Original Article

Role of superporous hydrogel particles as a superdisintegrant in fast disintegrating tablet of Glipizide

Abstract

Background: Superporous hydrogel (SPH) swells very rapidly in a shorter period of time to an equilibrium size and contains highly porous structure. The literature survey reflects the preparation of SPHs and its composite, but its application as an excipient in a drug delivery system is not well focused. **Aim:** Efforts were made to develop fast disintegrating tablets of Glipizide using superporous hydrogel particles (SPHPs) as a wicking agent, which act as a superdisintegrant to decrease disintegration time. **Materials and Methods:** The SPH of poly (acrylamide-co-acrylic acid) was prepared by solution polymerization and characterized. Prepared tablets were evaluated for concerned parameters. Formulation optimization was carried out using 3^2 full factorial design and analysis of variance. **Results:** Scanning electron microscopy pictures clearly confirmed the superporous structure of hydrogel. Batch F_4 containing 4% w/w of SPH of poly (acrylamide-co-acrylic acid) as a superdisintegrant showed extremely fast wicking effect and lesser disintegration time compared with other potential superdisintegrants. Drug release was good compared with conventional immediate release marketed product. **Conclusion:** It can be concluded that SPHPs can be used as a potential superdisintegrant in tablet formulation.

Key words:
Glipizide, superdisintegrant, superporous hydrogel particles

Introduction

The application of superporous hydrogel (SPH) as an excipient in a drug delivery system is not exploited much compared with their preparation with fast swelling and high superabsorbent properties.[1,2] SPHs particles possessing a unique water absorbent property and can be used as a wicking agent, which act as a superdisintegrant to decrease disintegration time of fast disintegrating tablets (FDTs).[3,4] The role of SPHs as a superdisintegrant is needed to be studied. Here, efforts are made to develop FDT using superporous hydrogel particles (SPHPs) with a very short disintegrating time.

The therapy of dysphagia becomes ineffective if patients' shows non-compliance due to difficulty in swallowing tablets.[5] The FDTs intended to be swallowed whole and to disintegrate and release their medicaments rapidly in the gastrointestinal tract still remains the dosage form of choice.[6,7] Disintegrants added to tablet formulations promotes the breakup of the tablet in an aqueous environment and thereby increasing the available surface area. This promotes a more rapid release of the drug substance. Various factors affect the disintegration behavior of tablets.[8] In recent years, increasing attention has been paid to formulating fast dissolving and/or disintegrating tablets.[9,10] An ideal disintegrant should have good hydration capacity, good compressibility, flow properties, poor solubility, poor gel formation and it should not form complexes with the drugs.

Glipizide is an oral blood glucose lowering drug of the sulfonylurea class. Glipizide is an antidiabetic drug act on sulfonylurea urea receptors on the pancreatic beta cell membrane and reduce conductance of adenosine triphosphate (ATP) sensitive potassium channels and causes depolarization, increases the time the cell spends in the calcium release stage of cell, results in signaling leading to the influx of calcium. The

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increased level of calcium will initiate more insulin release from each beta cell.[11,12] In type 2 diabetes mellitus, the kinetics of insulin release in response to meals and glucose is delayed and subdued. The sulfonylurea urea class primarily augments the second phase of insulin secretion with little effect on the first phase. Glipizide is fast acting as well as its insulinemic action is persistent even after prolonged use.[13]

Experimental

Materials

Glipizide, acrylic acid, Ac-Di-Sol, crospovidone and sodium starch glycolate were purchased from Yarrow chem., Mumbai, India. Acrylamide was purchased from Burgoyne Burbidges and Co., Pvt., Ltd., Mumbai. N,N'-methylene-bis-acrylamide and N,N,N',N'-tetramethylethylenediamine were purchased from Loba Chemie Pvt., Ltd., Mumbai, India. Ammonium persulfate, mannitol, sodium bicarbonate and sodium lauryl sulfate were purchased from Finar Chemicals Ltd., Ahmedabad, India. Span 80 and microcrystalline cellulose was purchased from Chemdyes Corporation, Mumbai, India. Polyvinylpyrollidone was purchased from Titan Biotech Ltd., Rajasthan. Double distilled water and phosphate buffer pH 6.8 were prepared in the laboratory. All other chemicals used were of analytical grade and used as obtained.

Preparation of SPH and SPHPs

Preparation of SPH of poly (acrylamide-co-acrylic acid) (poly [AM-co-AA]), poly (AM-co-AA) with Ac-Di-Sol and PVP and characterization for their density, porosity, swelling studies and mechanical strength are reported in our previous findings.[14] Dried SPHs were crushed, gently, using a mortar and pestle to get the SPHPs.[15] SPHPs were passed through 60# sieve and retained on 80# sieve. SPHPs were then stored in airtight container until further use.

Scanning electron microscopy (SEM)

Dried SPHs of poly (AM-co-AA), which showed fast wicking effect, were cut to expose their inner structure and their particles were used for SEM studies. The morphology of SPHs and SPHPs were examined using instrument JSM-5610 Scanning Electron Microscope (JEOL World-wide, India), with an operating voltage of 10 kV.

Preparation of FDTs

FDTs were prepared by direct compression method. SPHPs were used as a superdisintegrant. All the ingredients were passed through sieve 60#. The drug, superdisintegrant, mannitol and microcrystalline cellulose (MCC) were mixed uniformly with gentle trituration using a mortar and pestle to get a uniform mixture. Finally, magnesium stearate and talc were added and mixed well. The tablets were compressed using 6 mm flat-face surface punch on tablet compression machine (Rimek 10 station minipress). Table 1 shows compositions of FDT of Glipizide.

Solubility study

The solubility study was carried out as described by Higuchi and Connors[16] in phosphate buffer pH 6.8 containing different concentration of sodium lauryl sulfate (SLS). An excess amount of Glipizide was added to 10 ml of phosphate buffer pH 6.8 with 0-4% w/v SLS in glass vials. The closed vials were kept on a water bath incubator shaker (Hicon Instrument, Delhi) maintained at 37°C ± 0.5°C for 24 h. After that the solutions were centrifuge and filtered through 0.45 mm millipore filter. The filtrate was suitably diluted and analyzed using a double beam UV spectrophotometer (UV-1800, Shimadzu, Tokyo, Japan) at 275 nm.

Selection of solubilizing agent concentration

SLS was used as solubilizing agent and was added to prototype formulation T_2 in different concentration, mixed well and tablets were compressed.

Evaluation of FDT

Uniformity of weight

The 20 tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. Test was performed as per Indian Pharmacopeia (IP) 2010.[17]

Hardness

Hardness was determined by taking six tablets from each formulation, using a Monsanto hardness tester, which applies force to the tablet diametrically with the help of an inbuilt spring.

Table 1: Preliminary trial formulations of FDT for disintegration time

Ingredients (mg)	T_1	T_2	T_3	T_4	T_5	T_6	S_1	S_2	S_3	S_4
Glipizide	5	5	5	5	5	5	5	5	5	5
SPH particles	3	7.5	7.5	3	10	6	7.5	7.5	7.5	7.5
Microcrystalline cellulose	74	119	104	123	161	165	117.5	116	114.5	113
SLS	–	–	–	–	–	–	1.5	3	4.5	6
Mannitol	15	15	30	15	20	20	15	15	15	15
Talc	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Magnesium stearate	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Total weight (mg)	100	150	150	150	200	200	150	150	150	150

SPH – Superporous hydrogel; SLS – Sodium lauryl sulfate; FDT – Fast disintegrating tablet

Friability

The friability test was performed using Roche friabilator (Electrolab, Mumbai, India) as per IP 2010.[17] Sample comprising the tablets equivalent to 6.5 g were rotated at 25 rpm for 4 min. Tablets were reweighed after removal of fines (dedusted) and the percentage of weight loss was calculated. Friability below 1% was considered acceptable.

Wetting time

A piece of tissue paper folded twice was placed in a small petridish (internal diameter = 6.5 cm) containing 6 ml of phosphate buffer pH 6.8. A tablet was put on the paper and the time for complete wetting was measured.[18]

In-vitro disintegration time

The disintegration time of the tablet was measured in water (37°C ± 2°C) using disintegration test apparatus with disk in accordance with IP 2010.[17] The time in seconds taken for the complete disintegration of the tablet with no palpable mass in the test tubes was measured in seconds.

Content uniformity

Five tablets were powdered and 10 mg equivalent weight of Glipizide was accurately weighed and transferred into a 100 ml volumetric flask. Initially, 10 ml of methanol was added and shaken for 10 min. Then, the volume was made up to 100 ml with phosphate buffer pH 6.8. The solution in the volumetric flask was filtered, diluted suitably and analyzed spectrophotometrically at 275 nm using UV-visible double beam spectrophotometer.

In-vitro drug release study

The *in-vitro* drug release study of Glipizide FDT was performed using United State pharmacopeia (USP) Type 2 apparatus paddle (50 rpm) at 37°C ± 0.5°C using phosphate buffer pH 6.8 (900 mL) as a dissolution medium. At the predetermined time intervals, 10 ml samples were withdrawn and replaced with fresh dissolution media. Withdrawn samples was filtered through a 0.45 µm membrane filter, diluted and assayed at 275 nm using a Shimadzu UV-1800 double-beam spectrophotometer. Cumulative percentage drug release was calculated using an equation obtained from a calibration curve.

Experimental design

A 3^2 randomized full factorial design was applied.[19,20] In this experimental design two independent factors, each at three levels, were evaluated and experimental trials were performed for nine possible combinations. The X_1 is the concentration of SPH (3, 4 and 5% w/w) and X_2 is types of SPH (AM-co-AA, Ac-Di-Sol and polyvinylpyrrolidone [PVP]) were chosen as independent variables. Disintegration time and % cumulative drug release at 15 min were dependent variables. Tables 2 and 3 show the coding of variables and formulation layout for factorial design batches, respectively. The composition of factorial design batches (F_1-F_9) is shown in Table 4. The prepared formulations were evaluated for

Table 2: Coding of variables for factorial design batches

Levels	X_1, concentration of SPH (%)	X_2, type of SPH
−1	3	AM-co-AA
0	4	Ac-Di-Sol
1	5	PVP

SPH – Superporous hydrogel; PVP – Polyvinylpyrrolidone

Table 3: Formulation layout for factorial batches

Batch	X_1	X_2
F_1	−1	−1
F_2	−1	0
F_3	−1	+1
F_4	0	−1
F_5	0	0
F_6	0	+1
F_7	+1	−1
F_8	+1	0
F_9	+1	+1

Table 4: Formulations of 3^2 full factorial design

Ingredient (mg)	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9	SD_1	SD_2
Glipizide	5	5	5	5	5	5	5	5	5	5	5
SPHP (AM-co-AA)	4.5	–	–	6	–	–	7.5	–	–	–	–
SPHP (Ac-Di-Sol)	–	4.5	–	–	6	–	–	7.5	–	–	–
SPHP (PVP)	–	–	4.5	–	–	6	–	–	7.5	–	–
Crospovidone	–	–	–	–	–	–	–	–	–	6	–
SSG	–	–	–	–	–	–	–	–	–	–	6
MCC	119	119	119	117.5	117.5	117.5	116	116	116	117.5	117.5
SLS	3	3	3	3	3	3	3	3	3	3	3
Mannitol	15	15	15	15	15	15	15	15	15	15	15
Talc	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Magnesium stearate	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Total weight (mg)	150	150	150	150	150	150	150	150	150	150	150

SPHP – Superporous hydrogel particles; SLS – Sodium lauryl sulfate; SSG – Sodium starch glycolate; MCC – Microcrystalline cellulose

disintegration time, wetting time, friability, hardness, drug content and *in-vitro* release study. Tests for significant differences were performed by one-way analysis of variance (ANOVA) using Microsoft Excel 2007. Differences were considered significant at $P < 0.05$ level. A statistical model incorporating interactive and polynomial term was used to evaluate the response:

$$Y = B_0 + B_1X_1 + B_2X_2 + B_{12}X_1X_2 + B_{11}X_1^2 + B_{22}X_2^2$$

Where, Y is dependent variables, B_0 is arithmetic mean response of the nine runs, B_1 and B_2 are estimated coefficients for X_1 and X_2, respectively. The main effects (X_1 and X_2) represent the average result of changing one factor at a time from its low to high value. The interaction terms (X_1 and X_2) show how the response changes when two factors are simultaneously changed. The polynomial terms (X_1^2 and X_2^2) are included to investigate non-linearity.

Comparison of SPHPs with potential superdisintegrants

Optimized formulation F_4 was compared with different others potential superdisintegrants sodium starch glycolate and crosspovidone with 6% concentration. The prepared formulations SD_1 and SD_2 were evaluated and compared for disintegration time, wetting time and *in-vitro* drug release studies.

Fourier transforms infra-red (FTIR) Study

FTIR spectra of Glipizide, SPH, mixture of Glipizide and SPH and powder of crushed tablet were recorded using FTIR instrument (FTIR-1700, Shimadzu, Kyoto, Japan). The samples were powdered and mixed with KBr (potassium bromide) and the spectra were recorded over the ranges from 600 to 4000 cm^{-1}.

Differential scanning calorimetry (DSC) Study

DSC study was carried out using DSC-60 (Shimadzu, Kyoto, Japan) to check the compatibility of ingredients. DSC thermograms of pure drug and prepared tablet were individually taken for their endothermic reaction. Finally, physical mixture of above ingredients was scanned for DSC. At a constant nitrogen flow rate of 40 ml/min, samples were heated at a linear heating rate of 10°C/min between 30°C and 300°C.

Stability study

The stability studies were carried out on the most satisfactory formulations, which was sealed in aluminum packaging and kept in a humidity chamber maintained 40°C ± 2°C / 75% ± 5% RH for 6 month. The optimized formulation sealed in aluminum foil was also kept at room temperature and humidity condition. At the end of studies, samples were analyzed for the *in-vitro* drug release. Comparison of both the batches was carried out using similarity factor (f_2).

Results and Discussion

SEM study

Figure 1 shows the SEM images of SPH of poly(AM-co-AA) and its particles. SPH possessed numbers of interconnected pores, indicating that formation and retention of superporous structure of hydrogel. The pore size of SPHPs was very less compared with SPH of AM-co-AA because porous structure of SPH was broken during the crushing of SPH to make SPHPs.

Preliminary trial formulations of FDT

In the preparation of FDTs, SPHs particles were used as the superdisintegrants. MCC was used as filler. Mannitol was used as a sweetening agent. From Table 5, it concluded that T_1 formulation showed less hardness and rough surface. T_2 and T_3 formulations showed almost same disintegrating time and from that it could be concluded that disintegration time was not dependent on quantity of mannitol. T_4 and T_6 formulation showed longer disintegration time compared

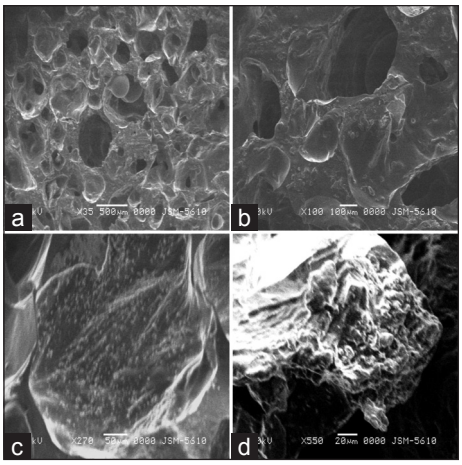

Figure 1: Scanning electron microscopy images of superporous hydrogel (SPHs) of poly (AM-co-AA) (a) at ×35; (b) at ×100; (c) particles at ×270; (d) particles at ×550 and SPH particles of poly (AM-co-AA)

Table 5: Evaluation of preliminary trial formulations of FDT

Batch	T_1	T_2	T_3	T_4	T_5	T_6	S_1	S_2	S_3	S_4
Disintegration time (s)	11±3	9±2	10±2	24±1	19±4	21±1	10±5	11±2	45±4	105±3
CPR at 20 min	65.14±1.22	81.04±0.58	79.99±2.49	67.10±0.16	74.42±0.91	69±1.27	83.12±0.11	97.90±2.17	95.04±0.68	96.91±1.55

*Mean ± SD, $n = 3$; For T1-T6 CPR at 20 min; For S1-S4 CPR at 15 min; CPR – Cumulative percentage drug release; SD – Standard deviation; FDT – Fast disintegrating tablet

with T_2. Here, T_5 and T_6 batch showed longer disintegration time with a large quantity of fillers and 5% concentration of SPH as compared with T_2. So, T_2 batch was taken as a prototype formulation which shown less disintegration time with less concentration of mannitol as compared to batch T_3 to T_5. From Table 5, drug release profile for preliminary trial formulations showed that prototype T_2 formulation showed 81% drug release after 20 min.

Solubility study

The solubility study of Glipizide was carried out in the phosphate buffer pH 6.8 containing different concentration of SLS (1-4% w/w). The result of solubility study is shown in Table 6. The solubility of Glipizide in the phosphate buffer pH 6.8 without SLS was very low. As increasing the concentration of SLS, the solubility also increased, but after 2% w/w of SLS there was no significant enhancement of solubility. From Table 5, it concluded that S_1 and S_2 showed longer disintegration time and nearly drug release compared with S_3 and S_4. Here, S_4 showed less disintegration time but showed same drug release as T_2 as shown in Table 5. From Table 5 S_2 formulation was taken as a prototype formulation, which showed less disintegration time with increase drug release.

Evaluation of factorial batches

Uniformity of weight

Percent weight variation was observed from 1.05 to 2.9 as shown in Table 7 which was within the acceptable limit for uncoated tablets as per USP.

Table 6: Solubility study

SLS concentration (%)	Solubility (μg/ml)
0	4.01
1	9.15
2	13.12
3	13.71
4	14.06

SLS – Sodium lauryl sulfate

Tablet hardness

The hardness of tablets was found to be in the range of 3.0-4.0 kg/cm^2 as shown in Table 7.

Tablet friability

Friability was observed between 0.33% and 0.61%, which were below 1% indicating sufficient mechanical integrity and strength of prepared tablets as shown in Table 7.

Drug content

Percentage drug content for all formulations was found to be between 97% and 101% as shown in Table 7.

Wetting time

Wetting time for F_4 batch was shown 12 s, which was very less, compared with all other batches. From Table 7, it can be concluded that SPHP with AM-co-AA as a superdisintegrant showed very less wetting time compared with other types of SPHP of Ac-Di-Sol and PVP. From Table 7, it concluded that conventional marketed product (Glucotrol) showed longer wetting time than all formulations, which containing SPH as superdisintegrant.

In-vitro disintegrating time

The lowest disintegration time from all formulations, which containing SPHP as a superdisintegrant was found to be 7 s (F_4 batch) as shown in Table 7. From that it can be concluded that SPHP (4%) with AM-co-AA can be used as a wicking agent with high swelling ratio which act as a superdisintegrant and showed less disintegration time compared to other types of SPHP. Conventional marketed product (Glucotrol) showed longer disintegration time than all formulations containing SPHPs as superdisintegrant.

In-vitro drug release study

The *in-vitro* dissolution study was performed for all formulations and the results are shown in Table 8. *In-vitro* drug release studies showed that more than 50%

Table 7: Evaluation of factorial batches

Batch	Weight variation (%) (n = 20)	Hardness (kg/cm^2)	Friability (%)	Drug content (%)	Disintegration time (s)	Wetting time (s)	CPR at 15 min
F_1	149.4±1.20	3.81±0.50	0.49	97.9±1.22	12±3	22±7	91.76
F_2	150.6±2.62	3.43±0.45	0.51	100.5±2.12	14±2	39±3	85.59
F_3	151.4±1.08	4.01±0.46	0.39	97.8±1.48	18±2	44±9	84.43
F_4	150.1±2.81	3.42±0.15	0.48	99.7±0.80	7±1	12±5	97.98
F_5	152.2±2.78	3.18±0.52	0.56	99.2±1.70	10±2	31±8	88.48
F_6	150.0±2.41	3.71±0.45	0.33	97.5±0.95	11±4	36±4	85.62
F_7	152.1±2.30	3.26±0.41	0.48	98.4±2.05	8±3	19±9	95.88
F_8	148.4±2.05	3.08±0.45	0.61	99.3±2.23	9±5	21±11	91.87
F_9	151.4±1.15	3.10±0.51	0.36	96.9±1.41	11±5	27±7	90.93
SD_1	149.4±1.48	3.91±1.32		97.5±1.38	16±3	29±3	92.87
SD_2	151.6±1.03	4.18±0.09		98.9±2.13	18±3	32±1	90.99
MP	–	–	–	–	240±8	65±4	79.63

*Mean ± SD, n=3; MP – Conventional marketed IR product (Glucotrol); CPR – Cumulative percentage drug release; IR – Immediate release

of the drug was released from all formulations containing SPHP within 5 min as compared to conventional marketed product (Glucotrol). From the drug release studies, it was confirmed that the more than 85% drug release was released for factorial formulations within 15 min compared to conventional MP (Glucotrol). Among all factorial batches, formulation F_4 containing 4% SPHP of AM-co-AA was considered as the optimized formulation as it shows the highest drug release in Table 8 and Figure 2.

Statistical analysis of factorial design batches

The statistical analysis of the factorial design batches was performed by multiple linear regression analysis carried out in Microsoft Excel 2007.[21] The results are shown in Table 7. The data clearly indicate that the values of disintegration time and cumulative percentage drug release (CPR) at 15 min were strongly dependent on the independent variables. The fitted equations (full and reduced model) relating the responses disintegration time and CPR at 15 min to the transformed factors are shown in Table 8.

Table 8: Summary of results of regression analysis

	b0	b1	b2	b12	b11	b22
FOR disintegrating time						
Response (DT)						
FM	9.22	−2.67	2.17	−0.75	2.67	0.17
RM	9.33	−2.67	2.17	—	2.67	—
For CPR at 15 min						
Response (CPR)						
FM	89.06	2.82	−4.11	0.59	−0.62	2.45
RM	90.28	2.81	−4.11	—	—	—

FM – Full model; RM – Reduced model; DT – Disintegration time; CPR – Cumulative percentage drug release

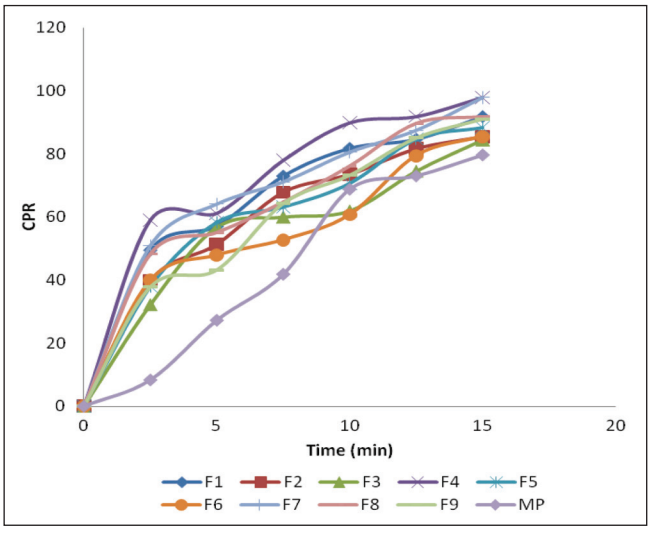

Figure 2: *In-vitro* drug release profile of factorial batches (F_1 to F_9) and conventional marketed infra-red product (Glucotrol)

The polynomial equations can be used to draw conclusions after considering the magnitude of coefficient and mathematical sign it carried (i.e. positive or negative). Table 8 shows the results of the ANOVA, which was performed to identify insignificant factors. R^2 value for disintegration time and CPR at 15 min was 0.9828 and 0.9211 respectively indicating good correlation between dependent and independent variables. The reduced models were developed by omitting response variable terms (insignificant) with $P > 0.05$ and retaining the terms with $P < 0.05$ (significant). The coefficients for response variables are shown in Table 8.

Full and reduced model for disintegrating time

The results of statistical analysis are shown in Table 8. The coefficient b_1, b_2 and b_{11} were found to be significant. The terms b_{12} and b_{22} was not contributed significantly to the prediction of disintegrating time and can be omitted from the full model to generate the reduced model. The results of model testing are shown in Table 9. Figure 3 shows response surface plot, drawn using Design Expert 8.0.4 (Stat-Ease Inc., Minneapolis), showing effect of concentration of SPH and type of SPH on disintegrating time. It is observed that the type and concentration of SPH both affect the disintegration time. The particles of SPH alone, compared to SPHs of Ac-Di-Sol and PVP, showed less disintegration time. Higher amount of SPHPs also reduced disintegration time of tablets.

Full model

$$Q1 = 9.22 - 2.67\,X_1 + 2.16\,X_2 - 0.75\,X_{12} + 2.67\,X_{11} + 0.167\,X_{22}$$

Reduced model

$$Q1 = 9.33 - 2.67\,X_1 + 2.17\,X_2 + 2.67\,X_{11}$$

Full and reduced model for CPR at 15 min

The results of statistical analysis are shown in Table 8. The coefficient b_1 and b_2 were found to be significant. The results of model testing are shown in Table 9. The critical value of F for $\alpha = 0.05$ is equal to 9.11 (df = 4, 3). Since the calculated value ($F = 2.55$) is less than the critical value ($F = 9.11$), it

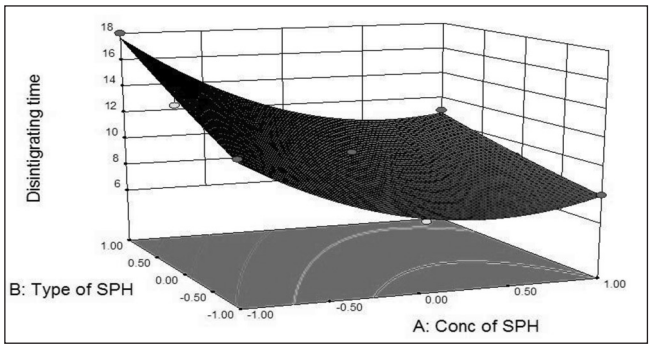

Figure 3: Response surface plot showing effect of concentration of superporous hydrogel (SPH) and type of SPH on disintegrating time

concluded that the term b_{12}, b_{11} and b_{22} was not contribute significantly to the prediction of Q5 and can be omitted from the full model to generate the reduced model. Figure 4 shows response surface plot showing the effect of concentration of SPH and type of SPH on CPR at 15 min. The particles of SPH alone, compared with SPHs of Ac-Di-Sol and PVP, showed higher drug release. Higher amount of SPHPs leads to improve the drug release at 15 min.

Full model

$Q5 = 89.06 - 2.82\,X1 - 4.11\,X_2 - 0.60\,X_{12} - 0.62\,X_{11} + 2.45\,X_{22}$

Reduced model

$Q5 = 90.28 + 2.81\,X_1 - 4.11\,X_2$

Comparison of SPHPs with potential superdisintegrants

From Table 7, it was confirmed that optimized formulation F_4 which containing SPHP as a superdisintegrant showed less disintegration time and wetting time as compared to potential superdisintegrants. As shown in Table 7, SD_1 and SD_2 showed drug release below 90% at 15 min as compared to optimized formulation F_4.

FTIR study

As shown in Figure 5 the FTIR spectra of Glipizide, SPHP, Glipizide and SPHP and FDT of Glipizide containing SPHP respectively. FTIR study revealed that there was no interaction between drug, SPHP and other ingredients present in formulations. Peaks at 1636 cm^{-1} and 1738 cm^{-1} revealed the presence of amide and carboxylic groups, which confirmed the formation of poly (AA-co-AM) SPH. Locations of the peaks

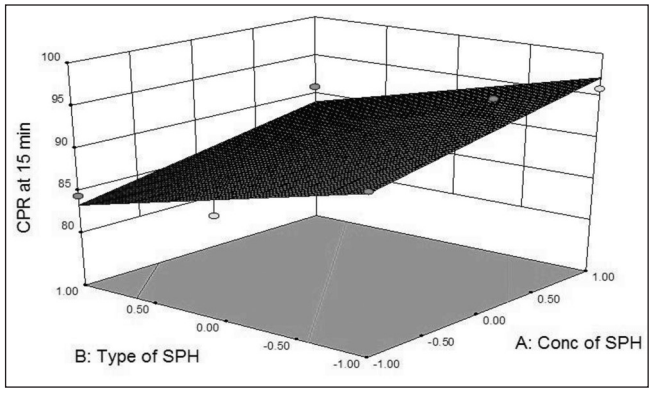

Figure 4: Response surface plot showing effect of concentration of superporous hydrogel (SPH) and type of SPH on CPR at 15 min

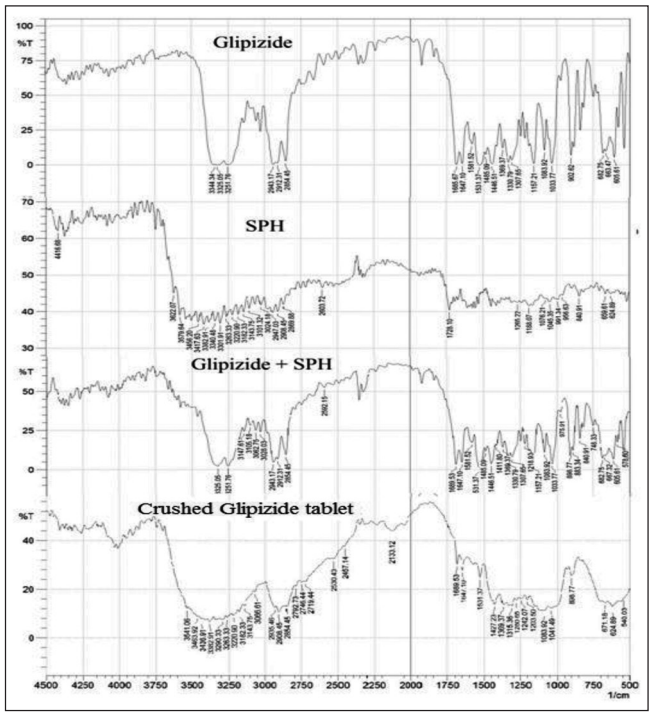

Figure 5: Fourier transforms infra-red spectra of Glipizide, superporous hydrogel particles (SPHP), Glipizide + SPHP and Glipizide tablet

Table 9: Calculation for testing the model in portions

	DF	SS	MS	F	R^2	
For disintegrating time						
Regression						$F_{cal} = 2.26$
FM	5	87.36	17.47	34.31	0.9828	$F_{tab} = 9.28$
RM	3	85.06	28.35	366.98	0.9569	df (3,3)
Error						
FM	3	1.52	0.51	–	–	
RM	5	3.83	0.77	–	–	
For CPR at 15 min						
Regression						$F_{cal} = 2.55$
FM	5	163.00	32.60	7.01	0.9211	$F_{tab} = 9.11$
RM	2	148.79	74.39	15.84	0.8408	df (4,3)
Error						
FM	3	13.96	4.65	–	–	
RM	6	28.18	4.69	–	–	

DF – Degree of freedom; SS – Sum of squares; MS – Mean of squares; R^2 – regression coefficient; FM – Full model; RM – Reduced model

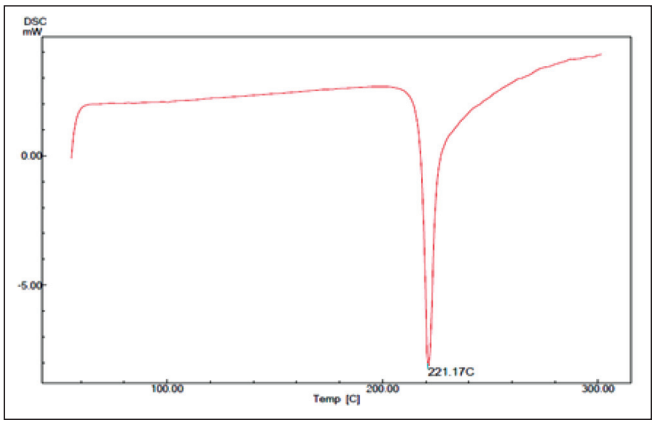

Figure 6: Differential scanning calorimetry of Glipizide

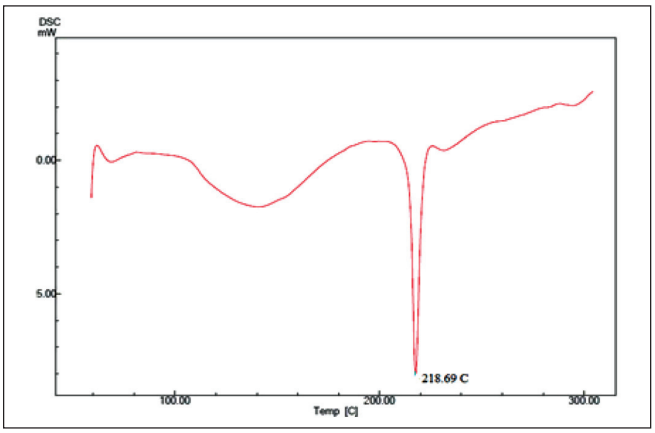

Figure 7: Differential scanning calorimetry of Glipizide and excipients

slightly changed which might be attributed to the cross-linking. At the end of the study the FTIR data obtained reveals that Glipizide was stable throughout with SPHP used in the study.

DSC Study

DSC curves obtained for pure Glipizide and prepared tablet mixture of all ingredients is shown in Figures 6 and 7. Pure powdered Glipizide showed a sharp melting endotherm at 221.17°C. DSC thermo grams of physical mixture of drug and excipients showed the melting peak of the drug at 218.69°C and broad endothermic peak at a sharp melting endotherm at physical mixture of all ingredients of prepared tablet showed their identical peaks at defined temperature range. Presence of peaks indicated that all ingredients and Glipizide were compatible with each other means there is no incompatibility between the selected ingredients and drug.

Stability study

Samples withdrawn after 6 month showed no significant change in appearance of tablets drug release. Disintegration time was 8 s, which was not shown much significant difference compared to initial batch F_4. Similarity factor of F_4 after storage was found 85.18 to initial drug releases. The result of short term stability studies indicated that the formulation was stable on the required storage condition.

Conclusion

From this research study, it can be concluded that SPHs was successfully formulated. FDT of Glipizide was prepared by using SPHPs as a superdisintegrant. SPHs possessed the porous structure which was showed by SEM analysis. F_4 was optimized as containing 4% SPH of AM-co-AA, showed extremely fast wicking effect into the tablet core and which provided less disintegration time compared to other potential superdisintegrant and also increased in drug release compared with conventional IR marketed product. From this research study, it can be concluded that SPHPs can be used as a potential superdisintegrant in FDT.

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