in treatment of breast cancer. But it has poor water solubility property. The research work is based on improvement of solubility by formulation and development of polymeric nanoparticles by nanoprecipitation technique. HPMCK15M is used as polymer and Polaxmer 407 is used as surfactant. After pre formulation study the drug interaction study is performed by FTIR and DSC analysis. After preparation various evaluation methods are adopted as per the specification. Evaluation method shows F6 formulation produce good entrapment capacity. The result of various kinetic studies is also acceptable. So we concluded that HPMCK15M is the appropriate polymer and Polaxmer 407 is the appropriate surfactant and nanoprecipitation is the best technique to enhance the stability of and able to enhance the anticancer activity.

Keywords: Carvedilol, Nanoprecipitation technique, HPMCK15M, Polaxmer 407

How to cite this article: Tamminana M, Ravikumar BVV; Solubility enhancement of Carvedilol Polymeric Nanoparticles by Nanoprecipitation Technique. Int J Drug Deliv Technol. 2026;16(1): 490-493. DOI: 10.25258/ijddt.16.1.52

Source of support: Nil.

Conflict of interest: None

INTRODUCTION

The size range of polymeric nanoparticles is from 1 to 1000 nm, and they are colloidal particles. [1] The oxidative stress, cytotoxicity, and genotoxicity toxicity [2]. are affected by polymeric NPs because of the quantum size effect [3]. It takes two solvents that are not incompatible to perform nanoprecipitation. Since they are insoluble in water, they are quickly depleted by evaporation. Placing the organic solvent out of a lipophilic solution and into an aqueous phase causes polymers to deposit at surfaces; this is the fundamental idea behind this method. Nanocapsules or nanospheres [4] of polymer precipitate out of nanodroplets when solvent diffuses from them [5]. Nanoparticle production is unaffected by switching the order of the phases. To stabilize colloidal suspensions, surfactants are commonly used, yet they are not required for nanoparticles production. [6, 7].

Through the absorption of polymeric nanoparticles which shows both internal and external stimuli, polymeric nanoparticles from a variety of nanostructures, including vesicles, hybrid nanoparticles, crosslinked nanoparticles, and micelles [8]. Polymeric nanoparticles may change their physical or chemical characteristics in reaction to one, two, or even more stimuli. They are able to target the affected area, keep their payloads in circulation [9].

MATERIALS AND METHODS

Materials:

Carvedilol is free sample collected from Reddy's Lab, Hyderabad, and required polymers as were collected from Sigma Aldrich of India.

Methods:

Pre formulation studies

Solubility Analysis

1 millilitre of ethanol is used as co-solvent. 0.1 N Hydrochloric acid of 9 ml is added with drug of 10 mg. Other components were investigated by the drug's quantitative solubility tests. Finally, it was shaken for about three hours. Then, it was possible to determine which solvents dissolved the medicine. "Taking 2 ml of each solvent and adding the medication till it reached its saturation point, the mixture was shaken for 3 hours to see whether it was completely soluble.

We then used a UV spectrophotometer to examine the filtrates from each solvent. Tabulated and shown in Figure 1 are the results of the solubility tests conducted on pure pharmaceuticals in various solvents.

Determination of λ_{max} of carvedilol

An ethanol-and-0.1N HCl combination was used to dissolve 100 mg of carvedilol in 90 ml to make the stock solution. Hence, 1000 μ g/liter. After that, 1 milliliter was collected and made into a solution containing 100

*Author for Correspondence: mallikatamminana@gmail.com

microgram's per litre. In the end, the UV technique was used to analyse it at λ_{max} 282nm.

Method of preparation of polymeric nanoparticles

Solvent evaporation and nanoprecipitation were used to create nanoparticles. The first thing to do is to measure out 1:3, 1:2, or 1:1 medication to water ratios. (20 milligrammes of medication): 20 milligramme polymer, 40 milligrammes of medication: (80 mg polymer, 60 mg medication) 5 millilitres of glacial acetic acid and acetone were used to dissolve 180 milligrammes of chitosan and HPMC K15M. A magnetic stirrer was used to combine the polymeric and drug solutions after 10 millilitres of acetone had been used to dissolve the pure prescription carvedilol. The solution of drug and polymer and 5 ml of the solution were combined. Then 20 ml of distilled were added. Slowly added the drug to the polymer mixture. Procedure is completed in one hour at 1000 rpm. Up until 20 ml of acetone remained. A capacity of 10 ml was specified. Then the product was freeze-dried for 36 hours to generate the nanoparticles.

IDENTIFICATION OF CHARACTERISTICS

Fourier Transform Infrared Spectroscopy

The solid substance (drug) should be ground into a fine powder using dry potassium bromide. Make sure the dosage is enough to cover the disc's area in terms of the substance's weight. Use a specialised die to place a little amount of the mixture and push it down under intense suction. Then, place the finished disc in an appropriate mount. Potassium bromide undergoes 45 IR scans. Scannable samples included both polymer-only and medication-containing formulations.

Entrapment Efficiency:

An additional 2 mL of each formulation was added to a centrifuge tube. We spun the sample for around 25 minutes at 8000 rpm after we got the tube. At the end of the 25-minute period, we carefully removed the tube from the centrifuge and observed if a layer of supernatant had formed above the sample. After that, 1 millilitre of the liquid's supernatant was carefully transferred to a test tube, and then 10 millilitres of solution containing ethanol and 0.1 N hydrochloric acid was added. Afterwards, the sample solution was examined using ultraviolet light at a wavelength of 281 nano meter .

Statistical analysis:

Statistical experiments are done by Design-Expert® (Version 12), a sophisticated statistical program developed by Stat-Ease Inc. of Minneapolis, MN, USA. Microsoft Excel 2007 (Microsoft, USA) was used to evaluate the data.

Optimization of process variables:

A number of formulation and preparative factors of the nanoprecipitation technology were investigated in order to regulate and improve the process. We conducted this experiment to see how various stabilizer concentrations, temperatures, and solvent/non-solvent ratios affected the nanoprecipitation of Carvedilol nanoparticles. We also

wanted to know how varied stirring rates affected nanoparticle production.

In-vitro diffusion study

0.1 N HCl of 150 ml is taken in each beaker. Then, via thread, about 5 millilitres of each formulation sample (F1–F9) was delivered to the dialysis membrane bag. Correct position of the dialysis membrane is maintained within the solution, spin it at 100 rpm using the magnetic stirrer. Start by pipetting 2 millilitres of the sample into the centrifuge tube at 0 hours. To keep the sink condition going, add 2 millilitres of 0.1 N HCl to the beaker. At 2,4,6,8,12, 18, and 24 hours, the same procedure was performed. At the end of the first 24 hours, after dividing the 2 millilitres of sample, 1 millilitre of sample was combined with 1 millilitre of ethyl acetate. Prior to setting aside for another fifteen minutes, the aforementioned solution was vortexed in a cyclo mixture. The liquid layer of supernatant was carefully transferred. Test tubes were prepared for ultraviolet (UV) analysis by adding the correct solvent after complete drying.

RESULTS AND DISCUSSION

Particle size analysis:

Particle size peaked in Run 11 at 1329.35 nm, or (1, 1), and peaked in Run 6 at 263.8 nm, or (-1, 0).

Entrapment efficiency:

This study examines how different process factors affect The amount of medication placed into polymeric matrices is known as the EE. The entrapped drug was 35.448, or (1,1). In run 11 and (-1, 0) in run 6. The percentage of entrapped pharmaceuticals reached its highest of 86.225%. There may be an effect on the formulation's stability due to the much lower zeta potential measurements taken for the individual formulations.

In vitro drug release

Cumulative Percentage Drug Release is presented in table No-2. In run 6, Cumulative Percentage Drug Release was 96.58%,.

CONCLUSIONS

The optimized polymeric nanoparticles formulation had a 99.5% entrapment rate . More than 90% of the medication was liberated" after 24 hour in in evaluation method using a sustained release profile. The results shows that the Carvedilol nanoparticles efficiently released their payload when suspended. The regulated release and improved solubility of hydrophobic medicines, such as Carvedilol, make NPs an ideal delivery vehicle.

REFERENCES

1. Jeevanandam J, Barhoum A, Chan YS, Dufresne A, Danquah MK. Review on nanoparticles and nanostructured materials: history, sources, toxicity and regulations. Beilstein J Nanotechnol. 2018; 9:1050-1074.
2. Crucho CIC, Barros MT. Polymeric nanoparticles: A study on the preparation variables and

- characterization methods. *Mater Sci Eng C Mater Biol Appl.* 2017; 80:771-784. doi: 10.1016/j.msec.2017.06.004. Epub 2017.
- Prabha AS, Dorothy R, Jancirani S, Rajendran S, Singh G, Kumaran SS. Chapter-7: Recent advances in the study of toxicity of polymer-based nanomaterials, Editor(s): Susai Rajendran, Anita Mukherjee, Tuan Anh Nguyen, Chandraiah Godugu, Ritesh K. Shukla, In *Micro and Nano Technologies, Nanotoxicity*, Elsevier, 2020, Page: 143-165.
 - Muddana Eswara Bhanaji Rao, Suryakanta Swain, and Sitty Manohar Babu. Chapter-8, *Polymeric nanoparticles as carrier for controlled release. Pharmaceutical Drug Delivery Systems and Vehicles.* Woodhead Publishing India Medicine Pvt. Ltd., an Elsevier imprint, India, 2015, ISBN: 9789385059001, 216-244.
 - Muddana Eswara Bhanaji Rao, Suryakanta Swain*, Chinam Niranjana Patra, Shakti Prasad Mund. Formulation design, optimization, and characterization of eprosartan mesylate nanoparticles. *Nanoscience & Nanotechnology-Asia.* 2018; 8(1): 130-143.
 - Zielinska A, Carreiro F, Oliveira AM, Neves A, Pires B, Venkatesh DN, Durazzo A, Lucarini M, Eder P, Silva AM, Santini A, Souto EB. Polymeric Nanoparticles: Production, Characterization, Toxicology and Ecotoxicology. *Molecules.* 2020;25(16):3731.
 - Sameer S. Sheikh & Shrikrishna K. Harkal & Rahul P. Gaikwad & Rahul W. Gawali & Dinesh P. Deshmukh, 2018. "Formulation and Evaluation of Polymeric Nanoparticles of Rifampicin for Anti-Tubercular Therapy, *Int J Healthcare Medical Sci.* Academic Research Publishing Group. 2018; 4(6), 117-122.
 - Kesarla R, Tank T, Vora PA, Shah T, Parmar S, Omri A. Preparation and evaluation of nanoparticles loaded ophthalmic in situ gel. *Drug Deliv.* 2016;23(7):2363-2370. doi: 10.3109/10717544.2014.987333.
 - Li Y, Gao GH, Lee DS. Stimulus-sensitive polymeric nanoparticles and their applications as drug and gene carriers. *Adv Healthc Mater.* 2013;2(3):388-417.
 - El-Say KM, Hosny KM. Optimization of carvedilol solid lipid nanoparticles: An approach to control the release and enhance the oral bioavailability on rabbits. *PLoS One.* 2018;13(8): e0203405. doi: 10.1371/journal.pone.0203405.
 - Singh B, Khurana L, Bandyopadhyay S, Kapil R, Katare OO. Development of optimized self-nano-emulsifying drug delivery systems (SNEDDS) of carvedilol with enhanced bioavailability potential. *Drug Deliv.* 2011;18(8):599-612. doi: 10.3109/10717544.2011.604686. Epub 2011.
 - Arun JK, Vodeti R, Shrivastava B, Bakshi V. Integrated Quality by Design Approach for Developing Nanolipidic Drug Delivery Systems of Olmesartan Medoxomil with Enhanced Antihypertensive Action. *Adv Pharm Bull.* 2020;10(3):379-388. doi: 10.34172/apb.2020.046. Epub 2020.
 - Mishra A, Imam SS, Aqil M, Ahad A, Sultana Y, Aameeduzzafar, Ali A. Carvedilol nano lipid carriers: formulation, characterization and in-vivo evaluation. *Drug Deliv.* 2016;23(4):1486-94. doi: 10.3109/10717544.2016.1165314. Epub 2016.
 - Ravikumar AA, Kulkarni PK, Osmani RAM, Hani U, Ghazwani M, Fatease AA, Alamri AH, Gowda DV. Carvedilol Precipitation Inhibition by the Incorporation of Polymeric Precipitation Inhibitors Using a Stable Amorphous Solid Dispersion Approach: Formulation, Characterization, and In Vitro In Vivo Evaluation. *Polymers (Basel).* 2022;14(22):4977. doi: 10.3390/polym14224977.
 - Selselehjonban S, Garjani A, Osouli-Bostanabad K, Tanhaei A, Emami S, Adibkia K, Barzegar-Jalali M. Physicochemical and pharmacological evaluation of carvedilol-eudragit® RS100 electrospayed nanostructures. *Iran J Basic Med Sci.* 2019;22(5):547-556. doi: 10.22038/ijbms.2019.34246.8139.
 - Xia D, Quan P, Piao H, Piao H, Sun S, Yin Y, Cui F. Preparation of stable nitrendipine nanosuspensions using the precipitation-ultrasonication method for enhancement of dissolution and oral bioavailability. *Eur. J. Pharm. Sci.* 2010; 40, 325-334

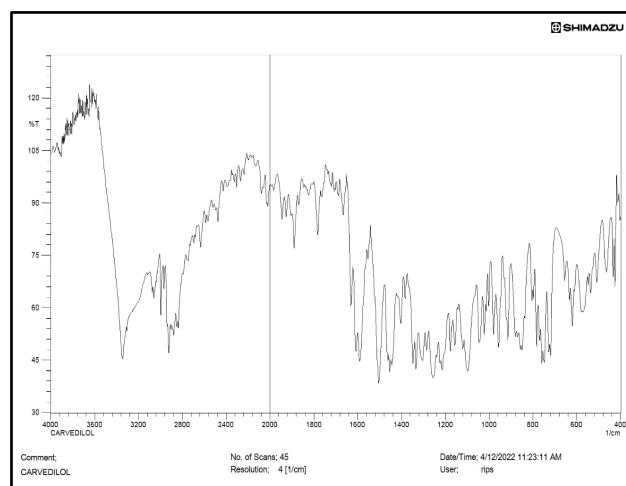


Figure-1. FT-IR -spectra of drug Carvedilol

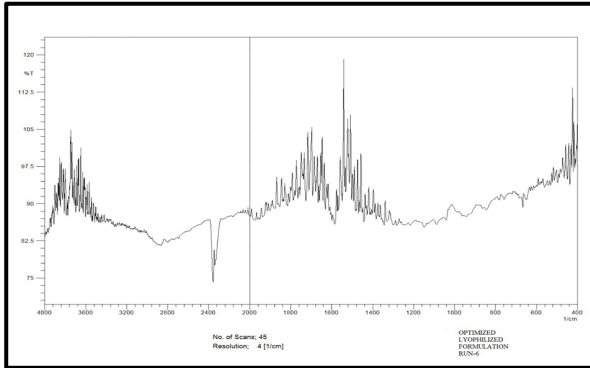


Figure-2. FT-IR spectra of mixture of carvedilol + poloxamer 407 + HPMC K15M + chitosan

Time vs Cumulative % drug release of formulations F1 to F13

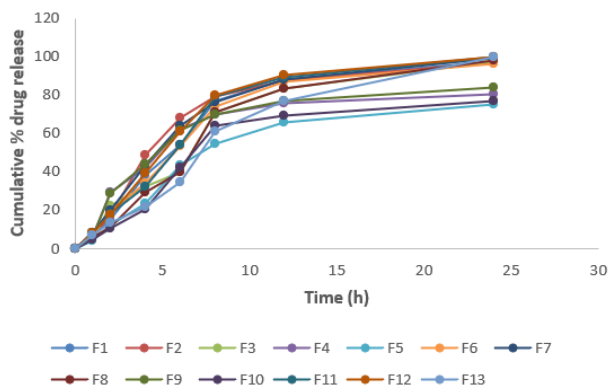


Fig: 3: Percentage of Drug Release of Formulations F1-F13

Table-1. Solubility Data Analysis of Pure Drug with different Solvents.

| SOLVENT NAME. | DILUTION FACTOR (DF) | ABSORBANCE (NM) | CONCENTRATION (µG/ML) | CONCENTRATION (MG/ML) |
|-------------------------|----------------------|-----------------|-----------------------|-----------------------|
| WATER | 100.0 | 0.33 | 14.83 | 1.48 |
| ACETONE | 100.0 | 0.02 | 1.83 | 0.18 |
| PHOSPHATE BUFFER PH 6.8 | 100.0 | 0.01 | 1.75 | 0.17 |

| | | | | |
|-------------------------|----------|-------|-------|---------|
| PHOSPHATE BUFFER PH 7.4 | 100.0 | 0.03 | 2.45 | 0.24 |
| 0.1N HCL | 100.0 | 0.01 | 1.54 | 4789.09 |
| METHANOL | 100.0 | 0.56 | 24.41 | 2.44 |
| N-OCTANOL | 100.0 | 0.16 | 7.91 | 0.79 |
| PEG-200 | 100.0 | 0.36 | 16.16 | 1.61 |
| PEG-400 | 10000.0 | 0.097 | 5 | 50 |
| DMSO | 10000.0 | 0.24 | 11.33 | 113.3 |
| Ethanol | 100000.0 | 0.57 | 24.70 | 2470.83 |

Table No-2- Cumulative Percentage Drug Release

| Time in (Hour) | Cumulative Percentage Drug Release | | | | | | | | | | | | |
|----------------|------------------------------------|---------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| | F-1 | F-2 | F-3 | F-4 | F-5 | F-6 | F-7 | F-8 | F-9 | F-10 | F-11 | F-12 | F-13 |
| 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 |
| 1 | ±6.393 | ±7.231 | ±4.837 | ±5.872 | ±4.215 | ±7.282 | ±8.221 | ±5.363 | ±5.863 | ±4.773 | ±8.323 | ±8.213 | ±6.123 |
| 2 | ±15.299 | ±16.923 | ±2.341 | ±2.221 | ±1.392 | ±1.927 | ±1.998 | ±1.122 | ±2.892 | ±1.327 | ±1.393 | ±1.482 | ±1.783 |
| 4 | ±38.331 | ±48.822 | ±3.341 | ±4.231 | ±2.382 | ±3.222 | ±4.221 | ±3.383 | ±4.783 | ±2.333 | ±3.343 | ±3.383 | ±2.633 |
| 6 | ±88.929 | ±67.789 | ±3.938 | ±6.289 | ±4.387 | ±5.728 | ±6.283 | ±3.839 | ±6.973 | ±4.333 | ±5.223 | ±6.383 | ±3.733 |
| 8 | ±93.929 | ±79.131 | ±7.387 | ±6.976 | ±5.439 | ±7.442 | ±7.222 | ±7.383 | ±6.978 | ±6.487 | ±7.333 | ±7.893 | ±6.233 |
| 12 | ±332.533 | ±87.453 | ±8.383 | ±7.828 | ±6.599 | ±8.237 | ±8.383 | ±8.983 | ±7.661 | ±6.223 | ±8.493 | ±9.343 | ±7.873 |
| 24 | ±389.738 | ±96.677 | ±9.707 | ±8.283 | ±7.539 | ±9.636 | ±9.833 | ±9.833 | ±8.361 | ±7.623 | ±9.933 | ±9.783 | ±9.768 |