

Solubility Enhancement Of Mangiferin By Solid Dispersion

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DOI: 10.47750/pnr.2022.13.S09.850

Abstract

The main intension of the present study is to enhance solubility and oral bioavailability of mangiferin naturally occurring bioactive compound having poor solubility by the different methods like kneading method and solvent evaporation method. The solid dispersions were made by using variety polymers like cross povidone, sodium starch glycolate, lecithin, β -cyclodextrin in ratios of 1:1,1:2,1:3,1:4 and 1:5. Phase solubility studies, Differential scanning calorimetry, X-Ray powder diffraction and fourier transform infrared spectroscopy were used to evaluate compatibility of mangiferin with selected polymers. Solid dispersions prepared by kneading method with sodium starch glycolate in 1:2 ratio shown maximum solubility of 791micrograms per ml (0.791mg/ml) compared with pure drug 57 μ g/ml (0.057mg/ml). Therefore it is formulated as tablet by direct compression method. Physicochemical properties and invitro dissolution studies are conducted to characterise tablets. The prepared solid dispersion shown maximum 98.3% release in 1h.

Key Words: Lecithin, sodium starch glycolate, cross povidone

1. Introduction

The Natural compounds and herbal plants have been traditionally used to treat various diseases associated with imbalanced metabolism. Mango considered as one of the important tropical fruit in the medicinal world which is originated from Asia (Lee et al., 2022). The various parts of mango tree have different tremendous Pharmacological Activities. The oral route is the most used drug administration method due to its practicality, high patient compliance, and affordable manufacturing (Thiengkaew et al., 2021). After oral administration drug should have capacity to dissolve in gastric fluids to get into systemic circulation. The dissolving process, which controls the rate and extent of absorption for hydrophobic medicines, operates as a rate-limiting phase. BCS class 4 drugs are the drugs having less solubility and low permeability (Mohana and Vijayalakshmi, 2022). These drugs are formulated in such a way that it becomes more permeable and more soluble with help of different formulation methods. Solid dispersion is the commonly used technique for solubility enhancement by various researchers due to its simplicity, economical with kneading and solvent evaporation method. BCS class 4 drug used for present research is Mangiferin. Solid dispersion is the effective method to enhance the bioavailability of insoluble drugs. Solid dispersions are made by mixing a pharmaceutical active ingredient with a hydrophilic polymer (Agrawal, Maheshwari and Mishra, 2022). The mixture is then ground into a powder using milling techniques. The resulting powder is then mixed with other excipients to form a tablet. The hydrophilic polymer helps to keep the drug

dispersed throughout the tablet. As the tablet dissolves, the drug will dissolve first and then release into the stomach. If the drug does not dissolve completely, it will remain in the tablet as a solid dispersion. This allows the drug to stay in contact with the gastrointestinal fluids longer and increases its absorption. Solid dispersions are made by mixing two or more substances together. One substance is called the “matrix” and the other is called the “drug”. A solid dispersion is considered to be a type of solid solution. Solid solutions are formed when two or more substances are mixed together and form a single phase. When the substances are melted together, they become a homogeneous mixture. Solid dispersions are often referred to as "molecular solids" because the drugs are dispersed in the matrix (Savjani, Gajjar and Savjani, 2012). In our research we have explored capacity of different polymers and super disintegrate as a carrier for the solid dispersion (SD) of the mangiferin. The solid dispersion of mangiferin was evaluated for its solubility and invitro dissolution studies. The solid-state characterization of SD was done using FTIR, DSC, and XRD.

2. Materials and methods

2.1 Materials

Cross povidone from FMC BioPolymer, India, Sodium starch glycolate gifted by DMV International India, Lecithin, β -cyclodextrin, Tween 80 and Methaol purchased from Sigma Aldrich, Bangalore, India.

2.2. Methods

2.2.1. Fourier transforms infrared spectroscopy (FTIR)

The compatibility of drug substance with other ingredients of formulation can be studied by using Fourier transform infrared spectroscopy. FTIR studies were done by using potassium bromide disks employing a Shimadzu Corporation (Koyto, Japan) facility (model - 8400S). Disc was prepared by making combination of small amount of drug with potassium bromide in exceedingly hydraulics press below vacuum at 6-8 tons pressure. The prepared disc was placed in an exceedingly appropriate holder in IR photometer and also the infrared spectrum was noted from 4000 cm^{-1} to four hundred cm^{-1} in an appropriate scan time of twelve minutes. The resultant spectrum was compared with pure drug spectra for spectral changes.

2.2.2. Differential scanning calorimetry (DSC)

Physical nature of medicine, excipients and selected dosage form was determined by DSC. DSC analysis was done using Shimadzu DSC-60 differential scanning calorimeter (DSC). Indium was used for calibration of instrument. In a sample pan, 3-5 mg of sample was weighed and placed. Thermo grams were recorded by heating the sample at a constant rate $10\text{ }^{\circ}\text{C}/\text{min}$. The melting point, heat of fusion, disappearance of the crystalline sharp peak of the drug and appearance of any new peak and peak shape were noted.

2.2.3. Preparation and characterization of solid dispersions

Solid dispersions were made using Cross Povidone (CP), Sodium Starch Glycolate (SSG), Beta cyclodextrin and Lecithin by Physical Mixture (PM), Solvent Evaporation (SM) and Kneading Method (KM).

2.2.3.1. Preparation of physical mixture method (PM)

Physical mixture of medicament with Variety of polymers were made by mixing method (Table 1). The formulations were made by using drug and polymers ratio in gradually increase method.

Physical mixture method:

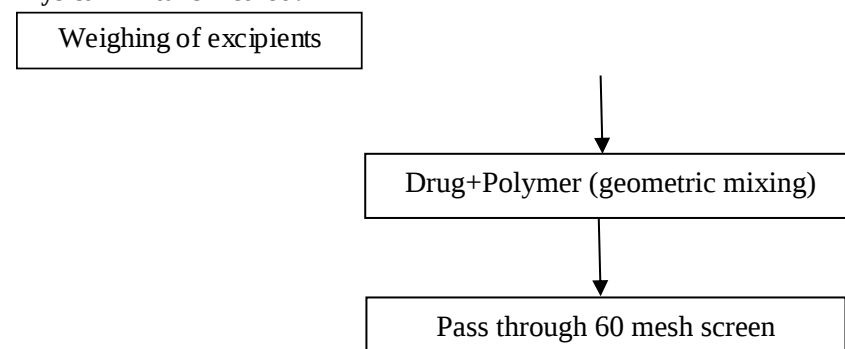


Table 1: Composition of physical mixtures of Mangiferin and various polymers

Formulation code	Drug: Carrier D:C	Weight of the drug (mg)	Weight of the carrier (mg)
PMCP-1	1:1	100	100
PMCP-2	1:2	100	200
PMCP-3	1:3	100	300
PMCP-4	1:4	100	400
PMCP-5	1:5	100	500
PMSSG-1	1:1	100	100
PMSSG-2	1:2	100	200
PMSSG-3	1:3	100	300
PMSSG-4	1:4	100	400
PMSSG-5	1:5	100	500
PMBCD-1	1:1	100	100
PMBCD-2	1:2	100	200
PMBCD-3	1:3	100	300
PMBCD-4	1:4	100	400
PMBCD-5	1:5	100	500
PMBCDL-1	1:1:2	100	100
PMBCDL-2	1:2:2	100	200
PMBCDL-3	1:3:2	100	300
PMBCDL-4	1:4:2	100	400
PMBCDL-5	1:5:2	100	500

Note: D-drug (Mangiferin), C-carrier, CP-Cross povidone, SSG-sodium starch glycolate, BCD- Beta cyclodextrin, L- Lecithin

2.2.3.2. Preparation of solid dispersion by Kneading Method (KM)

The formulations of the medicament with variety of polymers by kneading method were made using mortar and pestle. The solid dispersions were made by using different ratios of polymers and drug substance (**Table 2**).

Kneading method

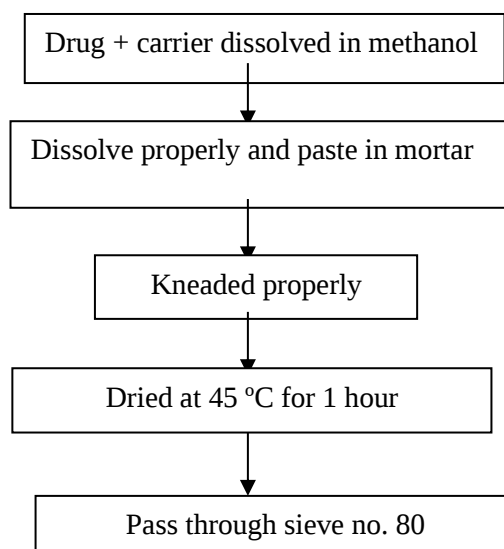


Table 2: Composition of kneading method of Mangiferin and various polymers

Formulation code	Drug: Carrier D:C	Weight of the drug (mg)	Weight of the carrier (mg)
KMCP-1	1:1	100	100
KMCP-2	1:2	100	200
KMCP-3	1:3	100	300
KMCP-4	1:4	100	400
KMCP-5	1:5	100	500
KMSSG-1	1:1	100	100
KMSSG-2	1:2	100	200
KMSSG-3	1:3	100	300
KMSSG-4	1:4	100	400
KMSSG-5	1:5	100	500
KMBCD-1	1:1	100	100
KMBCD-2	1:2	100	200
KMBCD-3	1:3	100	300
KMBCD-4	1:4	100	400
KMBCD-5	1:5	100	500
KMBCDL-1	1:1:2	100	100
KMBCDL-2	1:2:2	100	200
KMBCDL-3	1:3:2	100	300
KMBCDL-4	1:4:2	100	400
KMBCDL-5	1:5:2	100	500

Note: D-drug (Mangiferin), C-carrier, CP-Cross povidone, SSG-sodium starch glycolate, BCD- Beta cyclodextrin, L- Lecithin

2.2.3.3. Preparation of solid dispersion by using solvent evaporation method (SM)

The formulation of the medicament was made by using different carriers by solvent evaporation method using rotary flash evaporator. The solid dispersions were by using different ratios of polymers with drug (Table 3).

Solvent evaporation method

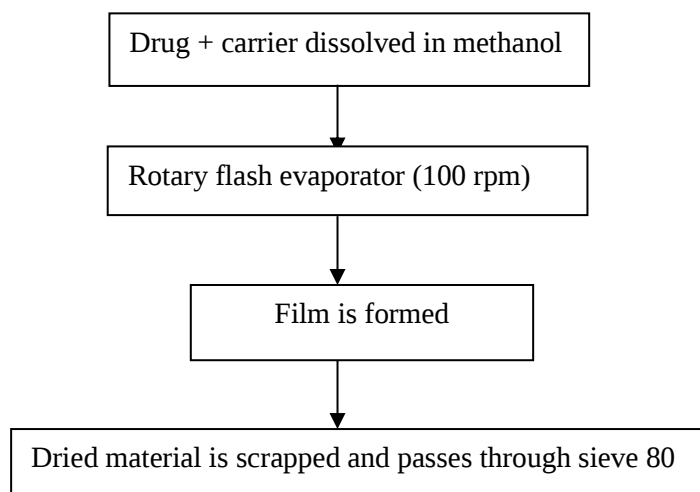


Table 3: Composition of Solvent evaporation method of Mangiferin and various polymers

Formulation code	Drug: Carrier D:C	Weight of the drug (mg)	Weight of the carrier (mg)
SECP-1	1:1	100	100
SECP-2	1:2	100	200
SECP-3	1:3	100	300
SECP-4	1:4	100	400
SECP-5	1:5	100	500
SESSG-1	1:1	100	100
SESSG-2	1:2	100	200
SESSG-3	1:3	100	300
SESSG-4	1:4	100	400
SESSG-5	1:5	100	500
SEBCD-1	1:1	100	100
SEBCD-2	1:2	100	200
SEBCD-3	1:3	100	300
SEBCD-4	1:4	100	400
SEBCD-5	1:5	100	500
SEBCDL-1	1:1:2	100	100
SEBCDL-2	1:2:2	100	200
SEBCDL-3	1:3:2	100	300
SEBCDL-4	1:4:2	100	400
SEBCDL-5	1:5:2	100	500

Note: D-drug (Mangiferin), C-carrier, CP-Cross povidone, SSG-sodium starch glycolate, BCD- Beta cyclodextrin, L- Lecithin

2.2.4. Characterization of solid dispersions

2.2.4.1. Solubility studies

A saturated solution of pure drug mangiferin and prepared solid dispersion was prepared in distilled water and buffer pH6.8 in a screwed bottles. Bottles are shaken mechanically at 26 °C for 24 hours and aliquots are withdrawn filtered and determined drug content at 242 nm using UV Spectrophotometer.

2.2.5. Precompression parameters of the powder blend

2.2.5.1. Angle of repose

100 grams of the prepared solid dispersion blend was weighed and placed in a funnel. The blend was allowed to pass through the funnel whose height is adjusted as 2.5cm above the graph paper. The pouring of powder mixture was continued until the cone of pile reaches the flat tip of funnel. Angle of repose is measured by using the formula (1).

$$\text{Angle of repose} = \tan^{-1} \left(\frac{h}{r} \right) \dots (1)$$

2.2.5.2. Bulk density

The bulk density of the blend was determined by placing the blend into a graduated measuring cylinder. The volume occupied by the powder and mass of the mixture was calculated the following formula (2).

$$\text{Bulk density} = \left(\frac{\text{MASS}}{\text{Bulk Volume}} \right) \dots (2)$$

2.2.5.3. Tapped density

Known amount of blend was placed in a measuring cylinder and tapped for a fixed toppings. The tapped volume and mass of the blend was determined. The tapped density was calculated using the formula (3).

$$\text{Tapped density} = \left(\frac{\text{MASS}}{\text{True Volume}} \right) \dots (3)$$

2.2.5.4. Carr's index

The simplest way of determination of flow characteristic of any powder is compressibility which indicates that how much fast the material flow property is enhanced by compressibility index (C.I) which is calculated using the formula (4).

$$CI(\%) = \left(\frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \right) \times 100 \dots (4)$$

2.2.5.5. Hausner's ratio

The indirect index which is used for the determination of ease of powder is called as hausner ratio. It is calculated by following formula (5).

$$\text{Hausner's ratio} = \left(\frac{\text{Tapped density}}{\text{Bulk density}} \right) \dots (5)$$

2.2.6. In vitro evaluation of mangiferin solid dispersion

2.2.6.1. In vitro Dissolution study

The in vitro dissolution studies of all solid dispersion formulations were conducted and also compared with the pure mangiferin drug. 0.1% Tween 80 was added while conducting dissolution studies. The conditions for dissolution test given below:

Temperature used: $37 \pm 0.5^\circ\text{C}$

Dissolution media used: 6.8 pH phosphate buffer

Volume of media: 900 ml

Sample withdrawn: 5 ml

Sample replaced: 5 ml of the fresh buffer solution

Dissolution test apparatus: USP type II (paddle)

Revolutions per minute (speed): 100 RPM

Sampling time intervals: 10 minutes

3. Results and discussion

3.1. Solubility studies

With kneading method KMSSG-5 have maximum solubility of 0.791 ± 0.008 mg/ml with Physical mixture method KMCP-5 showed 0.652 ± 0.009 mg/ml solubility. With solvent evaporation method SECP-5 formulation showed solubility of 0.562 ± 0.010 mg/ml and. It has been observed as the concentration of carrier (SSG) increased, the solubility was enhanced. Among the three different methods, solvent evaporation method showed maximum solubility of 0.791 ± 0.008 mg/ml when compared with pure drug (0.025 ± 0.0012 mg/ml).

3.2. Pre-compression parameters

Solid dispersions made by kneading method and solvent evaporation method were evaluated for pre-compression parameters, mainly flow properties. The values are given in table 4.

Table 4: Pre-compression parameters of the powder blend of mangiferin containing various polymers

Solid dispersion number	Angle of repose	Bulk density (gm/cm ³)	Tapped density (gm/cm ³)	Hausner ratio	Carr's index(%)	Solubility (mg/ml)
PMCP-1	40.0±0.36	0.224±0.01	0.317±0.02	1.15±0.01	15±0.08	0.136±0.007
PMCP-2	38.0±0.13	0.227±0.02	0.329±0.03	1.19±0.01	17±0.02	0.252±0.011
PMCP-3	35.0±0.02	0.229±0.02	0.341±0.03	1.25±0.02	19±0.08	0.362±0.009
PMCP-4	32.0±0.22	0.234±0.04	0.359±0.01	1.37±0.12	22±0.04	0.421±0.007
PMCP-5	30.0±0.14	0.237±0.02	0.365±0.02	1.52±0.01	23±0.06	0.652±0.008
PMSSG-1	41.0±0.36	0.324±0.01	0.327±0.02	1.25±0.01	14±0.08	0.116±0.007
PMSSG-2	39.0±0.13	0.327±0.02	0.339±0.03	1.29±0.01	16±0.02	0.212±0.011
PMSSG-3	35.0±0.02	0.329±0.02	0.341±0.03	1.25±0.02	18±0.08	0.262±0.009

PMSSG-4	33.0±0.22	0.234±0.04	0.359±0.01	1.37±0.12	21±0.04	0.321±0.007
PMSSG-5	31.0±0.14	0.237±0.02	0.365±0.02	1.52±0.01	23±0.06	0.452±0.008
PMBCD-1	41.0±0.36	0.324±0.01	0.327±0.02	1.25±0.01	14±0.08	0.116±0.007
PMBCD-2	39.0±0.13	0.327±0.02	0.339±0.03	1.29±0.01	16±0.02	0.212±0.011
PMBCD-3	35.0±0.02	0.329±0.02	0.341±0.03	1.25±0.02	18±0.08	0.262±0.009
PMBCD-4	33.0±0.22	0.234±0.04	0.359±0.01	1.37±0.12	21±0.04	0.321±0.007
PMBCD-5	31.0±0.14	0.237±0.02	0.365±0.02	1.52±0.01	23±0.06	0.452±0.008

The angle of repose of above physical mixture ranged between 30±0.14 to 40.0±0.36 inferring fair flow property. Carr's value is in the range of 0.317±0.02 to 0.365±0.02 which so it is considered as the fair. Hausner's ratio ranged from 1.15±0.01 to 1.52±0.01 inferring fair flow property. The angle of repose of above physical mixture ranged between 31±0.14 to 41.0±0.36 inferring fair flow property. Carr's value is in the range of 0.327±0.02 to 0.365±0.02 so it is considered as the fair. Hausner's ratio ranged from 1.25±0.01 to 1.52±0.01 inferring fair flow property. The angle of repose of above physical mixture ranged between 31±0.14 to 41.0±0.36 inferring fair flow property. Carr's value is in the range of 0.327±0.02 to 0.365±0.02 so it is considered as the fair. Hausner's ratio ranged from 1.25±0.01 to 1.52±0.01 indicates the flow property as fair (Baán et al., 2019).

Table 5: Pre-compression parameters of the powder blend of mangiferin containing various polymers by kneading method

Solid dispersion number	Angle of repose	Bulk density (gm/cm ³)	Tapped density (gm/cm ³)	Hausner's ratio	Carr's index(%)	Solubility (mg/ml)
KMCP-1	39.0±0.36	0.234±0.01	0.347±0.02	1.25±0.01	14±0.08	0.236±0.003
KMCP-2	337.0±0.13	0.237±0.02	0.349±0.03	1.29±0.01	15±0.02	0.265±0.001
KMCP-3	36.0±0.02	0.239±0.02	0.341±0.03	1.25±0.02	17±0.08	0.312±0.008
KMCP-4	33.0±0.22	0.234±0.04	0.369±0.01	1.47±0.12	21±0.04	0.452±0.007
KMCP-5	31.0±0.14	0.237±0.02	0.375±0.02	1.62±0.01	22±0.06	0.552±0.009
KMSSG-1	41.0±0.36	0.324±0.01	0.327±0.02	1.25±0.01	14±0.08	0.216±0.007
KMSSG-2	39.0±0.13	0.327±0.02	0.339±0.03	1.29±0.01	16±0.02	0.322±0.011
KMSSG-3	35.0±0.02	0.329±0.02	0.341±0.03	1.25±0.02	18±0.08	0.462±0.009
KMSSG-4	33.0±0.22	0.234±0.04	0.359±0.01	1.37±0.12	21±0.04	0.591±0.006
KMSSG-5	31.0±0.14	0.237±0.02	0.365±0.02	1.52±0.01	23±0.06	0.791±0.008
KMBCD-1	41.0±0.36	0.324±0.01	0.327±0.02	1.25±0.01	14±0.08	0.161±0.007
KMBCD-2	39.0±0.13	0.327±0.02	0.339±0.03	1.29±0.01	16±0.02	0.212±0.011
KMBCD-3	35.0±0.02	0.329±0.02	0.341±0.03	1.25±0.02	18±0.08	0.282±0.009
KMBCD-4	33.0±0.22	0.234±0.04	0.359±0.01	1.37±0.12	21±0.04	0.341±0.007
KMBCD-5	31.0±0.14	0.237±0.02	0.365±0.02	1.52±0.01	23±0.06	0.462±0.008

The angle of repose of above physical mixture ranged between 31±0.14 to 39.0±0.36 inferring fair flow property. Carr's value is in the range of 0.347±0.02 to 0.375±0.02 so it is considered as the fair. Hausner's ratio ranged from 1.25±0.01 to 1.62±0.01 inferring fair flow property. The angle of repose of above physical mixture ranged

between 32 ± 0.14 to 41.0 ± 0.36 inferring fair flow property. Carr's value is in the range of 0.327 ± 0.02 to 0.365 ± 0.02 so it is considered as the fair. Hausner's ratio ranged from 1.25 ± 0.01 to 1.52 ± 0.01 indicates fair flow property. The angle of repose of above physical mixture ranged between 32 ± 0.14 to 41.0 ± 0.36 inferring fair flow property. Carr's value is in the range of 0.327 ± 0.02 to 0.365 ± 0.02 so it is considered as the fair. Hausner's ratio ranged from 1.25 ± 0.01 to 1.52 ± 0.01 inferring fair flow property (Long et al., 2021).

Table 6: Pre-compression parameters of the powder blend of mangiferin containing various polymers by solvent evaporation method.

Solid dispersion number	Angle of repose ($^{\circ}$)	Bulk density (gm/cm^3)	Tapped density (gm/cm^3)	Hausner ratio	Carr's index	Solubility (mg/ml)
SECP-1	41.0 ± 0.36	0.324 ± 0.01	0.327 ± 0.02	1.25 ± 0.01	14 ± 0.08	0.161 ± 0.007
SECP-2	39.0 ± 0.13	0.327 ± 0.02	0.339 ± 0.03	1.29 ± 0.01	16 ± 0.02	0.262 ± 0.011
SECP-3	35.0 ± 0.02	0.329 ± 0.02	0.341 ± 0.03	1.25 ± 0.02	18 ± 0.08	0.382 ± 0.009
SECP-4	33.0 ± 0.22	0.234 ± 0.04	0.359 ± 0.01	1.37 ± 0.12	21 ± 0.04	0.441 ± 0.007
SECP-5	31.0 ± 0.14	0.237 ± 0.02	0.365 ± 0.02	1.52 ± 0.01	23 ± 0.06	0.562 ± 0.008
SESSG-1	41.0 ± 0.36	0.324 ± 0.01	0.327 ± 0.02	1.25 ± 0.01	14 ± 0.08	0.016 ± 0.007
SESSG-2	39.0 ± 0.13	0.327 ± 0.02	0.339 ± 0.03	1.29 ± 0.01	16 ± 0.02	0.222 ± 0.011
SESSG-3	35.0 ± 0.02	0.329 ± 0.02	0.341 ± 0.03	1.25 ± 0.02	18 ± 0.08	0.362 ± 0.009
SESSG-4	33.0 ± 0.22	0.234 ± 0.04	0.359 ± 0.01	1.37 ± 0.12	21 ± 0.04	0.391 ± 0.006
SESSG-5	31.0 ± 0.14	0.237 ± 0.02	0.365 ± 0.02	1.52 ± 0.01	23 ± 0.06	0.401 ± 0.008
SEBCD-1	41.0 ± 0.36	0.324 ± 0.01	0.327 ± 0.02	1.25 ± 0.01	14 ± 0.08	0.141 ± 0.007
SEBCD-2	39.0 ± 0.13	0.327 ± 0.02	0.339 ± 0.03	1.29 ± 0.01	16 ± 0.02	0.212 ± 0.011
SEBCD-3	35.0 ± 0.02	0.329 ± 0.02	0.341 ± 0.03	1.25 ± 0.02	18 ± 0.08	0.342 ± 0.009
SEBCD-4	33.0 ± 0.22	0.234 ± 0.04	0.359 ± 0.01	1.37 ± 0.12	21 ± 0.04	0.411 ± 0.007
SEBCD-5	31.0 ± 0.14	0.237 ± 0.02	0.365 ± 0.02	1.52 ± 0.01	23 ± 0.06	0.432 ± 0.008

The angle of repose of above physical mixture ranged between 32 ± 0.14 to 41.0 ± 0.36 inferring fair flow property. Carr's value is in the range of 0.327 ± 0.02 to 0.365 ± 0.02 so it is considered as the fair. Hausner's ratio ranged from 1.25 ± 0.01 to 1.52 ± 0.01 inferring fair flow property. The angle of repose of above physical mixture ranged between 32 ± 0.14 to 41.0 ± 0.36 inferring fair flow property. Carr's value is in the range of 0.327 ± 0.02 to 0.365 ± 0.02 so it is considered as the fair. Hausner's ratio ranged from 1.25 ± 0.01 to 1.52 ± 0.01 inferring fair flow property. The angle of repose of above physical mixture ranged between 31.5 ± 0.14 to 41.0 ± 0.36 which indicates that the flow property is fair. Carr's index is in the range from 0.327 ± 0.02 to 0.365 ± 0.02 inferring fair flow property. Hausner's ratio ranged from 1.25 ± 0.01 to 1.52 ± 0.01 inferring fair flow property. The precompression parameters were found to be excellent as related to other formulations. The solubility of the drug is increased gradually and is nearer to that of the optimized Formulation KMSSG ($0.791 \text{ mg}/\text{ml}$). Sodium starch glycolate is a hydrophilic carrier having more capacity to absorb water, hence it enhances the solubility of the drugs having poor solubility, by imparting its hydrophilic nature (Lum et al., 2022).

3.3. Dissolution studies

The in vitro drug release studies of the solid dispersions were conducted as per the standards.

The pure drug showed only 10.52% drug release in 60 min.

Table 7: Percentage drug release of pure drug in 6.8 pH phosphate buffer

Time (min)	% release of drug
0	0
10	1.981
20	2.01
30	4.490
40	5.059
50	8.674
60	10.521

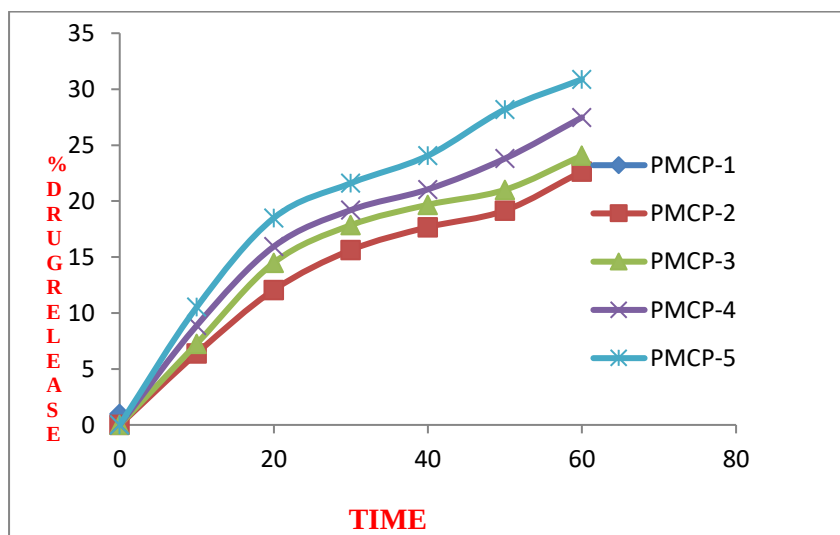


Figure 1: In vitro drug release profiles of physical mixtures of Mangiferin and Cross Povidone

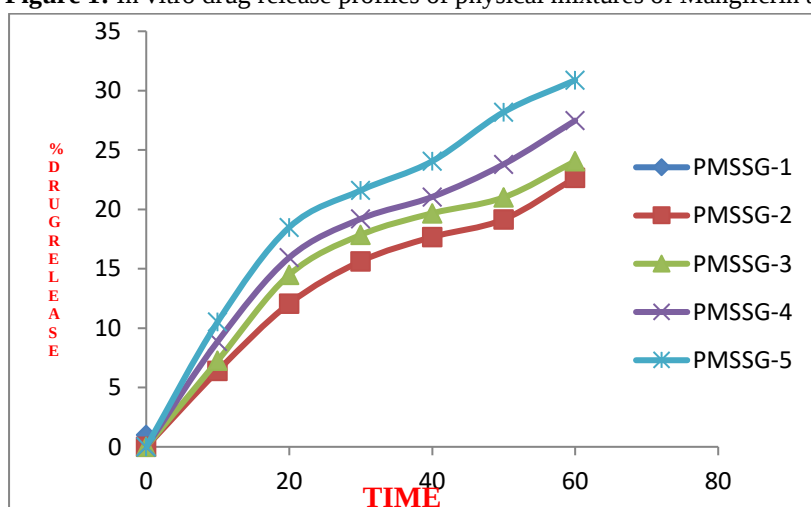


Figure 2: In vitro drug release profiles of physical mixtures of Mangiferin and Sodium starch glycol ate

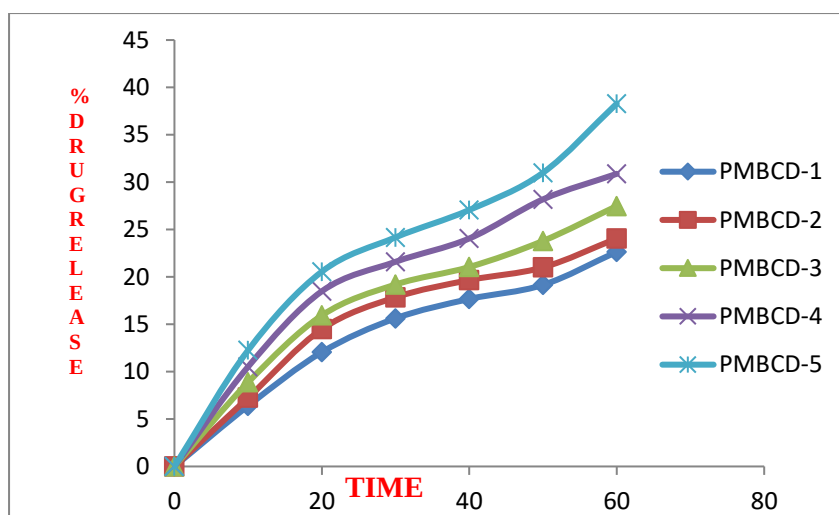


Figure 3: In vitro drug release profiles of physical mixtures of Mangiferin and beta cyclodextrin

From the in vitro drug release studies it was found that the drug is releasing in high amount from the solid dispersion containing physical mixture with cross povidone compare to pure drug. This is may be due to enhanced wettability of drug which is acquired due to hydrophilic nature of carriers (Walia, Chaudhary and Kumar Sethiya, 2021). Due to wetting process more amount of drug is available for dissolution. There is less drug release from solid dispersion containing pure drug due to its hydrophobic nature. The drug forming aggregates and floating on surface which leads to decrease in surface area and decrease the release of drug. It was observed that the drug release was increased as the carrier concentration increase's 1:5 ratio of drug to carrier have greater drug release (27.29%) compare to pure drug (10.52%). It was observed that the drug release was increased as the carrier concentration increases. 1:5 ratio of drug to carrier have greater drug release (35.29%) compare to pure drug (10.521%). It was observed that the drug release was increased as the carrier concentration increases. Solid dispersion containing 1:5 ratio of drug to carrier have greater drug release (28.29%) compare to pure drug (10.521%).

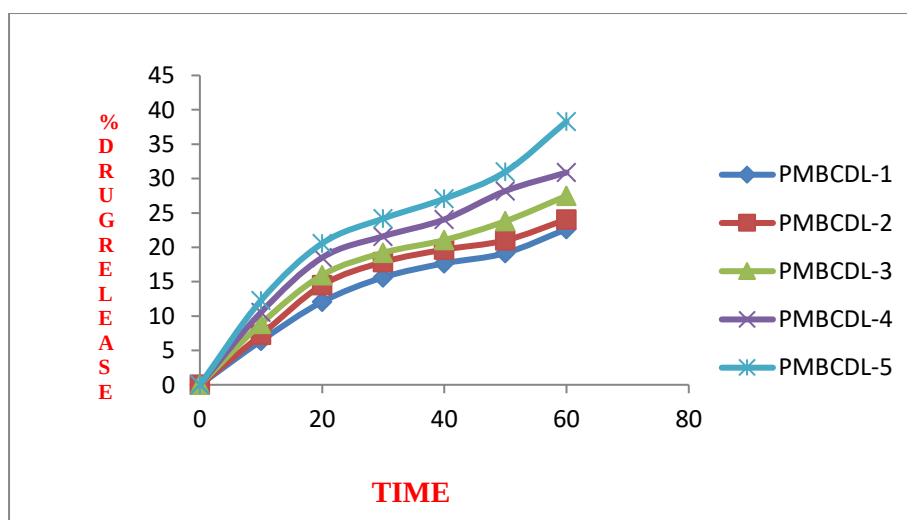


Figure 4: In vitro drug release profiles of physical mixtures of Mangiferin and beta cyclodextrin and lecithin. It was observed that the drug release was increased as the carrier concentration increases. Solid dispersion containing 1:5 ratio of drug to carrier have greater drug release (38.29%) compare to pure drug (10.521%).

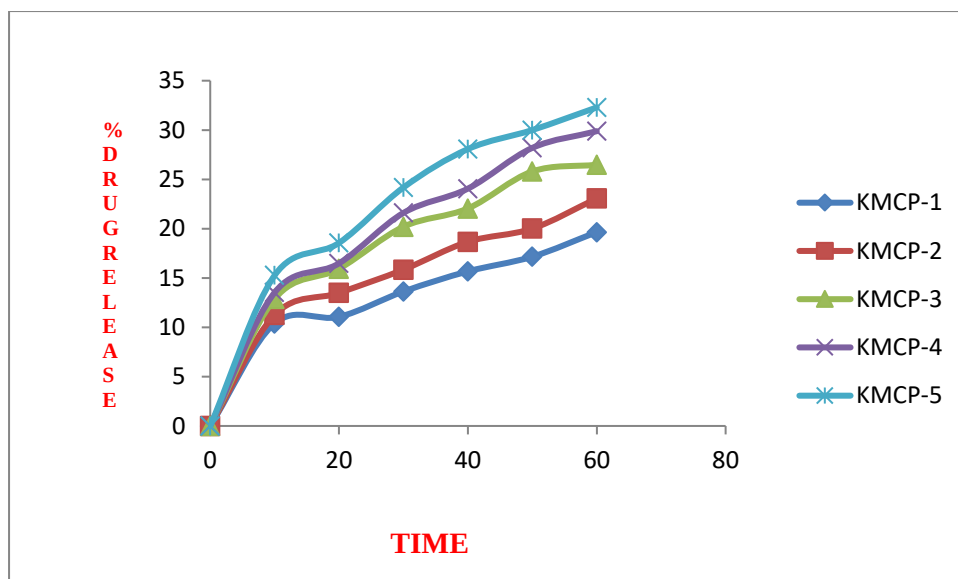


Figure 5: In vitro drug release profiles of solid dispersion containing cross povidone by kneading method
It was observed that the drug release was increased as the carrier concentration increases. Solid dispersion containing 1:5 ratio of drug to carrier have greater drug release (65.29%) compare to pure drug (10.521%).

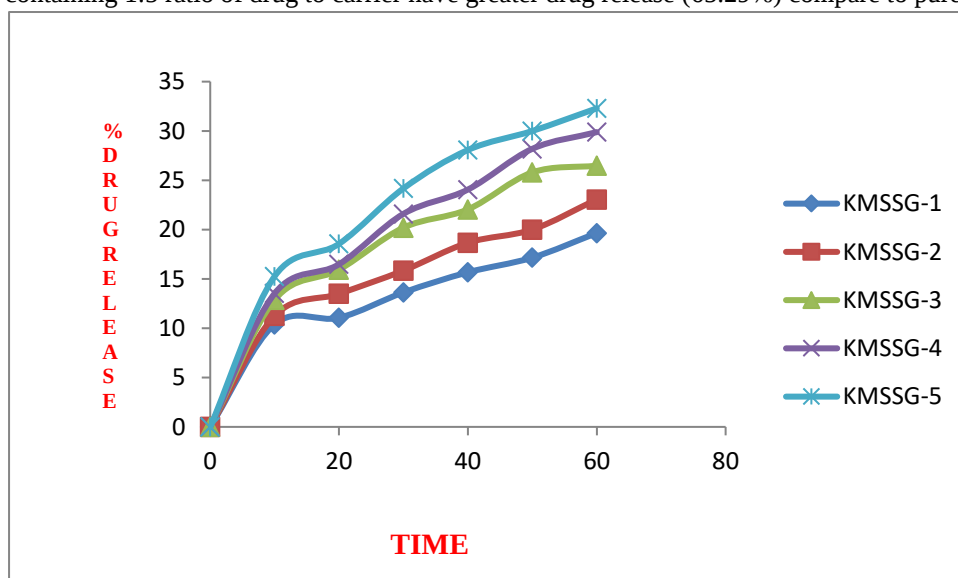


Figure 6: In vitro drug release profiles of solid dispersion containing sodium starch glycolate by kneading method
It was observed that the drug release was increased as the carrier concentration increases. Solid dispersion containing 1:5 ratio of drug to carrier have greater drug release (98.3%) compare to pure drug (10.521%).

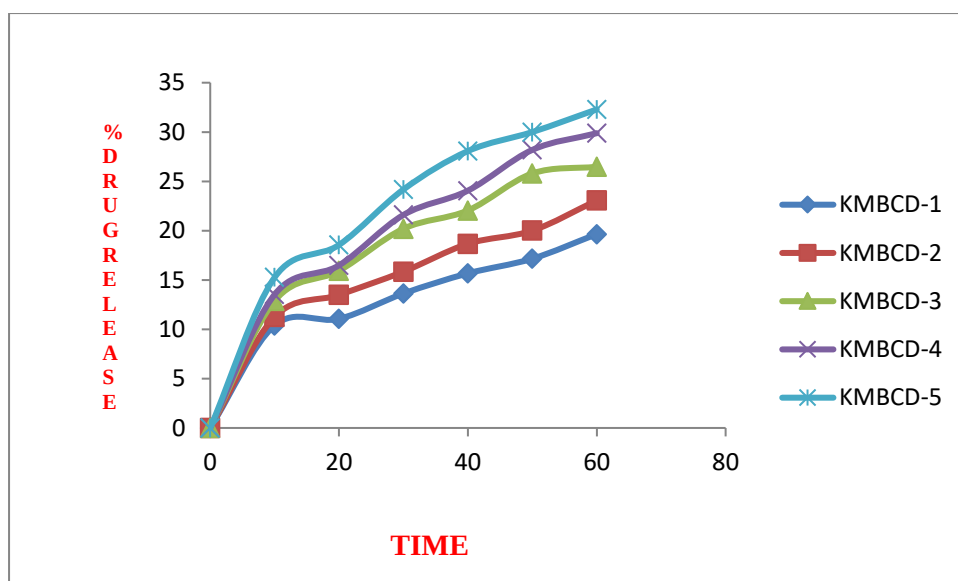


Figure 7: In vitro drug release profiles of solid dispersion containing beta cyclodextrin by kneading method
It was observed that the drug release was increased as the carrier concentration increases. Solid dispersion containing 1:5 ratio of drug to carrier have greater drug release (45.29%) compare to pure drug (10.521%).

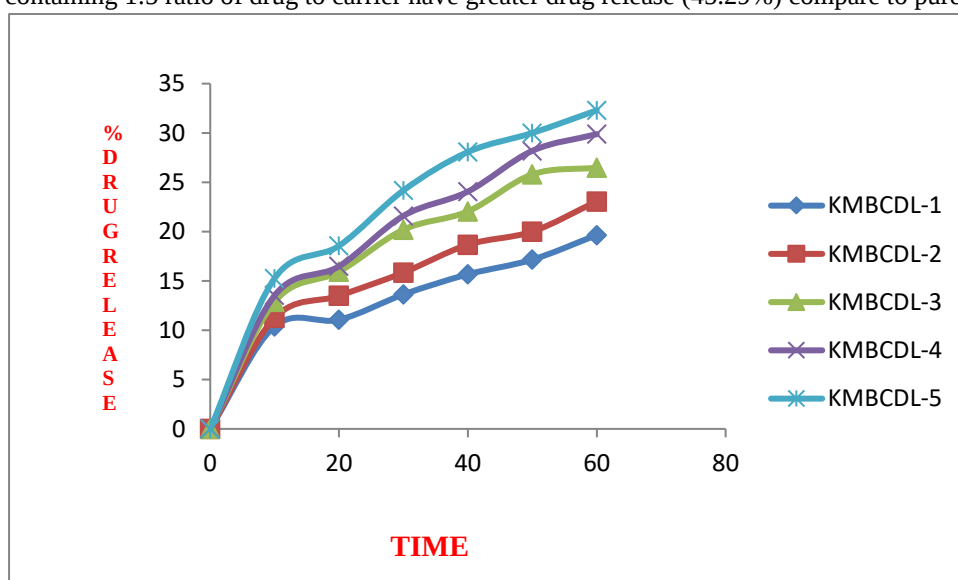


Figure 8: In vitro drug release profiles of solid dispersion containing beta cyclodextrin and lecithin by kneading method
It was observed that the drug release was increased as the carrier concentration increases. Solid dispersion containing 1:5 ratio of drug to carrier have greater drug release (44.29%) compare to pure drug (10.521%).

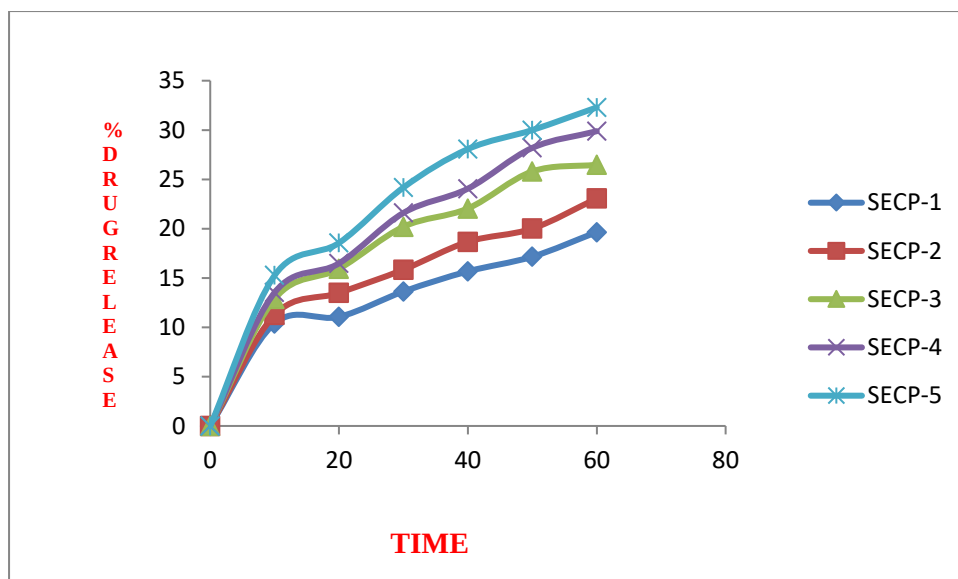


Figure 9: In vitro drug release profiles of solid dispersion containing cross povidone by solvent evaporation method

It was observed that the drug release was increased as the carrier concentration increases. Solid dispersion containing 1:5 ratio of drug to carrier have greater drug release (48.29%) compare to pure drug (10.521%).

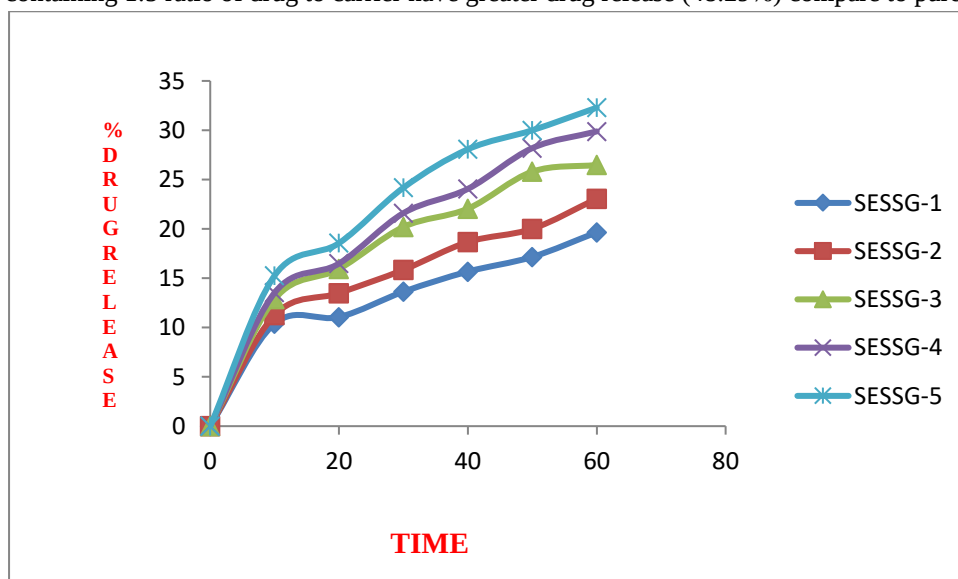


Figure 10: In vitro drug release profiles of solid dispersion containing sodium starch glycolate by solvent evaporation method

It was observed that the drug release was increased as the carrier concentration increases. Solid dispersion containing 1:5 ratio of drug to carrier have greater drug release (82.29%) compare to pure drug (10.521%).

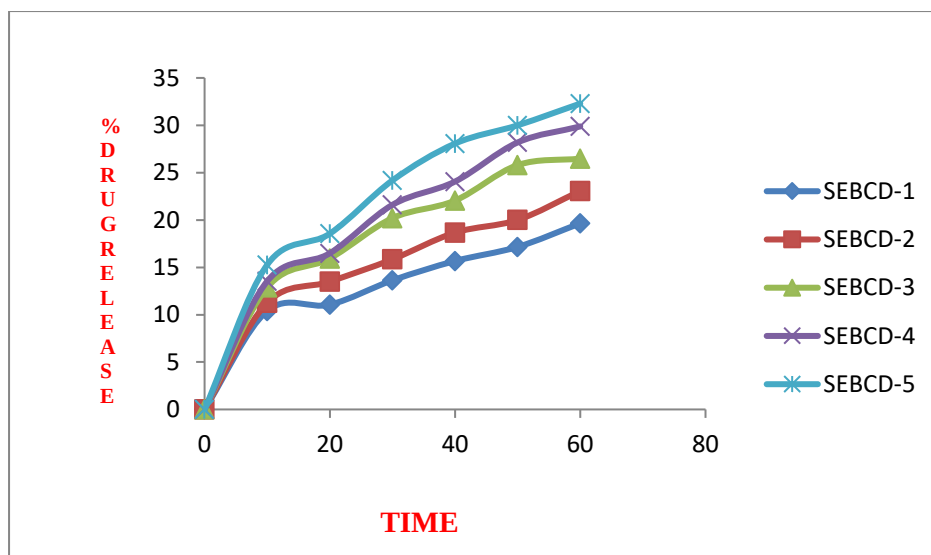


Figure 11: In vitro drug release profiles of solid dispersion containing beta cyclodextrin by solvent evaporation method

It was observed that the drug release was increased as the carrier concentration increases. Solid dispersion containing 1:5 ratio of drug to carrier have greater drug release (38.29%) compare to pure drug (10.521%).

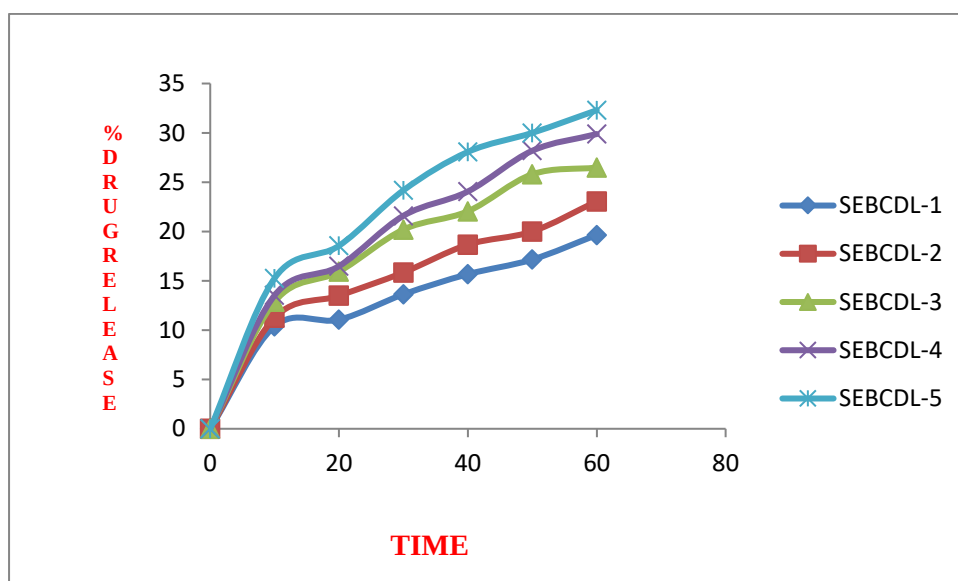


Figure 12: In vitro drug release profiles of solid dispersion containing beta cyclodextrin and lecithin by solvent evaporation method

It was observed that the drug release was increased as the carrier concentration increases. Solid dispersion containing 1:5 ratio of drug to carrier have greater drug release (32.29%) compare to pure drug (10.521%).

3.4 DSC studies As discussed in previous researches, mangiferin is a poorly soluble xanthenes' compound which is having partition coefficient log P of 2.5, but it is having strong intra and intermolecular hydrogen bonds (Demeyer et al., 2021). Due to strong hydrogen bonds, it is in crystalline form which makes the drug to difficulty in solubility. Generally, solid dispersion was used to enhance the solubility of poorly soluble drugs which change the compound from crystalline state to amorphous state (Septiana et al., 2020). Differential scanning calorimeter was studied to understand the melting point and crystalline profile of powdered mangiferin, physical mixture of sodium starch glycolate and mangiferin. The DSC curve of mangiferin has a single endothermic peak at 282 mm

which is confirming that the crystal melting factor. The DSC thermogram curves of the prepared stable dispersions, did not show any obvious endothermic peak around the melting factor of mangiferin, suggesting that mangiferin may also lose its crystalline in the starch glycolate polymer matrix. Mangiferin may exist in the amorphous ground inside the SD, which is consistent with our previous observation. Our result suggests that mangiferin in SD maintained an amorphous nation after rotation to similarly verify the alternative physical nation of mangiferin after entrapment in a sodium starch glycolate matrix.

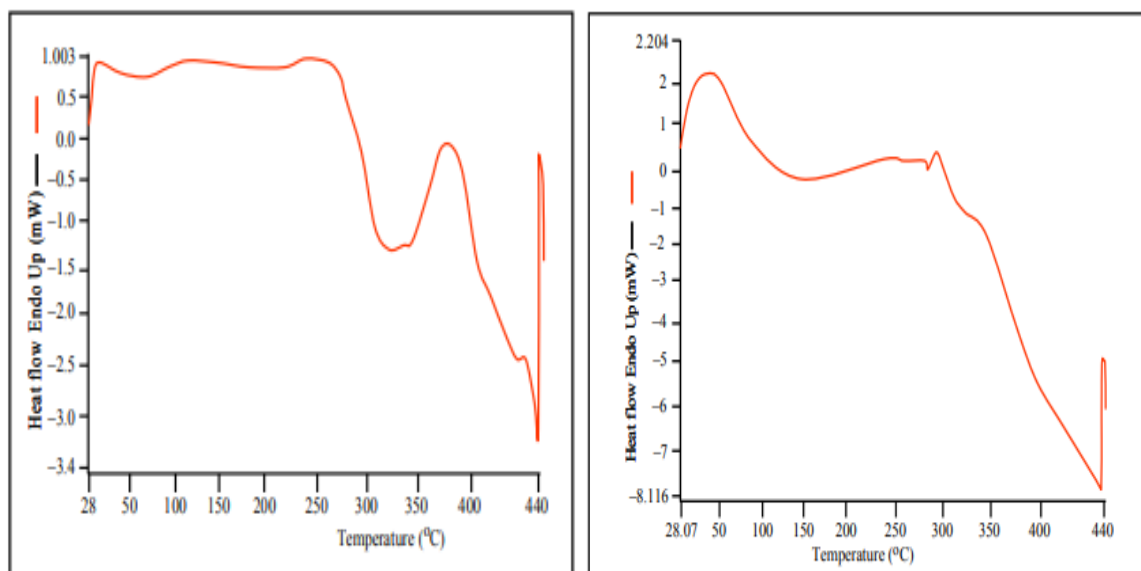


Figure 13: Differential scanning calorimetry of pure compound and solid dispersion

3.5. X-ray diffraction studies XRD was used to encounter crystallization houses. The XRD pattern of the SSG polymers showed no full-size diffraction peaks, which is consistent with the amorphous nature of these three acrylic polymers as previously suggested (Navarro-Orcajada et al., 2022). The halo XRD pattern of the mangiferin SDs indicates that there is no crystalline compound, thus confirming the DSC claim that within all 3 acrylic polymerbased SDs, mangiferin exists in amorphous nation instead of crystal country.

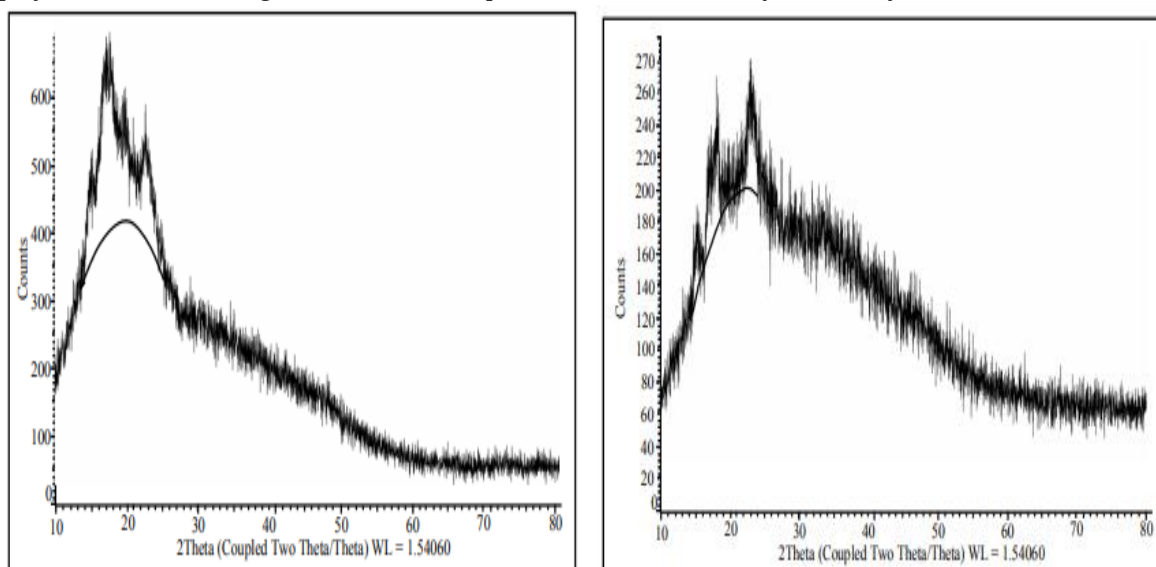


Figure 14: X-ray diffraction pattern of pure drug and solid dispersion

In this study, mainly we focused on development of suitable dissolution media for poorly soluble drugs. Mangiferin sold dispersion is prepared for enhancement of solubility. The solubility of mangiferin was increased

in kneading method by using sodium starch glycolate as a carrier in 1:5 ratios. There is 14 fold increase (0.79 mg/ml) in solubility compare to pure drug (0.057 mg/ml). Based on solubility, study the optimized formulation was used for the in vitro drug release studies. In vitro drug release was greater in pH 6.8 phosphate buffer along with 1% tween 80. The drug release was 98.3% in 1 h. So, phosphate buffer with 1% tween 80 confirmed as suitable dissolution media for mangiferin drug. Differential scanning calorimeter was conducted to understand the melting point and crystalline of mangiferin (Jamil and Polli, 2022a; Sales et al., 2022). The DSC curve of mangiferin has a single endothermic peak at 282 mm which is confirming that the crystal melting factor. The DSC thermogram curves of the prepared stable dispersions did not show any obvious endothermic peak around the melting factor of mangiferin, suggesting that mangiferin may also lose its crystalline in the starch glycolate polymer matrix. XRD was used to encounter crystallization houses (Jamil and Polli, 2022b; Nel, Samsodien and Aucamp, 2022). The XRD pattern of the SSG polymers showed no full-size diffraction peaks, which is consistent with the amorphous nature of these three acrylic polymers as previously suggested. The halo XRD pattern of the mangiferin SDs indicates that there is no crystalline compound, thus confirming the DSC claim that within all 3 acrylic polymer-based SDs, mangiferin exists in amorphous nation instead of crystal form.

4. Conclusion:

Optimised solid dispersion containing sodium starch glycol ate in 1:5 ratios have good solubility and maximum drug release compared to pure drug. So sodium starch glycolate is teh potential carrier for solubility enhancement of mangiferin drug.

5. References

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