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Formulation Development of Solid Dispersions of Nateglinide using meltable hydrophilic carrier

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ABSTRACT

The objectives of the present research work are to improve the solubility and dissolution rate of nateglinide. Solid dispersions of nateglinide were prepared by fusion method by using three selected hydrophilic meltable carriers vis-a-vis gelucire 44/14, poloxamer 188 and polyethyleneglycol (PEG6000). Sylysia 550 was used as an adsorbent. Solid dispersions were evaluated for solubility, phase solubility, flowability, compressibility, Fourier transform infrared spectra (FT-IR), differential scanning calorimetry (DSC). Solubility studies showed 10, 16 and 7 fold increase in solubility for gelucire 44/14, poloxamer 188 and PEG6000 based solid dispersions respectively. The Gibbs free energy ΔGtr° values were all negative for all the three carriers indicating spontaneous nature of solubilisation. FT-IR and DSC spectra showed that drug and carriers are compatible with each other. Solid dispersions exhibiting highest solubility for each were compressed into immediate release tablets by using crosscaramellose sodium as superdisintegrant. In vitro dissolution studies, exhibited more than 90 % drug dissolution in 1 h for poloxamer 188 based solid dispersion tablets (F11). The adsorbent, sylysia 550 may be used to impart good flow and compressibility to solid dispersions. Among the three carriers, poloxamer 188 exhibited better solubility and dissolution enhancement potential for nateglinide.

***Key Words:** Solubility, Gelucire44/14, Poloxamer 188, PEG6000*

INTRODUCTION

Several approaches have been attempted for improvement of solubility and dissolution rate of poorly water-soluble drugs [1]. The most commonly adopted and successful approaches include reducing particle size, solubilization in surfactant systems, formation

of water soluble complexes, use of prodrug and drug derivatization approaches such as strong electrolyte salt forms, lyophilization, manipulation of the solid state of the drug substance to improve drug dissolution, i.e., by decreasing crystallinity of the drug substance through formation of solid dispersions [2]. Solid dispersion can be defined as distribution of active ingredients in molecular, amorphous, and/or crystalline forms surrounded by an inert carrier. The solid state characteristics of solid dispersions have been extensively studied and reported [3]. Formulation of poorly water-soluble drugs as solid dispersions leads to a marked improvement in their dissolution rates and is often accompanied by an increase in their relative bioavailability [4].

In recent times, many scientists have reported improvement in solubility and dissolution rate for poorly soluble drugs by using meltable hydrophilic carriers like gelucire 44/14 [5], poloxamer 188 [6] and polyethylene glycol (PEG6000) [7]. Gelucire is a varying mixture of mono, di and triglycerides with polyethylene glycol esters of fatty acids. They are inert, semisolid and waxy amphiphilic excipients. A low hydrophilic-lipophilic balance (HLB) value in gelucire decreases the dissolution rate whereas high HLB value enhances the dissolution rate. The low HLB compounds are composed of partial glycerides while those with HLB values above 10 are mixtures of partial saturated glycerides and polyethylene glycol (PEG) esters. Gelucire 44/14 is a semisolid excipient with an HLB value of 14 and melting point of 44^0C. Its hydrophilic property and low melting point makes it a good choice for use as carrier in preparation of solid dispersions by fusion method [8]. Poloxamers are polyoxyethylene-polypropylene block copolymer nonionic surfactants that have been widely used as wetting and solubilising agents. Poloxamer consists of hydrophilic corona ethylene oxide and hydrophobic core (polypropylene oxide) blocks arranged in a triblock structure resulting in an amphiphilic copolymer. Poloxamer 188 exhibits low melting point (about 52-57^0C) with an HLB value of 29. Poloxamer 188 based solid dispersions have been considered as an effective method for improving drug dissolution rate and their saturation solubility in the gastrointestinal fluids [9]. Polyethylene glycol is also one of the most commonly used excipient for enhancement of solubility. It shows excellent water solubility and vary significantly in molecular weight, ranging from 200 to >300,000 with an HLB value of 19. The molecular size of favors the formation of interstitial solid solutions. It is often employed as vehicles due to their low toxicity, low melting point, rapid solidification rate, high aqueous solubility, availability in various molecular weights, economic cost, and physiological tolerance. These and other properties make it a very suitable vehicle in the formulation of dosage forms [10].

Although gelucire 44/14, poloxamer 188 and PEG6000 based solid dispersions significantly improve the dissolution rate of poorly water soluble drugs, but they have some limitations such as poor flow and sticking to tablet punches [11]. This will create problems in formulation of solid dosage forms like tablets and capsules. In order to overcome these problems, an inert material with good flow and compressibility may be used to adsorb the dispersion on its surface. Sylysia 550 is an amorphous SiO_2 with high specific surface area and porosity, is a dry, white micronized porous powder having an average particle size of 3.9 mm, and is tasteless and odorless. It has a high specific surface area (300 m^2/g) and high adsorption capacity (310 mL/100 g), making it a

suitable material for adsorption of a high proportion of drug [12]. It is used primarily as a tablet excipient to improve the ease of powder flow through the tableting process, which provides more accurate dosage. It can be also used for powderizing liquids, to increase the viscosity of liquids and gels, or to protect sensitive compounds from moisture.

Nateglinide is selected as the model drug for the above proposed research. Netaglinide is use as monotherapy to lower blood glucose in patients with Type-2 diabetes, whose hyperglycemia cannot be adequately controlled by diet and physical exercise and have not been chronically treated with other anti-diabetic agents. It is practically insoluble in water [13]. Nateglinide is rapidly and almost completely (greater than or equal to 90%) absorbed from an oral solution. Absolute oral bioavailability is estimated to be 72%. The nateglinide which has a half life of about 1 hr [14]. Hence the primary objective of the present research work is to improve the solubility and dissolution rate of nateglinide by using three different hydrophilic meltable carriers vis-a-vis gelucire 44/14, poloxamer 188 and PEG 600. The secondary objective is to formulate an immediate release (IR) tablet from the solid dispersion exhibiting highest solubility.

MATERIALS AND METHODS

Materials Used

Nateglinide was obtained as a gratis sample from M/S Dr Reddy's Laboratories Ltd, Hyderbad. Gelucire 44/14 was obtained as gift sample from Gattefosse India Pvt Ltd, India. Sylysia 550 was a gift sample from Fuji sylysia, Japan. Poloxamer 188 was procured from Sigma Aldrich, India. PEG 6000 was procured from Fine Chemicals, India. All other chemicals and reagents used were of analytical grade.

Method

Phase solubility studies were performed as per method described by Higuchi et al, 1965 [15]. An excess amount of powdered nateglinide was placed in a screw-cap glass vial to which 20 mL of distilled water containing various concentrations (0, 2, 4, 6, 8 and 10 % w/v) of gelucire 44/14 poloxamer 188 (0, and 1 % w/v) and PEG 6000 (0, 2, 4, 6, 8 and 10 % w/v) (Table-1). The samples were shaken at 37 ± 0.5 °C for 72 h on a Remi mini rotary shaker-12R-DX. After 72 h of shaking, the samples were filtered through a 0.45 µm membrane filter (Auroco, Thailand). The filtrate was diluted suitably and analyzed in an UV-Vis spectrophotometer UV-1800 (Shimadzu, Japan).

The value of the apparent stability constant, Ks for nateglinide-gelucire 44/14, nateglinide-poloxamer 188 and nateglinide-PEG6000 combinations was computed from the phase-solubility profiles, as described by

$$Ks = {Slope}/{Intercept\ (1 - Slope)} \quad (1)$$

The Gibb's free energy of transfer (ΔG_{tr}^{0}) of nateglinide from distilled water to solutions of carrier was calculated by using formula:

$$\Delta G_{tr}^{0} = -2.303RT\left\{log\frac{S_0}{S_s}\right\} \quad (2)$$

Where S_0/S_s is the ratio of the molar solubility of nateglinide in distilled water of gelucire 44/14, poloxamer 188 and PEG 6000 to that in the same medium.

FT-IR spectroscopy study

Nateglinide-carriers (1:1) interactions were assessed by FT-IR spectroscopy (IR-Affinity-1, Shimadzu, Japan). FT-IR spectra of pure drug nateglinide and its 1:1 solid dispersions with gelucire 44/14, poloxamer 188 and PEG 6000 were recorded on IR using KBr discs. The instrument was operated under dry air purge and the scans were collected at a scanning speed of 2 mm/sec with resolution of 4 cm^{-1} over the region 4000-400 cm^{-1}. The FT-IR spectra are shown in **(Figure 1)**.

Differential scanning calorimetry (DSC) study

The DSC measurements were performed on a DSC with thermal analyzer (DSC-60, Shimadzu, Japan). All the accurately weighed samples (about 2 mg) were placed in sealed aluminum pans before heating under nitrogen flow (20 mL/min) at a scanning rate of 10 °C/min from 25 to 175°C. An empty aluminum pan was used as reference. DSC measurements were performed for nateglinide and its 1:1 solid dispersions with gelucire 44/14, poloxamer 188 and PEG6000 to study drug carrier interaction. The results are shown in **(Figure-2)**.

Formulation of solid dispersion

Preparation of solid dispersions of Nateglinide with Gelucire 44/14, Poloxamer 188 and PEG6000

Solid dispersions were prepared by melt dispersion method. Nateglinide was added to the melt of gelucire 44/14, maintaining a temperature of 50^{o}C to obtain a clear molten mixture. The molten mixture was then added drop-wise to sylysia 550 with continued mixing. The solid dispersions were allowed to cool to room temperature by air-cooling followed by sieving through mesh 40. The compositions of solid dispersions are shown in Table-2. Batch size of each formulation was 50 g. Poloxamer 188 and PEG 6000 based solid dispersions of nateglinide were also prepared by similar method **(Table-2)**.

Solubility measurement of solid dispersions

Solubility of nateglinide and its solid dispersions was determined [16]. An excess amount of nateglinide and solid dispersions were added to 20 mL of freshly prepared distilled water in clean vials with continuous shaking on a Remi mini rotary shaker-12R-DX at 25 ± 0.5 °C for 24 h to achieve equilibrium. The filtered solutions were suitably diluted and analyzed spectrophotometrically. The results are shown in **(Table 3)**.

Flowability and compressibility measurement

Solid dispersions were characterized for flow and compressibility by measuring Compressibility index (%), Hausner's ratio (H.R) and angle of repose (Ɵ) [17]. The results are shown in Tabl-3.

The Hausner's ratio is a number that is correlated to the flowability of powder. The Hausner's ratio is determined by following formula.

$$Hausner's\ Ratio = \frac{Tapped\ Density}{Bulk\ Density} \quad (3)$$

Compressibility index (CI) was determined according to the formula

$$C.I = \frac{(Tapped\ Density - Bulk\ Density)}{Tapped\ Density} \times 100 \quad (4)$$

Angle of repose was determined by allowing the solid dispersions to flow through a funnel (with a 10 mm orifice diameter) and measuring the angle between the horizontal and the slope of the heap of solid dispersions. The radius (r) and height (H) of the pile were measured. Then the angle of repose (θ) was calculated using following formula.

$$\theta = tan^{-1}\ {}^{h}/_{r} \quad (5)$$

Preparation of Immediate Release (IR) Tablet

The composition exhibiting highest solubility for each carrier were mixed with superdisintegrant crosscaramellose sodium, talc and magnesium stearate and then compressed on a multistation tablet press (karnavati MiniPress II, Ahmedabad) with a flat, circular punch of 8 mm diameter to produce nateglinide IR tablet. The composition is shown in (Table 4).

Quality Control tests for tablets

The prepared tablets were subjected to standard quality control tests. Weight variation was determined by weighing 20 tablets individually, the average weight was calculated and the percentage variation of each tablet was determined. Hardness was determined by testing 6 tablets from each formulation using a Electrolab digital portable hardness tester EH-01 (Electrolab, India) and the average applied pressure (kg/cm^2) required to crush each tablet was determined. Friability was determined by firstly weighing 10 tablets then placing them in a friability tester EF-2W (Electrolab, India) which was rotated for 4 min at 25 rpm. After dusting, the total remaining weight of the tablets was recorded and the percentage of friability was calculated. The disintegration time for the tablets was determined in 900 mL of distilled water using a programmable tablet disintegration tester ED-2L (Electrolab, India).

In-vitro dissolution test

The release of nateglinide from gelucire 44/14, poloxamer 188 and PEG600 based IR tablets was determined using USP paddle type Dissolution Tester at 50 rpm. Dissolution was examined using 900 mL of simulated intestinal fluid (SIF) without enzyme. The temperature was maintained at 37 ± 0.2°C. Samples each containing 5 mL were withdrawn at 5, 10, 15, 30, 45 and 60 min intervals, filtered through a Whatman filter of 0.45 µm and replaced with an equal amount of fresh dissolution medium to maintain sink condition. Samples were then suitably diluted and analyzed spectrophotometrically at 210 nm. The dissolution studies were conducted in triplicate. The dissolution profiles were evaluated for amount of drug released in initial 15 min (Q_{15} min) and time taken to release 50% of the drug (T_{50}).

Dissolution Efficiency

The percent dissolution efficiency (% DE) was computed to compare the relative performance of various formulations. The % DE of a pharmaceutical dosage form is defined as the area under the dissolution curve up to a certain time, *t*, expressed as a percentage of the area of the rectangle described by 100% dissolution at the same time. The % DE can be calculated from the following equation

$$\% DE = \frac{\int_0^t Y dt}{Y_{100} t}$$

Where, Y is the percent drug dissolved at time t.

Hixson Crowell Cube root law

Finally Hixson and Crowell's cubic root law of dissolution was applied to evaluate the effect of change in surface area on dissolution rate of all the formulations. The dissolution data of Nateglinide and IR tablets were analyzed as per Hixson-Crowell's cube root equation. Hixson-Crowell introduced the concept of changing surface area during dissolution and derived the "cube-root law" to nullify the effect of changing surface area and to linearize the dissolution curves. Hixson-Crowell's cube root law is given by the following equation.

$$(W_0)^{1/3} - (W_t)^{1/3} = Kt$$

Where W_0 is initial mass and W_t is the mass remained at time't', K is Hixson crowell cube root constant.

RESULTS AND DISCUSSION

Phase solubility study

The phase-solubility diagram investigated in distilled water was linear with respect to the increased weight fraction of the gelucire 44/14, poloxamer 188 and PEG6000 (0 to 10 % *w/v*) indicating the solvent properties of all the three carriers for nateglinide, giving A_L type solubility. The values of the stability constant depend on slope values. The greater the value of the slope, greater is the capacity of the carrier to solubilize. The slope value for gelucire 44/14, poloxamer 188 and PEG 6000 was

found to be 0.268, 0.931 and 0.221 respectively. Higher slope value for poloxamer 188 suggests that it has better capacity to solubilize the drug. The Gibbs free energy $\Delta G_{tr}°$ values were all negative for gelucire 44/14, poloxamer 188 and PEG6000 at various concentrations (Table-1), indicating the spontaneous nature of solubilization [18]. Gibbs free energy decreased with increase in concentration of all the three carriers demonstrating that the reaction became more favorable as the concentration of carriers increased. Increased solubility may be due to the improved wettability of the nateglinide particles in aqueous solution of carriers. These results agreed with the well-established formation of soluble complexes between the water-soluble polymeric carriers like gelucire 44/14, poloxamer 188 and PEG6000 with poorly water-soluble drug nateglinide [19] **(Table 1)**.

Table 1: Effect of Concentration of carriers (gelucire 44/14, Poloxamer 188 and PEG6000) on Gibbs free energy

Concentration of carrier (% w/v)	ΔG_{tr}° (J/mol)*		
	Gelucire 44/14	Poloxamer 188	PEG6000
0	0	0	0
2	-2.418	-3.231	-1.124
4	-2.748	-4.343	-1.189
6	-2.92703	-6.765	-1.897
8	-3.12286	-8.582	-2.265
10	-3.29443	-9.343	-2.278

Table 2: Composition Nateglinide solid dispersions

Formulation Code	Nateglinide	Poloxamer 188	Gelucire 44/14	PEG 6000	Sylysia 550
F1	1	1	-	-	0.5
F2	1	2	-	-	1
F3	1	3	-	-	1.5
F4	1	-	1	-	0.5
F5	1	-	3	-	1
F6	1	-	5	-	1.5
F7	1	-	-	1	0.5

F8	1	-	-	3	1
F9	1	-	-	5	1.5

FT-IR Spectroscopy

When the FTIR spectrum of pure Nateglinide is taken into account it showed an absorption band at 2924.52 cm^{-1} (aliphatic C-H stretching; asymmetric), 2859.92 cm^{-1} (aliphatic CH stretching; symmetric), 1649.80 & 1713.44 cm^{-1} (C=O stretching for Ketone). Conformation of C-O stretching OH bending of carboxylic acid spectra was given by the band at 1240.97 cm^{-1} owing to hydrogen bonded O-H of COOH. The peak at 3299.61 cm^{-1} is attributed to secondary amide (-NH stretching). The absorption band at 1540.85 cm^{-1} corresponds to alkene C=C stretching bonds. The sharp band at 756.92 cm^{-1} & 700.03 cm^{-1} indicates the mono-substituted benzene. The FTIR spectrum of nateglinide with gelucire 44/14, poloxamer 188 and PEG6000 showed all the peaks for nateglinide **(Figure 1)**. There is no significant change in the absorption bands; hence no interaction was observed between them.

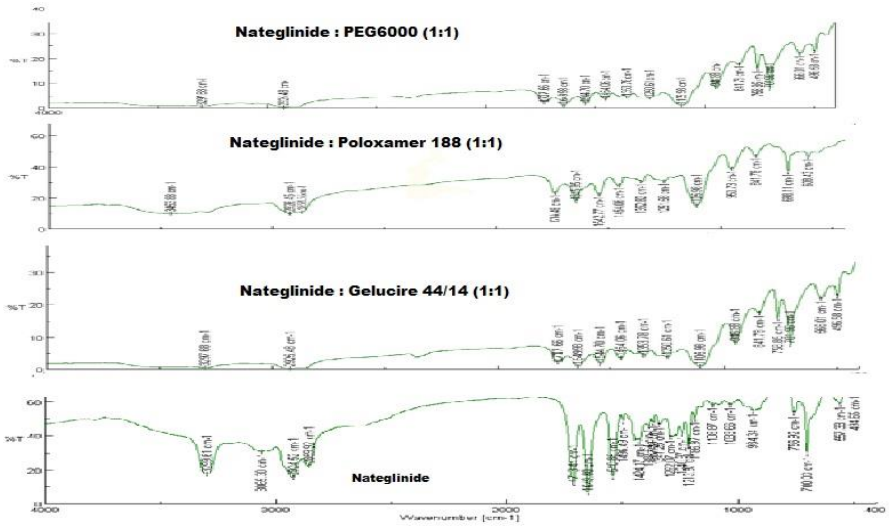

Figure-1: FTIR spectrum of nateglinide with gelucire 44/14, poloxamer 188 and PEG6000

Differential Scanning Calorimetry (DSC)

Figure 2 represents the DSC thermogram of nateglinide and its 1:1 solid dispersion with gelucire 44/14, poloxamer 188 and PEG6000. The DSC thermogram of nateglinide exhibited a sharp endothermic peak at 138.8˚C *(T_{fus}).* The endothermic peak indicated the crystalline nature of the drug whereas the DSC thermogram of its 1:1 formulation with all the three carriers also

exhibited peak at 138^{0}C. The DSC thermogram of formulations exhibited no shift in peaks indicating all the carriers are compatible with nateglinide.

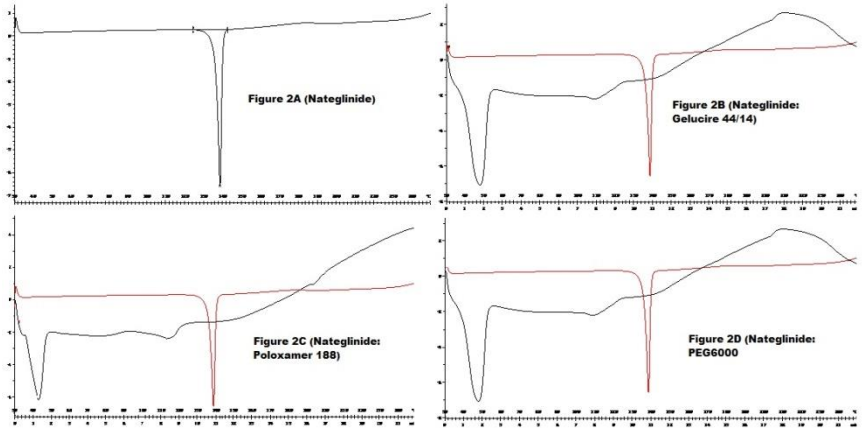

Figure-2: DSC thermogram of nateglinide and its 1:1 solid dispersion with gelucire 44/14, poloxamer 188 and PEG6000.

Solubility

Solubility data of nateglinide and its solid dispersion with gelucire 44/14, poloxamer 188 and PEG6000 in distilled water suggests more than tenfold, sixteenfold and sevenfold increase in solubility of nateglinide respectively (Table-3). The solubility of nateglinide increased with increase in the ratio of carriers. The improved solubility of nateglinide in gelucire 44/14 solid dispersions can be explained by the improved wettability of the nateglinide particles, and improved surfactive power [20]. Whereas the improved solubility of nateglinide from poloxamer 188 based solid dispersions could possibly be because of the combined action of the surface activity, solubilization and wetting effect of poloxamer 188 [21]. Improvement in solubility of nateglinide in PEG6000 based solid dispersions was due to higher hydrophilicity and water solubility of the high molecular weight PEG6000.

Table-3: Solubility and micromeritic properties of Nateglinide and solid dispersions.

Formulations	Solubility (µg/mL)	Angle of repose (^{0})*	Compressibility Index (%)*	Hausener's ratio*
Nateglinide	27 ± 1	42 ± 1.4	32 ± 1.5	1.39 ± 0.3
F1	130 ± 1.5	27 ± 2.5	18 ± 1	1.14 ± 0.2
F2	248 ± 3	24 ± 2.1	19 ± 2	1.31 ±0.4
F3	277 ± 4	25 ± 1.5	18 ± 1	1.19 ±0.4
F4	84 ± 3	22 ± 2.4	18 ± 2	1.17 ±0.3
F5	369 ± 4	24 ± 1.5	17 ± 2	1.21 ± 0.2

F6	435 ± 6	23 ± 2.1	19 ± 1	1.25 ±0.2
F7	103 ± 7	24 ± 2.2	18 ± 2	1.22 ±0.7
F8	127 ± 8	22 ± 3.0	17 ± 1	1.18 ±0.4
F9	189 ± 6	25 ± 2.5	16 ± 2	1.21 ±0.3

Flowability and compressibility

The values of angle of repose (42°), C.I (32 %) and H.R (1.39) for pure drug nateglinide revealed that it is a poorly flowable drug. Whereas flowability and compressibility of solid dispersion formulations were within the theoretical range for processing into tablet dosage form (Table-3). Addition of Sylysia 550 (50 % of the quantity of carrier) in each solid dispersion formulations was found to be the optimum quantity for converting the waxy solid dispersions into freely flowable powders which can be processed into a tablet. This could be attributed to high oil adsorption capacity and high specific surface area of sylysia 550 [22].

Table 4: Composition of Nateglinide IR tablets.

Ingredients	**F10**	**F11**	**F12**
Nateglinide	60	60	60
Gelucire 44/14	180	-	-
Poloxamer 188	-	180	-
PEG6000	-	-	180
Sylysia 350	90	90	90
Cross caramellose sodium	10	10	10
Talc	5	5	5
Magnesium stearate	5	5	5
TOTAL	350 mg	350 mg	350 mg

Evaluation of immediate release tablets of Nateglinide

Drug content values (97-99%) ensured uniform mixing of nateglinide, gelucire 44/14, poloxamer 188, PEG6000 and Sylysia 550. Hardness of the tablets was in the range of 5.1 kg/cm^2 to 5.4 kg/cm^2. This revealed that the required compressibility was imparted

by sylysia 550. Gelucire 44/14, poloxamer 188 and PEG6000 are waxy materials and tend to stick to the punches during compression. This problem was also resolved by uniform mixing with sylysia 550. Friability values were in the range of 0.29% and 0.64%, which ensured no loss of material from the surface or edge of tablets. This may be attributed to the waxy nature of carriers. All the formulations passed weight variation test which was an indication of good flowability. Formulation F10, F11 and F12 showed disintegration time of 3, 2.8 and 3.2 min respectively. Crosscaramellose sodium produced quick disintegration because of higher swelling and hydration capacity [23]. The results of evaluation tests are summarized in (Table-5).

Table-5: Quality Control Tests of Nateglinide IR Tablets.

Formulation code	Hardness (Kg/cm^2)*	D.T. (min)*	Friability (%)*	Weight Variation	Drug Content (%)*
F10	5.1 ± 0.36	3 ± 0.2	0.64	PASS	98.9 ± 1.6
F11	5.4 ± 0.32	2.8 ± 0.3	0.29	PASS	97.4 ± 2.2
F12	5.2 ± 0.89	3. 2 ± 0. 3	0.45	PASS	98.9 ± 3.1
Note: * Mean ± SD, n=6					

***In vitro* dissolution test**

The dissolution profile of nateglinide is very poor as around 27% of drug was dissolved in 2 h of dissolution study whereas the entire three carriers based IR tablets exhibited improved dissolution rate. The highest dissolution of nateglinide was observed for poloxamer 188 based IR tablet. The observed enhancement may be attributed to the effects of solid dispersion and surface adsorption. Poloxamer 188 solid dispersion based IR tablets (F11) exhibited more than 90 % drug dissolution with in 15 min. This may attributed to the following reasons such as HLB value 29, molecular dispersion of drug in polymer chain, formation of glassy solution which resulted in quick dissolution upon contact with dissolution medium [24]. The results are shown in Figure-3.

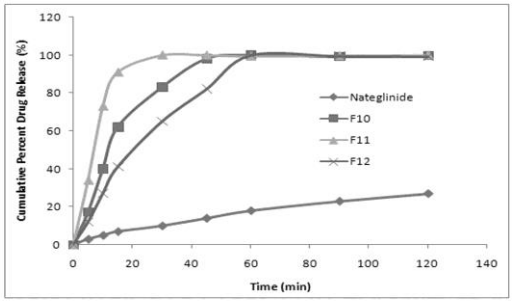

Figure 3: Dissolution profile of nateglinide

The DE_{15} value for each formulation is presented in Table-6. The DE_{15} value for pure drug nateglinide was significantly lower than solid dispersion based IR tablets. Dissolution onset of F10, F11 and F14 was very fast. Formulation F10, F11 and F12 showed very high dissolution efficiency values 54, 82 and 57 respectively. Maximum was obderved for poloxamer 188 based IR

tablet (F11). Q_{15} values for formulation F10, F11 and F12 showed more than 9, 13 and 6 fold increase in dissolution rate respectively. Similarly T_{50} values for pure drug nateglinide could not be determined as only 27 % of drug didssolved in 2 h of dissolution study. Lowest time of T_{50} was observed for F11 indicating higher dissolution potential of poloxamer 188. Correlation coefficient for Hixson Crowell's equation was higher for all formulations suggesting that the rate of dissolution increased with increase in surface area.

Table-6: Dissolution parameters of Nateglinide and IR tablet formulations

Formulation	% DE_{15}	Q_{15}	T_{50} (min)	Hixson Crowell's cube root constant (r^2)
Bosentan	6	7	*	0.902
F10	54	62	12	0.969
F11	82	91	7	0.989
F12	57	41	25	0.989
Note: % DE15 is the percent dissolution efficiency at 15 min and MDT is the mean dissolution time in min, *50 % of drug was not dissolved within 1 h of dissolution study.				

CONCLUSION

Hence from the above research work, it may be concluded that gelucire 44/14, poloxamer 188 and PEG600 can be used to enhance the dissolution of a poorly water soluble drug nateglinide. Gelucire 44/14, poloxamer 188 and PEG6000 played a significant role in enhancement of drug solubility and dissolution. The surface adsorbent, sylysia 550 may be used to impart good flow and compressibility to solid dispersions. Presence of crosscaramellose sodium as superdisintegrant also contributed significantly in dissolution enhancement of drug. Among the three carriers, poloxamer 188 exhibited better solubility and dissolution enhancement potential.

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