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Research Article

Formulation and Evaluation Controlled Release Solid Lipid Microparticles of Antihypertensive Drug

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Abstract:

Objective: To prepare and optimize solid dispersion of isradipine, an antihypertensive drug with poor aqueous solubility using two different methods, namely, solvent evaporation and fusion.

Methods: Twenty-two formulas of isradipine solid dispersion were prepared using one of the following carriers: Poloxamer 407 (PXM 407), Polyethylene Glycol 4000 (PEG 4000), Polyethylene Glycol 6000 (PEG 6000) and urea at different carrier-to-drug ratios. The produced solid dispersion formulations were evaluated for their percentage yield, drug content, solubility, and in vitro dissolution. Further investigations were performed for the selected formula; these include Differential Scanning Calorimetry (DSC), and Powder X-Ray Diffraction (PXRD) studies to evaluate the crystalline state of the drug. Besides Fourier Transformation Infrared (FTIR) spectroscopy was conducted to evaluate drug-carrier compatibility.

Results: The results of this study showed that all the prepared formulas resulted in improvement in saturation solubility. Run 14 (which consists of PXM 407: isradipine in a 5:1 ratio) demonstrated a substantial increase in solubility, resulting in approximately 16 times higher solubility than the pure drug. The results of DSC and PXRD studies demonstrated complete dispersion of the drug in the carrier or amorphization of the drug. Furthermore, FTIR results indicated drug-carrier compatibility.

Conclusion: From this study, it was evident that solid dispersion of isradipine in the previously mentioned carriers is an effective and efficient method to enhance its solubility. The best solubility enhancement and release profile was observed in run 14 (which combines PXM 407: isradipine in a 5:1 ratio), which was selected as the optimum formula.

Keywords: Poloxamer 407, Isradipine, Dissolution rate, Solubility, Solid dispersion, polymer, Solvent evaporation.

Introduction

Many important pharmaceutical compounds for treatment of wide range of diseases suffer from poor aqueous solubility. This obstacle continues to be a major challenge to the formulators [1]. The water solubility of an orally administered drug highly determines its bioavailability. Low

solubility and dissolution rates make Biopharmaceutics Classification System (BCS) class II drugs difficult to develop into pharmaceutical products. Formulation development should focus on improving their solubility and dissolution rates [2]. Isradipine is a type of antihypertensive medication that belongs to the Dihydropyridine (DHP) calcium channel blocker class.

Its mechanism of action for managing hypertension (and, to some extent, angina) involves inhibiting calcium entry into the smooth muscle cells of the arteries [3]. Isradipine is practically water-insoluble (<10 mg/l at 37°C), but it is soluble in ethanol and freely in acetone and chloroform. It has a log p of 4.28 and an oral bioavailability of 15–24% [4]. The poor oral bioavailability of isradipine, a BCS class II drug, is due to its extensive first-pass metabolism and poor aqueous solubility (<10 mg/l) [5]. To address specific issues related to drug formulation, such as solubility, we can employ various techniques to alter the physical characteristics of drugs.

These techniques involve inclusion complexes, solid dispersion, surfactants, nanosuspension, particle size reduction, cocrystal formation, and salt formation [6]. Amorphous solid dispersions are widely used to improve the solubility and bioavailability of poorly water-soluble drugs [7]. The term "solid dispersion" refers to the concept of dispersing a drug in an inert, water-soluble carrier in a solid state. By formulating a solid dispersion, it is feasible to enhance the drug's dispersibility and wettability through the use of a carrier material [8]. The aim of this study is to enhance the solubility and dissolution rate of isradipine by formulating it as a solid dispersion using different hydrophilic carriers, namely PEG 6000, PEG 4000, urea and PXM 407, and different methods, specifically solvent evaporation and melting methods.

Materials and Methods

Isradipine was purchased from Hyperchem, China. PEG 4000 was provided by Loba chemie, India. PXM 407 and PEG 6000 were supplied by Sigma-Aldrich, Germany. Urea was supplied by Thomas baker, India.

Methods Experimental design

To systematically evaluate the prepared solid dispersion formulations, a Design of Experiment (DOE) approach was employed.

The DOE included three factors-two: categorical (Carrier type and method) and one numerical factor (carrier to drug ratio). The first categorical factor consisted of four levels while the second one consisted of two levels on the other hand, the numeric factor consisted of three levels.

The factors and their levels are listed in the table 1. Design of expert 13® was used to create response surface design according to the mentioned factors and the intended responses (percentage of yield of the prepared solid dispersion, drug content, saturation solubility). The suggested design composed of 22 runs as shown in table 2.

Table 1: Factors of the experimental design to manufacture isradipine solid dispersion

Factor	Name	Type	Minimum	Maximum
1	Carrier to drug ratio	Numeric	1	5
2	Carrier type	Categoric	PEG 4000	PEG 6000
3	Preparation method	Categoric	Solvent evaporation	Melting

Table 2: Design of experiment for solid dispersion loaded with isradipine

Run	Factor 1	Factor 2	Factor 3
	A: carrier to drug ratio	B: carrier type	C: Method
1	1	PEG 4000	Solvent evaporation
2	3	PEG 6000	Melting
3	5	Urea	Solvent evaporation

4	3	PEG 4000	Melting
5	1	PEG 6000	Solvent evaporation
6	1	Urea	Melting
7	1	PXM 407	Melting
8	5	Urea	Melting
9	5	PEG 6000	Solvent evaporation
10	1	PXM 407	Solvent evaporation
11	1	PXM 407	Melting
12	3	Urea	Solvent evaporation
13	5	PXM 407	Melting
14	5	PXM 407	Solvent evaporation
15	3	PEG 6000	Melting
16	1	PEG 6000	Melting
17	3	PEG 4000	Melting
18	3	Urea	Melting
19	3	Urea	Solvent evaporation
20	1	PEG 4000	Melting
21	5	PEG 4000	Solvent evaporation
22	3	PEG 6000	Solvent evaporation

Preparation of isradipine solid dispersion by conventional fusion (melting) technique

In conventional melting method, an accurately weighed amount of isradipine and carrier were prepared at different weight-to-weight ratios as illustrated in table 2. The required amount of carrier powder (PXM 407, PEG 6000, PEG4000, urea) was placed in a porcelain petri dish and heated on a water bath gradually until the carrier was melted; then, the previously weighed amount of the drug was added to the molten carrier and subjected to continuous stirring until a uniform dispersion was achieved then, the mixture was transferred into ice bath to cool down. The produced solid mass was grinded and sieved through a No.60 sieve and subsequently stored, protected from moisture, for further evaluation [9].

Preparation of isradipine solid dispersion by solvent evaporation

In this method, a predetermined amount of the carrier was dissolved in ethanol with gentle stirring using a magnetic stirrer until a clear solution was obtained; then, the required amount of the drug was added with continuous stirring. The solution was poured into a Petri dish and transferred to an oven and dried at 40 °C for 24 h. Finally, the mass was Grinded and sieved using No. 60 mesh sieve and stored protected from moisture for further investigations [10].

Determination of percentage yield of the prepared isradipine solid dispersion

In order to assess the impact of each method, the percentage yield was determined for each formula of isradipine solid dispersion. It was calculated by dividing the actual weight of the solid dispersion formula by the theoretical weight using the following formula [11].

Determination of saturation solubility: The saturation solubility of isradipine and the prepared solid dispersion formulas were determined by adding excess amount of the drug and 5 mg dose equivalent of isradipine prepared solid dispersion to 10 ml of phosphate buffer (pH=6.8). The prepared samples were then placed in a water bath shaker and allowed to stand for 48 h at 37 °C for both samples. After incubation, the samples were filtered with a 0.45µm filter syringe. Following appropriate dilutions, The Dissolved isradipine was determined in the filtrate using a UV spectrophotometer at the drug λ max (328 nm).

Additionally, this procedure was carried out in triplicate [13].

In vitro dissolution studies

Pure isradipine and prepared solid dispersion formulas have been evaluated for in vitro dissolution using a USP apparatus II (Erweka DT720 GmbH, Germany). An equivalent amount of 5 mg of the drug was dispersed in 500 ml of pH 6.8 phosphate buffer. A thermostatic water bath was used to maintain the temperature at 37±0.5 °C. The device was set up to revolve at a rate of 75 revolutions per minute [14]. This evaluation was performed in triplicate on the prepared formulations that showed the highest solubility (run 2,13,14 and 22) when compared to the pure drug. A sample of 10 ml was collected from the dissolution medium at specific intervals of 10, 20, 30, 45, 60, 90, and 120 min and replaced with a fresh dissolution medium. After filtration, each sample was filtered using a 0.45-micron syringe filter, and the amount of dissolved isradipine was measured using a spectrophotometer at the drug λmax (328 nm).

Determination of drug content

Drug content was determined for all the prepared solid dispersion formulations by dissolving an exactly weighed amount of isradipine solid dispersion equivalent to 5 mg in 50 ml of ethanol using 50 ml volumetric flask; then, the solution was evaluated for drug content using a UV-spectrophotometer at its specified λmax (326 nm) after being appropriately diluted with ethanol. The formula below was applied to calculate the percentage of drug content [12]. The reference dissolution value (Rt), the test dissolution value (Tt), and the number of dissolution time points (n) are all represented at time t. When the $f2$ value is greater than 50 (within a range of 50 to 100), dissolution patterns are considered similar. On the other hand, dissimilar profiles are defined as those with a $f2$ value less than 50 [15].

Fourier transforms infrared spectroscopy (FTIR)

The FTIR spectra of pure isradipine, PXM 407 and the optimum formula were analyzed to examine potential interactions between the drug and the ingredients of the formula. The test was performed over a scanning range of 600–4000 cm using IRAffinity-1, Shimadzu, Drug content % = Theoretical amount of drug × 100

Japan. Few milligrams of the formulation samples were finely ground and mixed with dry potassium bromide. The mixture was then compressed using a hydraulic press to form a disc, which was subsequently scanned [16].

Powder x-ray diffraction (PXRD)

The crystalline state of pure isradipine, PXM 407, and the selected formula were assessed using Powder X-ray diffraction (DX2700BH, China). The measurement was conducted with a wavelength of 1.5406 Å over a 2θ range of 5-80° [17].

Differential scanning calorimetry (DSC)

The thermal behavior of pure isradipine, PXM 407, and the selected formula were evaluated using DSC (Shimadzu, Japan). A closed aluminum pan containing ten milligrams of each sample was heated at 10 °C per minute over a temperature range of 10 °C to 300 °C [18].

Results and Discussion

Percentage of yield and drug content

Table 3 illustrates percentage of yield and drug content of the successful formulas. The percentage of yield was evaluated for the prepared formulations to investigate the efficiency of each method. Both solvent evaporation and melting methods produced a good yield ranging between 80 and 99%. This result indicates that both methods were suitable and effective. The drug content of the obtained formulas ranged between 94% and 103%, which agrees with British pharmacopeia for most formulas [14]. This observation suggests that both methods resulted in uniform dispersion of isradipine in the employed carrier.

Saturation solubility

The solubility of isradipine in phosphate buffer (pH=6.8) was determined. The obtained value was 1.2µg/ml which indicates the lipophilic property of the drug [4]. The saturation solubility of isradipine was significantly (P-value<0.05) improved in all solid dispersion formulations. This enhancement may be attributed to the improvement in drug wettability and/or hydrophilic character of the utilized carriers [19, 20]. Besides, the solubility enhancement was affected by the type of the carrier. Among the employed carriers, PXM 407 achieved the best improvement in solubility. This may be attributed to the surfactant properties of the former [21]. The ratio of the carrier to the drug was directly proportional to the solubility enhancement as more drug incorporated into the carrier [22]. Except for PEG 6000 in 5:1 ratio (run 9) and urea in 5:1 ratio (run 3 and 8) where the solubility paradoxically decreased when the carrier ratio further increased. This may be due to increased viscosity [23]. Furthermore, the preparation method also had an impact on the solubility of the prepared formulas. In most of the obtained formulations, solvent evaporation resulted in better improvement in isradipine solubility when compared with fusion method. This can be justified because the of the drug lattice structure is destroyed completely during the preparation process when using solvent evaporation. On the other hand, the melting method may lead to imperfect amorphization; that is, the presence of remaining nuclei or small crystals may lead to crystallization after preparation [24]. Table 3 shows the saturation solubility of isradipine solid dispersions using different carriers and different carrier-to-drug ratio.

Table 3: Effect of formulation factors and type of method on responses 1,2 and 3

Run	Factor 1 (A)	Factor 2 (B)	Factor 3 (C)	Response 1	Response 2	Response 3
	Carrier to drug ratio	carrier type	Method	Percentage of yield %	% of drug content*	Saturation solubility*
1	1	PEG 4000	Solvent evaporation	94%	98.4%±0.28	2.5±0.098
2	3	PEG 6000	Fusion	97%	98%±0.04	3.7±0.015
3	5	Urea	Solvent evaporation	90%	97.2%±0.2	2.92±0.065
4	3	PEG 4000	Fusion	98%	102%±0.05	1.92±0.2
5	1	PEG 6000	Solvent evaporation	92%	103%±0.087	1.96±0.039
6	1	Urea	Fusion	89%	99.2%±0.09	1.86±0.3
7	1	PXM 407	Fusion	92%	99%±0.07	2.65±0.11
8	5	Urea	Fusion	95%	101.6%±0.07	2.04±0.03
9	5	PEG 6000	Solvent evaporation	80%	99.4%±0.01	3.49±0.12
10	1	PXM 407	Solvent evaporation	96%	100%±0.12	3.49±0.065
11	1	PXM 407	Fusion	95%	98.2%±0.054	2.78±0.013
12	3	Urea	Solvent evaporation	92.5%	97.4%±0.14	3.48±0.3
13	5	PXM 407	Fusion	97%	98.6%±0.03	12±0.05
14	5	PXM 407	Solvent evaporation	93%	99.5%±0.08	19.2±0.65
15	3	PEG 6000	Fusion	99%	97.8%±0.05	3.45±0.02
16	1	PEG 6000	Fusion	96%	94%±0.075	2.03±0.089

17	3	PEG 4000	Fusion	94%	99.04%±0.06	2.3±0.13
18	3	Urea	Fusion	90%	99±0.09	2.62±0.03
19	3	Urea	Solvent evaporation	92.5	97.4±0.14	3.48±0.3
20	1	PEG 4000	Fusion	97%	101%±0.12	1.72±0.065
21	5	PEG 4000	Solvent evaporation	93.3%	100.6%±0.078	3.32±0.065
22	3	PEG 6000	Solvent evaporation	84.5%	98.4%±0.15	4.17±0.19

***Data are represented as mean ±SD, N=3 observations.**

In vitro dissolution studies

The formulas obtained by (run2, 13, 14, and 22) were selected to compare their in vitro dissolution behavior because they provided the highest enhancement in solubility. Fig. 1 demonstrated that the dissolution rate significantly improved by all of the previously mentioned formulations when compared to the pure drug with the following f2 values 27,75, 16.25, 11.35, 20.98, respectively.

Run 14 which is composed of PXM 407: isradipine in 5:1 ratio exhibited the highest release profile (80%) after 10 min. while run 2, 13, 22 and the pure drug showed (21%, 63%, 29%,19%) respectively. This enhancement in dissolution profile may be attributed to the solubility enhancement provided by PXM 407. The arrangement of ethylene oxide (EO) and propylene oxide (PO) blocks in PXM 407 permits the amphiphilic structure to self-assemble into micelles in aqueous solutions. In order to solubilize drugs, these monomolecular micelles can assemble into aggregates of varied sizes [25].

Selection of the optimum formula

Run14, which contained PXM 407: isradipine in 5:1 ratio was selected as the optimum formula and subjected to further investigations. This is because it had the highest solubility and the amount of released drug after 10 min is higher than the other formulas.

Fourier transforms infrared spectroscopy (FTIR)

The FTIR spectra of pure isradipine, PXM 407 and the selected formula are shown in fig. (2, 3, 4). The characteristic peaks of pure isradipine were observed at 3348 cm-1 (N-H stretching), 1,701.22 cm-1 (C=O stretching), 2941.44 cm-1 (C-H stretching), and 1,490.97 cm-1 (C=C vibration), in agreement with previous reports [26]. The characteristic peaks of isradipine still observed in the selected formula with reduced intensities, which may be attributed to the dilution effect of the polymer. This observation indicates that there is no chemical incompatibility between PXM 407 and isradipine.

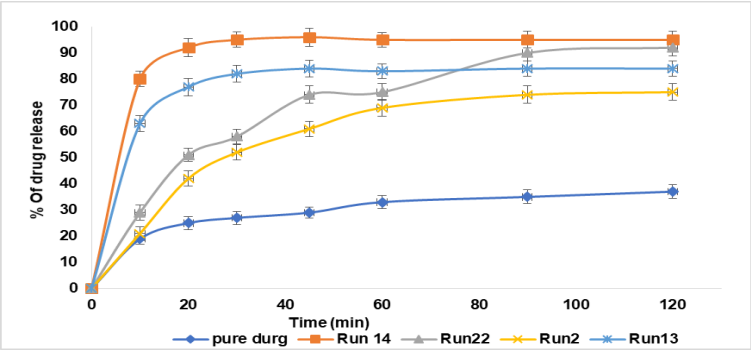

Fig. 1: Comparison between in vitro dissolution profile of pure drug (isradipine), run 2, 13, 14, 22) in phosphate buffer (pH 6.8) at 37 °C±0.5. Error bars represent the standard deviation of replicates (N=3)

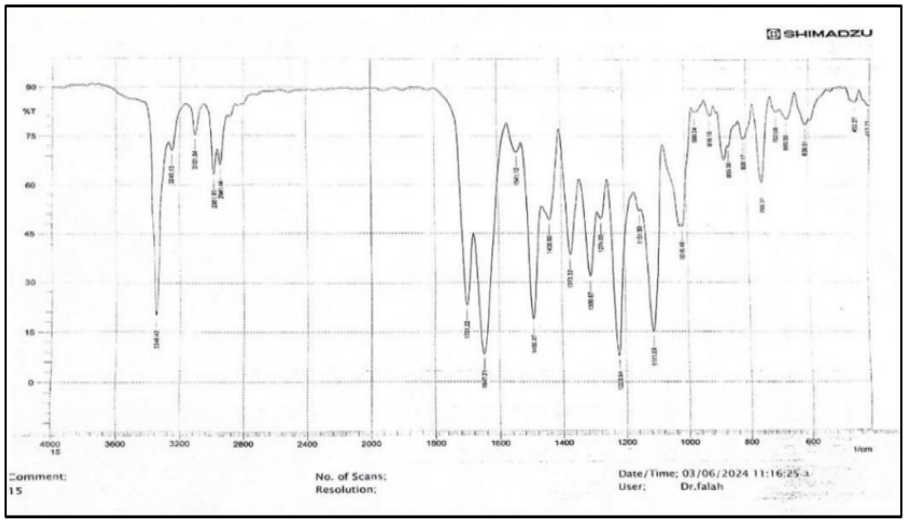

Fig. 2: FTIR spectrum of pure drug (isradipine)

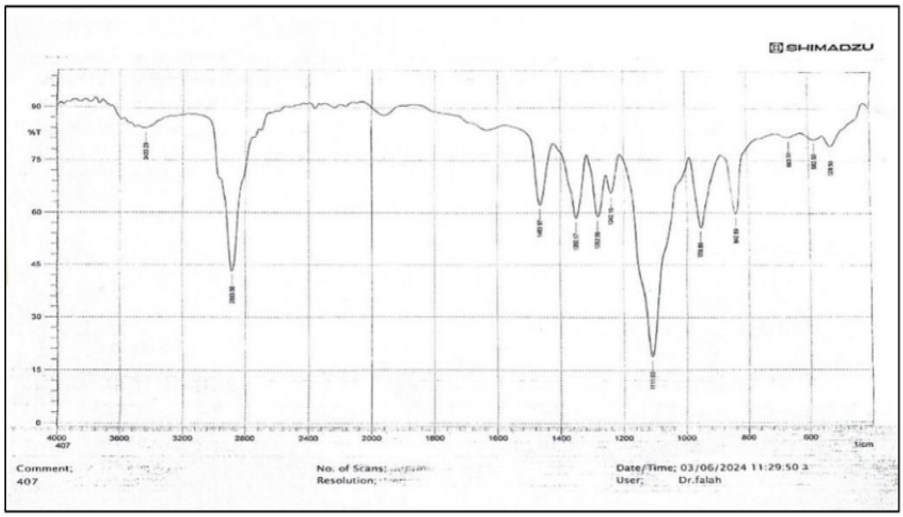

Fig. 3: FTIR spectrum of PXM 407

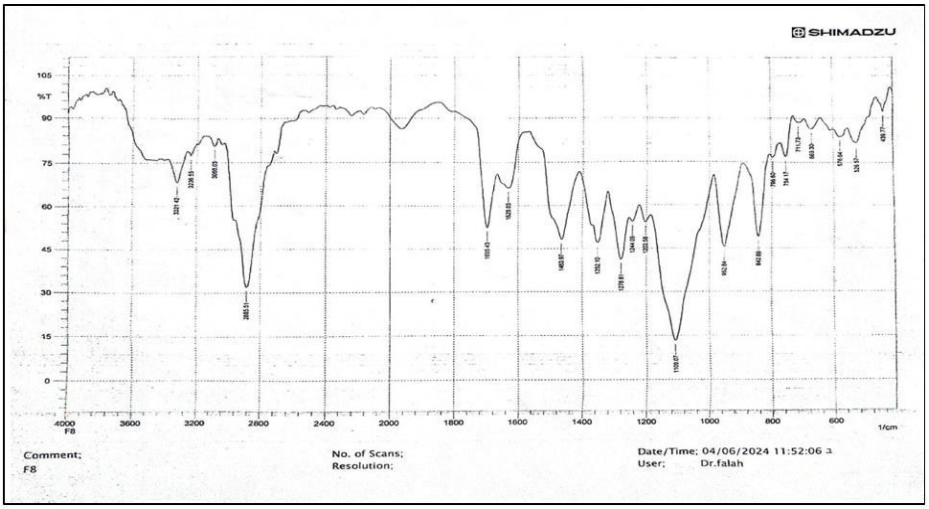

Fig. 4: FTIR spectrum of selected formula (run 14)

Powder x-ray diffraction (PXRD)

The XRD pattern of the pure drug, PXM 407 and the selected formula (run 14) are shown in fig. 5.

Pure-drug exhibited a high-intensity diffraction angle at 8.5º, 10.4°, 12.7º, 16.5º, 18.17º, 19.3º, 21.9º, 24.3º and 27.2º, indicating typical crystalline pattern. These results approached the previously documented data [27]. The XRD diffractogram of the selected formula showed a significant decrease or complete absence of the characteristic isradipine peaks. This indicates that either the prepared solid dispersion is mainly composed of an amorphous state or the drug is completely dispersed through the polymer [28].

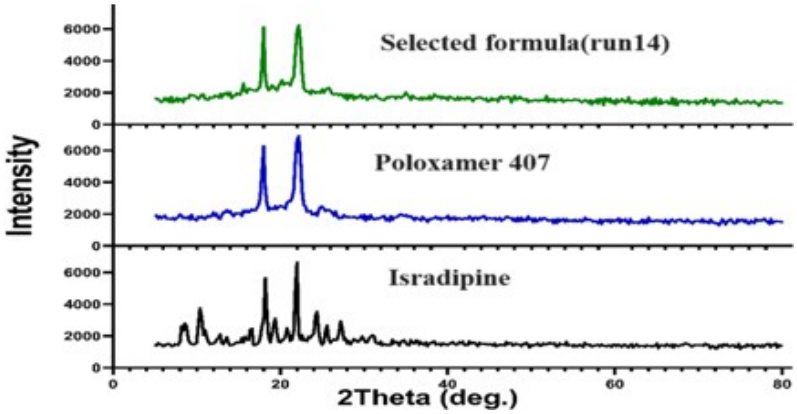

Fig. 5: XRD of pure drug, PXM 407 and selected formula (run 14)

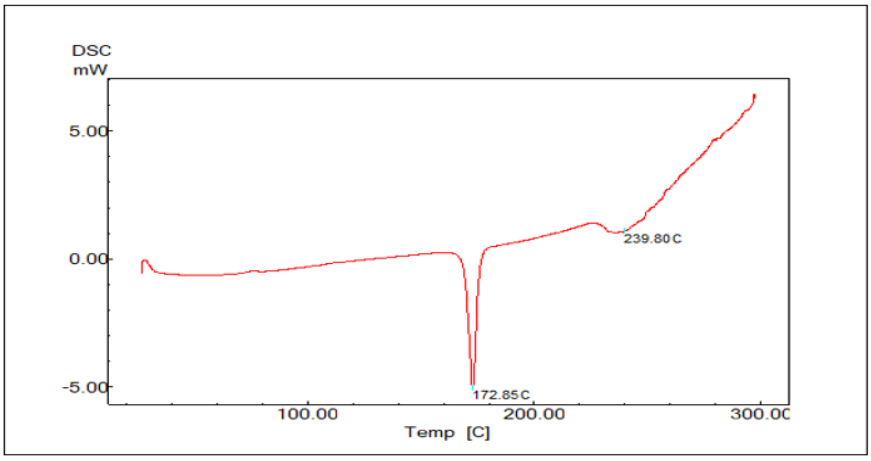

Fig. 6: Thermal analysis of isradipine

Differential scanning calorimetry (DSC)

The DSC thermogram of the pure drug, PXM 407 and the selected formula (run14) are shown in fig. (6, 7, 8). The pure drug thermogram showed sharp endothermic peak at 172 °C, which represents the drug melting point and indicates the drug crystallinity. While PXM 407 exhibited endothermic peak at 61 °C. These observations are in agreement with previous studies [29, 30]. On the other hand, the thermogram of the selected formula shows disappearance of isradipine peak.

This may be due to the complete dispersion of the drug in the utilized carrier or presence of isradipine in its amorphous form, which is further supported by the XRD data. Additionally, there was a slight shift in the peak of the carrier in the selected formula, which may indicate eutectic mixture formation between PXM 407 and the drug [31].

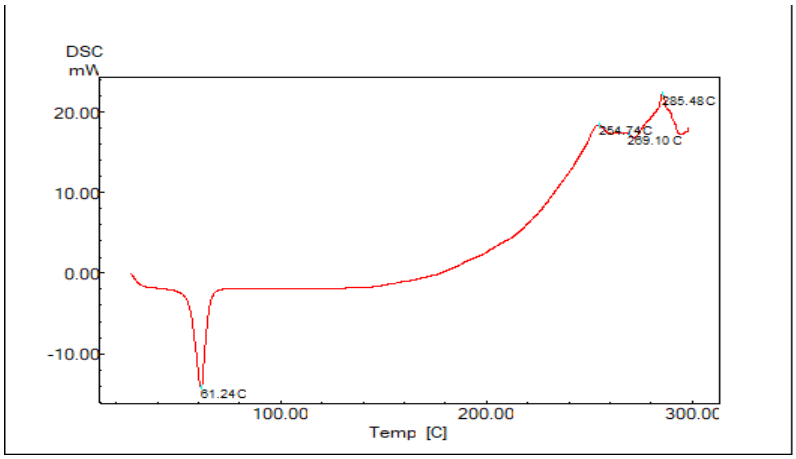

Fig. 7: Thermal analysis of PXM 407

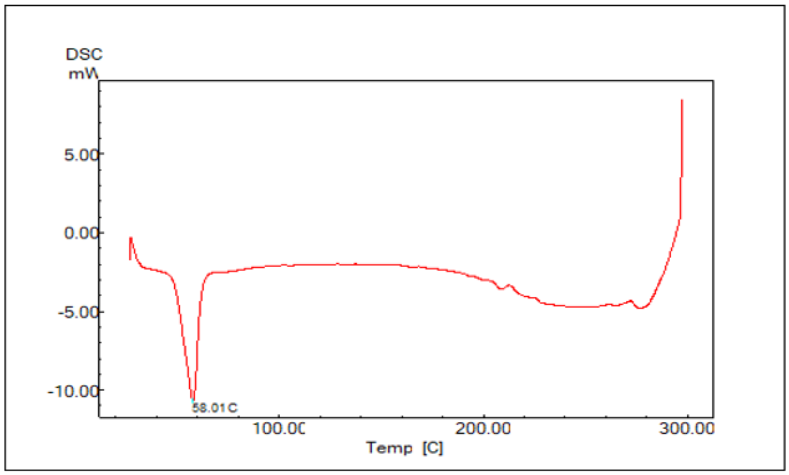

Fig. 8: Thermal analysis of selected formula

Conclusion

A solid dispersion of the poorly water-soluble drug isradipine was prepared in this study in order to enhance its solubility and dissolution. Design of experiment approach was used to systematically evaluate the prepared solid dispersion formulations.

Formulation variables such as carrier type and ratio in addition to processing variable for example, preparation method, significantly affect the solubility and the dissolution rate of the final product. Run 14 which is composed of (PXM 407: isradipine in 5:1 ratio) and prepared by solvent evaporation resulted in best result with 16 times increment in solubility compared to the parent drug. Besides the later formula released 80% of the drug in 10 min. The current research revealed Solid dispersion is a simple and highly efficient strategy to improve isradipine solubility and dissolution.

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Authors Contributions

All authors contributed equally to the development and execution of this research. Each author was actively involved in the conceptualization, data acquisition, analysis, and manuscript. The final manuscript has been thoroughly reviewed and approved by all authors prior to publication.

References

1. Boyd BJ, Bergstrom CA, Vinarov Z, Kuentz M, Brouwers J, Augustijns P. Successful oral delivery of poorly water-soluble drugs both depends on the intraluminal behavior of drugs and of appropriate advanced drug delivery systems. Eur J Pharm Sci. 2019 Sep 1;137:104967. doi: 10.1016/j.ejps.2019.104967, PMID 31252052.
2. Kumar S, Bhargava D, Thakkar A, Arora S. Drug carrier systems for solubility enhancement of BCS class II drugs: a critical review. Crit Rev Ther Drug Carrier Syst. 2013 Apr 24;30(3):217- 56. doi: 10.1615/critrevtherdrugcarriersyst.2013005964,PMID 23614647.
3. Benowitz NL. Antihypertensive agents. In: Katzung B Trevor A. Basic and clinical pharmacology. New York: McGraw-Hill; 2015.
4. Moffat A, Osselton M, Widdop B. Clarkes analysis of drug and poisons. 4th ed. London: Pharmaceutical Press; 2011.
5. Ramasahayam B, Eedara BB, Kandadi P, Jukanti R, Bandari S. Development of isradipine loaded self nano emulsifying powders for improved oral delivery: in vitro and in vivo evaluation. Drug Dev Ind Pharm.

2015 May;41(5):753-63. doi: 10.3109/03639045.2014.900081, PMID 24641324.
6. Ainurofiq A, Putro DS, Ramadhani DA, Putra GM, DO Espirito Santo LC. A review on solubility enhancement methods for poorly water-soluble drugs. J Rep Pharma Sci. 2021;10(1):137- 47. doi: 10.4103/jrptps.JRPTPS_134_19.
7. Bhujbal SV, Mitra B, Jain U, Gong Y, Agrawal A, Karki S. Pharmaceutical amorphous solid dispersion: a review of manufacturing strategies. Acta Pharm Sin B. 2021 Aug 1;11(8):2505-36. doi: 10.1016/j.apsb.2021.05.014, PMID 34522596.
8. Sharma B. Drugs dissolution enhancement by using solid dispersion technique: a review. EPRA International Journal of Multidisciplinary Research. 2021 Jan;7(1):1-2. doi: 10.36713/epra2013.
9. Kandwal M, Ghalan I, Patil S. Formulation and evaluation of nimodipine tablets using solid dispersion technique. APJHS. 2022 Jun 20;9(4):355-64. doi: 10.21276/apjhs.2022.9.4.66.
10. Mohana M, Vijayalakshmi S. Development and characterization of solid dispersion based orodispersible tablets of cilnidipine. Beni Suef Univ J Basic Appl Sci. 2022 Dec 1;11(1):83-94. doi: 10.1186/s43088-022-00259-3.
11. Sarkar P, Biswas Majee SB. Formulation development and in vitro characterization of ternary hydrotropic solid dispersions of aceclofenac. Asian J Pharm Clin Res. 2022 Jun 13;15(9):174-9. doi: 10.22159/ajpcr.2022.v15i9.45158.
12. Mankar SD, Rachh PR. Formulation development evaluation and solubility enhancement of lercanidipine hydrochloride by solid dispersion techniques. J Pharm Res Int. 2021 Dec 7;33(53B):195-213. doi: 10.9734/jpri/2021/v33i53B33697.
13. Tripathi D, Sharma K, Sahoo J, Chaudhary N. A recent advancement in approaches used for estimation of drug solubility: a review. Pharm Lett. 2020;12(4):15-29.
14. Pharmacopoeia B. British pharmacopoeia; 2016.
15. Muselik J, Komersova A, Kubova K, Matzick K, Skalicka B. A critical overview of FDA and EMA statistical methods to compare in vitro drug dissolution profiles of pharmaceutical products. Pharmaceutics. 2021 Oct 15;13(10):1703. doi: 10.3390/pharmaceutics13101703, PMID 34683995.
16. Al Edresi S, Albo Hamrah KA, Al Shaibani A. Formulation and validation of candesartan cilexetil loaded nanosuspension to enhance solubility. Pharmacia. 2024 Mar 19;71:1-13. doi: 10.3897/pharmacia.71.e114943.
17. Wannas AN, Abdul Hasan MT, Mohammed Jawad KK, Razzaq IF. Preparation and in vitro evaluation of self nano emulsifying drug delivery systems of ketoprofen. Int J App Pharm. 2023 May 1;15(3):71-9. doi: 10.22159/ijap.2023v15i3.46892.
18. Sopyan I, Riyaldi MR, Mita SR, Hariono M. Increasing solution in the drug simvastatin with solid dispersion technique using polymer soluplus. Int J App Pharm. 2023 Jul 1;15(4):160-5. doi: 10.22159/ijap.2023v15i4.48293.
19. VO CL, Park C, Lee BJ. Current trends and future perspectives of solid dispersions containing poorly water-soluble drugs. Eur J Pharm Biopharm. 2013 Nov;85(3 Pt B):799-813. doi: 10.1016/j.ejpb.2013.09.007, PMID 24056053.
20. Nair AR, Lakshman YD, Anand VS, Sree KS, Bhat K, Dengale SJ. Overview of extensively employed polymeric carriers in solid dispersion technology. AAPS Pharm Sci Tech. 2020 Nov 8;21(8):309. doi: 10.1208/s12249-020-01849-z, PMID 33161493.
21. Szafraniec J, Antosik A, Knapik Kowalczuk J, Chmiel K, Kurek M, Gawlak K. Enhanced dissolution of solid dispersions containing bicalutamide subjected to mechanical stress. Int J Pharm. 2018 May 5;542(1-2):18-26. doi: 10.1016/j.ijpharm.2018.02.040, PMID 29481948.
22. Abduljabbar HH, Abd Alhammid SN. Enhancement of the solubility and the dissolution rate of tamoxifen citrate solid

dispersion using soluplus by solvent evaporation technique. Asian J Pharm Clin Res. 2019 Jan 7;12(1):216-21. doi: 10.22159/ajpcr.2019.v12i1.28933.
23. Sarisuta N, Parrott EL. Relationship of dissolution rate to viscosity of polymeric solutions. J Pharm Sci. 1982;71(12):1375-80. doi: 10.1002/jps.2600711216, PMID 7153886.
24. Benes M, Pekarek T, Beranek J, Havlicek J, Krejcik L, Simek M. Methods for the preparation of amorphous solid dispersions a comparative study. J Drug Deliv Sci Technol. 2017 Apr 1;38:125- 34. doi: 10.1016/j.jddst.2017.02.005.
25. Eloy JO, Marchetti JM. Solid dispersions containing ursolic acid in poloxamer 407 and PEG 6000: a comparative study of fusion and solvent methods. Powder Technol. 2014 Feb;253:98-106. doi: 10.1016/j.powtec.2013.11.017.
26. Hussien RM, Ghareeb MM. Formulation and characterization of isradipine nanoparticle for dissolution enhancement. Iraqi J Pharm Sci. 2021;30(1):218-25. doi: 10.31351/vol30iss1pp218-225.
27. Ghose D, Patra CN, Swain S, Sruti J. Box-behnken design based development and characterization of polymeric freeze-dried nanoparticles of isradipine for improved oral bioavailability. Int J App Pharm. 2023 Jul 1;15(4):60-70. doi: 10.22159/ijap.2023v15i4.47728.
28. Tran TT, Tran PH. Investigation of polyethylene oxide-based prolonged release solid dispersion containing isradipine. J Drug Deliv Sci Technol. 2013;23(3):269-74. doi: 10.1016/S1773-2247(13)50040-2.
29. Sadoon NA, Ghareeb MM. Formulation and characterization of isradipine as oral nanoemulsion. Iraqi J Pharm Sci. 2020 Jun 25;29(1):143-53. doi: 10.31351/vol29iss1pp143-153.
30. Meruva S, Thool P, Shah S, Karki S, Bowen W, Ghosh I. Formulation and performance of irbesartan nanocrystalline suspension and granulated or bead layered dried powders Part Int J Pharm. 2019 Sep 10;568:118189. doi: 10.1016/j.ijpharm.2019.03.007, PMID 30851385.
31. Simonazzi A, Davies C, Cid AG, Gonzo E, Parada L, Bermudez JM. Preparation and characterization of poloxamer 407 solid dispersions as an alternative strategy to improve benznidazole bioperformance. J Pharm Sci. 2018 Nov 1;107(11):2829-36. doi: 10.1016/j.xphs.2018.06.027, PMID 30005984.