



DESIGN, DEVELOPMENT AND EVALUATION OF SOLIFENACIN SUCCINATE MODIFIED RELEASE MATRIX TABLETS USING NATURAL POLYMER

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ABSTRACT

To design, develop and evaluate the modified release matrix tablets by controlled drug delivery system for anti-muscarinic class drugs such as Solifenacin succinate with the objective overcome the existing problems using Hydroxypropyl methyl cellulose (HPMC K4M), Sodium carboxy methyl cellulose (NaCMC), Guar Gum and Xanthan Gum as rate controlling polymer for the treatment of overactive bladder. The tablets were prepared by wet granulation method and studied the effect of the matrix former such as Guar Gum and Xanthan Gum separately. Tablets were evaluated for uniformity of weight, drug content, friability, hardness, thickness, swelling study, in vitro drug release, kinetic studies and stability studies. All the formulation had shown compliance with pharmacopoeial standard. The drug release study shows that an increase amount of polymer resulted in retarded drug release. The maximum drug release was found to be 96% over a period of 24 hours in guar gum based formulations (SF 9-SF 12) at a concentration ranging from 15 to 60mg per tablet. Similarly maximum drug release was found to be 95% over a period of 24 hours in Xanthan gum based formulations (SF13-SF16) at a concentration ranging from 15 to 60mg per tablet. The drug release from optimized formulation (SF14) fitted to various kinetic models and the drug release was found to follow zero-order kinetics and diffusion release mechanism. The optimized formulation were subjected to stability studies and shown there were no significant changes in drug content, physicochemical parameters and release pattern. Results of the present study indicate the suitability of the above mentioned polymers in the preparation of controlled release formulation of Solifenacin.

Keywords: Solifenacin succinate, Hydroxypropyl methyl cellulose (HPMC K4M), Sodium carboxy methyl cellulose (NaCMC), Guar Gum and Xanthan Gum, matrix tablets.



INTRODUCTION

Anti-cholinergics are main medications to treat overactive bladder diseases. Anti-cholinergics medications target to decrease the overactivity of the detrusor muscle. Examples of Anti-cholinergics drugs are Oxybutynin, Tolterodine, Solifenacin, Darifenacin, Fesoterodine fumarate, Mirabegron and Onabotulinumtoxin A. Solifenacin is a competitive muscarinic acetylcholine receptor antagonist. The goal of any drug delivery system is to provide a therapeutic amount of drug to the proper site

in the body to achieve and then maintain the desired drug concentration i.e. the drug-delivery system should deliver drug over a specified period of time. The polymers which may be used to formulate matrix tablets depend on the physicochemical properties of the drug substance to be incorporated into matrix system and type of drug release required. Modified release products may be developed due to reduce dose frequency, maintains therapeutic drug concentrations over prolonged and patient convenience.

Nowadays, in order to investigate the suitability of a polymer as a matrix forming agent, it is necessary to gather sufficient information about its physical and mechanical properties, since the properties of the matrix will mainly depend on the characteristics of the polymer [1]. In light of the above, the aim of this present work is focused on knowing the swelling properties and sustained release hydrophilic matrices of Solifenacin succinate using new modified polymeric natural carbohydrates and compared with semi synthetic polymers.

Xanthan gum is a hydrophilic natural polymer, swells in gastric fluid to produce a highly viscous layer around the tablet core through which the drug can slowly diffuse. This property makes Xanthan gum as a useful candidate for developing modified release systems. Hydroxypropyl methyl cellulose (HPMC K4M) is a non-ionic aqueous soluble cellulose derivative for use in modified release dosage forms. Owing to high swellability and high gelling strength formation this effectively prolongs drug release, which has a significant effect on the release kinetics of incorporated drug.

The main objective of the present study is to provide an improved oral controlled release matrix dosage formulation at a therapeutic dose, in the tablet form containing 5mg of Solifenacin succinate for 24 hours release useful for the treatment of urge incontinence and other symptoms of an unstable or overactive urinary bladder.

MATERIALS AND METHODS

Materials

Solifenacin succinate was purchased from Hetro Drugs India, Hyderabad. HPMC K4M and SCMC were

obtained from AurobindoPharma, Hyderabad. Xanthan gum 80 mesh SR-2 and Guar gum 100 mesh Food Grade were purchased from SD fine Chemicals, Mumbai. All other ingredients, chemicals and solvents used were analytical reagent grade and were used as received.

Design of formula and composition

The modified release matrix tablets of Solifenacin succinate were prepared by wet granulation method by using natural polymer of guar gum, Xanthan gum and semi synthetic polymers of hydroxypropyl methyl cellulose (HPMCK4M), sodium carboxy methyl cellulose (NaCMC). The povidone (PVPK30) solution prepared with Polysorbate 80 which is act as granulating agent. Apart from that lactose was added as diluents to increase the bulk of the tablets, magnesium stearate and aerosol were added to increase the flow ability of the granules during tablet compression. The prepared matrix tablets were used for further evaluation studies.

Standard solutions

10mg of Solifenacin was accurately weighed and transferred into a 10mL volumetric flask and 7 mL of diluent was added and sonicate to dissolve it completely and the volume was adjusted with the mobile phase to get stock solution of 1000µg/mL.

Then 0.4 mL of stock solution is transferred into 10 ml volumetric flask and made up to volume with mobile phase and filtered through 0.45µm membrane filter, which gives a solution of strength of 40µg/mL. The concentration range of standard curve was diluted four times in mobile phase and the corresponding solution was subjected to

Table 1. Composition of matrix tablets of Solifenacin succinate

Ingredients in mg/tablet*	Solifenacin succinate	HPMC K4M	NaCMC	Guar Gum	Xanthan Gum	Lactose monohydrate
SF1	5	15	--	--	--	156.4
SF2	5	30	--	--	--	141.4
SF3	5	45	--	--	--	126.4
SF4	5	60	--	--	--	111.4
SF5	5	--	15	--	--	156.4
SF6	5	--	30	--	--	141.4
SF7	5	--	45	--	--	126.4
SF8	5	--	60	--	--	111.4
SF9	5	--	--	15	--	156.4
SF10	5	--	--	30	--	141.4
SF11	5	--	--	45	--	126.4
SF12	5	--	--	60	--	111.4
SF13	5	--	--	--	15	156.4
SF14	5	--	--	--	30	141.4
SF15	5	--	--	--	45	126.4
SF16	5	--	--	--	60	111.4

*All ingredients were taken in mg, 10% PVP K30 w/v solution was used as granulating agent, 0.2% w/w of Magnesium stearate and Aerosil were used as a lubricant and glident respectively for all formulations.

chromatographic analysis at 20-70µg/ml of Solifenacin succinate [2].

Chromatographic analyses

The HPLC system was employed using Shimadzu liquid chromatograph, model SPD 10A VP using a variable wavelength UV detector set at 220nm, an LC-10 ADVP pump, a Rheodyne injector and a model CR6-A integrator. Separation was performed on a C18 reversed-phase column at room temperature (28°C). A (50:50) acetonitrile:phosphate buffer pH 6.8 mixture was used as mobile phase, at a flow rate of 1ml/min and injection volume of 20µl.

Preformulation Study

The prepared granules were evaluated for micromeritic properties using the parameters such as derived properties like bulk density and tapped density, flow properties like Hausner's ratio, angle of repose and compressibility index (Carr's index). The values for drug and granules of all formulations are given in Table 2.

Bulk Density:

Apparent bulk density was determined by pouring pre-sieved drug excipients blend into a graduated cylinder and measuring the volume and weight "as it is". It is expressed in g/mL and is given by,

$$D_b = M / V_O$$

Where, D_b is the bulk density, M is the mass of powder and V_O is the Bulk volume of the powder.

Tapped density:

It was determined by placing a graduated cylinder, containing a known mass of drug- excipients blend, on mechanical tapping apparatus. The tapped volume was measured by tapping the powder to constant volume. It is expressed in g/mL.

$$D_t = M / V_t$$

Where, D_t is the tapped density, M is the mass of powder and V_t is the tapped volume of the powder.

Angle of repose

This is the maximum angle possible between the surface of the pile or powder and horizontal plane. The frictional forces in the loose powder can be measured by Angle of repose. The tangent of Angle of repose is equal to the coefficient friction between the particles. Angle of repose was determined by using funnel method.

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

Where, θ is the angle of repose, h is the height in cm and r is the radius in cm.

Carr's Index (I)

Compressibility index is an important measure that can be obtained from the bulk and tapped densities. A material having values less than 20 to 30% are defined as the free flowing material, based on the apparent bulk density and tapped density, the percentage compressibility of the bulk drug was determined by using the following formula.

$$I = D_t - D_b / D_t \times 100$$

Where, I is the Compressibility index, D_t is the tapped density of the powder and D_b is the bulk density of the powder.

Hausner's ratio

It indicates the flow properties of the powder. The ratio of Tapped density to bulk density of the powder or granules is called Hausner's ratio.

$$H = D_t / D_b$$

Where, H is the Hausner's ratio, D_t is the tapped density of the powder and D_b is the bulk density of the powder.

Table 2. Data obtained by preformulation study for pure drug and prepared granules containing Solifenacin succinate

F.Code	Derived Properties		Flow Properties		
	Bulk density (mean ± SD)	Tapped density (mean ± SD)	Angle of repose (mean ± SD)	Carr's index (mean ± SD)	Hausner's ratio (mean ± SD)
Pure drug	0.28±0.04	0.26±0.07	31.03±0.02	17.33±0.02	1.28±0.04
SF1	0.38±0.05	0.41±0.08	48.66±0.05	20.89±0.05	1.32±0.02
SF2	0.42±0.09	0.35±0.02	48.05±0.07	19.62±0.05	1.39±0.05
SF3	0.39±0.07	0.42±0.04	48.48±0.04	17.71±0.07	1.25±0.07
SF4	0.39±0.04	0.32±0.06	48.47±0.12	15.24±0.03	1.37±0.03
SF5	0.43±0.09	0.35±0.07	40.74±0.06	19.85±0.06	1.41±0.05
SF6	0.41±0.06	0.32±0.04	42.28±0.02	18.10±0.02	1.41±0.03
SF7	0.37±0.04	0.38±0.05	30.17±0.06	13.95±0.11	1.35±0.02
SF8	0.41±0.06	0.44±0.04	33.84±0.09	13.70±0.21	1.37±0.01
SF9	0.33±0.04	0.35±0.07	33.13±0.03	19.93±0.03	1.32±0.05
SF10	0.35±0.04	0.40±0.02	47.07±0.13	18.46±0.05	1.32±0.06
SF11	0.36±0.03	0.36±0.05	44.63±0.06	18.41±0.05	1.29±0.08
SF12	0.36±0.05	0.36±0.06	39.55±0.04	16.11±0.08	1.26±0.03
SF13	0.33±0.04	0.44±0.07	36.94±0.02	20.85±0.09	1.26±0.06
SF14	0.39±0.09	0.38±0.04	44.28±0.04	20.69±0.03	1.39±0.03
SF15	0.42±0.07	0.32±0.02	34.45±0.07	15.27±0.06	1.29±0.07
SF16	0.36±0.06	0.41±0.03	37.59±0.09	19.53±0.09	1.29±0.02

Compatibility studies

The compatibility of the drug in the formulation was confirmed by FTIR spectral analysis. FTIR spectra of pure drug, formulation containing Xanthan gum and Guar gum were determined by using Shimadzu FTIR spectrophotometer by KBr pellet method [4].

Physicochemical evaluation

The prepared matrix tablets were evaluated for weight variation, thickness, diameter, hardness, drug content, swelling and in vitro studies. Drug content was estimated by HPLC technique using a developed method. Solifenacin from accurately weighed samples was extracted into methanol and the extracts were suitably diluted and assayed for drug content. The samples were performed using UV detector with flow rate 2ml/min [4].

Physicochemical evaluation of matrix tablets

Dimension measurement:

The thickness and diameter of the tablets was carried out using digital vernier caliper. Three tablets were used from each batch and results were expressed in millimeter. All tablets from individual batch have shown uniform thickness and diameter.

Hardness test: Tablet requires a certain amount of strength or hardness and resistance to friability to withstand mechanical shocks of handling in manufacture, packing and shipping. Monsanto hardness tester was used to measure the hardness of tablet. Three tablets from each batch were used for hardness test and results were expressed in Kg/cm².

Friability test: It was done in Roche friabilator apparatus where the tablets were subjected to the combined effect of

abrasion and shock by utilizing a plastic chamber that revolves at 25 rpm for dropping the tablets at a distance of six inches with each revolution. Pre-weighed samples of 20 tablets were placed in the friabilator, which is then operated for 100 revolutions. The tablets are then dusted and reweighed. Compressed tablets that loss less than 0.5 to 1.0% of their weight are generally considered acceptable. The percentage friability was calculated by the following expression,

$$\text{Friability} = \frac{\text{Weight loss}}{\text{Weight of tablets before operations}} \times 100$$

Weight variation test: Twenty tablets were selected randomly, individually weighed in a single pan electronic balance and the average weight was calculated. The uniformity of weight was determined according to I.P. specification. As per IP not more than two of individual weights should deviate from average weight by more than 5% and none deviate more than twice that percentage.

Drug content uniformity: Ten tablets were weighed and taken in a mortar and crushed to make powder form. A quantity of powder weighing equivalent to 100mg of drug was taken in a 100mL volumetric flask and pH 6.8 buffer solution was added. It was then heated at 60°C for 30 minutes. The solution was filtered using membrane filter (0.45µm) and then its absorbance was measured at 281nm using UV-Visible spectrometer. The amount of drug present in one tablet was calculated using standard graph. The results obtained for physicochemical evaluation of matrix tablets are given in Table [5].

Table 3. Results of physicochemical parameters of all formulations containing Solifenacin succinate

F.CODE	Diameter (mean±SD) (mm)	Thickness (mean±SD) (mm)	Hardness (mean±SD) (kg)	Friability (mean±SD) (%)	Weight variation (mean±SD) (mg)	Drug content (mean±SD)
SF1	2.8±0.2	3.93±0.4	4.85±0.3	0.03	180.57±0.43	101.63±0.15
SF2	2.8±0.4	3.98±0.5	5.19±0.5	0.04	182.85±0.37	99.61±0.14
SF3	2.8±0.5	4.10±0.3	4.71±0.6	0.01	180.77±0.52	100.54±0.18
SF4	2.8±0.3	4.03±0.6	5.23±0.5	0.08	182.90±0.63	98.29±0.09
SF5	2.8±0.5	3.93±0.3	4.56±0.3	0.08	180.93±0.64	103.01±0.23
SF6	2.8±0.5	4.06±0.1	4.95±0.6	0.02	183.31±0.34	100.10±0.12
SF7	2.8±0.2	3.88±0.6	4.72±0.7	0.03	183.23±0.78	98.45±0.14
SF8	2.8±0.4	3.95±0.3	4.59±0.3	0.03	181.14±0.46	102.68±0.08
SF9	2.8±0.2	4.08±0.5	4.75±0.2	0.06	182.01±0.47	103.55±0.15
SF10	2.8±0.6	3.80±0.4	5.47±0.5	0.02	181.50±0.63	102.69±0.13
SF11	2.8±0.3	4.05±0.6	4.72±0.7	0.01	183.53±0.62	101.13±0.21
SF12	2.8±0.5	3.92±0.3	5.36±0.4	0.03	183.64±0.53	97.92±0.15
SF13	2.8±0.4	4.02±0.6	4.59±0.3	0.06	181.61±0.57	100.13±0.13
SF14	2.8±0.3	3.85±0.4	5.21±0.6	0.08	181.04±0.35	98.72±0.15
SF15	2.8±0.6	3.99±0.3	4.94±0.3	0.06	182.79±0.72	101.14±0.18
SF16	2.8±0.2	3.98±0.3	4.66±0.5	0.08	181.09±0.52	101.62±0.15

Each value represents the mean ± standard deviation (n=3)

Swelling behavior of matrix tablets

The extent of swelling was measured in terms of percent weight gain by the tablet. The swelling behaviors of formulations were studied. One tablet from each formulation was kept in petri dish containing distilled water. At the end of one hour the tablet was withdrawn, soaked with tissue paper and weighed. The process is continued for 24 hours. The percentage weight gain by the tablet was taken as swelling index was expressed in terms

of percentage, and was calculated from the following equation.

$$SI (\%) = \frac{W_t - W_0}{W_0} \times 100$$

Where, SI is swelling index, W_t is weight of tablet at time t , W_0 is weight of tablet before immersion. The swelling indexes of tablets are given in Table 4.

Table 4. Swelling index of matrix tablets of Solifenacin succinate

Code	% of swelling with time in hrs Mean $\pm$ SD					
	2	4	6	8	10	12
SF1	45.7 $\pm$ 0.25	53.9 $\pm$ 0.15	69.9 $\pm$ 0.18	95.1 $\pm$ 0.52	123.3 $\pm$ 0.42	143.2 $\pm$ 0.35
SF2	37.1 $\pm$ 0.14	47.3 $\pm$ 0.14	78.1 $\pm$ 0.13	101.0 $\pm$ 0.53	127.1 $\pm$ 0.52	151.8 $\pm$ 0.26
SF3	49.9 $\pm$ 0.16	66.9 $\pm$ 0.18	89.5 $\pm$ 0.14	95.8 $\pm$ 0.24	126.6 $\pm$ 0.13	144.6 $\pm$ 0.36
SF4	41.3 $\pm$ 0.25	57.4 $\pm$ 0.26	94.0 $\pm$ 0.25	111.2 $\pm$ 0.52	135.5 $\pm$ 0.53	144.0 $\pm$ 0.32
SF5	45.5 $\pm$ 0.22	67.8 $\pm$ 0.42	88.8 $\pm$ 0.42	104.2 $\pm$ 0.32	120.3 $\pm$ 0.24	133.1 $\pm$ 0.35
SF6	41.3 $\pm$ 0.15	56.0 $\pm$ 0.52	76.2 $\pm$ 0.31	97.2 $\pm$ 0.46	113.8 $\pm$ 0.54	126.4 $\pm$ 0.37
SF7	40.8 $\pm$ 0.21	51.3 $\pm$ 0.14	77.2 $\pm$ 0.45	100.5 $\pm$ 0.24	111.2 $\pm$ 0.24	129.4 $\pm$ 0.26
SF8	33.1 $\pm$ 0.25	49.7 $\pm$ 0.52	66.0 $\pm$ 0.21	88.6 $\pm$ 0.42	104.7 $\pm$ 0.52	122.6 $\pm$ 0.25
SF9	35.0 $\pm$ 0.27	52.7 $\pm$ 0.12	71.1 $\pm$ 0.42	91.2 $\pm$ 0.42	110.1 $\pm$ 0.13	129.6 $\pm$ 0.24
SF10	38.2 $\pm$ 0.26	51.1 $\pm$ 0.17	67.2 $\pm$ 0.43	85.8 $\pm$ 0.15	104.7 $\pm$ 0.15	127.5 $\pm$ 0.26
SF11	40.6 $\pm$ 0.17	54.1 $\pm$ 0.14	71.3 $\pm$ 0.46	90.2 $\pm$ 0.32	113.3 $\pm$ 0.25	130.8 $\pm$ 0.24
SF12	30.3 $\pm$ 0.19	51.3 $\pm$ 0.23	67.6 $\pm$ 0.14	93.5 $\pm$ 0.24	114.9 $\pm$ 0.25	135.0 $\pm$ 0.31
SF13	35.0 $\pm$ 0.31	54.8 $\pm$ 0.34	77.4 $\pm$ 0.21	90.0 $\pm$ 0.35	121.0 $\pm$ 0.16	147.1 $\pm$ 0.45
SF14	28.9 $\pm$ 0.43	59.7 $\pm$ 0.42	87.2 $\pm$ 0.35	96.5 $\pm$ 0.25	117.0 $\pm$ 0.24	162.5 $\pm$ 0.24
SF15	35.7 $\pm$ 0.35	62.7 $\pm$ 0.62	86.0 $\pm$ 0.25	91.2 $\pm$ 0.27	112.2 $\pm$ 0.25	139.0 $\pm$ 0.52
SF16	40.3 $\pm$ 0.13	53.9 $\pm$ 0.54	73.4 $\pm$ 0.21	85.1 $\pm$ 0.24	103.8 $\pm$ 0.34	141.5 $\pm$ 0.44

In vitro drug release study

In vitro dissolution study was carried out using USP Type II apparatus (Lab India) at 50 rpm. Phosphate buffer pH 6.8 was used as dissolution medium, temperature was maintained at 37 $\pm$ 0.5°C. An appropriate time intervals samples were withdrawn from the dissolution medium and assayed by developed HPLC method to determine the amount of Solifenacin succinate release from the matrix tablet. Comparison of drug release pattern of all matrix tablets of Solifenacin succinate is shown in Figure 1 to Figure 4.

Kinetics of drug release

Dissolution data of all matrix tablets were subjected to the treatment of different kinetic equations. It was found to be that the drug release patterns were best fitted with zero order release equation and involves the combination of polymer relation and consequently swelling.

Zero-order release equation $C = K_0t$

First-order release equation $\log C = \log C_0 - Kt/2.303$

Higuchi's square root of time equation $Q = Kt^{1/2}$

KorsmeyerPeppas equation $Mt/M_\infty = Kt^n$

Figure 1. In vitro dissolution data trials for SF1 to SF4

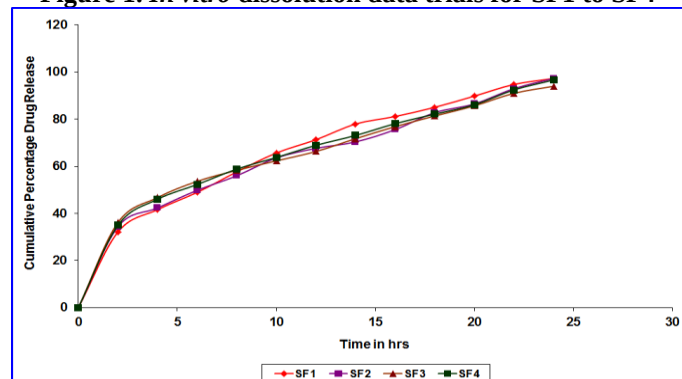


Figure 2. In vitro dissolution data trials for SF5 to SF8

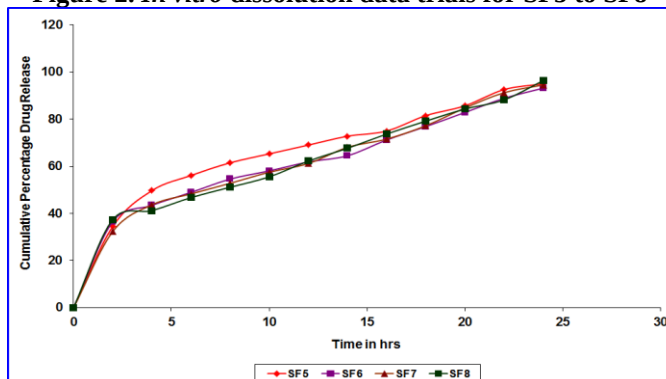


Figure 3. *In vitro* dissolution data trials for SF9 to SF12

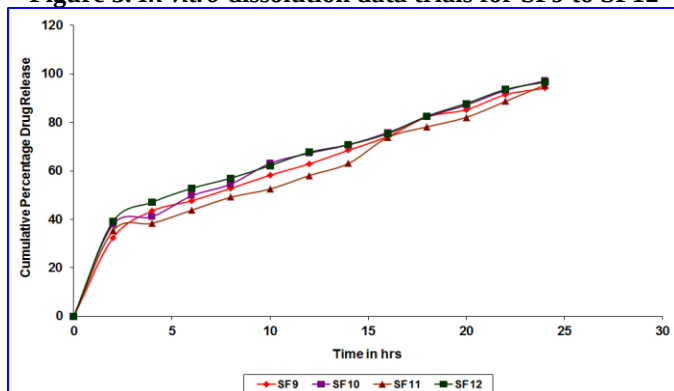
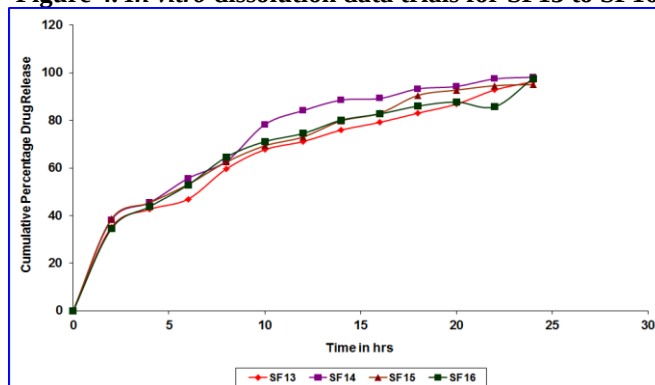


Figure 4. *In vitro* dissolution data trials for SF13 to SF16



Stability study

According to ICH Guidelines (Q1E Evaluation for stability Data) stability studies were carried out for optimized formulation SF 12 at two conditions i.e. Long term condition ($25 \pm 2^\circ\text{C}/60\% \pm 5\% \text{ RH}$) and Accelerated condition ($40 \pm 2^\circ\text{C}/70\% \pm 5\% \text{ RH}$) for a period of 12 months. The ten tablets were packed in Alu-Alu blister packing and stored in stability chambers.

Tablet samples were evaluated after 1st, 3rd, 6th, 9th, and 12th month for drug content as well as subjected for the *In vitro* drug release study. All the parameters have not shown any much variation when compared to the initial data. The *In vitro* dissolution was carried out for twelve months at the interval of four months.

Figure 5. FTIR Spectrum of Solifenacin succinate

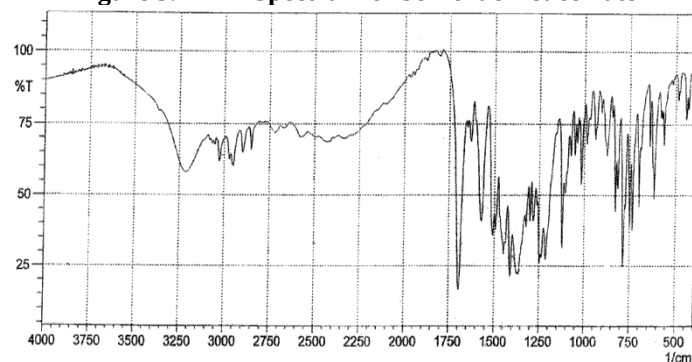
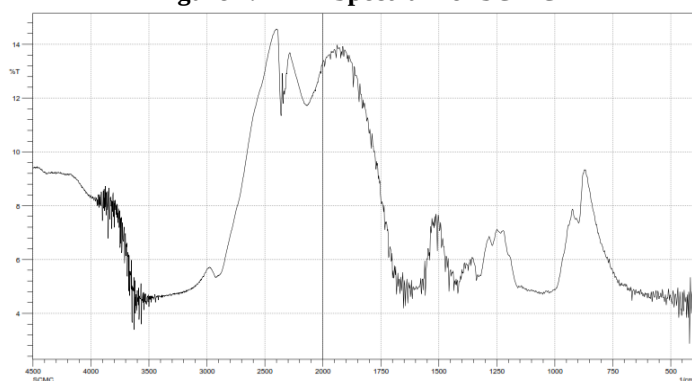


Figure 7. FTIR Spectrum of SCMC



RESULTS AND DISCUSSION

IR spectroscopy studies were carried out using Perkin Elmer model 2000 at LailaImpex Research centre, Vijayawada, Andhra Pradesh, India by KBr pellet method. Materials were compressed under 10 tones pressure in a hydraulic press to form a homogeneous sample/KBr pellet. The pellet was scanned over the frequency range from 4400 to 450 cm^{-1} and peaks obtained were identified [6]. FTIR spectra are shown from Figure 5 to Figure 9. The IR spectra of drug and polymer alone and prepared formulations shows no significant interaction between drug and polymer. The study confirmed the presence of all predominant peaks indicating its authenticity.

Figure 6. FTIR spectrum of HPMC

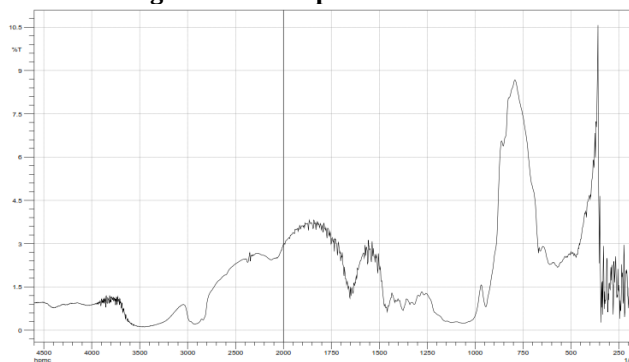


Figure 8. FTIR Spectrum of Guar Gum

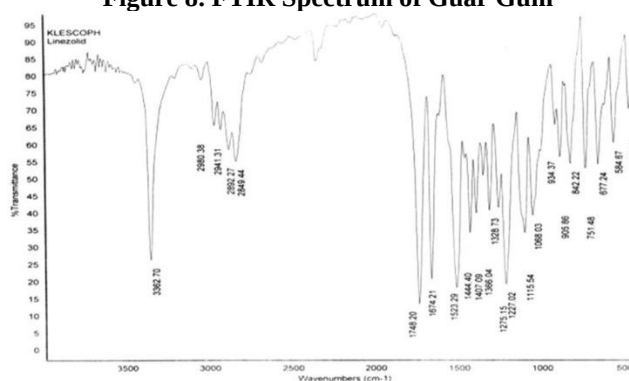
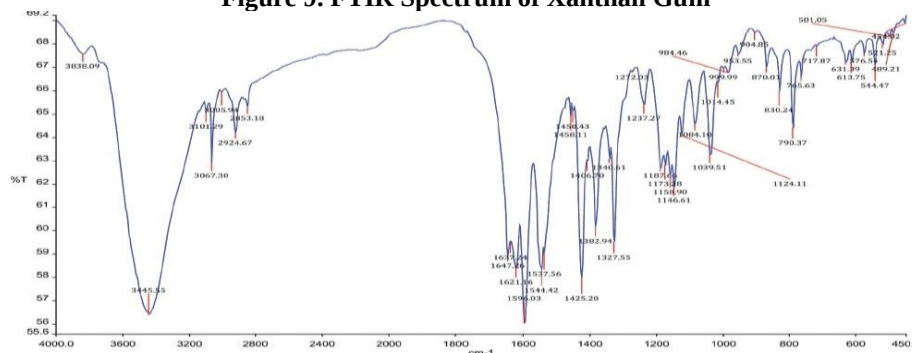


Figure 9. FTIR Spectrum of Xanthan Gum



Preformulation study

The angle of repose for pure drugs was very less and hence poor flow of drug was exhibited. Moreover, the Carr's index of the pure drug was found to be high confirming that the drug has poor flow property and compressibility.

In view of this, the formulations were prepared by wet granulation technique to improve the flow as well as compressibility. The flow properties and derived properties were evaluated for all formulations, which were proven to be within limits showing good flow properties, standard limits were tabulated in Table 5.

Table 5. Standard limits for flow properties of powder

S.NO	Type of flow	Angle of repose	Carr's index	Hausner's ratio
1	Excellent	25-30	10	1-1.11
2	Good	31-35s	11-15	1.12-1.18
3	fair	36-40 (aid not needed)	16-20	1.19-1.25
4	passable	41-45 (may hang up)	21-25	1.26-1.34
5	Poor	46-55 (must agitate)	26-31	1.35-1.45
6	very poor	56-65	32-37	1.46-1.54
7	very very poor	>66	>38	>1.60

Physicochemical evaluation

The hardness of the tablets was found to be between 4-6 kg/cm² and % friability of tablets ranged between 0.01 and 0.08%. The tablets have the enough hardness to withstand stress during the transport and handling. The tablet complies with the test for uniformity of weight. The drug content varied from 97.92-103.55% w/w and all the formulations exhibited uniformity of drug content.

Swelling index

As time increased the swelling index was increased, because weight gained by the matrix tablet was increased proportionally with the rate of hydration up to 5 hours. The direct relationship was observed between swelling index and gum concentration, as gum concentration increases, swelling index was increased, but drug release decreases. This is due to slow erosion of gelled layer from the core tablets containing a higher amount of matrix polymer. Comparisons between Xanthan gum and guar gum, it was observed that swelling index of guar gum was significantly more compared to Xanthan gum.

In vitro drug release study

The drug release was prolonged as the amount of polymeric concentration was increased. Comparison

between Xanthan gum and guar gum based matrix tablets, release of drug from guar gum based tablets were found to be more slowly compared to Xanthan gum based tablets. This sustained release is because of the formulation of thicker gel barrier structure around the matrix that delayed the drug release from the matrix tablets. Thus, maintain the integrity of tablet and retarding further penetration of the dissolution medium. The maximum drug release was found to be 94% over a period of 24 hours in guar gum based formulations (F9-F12) at a concentration ranging from 15 to 60mg per tablet. Similarly maximum drug release was found to be 95% over a period of 24 hours in Xanthan gum to gum based formulations (F13-F16) at a concentration ranging from 15 to 60mg per tablet. In vitro profiles of tablets could be best expressed by zero-order kinetics and Korsmeyer-Peppas kinetics. The 'n' value of drug release is 0.964. Therefore, the drug release followed non-fickian diffusion.

Stability studies

The stability studies were conducted as per ICH guidelines for the period of twelve months at various accelerated temperature and humidity conditions of 25°C/60%RH, 40°C/70%RH, 50°C/75%RH, 60°C/80%RH. The stability study revealed that the matrix tablets of SF14 may be stable for the period of two years.

CONCLUSION

The modified release matrix tablets contain Solifenacin succinate were prepared using Hydroxypropyl methyl cellulose (HPMC K4M), Sodium carboxy methyl cellulose (SCMC), Guar Gum and Xanthan Gum as rate controlling polymer for the treatment of overactive bladder. The tablets were prepared by wet granulation method and studied the effect of the matrix former such as Guar Gum and Xanthan Gum separately. Hydrophilic

polymers delivers drug over a period of 24 hours. Formulation SF14 shows satisfactory results by releasing 98.13% of drug in 24 hours and followed zero-order and Korsmeyer-Peppas release mechanism. The overall results indicate that the formulation SF14 was better and that satisfied all the criteria as modified release tablets. This modified release dosage form will be good in treatment of over active bladder/urinary incontinence by improving patient compliance and reducing dosing frequency.

REFERENCES

1. Bruce LD, Shah NH, Malick AW, Infeld MH, McGinity JW. Properties of hotmelt extruded tablet formulations for the colonic delivery of 5-aminosalicylic acid. *Eur J Pharm Biopharm*, 59, 2005, 85–97.
2. Saroj Kumar Raul, BVV Ravi kumar, Ajaya Kumar Patnaik, a RP-HPLC method development and validation for the estimation of solifenacin in bulk and pharmaceutical dosage forms, *International Journal of Bioassays*, 1(12), 2012, 210-213.
3. Chavda HV, Patel MS, Patel CN. Preparation and *in vitro* evaluation of guar gum based triple-layer matrix tablet of diclofenac sodium. *Research in Pharmaceutical Sciences*, 7(1), 2012, 57-64.
4. Patel CN, Patel SA, Patel MM. Spectrophotometric Methods for the Estimation of Nicorandil in Tablet Dosage form. *IJPS*, 67(1), 2005, 103-105.
5. Jaimini M, Rana AC. Formulation and Evaluation of Famotidine Floating Tablets. *Current Drug Delivery*, 4, 2007, 51-55.
6. Narayana Raju P, Prakash K, Lakshmi Narasu M. Compatibility Study of Lamivudine with Various Cellulose Polymers, *E-Journal of Chemistry*, 6(S1), 2009, S17-S20.