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Original Article

DEVELOPMENT OF AMORPHOUS BINARY AND TERNARY SOLID DISPERSIONS OF NATEGLINIDE FOR IMPROVED SOLUBILITY AND DISSOLUTION

SHRADHA S. TIWARI[1], SHAILESH J. WADHER[2], SURENDRA G. GATTANI[3]

[1]Department of Pharmaceutics, Indira College of Pharmacy, Sahyog Campus, Vishnupuri, Nanded, Maharashtra, India, 431606,
[2]Department of Pharmaceutical Chemistry, School of Pharmacy, University Department, SRTMU, Nanded, Maharashtra, India, 431606,
[3]Department of Pharmaceutics, School of Pharmacy, University Department, SRTMU, Nanded, Maharashtra, India, 431606
Email: shraddha.life10@gmail.com

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ABSTRACT

Objective: Nateglinide is a commonly used oral hypoglycemic, biopharmaceutical classification system Class II drug, which shows relatively poor water solubility and variable bioavailability. The objective of the present investigation was to develop the binary and ternary solid dispersions of nateglinide for improved solubility and dissolution.

Methods: Nateglinide solid dispersions were prepared by a common solvent evaporation method. Polymers like soluplus, kolliphor P188, sylloid 244FP, gelucire 48/16, affinisol (HPMCAS), HPβCD, βCD were used in different combinations. The physicochemical characterization of the optimized ternary dispersion was studied by using FT-IR, DSC, and PXRD. Solubility and dissolution behavior of all dispersions were studied.

Result: From all prepared ternary solid dispersions, nateglinide dissolution was significantly faster than pure nateglinide. With ternary solid dispersion of NTG, soluplus and kolliphor P188 there was a big improvement in solubility and dissolution. This combination enhanced the solubility of NTG by 23 folds. Another ternary dispersion of NTG with soluplus and gelucire 48/16 enhanced solubility by 25 fold.

Conclusion: Ternary solid dispersion found superior over binary dispersions. For the ternary dispersions, showing the best solubility, tablets were prepared. Dissolution and drug release from the formulated tablet was as good as a marketed product.

Keywords: Nateglinide, Solid dispersion, Dissolution, Solubility enhancement

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INTRODUCTION

Enhancement of the solubility of the poorly water-soluble drug is one of the most challenging issues in the pharmaceutical industry. Limited drug Dissolution and bioavailability depend on its solubility and permeability [1]. Amorphous solid dispersion has been proved as an effective method to enhance the solubility and dissolution behavior of many BCS II class drugs [2]. Nateglinide is an oral hypoglycemic agent used in the treatment of type II diabetes mellitus (non-insulin-dependent diabetes mellitus, NIDDM). Nateglinide is a non-sulfonylurea drug, belonging to BCS class II, low solubility and high permeability [3].

NTG is an amino-acid derivative; it stimulates insulin secretion from β-cells of the pancreas through inhibition of potassium-ATP channels. Thereby reduces blood glucose levels. NTG immediately gets absorbed from the gastrointestinal tract and eliminated through plasma. NTG has a half-life of about 1.5 h [4]. Nateglinide is the most effective antidiabetic drug; lipophilic, belongs to family meglitinide, recommended in 60 mg or 120 mg dose. It has very poor water solubility 0.061 mg/ml. Solubility is the main obstacle to prepare an oral dosage form of nateglinide. Studies say that NTG exhibits pH-dependent solubility and variable bioavailability [5].

Nateglinide can be used as monotherapy or in combination with other hypoglycemic agents. NTG is an elegant, flexible and effective treatment option to reduce mealtime glucose in patients with type 2 diabetes [6]. Vasanti Suvarna *et al.* have successfully prepared ternary solid dispersion of NTG with HP–β–CD and L-Arginine for Solubility and Dissolution Enhancement. The solubility of a drug is a critical parameter to enhance the oral bioavailability of drugs like NTG. Solubility and bioavailability of nateglinide have been enhanced previously by using different methods. In our study, we have used new combinations of polymers. The main objective of this work was to develop a new ternary and binary solid dispersion formulation to enhance the solubility of nateglinide. Preparation of polymer-based amorphous solid dispersions (ASD) has been widely used as a strategy to improve the solubility of poorly water-soluble drugs.

The literature reveals that the solubility of NTG is less at acidic pH, while more in alkaline pH. pH-dependent solubility is a major concern while designing NTG into the dosage form. As per the previous studies nateglinide proved to have good solubility with alkalizes like Na2CO3, NaCO3, and NaOH. For the preparation of amorphous solid dispersion with a drug like NTG, one must be very selective in the choice of polymers [7].

Soluplus is polyvinyl caprolactam polyvinyl acetate-polyethylene glycol graft copolymer. It is an outstanding matrix polymer and enhances solubility dramatically. Soluplus is unique in that it is an amphiphilic i.e. it can enhance the solubility of both hydrophilic and lipophilic drug molecules. Soluplus has been found to have an excellent solubilizing efficiency of the BCS class II drugs. It can be used for preparing immediate-release formulations of a poorly water-soluble BCS class II drug. Soluplus is an interesting polymer, acts as a matrix polymer for superior performance in forming solid solutions and an active solubilizer through micelle formation in water [8, 9].

β-Cyclodextrin (β-CD) is the most widely used natural cyclodextrin, which forms inclusion complexation with drug molecules and enhances solubility. From the previous studies it has been proved that with β-CD nanocomposites formation by solvent evaporation, the solubility of drugs can be enhanced significantly [10, 11].

The surfactants can be employed in pharmaceutical dosage forms as a solubilizer, emulsifier, wetting agent, suspending agent, detergent, etc. Gelucire 48/16 is a novel hydrophilic grade of polymer, extensively used to enhance solubility and bioavailability of the drug. We have used gelucire 48/16 along with Soluplus to prepare ternary solid dispersion [12].

Solid dispersion prepared by the solvent evaporation method has been proved to enhance the solubility of drugs successfully. Ternary solid dispersions were developed using different polymers like soluplus, kolliphor P188, affinisol, sylloid 244 FP, gelucire 48/16, etc. In this drug and carrier were dissolved in a volatile solvent with homogeneous mixing. The volatile solvent was later evaporated at normal room temperature [13].

The present research work was aimed to study and explore new combinations of polymers for solubility enhancement. NTG binary and ternary dispersions were prepared by the common solvent evaporation method for solubility and dissolution enhancement. Finally, the optimized dispersions were formulated as tablets. *In vitro* drug release through in house formulations and marketed tablets were studied.

MATERIALS AND METHODS

Materials

The pharmaceutical grade of Nateglinide was obtained as a generous gift from Cipla Ltd. Goa, India. β Cyclodextrin and Hydroxypropyl β Cyclodextrin were purchased from Sigma Aldrich (Mumbai, India). Affinisol, soluplus, kolliphor P 188, gelucire 48/16, sylloid 244FP were provided as a gift sample by Lupin Ltd Aurangabad, India. Ethanol was purchased from Himedia Laboratories, Mumbai, India. All remaining ingredients were purchased from S. D Fine Chemicals (Mumbai, India).

Solubility determination of nateglinide

Nateglinide solubility was determined in different media like Phosphate buffer pH 6.8, Phosphate buffer pH 7.4, 0.1 N HCl, and reported dissolution media 0.5 % SLS in 0.01 N HCl. Binary and ternary complexes of NTG were formulated with polymers like soluplus, β-cyclodextrin and hydroxypropyl β-Cyclodextrin, and affinisol. The Solvent co-evaporation method was employed to prepare solid dispersions. The complexes were scraped and collected. Table 1. Shows the Composition of different binary and ternary SD.

Table 1: Composition of different binary and ternary SD

Dispersion type	Combination	Code	Weight ratio
Binary dispersion	NTG and Soluplus	F1	1:1
	NTG and Soluplus	F2	1:2
	NTG and HPBCD	F3	1:1
	NTG and HPBCD	F4	1:2
	NTG and BCD	F5	1:2
	NTG and BCD	F6	1:3
	NTG and Affinisol	F7	1:1
	NTG and Affinisol	F8	1:2
	NTG and Affinisol	F9	1:3
	NTG and KolliphorP188	F10	1:2
Ternary dispersion	NTG+Soluplus+Kolliphor P188	F11	1:1:1
	NTG+Soluplus+Affinisol	F12	1:1:1
	NTG+Soluplus+Gelucire 48/16	F13	1:1:1
	NTG+BCD+Na2CO3	F14	1:1:1
	NTG+Soluplus+Sylloid FP244	F15	1:1:1

Formulation of binary and ternary solid dispersions

A weighed amount of nateglinide and polymer were mixed, dissolved in common solvent ethanol; the mixture was then sonicated for 10-20 min using ultra-probe sonication Model Frontline Sonicator FS-250 (Ahmedabad, India) to prepare the homogenous Solution later the solvent evaporated at room temperature. Nateglinide and polymers were dissolved in ethanol in different ratios (1:1,1:2, 1:3.1:4) to prepare SD by the solvent evaporation technique until we find the best proportion of drug and polymer. The prepared complexes were studied for solubility. In this same way, complexes were prepared with Soluplus, βCD, HPβCD, and Affinisol. Solubility for all prepared complexes was determined and the best ratios of the drug: polymer was decided. To formulate a ternary complex, a binary complex with the best solubility was selected and formulated. The combinations of polymers given in the following table 1. In the given ratio, the drug and polymers were dissolved in ethanol with continuous stirring and the solvent was evaporated at room temperature. Prepared complexes were then scraped and studied [14, 15]. The graphical abstract of the formulation is shown in fig. 1.

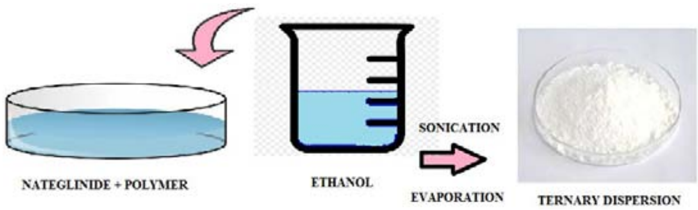

Fig. 1: Formulation of ternary solid dispersions

Determination of saturated solubility of NTG and prepared solid dispersions

To determine the solubility of the Nateglinide pure drug and dispersions, an excess quantity of the drug or its dispersions equivalent to 50 mg nateglinide were added to a 10 ml Volumetric flask containing 5 ml of the 0.5% SLS in 0.01 N HCl (Dissolution media of Nateglinide), the vials were stirred at 100 RPM with a magnetic stirrer for 24 h, the aliquots were filtered through 0.45-micron filter paper. The aliquots were diluted and assayed spectrophotometrically at 210 nm using a UV-Vis spectrophotometer (UV-1700 Pharmspec, Shimadzu, Kyoto, Japan). The calibration curve in different media was previously prepared for Nateglinide at 210 nm [16]. Similarly, Solubility of pure nateglinide is also determined in phosphate buffers pH 6.8, pH 7.4 and pH 1.2.

Fourier transform infrared spectroscopy

IR spectra of the pure NTG, all the formulated dispersion, were recorded on the FTIR spectrophotometer (Shimadzu 8400S, Japan) with KBr as the reference standard. FTIR study was conducted to study the alteration in the structure of pure NTG after the formulation of ternary dispersions. FTIR determines drug-polymer compatibility. 2–3 mg samples were mixed with about 4 mg of potassium bromide, compressed through the manual press to form a thin disc. The IR spectra were recorded at a scanning range from 4000–400 cm^{-1}.

Powder X-ray diffraction

The PXRD patterns of the pure nateglinide and the optimized NTG-ternary dispersion were obtained using an X-ray diffractometer, Miniflex II (Regaku, USA). The samples were scanned in the range of 5 ° to 50 ° (diffraction angle 2θ), Cu K α line as the source of radiation with nickel filter, at the 40-kV voltage and 25-mA current.

Differential scanning calorimetry

DSC thermograms of pure NTG and the optimized ^{NTG}-ternary dispersion were obtained by scanning from 10–400 °C at 10 °C/min with a differential scanning calorimeter (Mettler toledo, Japan). Each sample (approximately 5 mg) was weighed in a standard open aluminum pan using an empty pan as a reference.

Dissolution study of ternary dispersions

In vitro drug release through ternary solid dispersions and the pure drug (equivalent to 60 mg) was carried out in different Dissolution media, including 0.5% SLS in 0.01 N HCl, 0.1 N HCl, phosphate buffer having pH 6.8 and 7.4. Dissolution studies were carried out using the Electrolab USP II paddle apparatus at 37±0.5 °C in 1000 ml dissolution media; paddle speed was 50rpm, sampling was done at the time interval of 10, 20, 30 and 45 min. Aliquots were collected at different time intervals and filtered through a 0.45 µm filter. The fresh dissolution media was replaced again. The aliquots were subsequently diluted and the concentration of the drug was determined using a UV spectrophotometer at 210 nm.

Tablet formulation

After the solubility and dissolution study, the best ternary complexes were selected. For the best ternary complexes, tablets were formulated. For the formulation of a tablet karnavati tablet punching machine was used. For the prepared tablet dissolution, Disintegration, Hardness, Friability, Weight variation test was performed [17]. Table 2 shows the composition of formulated tablets.

Tablet 2: Formulation of NTG tablets

S. No.	Ingredient	N1 Quantity (mg)	N2 Quantity (mg)	N3 Quantity (mg)
1.	Nateglinide	60	60	60
2.	Soluplus	60	60	60
3.	Affinisol	60	-	-
4.	Kolliphor P188	-	60	-
5.	Sylloid 244 FP			60
6.	Avicel 102	36	36	36
7.	Croscarmellose sodium	2	-	-
8.	Lactose	-	20	-
9.	Magnesium Stearate	-	2	2
10.	Talc	2	2	2
The total weight (mg)		220	240	220

Dissolution study of formulations

For optimized formulations and marketed formulation dissolution study was performed in different dissolution media. All the parameters were kept similar to the dissolution study. The percentage of drug release from the optimized formulation and marketed formulation was calculated and compared. Sampling was done at the time interval of 10, 20, 30 and 45 min. The speed of the peddle was kept at 50 RPM.

RESULTS AND DISCUSSION

Saturation solubility of NTG

Saturation solubility of NTG was determined in various media like reported dissolution media 0.5% SLS in 0.01N HCl, Phosphate buffer pH 6.8 and pH 7.4 and 0.1 N HCl. Values of Saturation solubility of NTG in various Dissolution media are given in the following table 3. Preliminary studies revealed that NTG is a poorly water-soluble drug and shows pH-dependent solubility at different physiological pH ranges. It was found that Solubility of NTG gradually increased from acidic pH to alkaline pH.

Saturation solubility study of the prepared solid dispersions

All the batches of the above Binary mixtures, ternary mixtures, and pure drugs were subjected to saturation solubility studies at room temperature in 0.5% SLS in 0.01N HCl, which is reported dissolution media for nateglinide. The amount of drug dissolved was analyzed by the UV-Vis spectroscopy at 210 nm. Nateglinide forms a very transparent solid solution after solvent evaporation with Soluplus and Affinisol. Saturation solubility study of NTG and all prepared dispersion was found as follows. Fold enhancement in solubility was calculated. Ternary solid dispersion of NTG with soluplus and kolliphor P188 shows the highest fold enhancement solubility. Table 4. Shows saturation solubility data of nateglinide in various ternary dispersion.

Table 3: Saturation solubility data of nateglinide in various dissolution media: (mean±SD, n = 3)

S. No.	Nateglinide saturation solubility different media	Solubility (mg/ml)
1.	In 0.1 N HCl	0.525±0.027
2.	In Phosphate buffer Ph 6.8	2.134±0.123
3.	In Phosphate buffer Ph 7.4	6.864±0.145
4.	In 0.5% SLS in 0.01 N HCl	2.856±0.032

Fourier transform infrared spectroscopy (FT-IR)

FT-IR is an important technique to predict a possible interaction of the drug with polymers in the solid-state. FT-IR spectroscopy was used to detect the presence of possible interactions between NTG, soluplus, affinisol, sylloid 244 FP, kolliphor P 188 that, if it should result in shifting of the absorption bands characteristic for functional groups, which is involved in the interaction.

FT-IR spectra of NTG showed characteristic absorption peaks at 2927 cm-1 (-OH stretching; asymmetric), 2866 cm-1 (aliphatic CH stretching; symmetric, 1741 cm-1 (C = O stretching), 3064 cm-1 (aromatic C-H Stretching), 3300 cm-1 (aromatic N-H Stretching). The FTIR spectrum of ternary solid dispersions and pure glinide shows all the peaks for drug and other excipients, hence no interaction was observed between them. Considerable shifting of the major absorption bands of NTG has been observed in the spectra of all the analyzed ternary formulations. On the spectrum of formulation F 11 (NTG: soluplus: kolliphor P 188), the sharp absorption peak of NTG, positioned at 2927 cm-1, changed to a broad absorption band positioned around 2883 cm-1, while the absorption band positioned at 1741 cm-1 shifted to 1743 cm-1. In pure drug IR, N-H Stretching is observed at 3300 cm-1, in the optimized ternary complexes showing the best solubility, almost disappearance of characteristic N-H stretching peak of NTG at 3300 cm-1, this indicated the hydrogen bond interaction between NTG and Polymer complexes. In this case,–OH groups present in the NTG may be interacting with the terminal–OH and ether oxygen groups present in soluplus and form hydrogen bonds.

Soluplus shows a characteristic peak at 1750 cm-1 and 1650 cm-1 corresponding to the carbonyl–C = O group, 2747 and 2890 cm-1 for–C-H, and broadband in the range 3200-3400 cm-1 representing the terminal–OH groups. The spectrum of Kolliphor P 188 is characterized by strong absorption peaks at 2880 cm–1 signifying the aliphatic–C-H stretch, 1339 cm–1 (in-plane O-H bend), and 1098 cm–1 (C-O-stretch) Other absorption bands of NTG became indistinguishable. Formulation F 12 (NTG-soluplus-affinisol), and formulation F 15 (NTG-soluplus-sylloid 244), showed very similar IR spectra. Comparative graphs of some ternary dispersion are shown in the following fig. 2.

Table 4: Saturation solubility data of nateglinide in 0.75% SLS (Reported dissolution media) (mean±SD, n = 3)

Formulation code	Combination	Saturation solubility (mg/ml)	Fold enhancement in solubility
	NTG pure drug	**2.85**±0.032	
F1	NTG and Soluplus (1:1)	59.96±0.263	20.96
F2	NTG and Soluplus(1:2)	57.26±0.127	20.02
F3	NTG and HPBCD (1:1)	28.02±0.243	9.79
F4	NTG and HPBCD(1:2)	30.18±0.115	10.55
F5	NTG and BCD (1:2)	32.88±0.247	11.49
F6	NTG and BCD(1:3)	35.90±0.362	12.55
F7	NTG and Affinisol (1:1)	45.84±0.136	16.02
F8	NTG and Affinisol(1:2)	42.24±0.261	14.76
F9	NTG and Affinisol (1:3)	32.11±0.344	11.22
F10	NTG and Kolliphor P188(1:1)	43.69±0.245	15.27
F11	NTG+Soluplus+KolliphorP188	**68.38**±0.453	**23.90**
F12	NTG+Soluplus+Affinisol	**49.89**±0.123	**17.44**
F13	NTG+Soluplus+Gelucire 48/16	**72.82**±0.595	**25.46**
F14	NTG+BCD+Na2CO3	38.57±0.183	13.48
F15	NTG+Soluplus+Sylloid 244FP	**48.86**±0.496	**17.08**

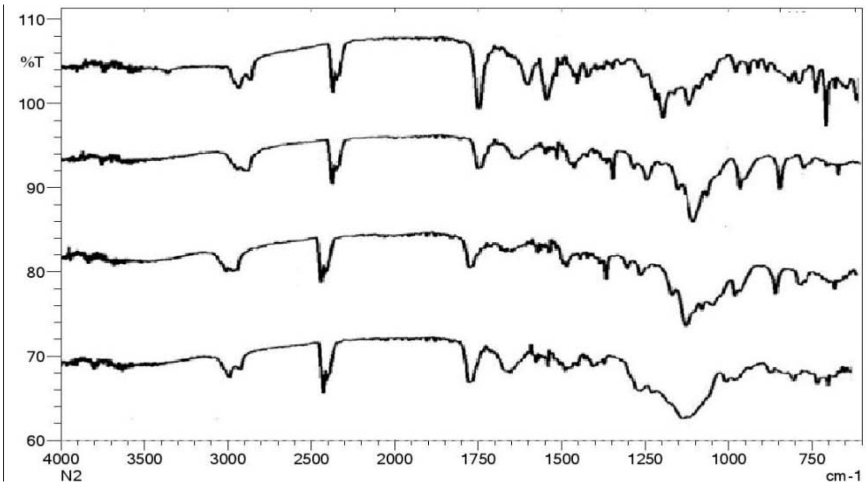

Fig. 2: Overley diagram of FTIR of pure nateglinide, NTG-soluplus-kolliphor, NTG-soluplus-gelucire, NTG-soluplus-sylloid ternary solid dispersions

Powder X-ray diffraction

The PXRD diffractograms of NTG and the optimized NTG-ternary dispersion are presented in fig. 3. As can be seen from the PXRD spectra of pure NTG, showed sharp characteristic diffraction peaks at 2θ diffraction angles of 5, 10.5, 12, 15 and 19 confirming the crystalline nature of the pure drug. In the PXRD spectra of optimized ternary solid dispersions, no characteristic peaks were observed. Broad hallows were observed, indicating the amorphous nature of NTG in ternary dispersions.

Differential scanning calorimetry

DSC thermograms of pure NTG and the optimized NTG-ternary dispersion are shown in fig. 4. The DSC curve of pure NTG exhibited a single endothermic peak at 130 °C, which indicates its melting point. Thus NTG exhibited in crystalline Form. The characteristic peak of the pure drug disappeared in the thermogram of ternary dispersions. This indicates a molecular dispersion of NTG in ternary dispersions. The total disappearance of the drug melting peak indicates the occurrence of the amorphous nature of NTG in ternary dispersions. The exothermic peak for the NTG-ternary dispersion was observed at 345.29 °C.

Dissolution Study of dispersions

Ternary dispersions with the highest solubility were selected and drug dissolution was studied through the selected combinations. The percentage of NTG release was calculated through all selected dispersion. The study was performed in different dissolution media. Table 5. Shows dissolution study of nateglinide ternary solid dispersions in different dissolution media (Percentage drug release) after 10 min of dissolution.

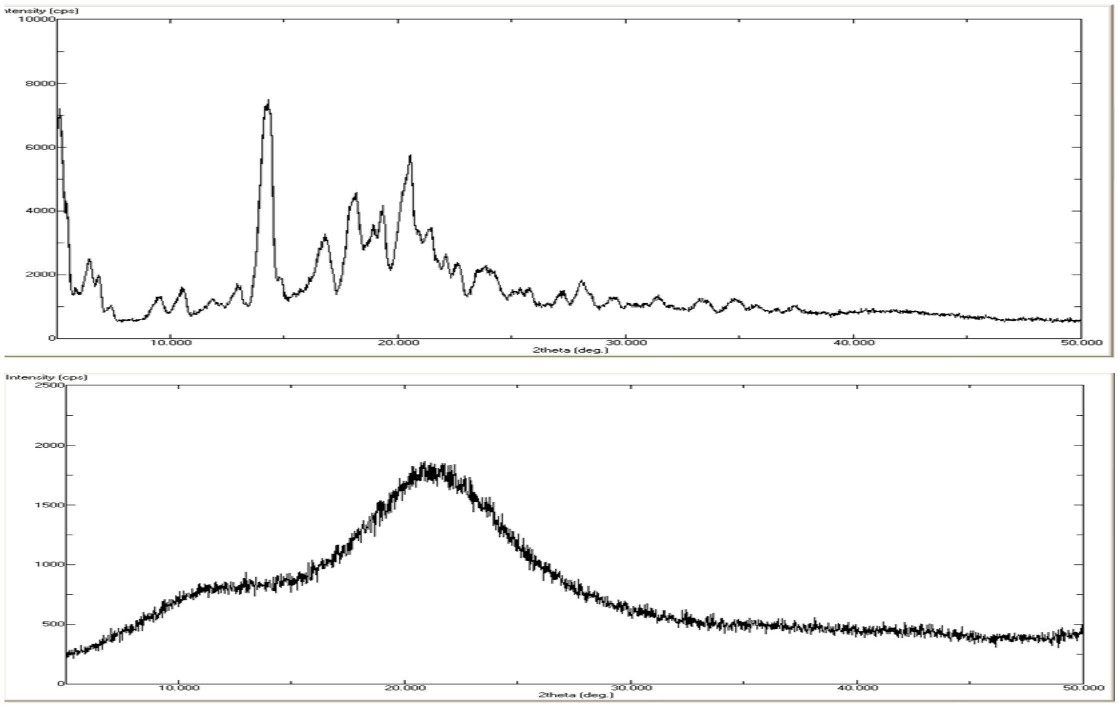

Fig. 3: PXRD thermogram of pure NTG and optimized ternary dispersion

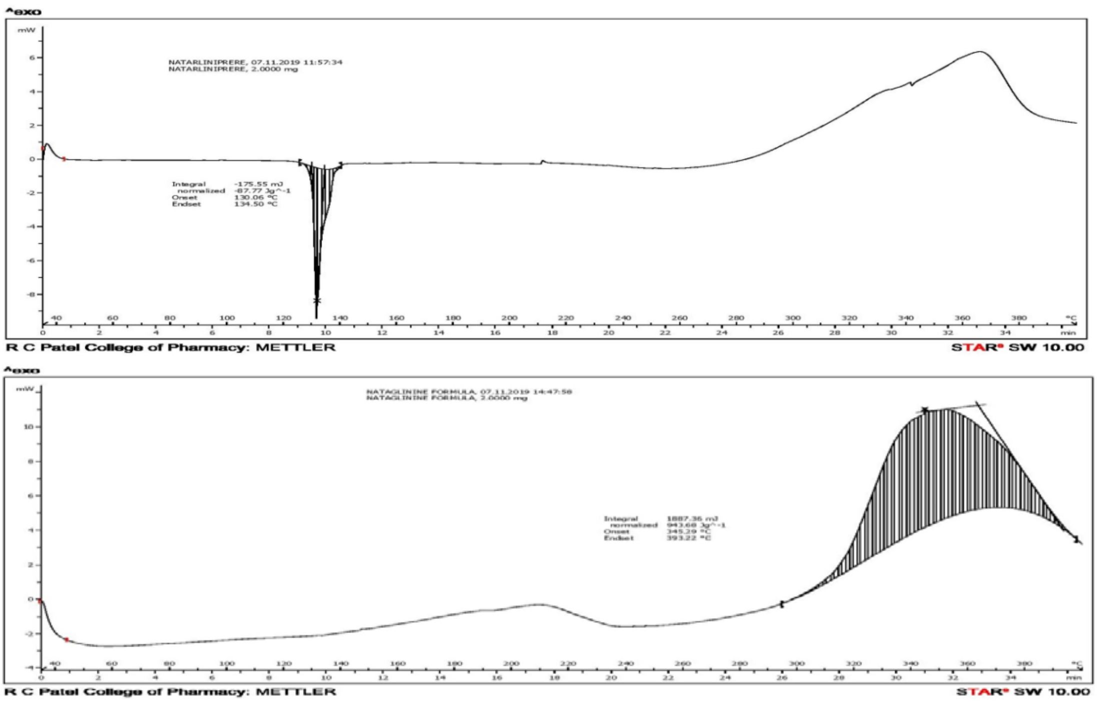

Fig. 4: DSC thermogram of pure NTG and optimized ternary dispersion

Table 5: Dissolution study of nateglinide ternary solid dispersions in different dissolution media (Percentage drug release) after 10 min of dissolution

Complexes	Dissolution media			
	0.5% SLS in 0.01 N HCl	0.1 N HCl	Ph. 6.8 buffer	Ph. 7.4 buffer
Pure NTG	29.87	10.07	26.67	28.56
NTG+Soluplus+KolliphorP188	100.89	100.54	89.54	94.67
NTG+Soluplus+Affinisol	100.38	72.87	100.03	100.18
NTG+Soluplus+Sylloid	98.89	100.35	93.53	95.67
NTG+Soluplus+Gelucire 48/16	100.13	98.92	94.36	96.55
NTG+BCD+Na2CO3	89.34	97.67	80.72	83.96s

NTG dissolution from solid dispersions

The complexes showing more fold enhancement in solubility were selected and their dissolution study was performed in all selected media. Dissolution profiles of NTG from the pure drug were studied in dissolution media and percentage drug release through prepared formulations in all dissolution media, are shown in table 5. From the presented dissolution profiles, it can be observed that pure NTG dissolves slowly and incompletely, with less than 30 % of NTG dissolved after 45 min of testing. Dissolution of all prepared Ternary dispersions in 0.5% SLS in 0.01 N HCl, was faster relative to pure NTG. The fastest NTG dissolution rate was achieved from the formulation From complex ternary F13 (NTG+Soluplus+Gelucire 48/16) 100.13% of the drug was released within 10 min of dissolution while from F11 (NTG+Soluplus+KolliphorP188), with 100.89% of NTG dissolved after 20 min of Dissolution. F 12 (NTG+Soluplus+Affinisol) dissolves 100.13% after 45 min. As all the prepared ternary dispersions were in powdered form, many were dissolved 100% within 10 min of dissolution. The percentage of drug release of all SD was very slow in 0.1 N HCl. All ternary dispersions prepared with soluplus were dissolved completely at all the dissolution media. Formulated combinations successfully enhanced the dissolution of NTG.

Dissolution study of formulations

Ternary dispersions showing improved drug release were formulated as NTG tablets. Dissolution study of optimized NTG tablets and marketed formulation, Glinate-60 was performed in different dissolution media. The comparative drug release was observed as follows. Table 6 shows comparative Percentage drug release from in house and marketed tablets in 0.5% SLS in 0.01% HCl dissolution media. Fig. 5 shows a Comparative percentage drug release from NTG marketed tablet and prepared tablets.

Table 6: Percentage drug release of tablets in 0.5% SLS in 0.01% HCl dissolution media

Time in min	N1	N2	N3	Marketed brand glinate 60
0	0	0	0	0
10	59.57	33.67	49.28	63.79
20	89.54	50.45	61.33	82.42
30	100.17	78.34	77.86	100.32
45	92.28	100.89	100.65	88.39

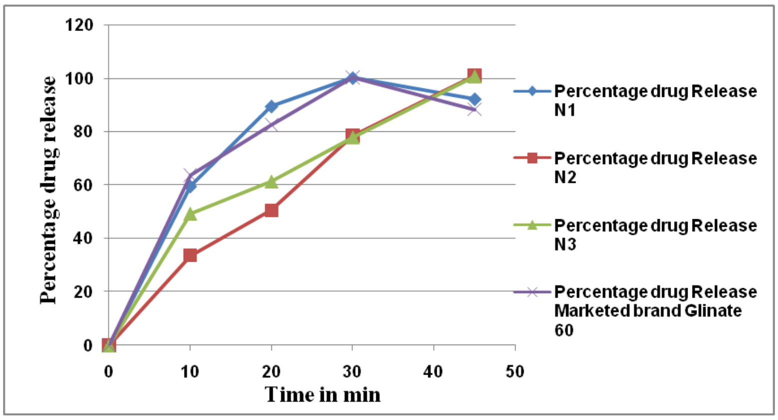

Fig. 5: Comparative percentage drug release from NTG marketed tablet and prepared tablets

DISCUSSION

After solubility and dissolution determination of binary solid dispersions, we found that with all selected polymers, the solubility of the drug increases up to a certain limit beyond that it remains the same. Soluplus forms a solid solution with drugs that allows the drug in a dissolved state and shows superior performance to enhance solubility. NTG with soluplus shows more solubility at 1:1 ratio and solubility decreases with increasing concentration of soluplus. This might be due to Higher concentration may result in a cloudy or turbid aqueous solution. This is due to the formation of colloidal soluplus micelles. Molecular dispersion might be the reason behind the enhanced solubility of drugs with soluplus. By considering the size of the dosage form, we have considered 1:1 as a good ratio to make formulation.

In ternary dispersions, NTG-Soluplus-KolliphorP188 combination enhanced solubility dramatically. Ternary dispersion with kolliphor P188 and soluplus, enhanced solubility of NTG Synergistically [18]. Another mechanism involved may be that, soluplus being hydrophilic makes a wet layer around the drug molecule which allows the transfer of solvent to the surface of the drug molecule which makes the drug molecule solubilize [19].

NTG-Soluplus-Gelucire 48/16 ternary combination was proved best. This combination enhanced the solubility of NTG by 25.46 fold. Gelucire 48/16 is a non-ionic surfactant proved as a solubilizer as well as a bioavailability enhancer. This polymer forms micelle solution with aqueous media, it enhances the wettability of the drug thereby improves solubility.

CONCLUSION

In the present investigation, there was a significant improvement in the solubility and dissolution profile of NTG by formulating ternary solid dispersions. Ternary solid dispersions prepared by the common solvent evaporation method proved a successful method to enhance the solubility of NTG. Solubility and dissolution were enhanced significantly with soluplus and kolliphor P188. Soluplus and gelucire 48/16 with NTG enhanced solubility dramatically. F11 and F13 ternary dispersions were having the best solubility. Prepared tablets show very good dissolution. All formulations N1, N2, N3 showed the complete drug release after 45 min. Among all prepared formulations N1 was found best. 100 % Drug was released from the marketed tablet and N1 after 30 min. Formulating ternary solid dispersions of NTG with Soluplus and Kolliphor could be a potential strategy to improve the solubility of NTG.

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AUTHORS CONTRIBUTIONS

Authors declare that the work done by the names mentioned in the article and all the liabilities and cl aims related to the content of the article will be borne by the authors.

CONFLICT OF INTERESTS

The authors declare that no conflict of interest associated with this work.

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