RESEARCH PAPER

DESIGN, DEVELOPMENT AND EVALUATION OF NATURAL EXCIPIENT BASED ITOPRIDE HYDROCHLORIDE CONTROLLED-RELEASE MATRIX TABLETS

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ABSTRACT

Maintaining drug levels within a desired range, requiring fewer administrations, making the best use of the drugs in question, and improving patient compliance are among the benefits of controlled drug delivery systems. The prokinetic agent itopride was chosen as the drug candidate for this investigation. The aim of the present study was to design, prepare and evaluate Itopride controlled release tablets using natural gums as excipients. Itopride was loaded into pellets (IC1 to IC5) by calcium silicate in increasing concentrations of 1 to 5%w/w. Itopride pellets that exhibited best drug load was selected and controlled release tablets were prepared (I1 to I18) with different amounts of polymers like Xanthan gum, Gum karaya and HPMC K4M using direct compression method. Various pre and post compression parameters followed by *in vitro* dissolution and characterization studies were also performed. The pellets with maximum quantity of calcium silicate showed delayed drug release. IC3 formulation was selected for preparation of Itopride controlled release tablets. The tablets prepared with gums and HPMC K4M exhibited good flow properties. Among all the formulations, I18 exhibited highest swelling index of 249%. *In vitro* drug release studies showed that the preparations made with higher concentrations of gums exhibited delayed drug release compared to HPMC K4M. The characterization studies revealed that the drug and excipients have no interactions. Incorporation of calcium silicate and gums in the formulations is good choice for the preparation of controlled release tablets. The optimized formulation could become a potential commercial prokinetic agent which showed good physicochemical properties and drug release.

KEYWORDS

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INTRODUCTION

Drugs which get readily absorbed from gastro-intestinal tract (GIT) along with very less half-life will be cleared off from the body. Such drugs are needed to be formulated as oral controlled release agents. This helps in slow and constant release of drug in GIT for a prolonged period of time.[1] Gastric retention time is another barrier in limiting the drug delivery through oral route. When a controlled system is developed, it also overcomes the issue of gastric retention. It also helps in maintaining plasma drug levels at a constant rate within the therapeutic window.[2] Nowadays, several techniques and polymers have been employed in preparation of controlled release formulations.[3]

Itopride is a drug which is used to treat variety of conditions like dyspepsia, anorexia, bloating and vomiting. It acts as a prokinetic agent. It has an elimination half-life of around 6 h.[4] Therefore, it is possible to develop a controlled release formulation which helps in longer plasma retainment of the drug that reduces frequent drug usage. Calcium silicate is one of the components used for entrapping drug. On exposure to water, calcium silicate absorbs water and swells which causes drug release. Due to its high capacity to load drug, most of the controlled release formulations prefer calcium silicate.[5] Despite the invention of a number of synthetic excipients, the use and advancement of natural excipients have gained attention recently because of their accessibility.[6] Among the biopolymers, xanthan gum and gum karaya were mostly employed in preparation of controlled release formulations. Xanthan gum is widely employed in controlled release preparations due to its high thermal stability and pseudoplastic behavior that can be easily changed.[7] Gum karaya is a natural derivative which takes up water easily and due to its extensive gelling and enzymatic degradation property, it is widely used in preparation of controlled release formulations.[8] The present study

was aimed to develop Itopride controlled release tablets using calcium silicate to delay the drug release using natural gums. The prepared matrix tablets were further evaluated for various parameters and characterization studies.

MATERIALS AND METHODS

Procurement of Materials

Itopride hydrochloride was procured from Yarrow Chem Products (Mumbai, India). Calcium silicate was procured from S.D Fine Chem. Ltd. (Mumbai, India). Xanthan gum and gum karaya were procured from Yarrow Chem Products (Mumbai, India). Sodium hydroxide, magnesium stearate and talc were procured form Qualigens fine chemicals (Mumbai, India).

Preparation of Itopride Absorbed Calcium Silicate

Calcium silicate dispersion in increasing concentrations (1% to 5%w/w) was prepared in a beaker with distilled water. Itopride solution was made using 25ml of ethanol. Then the calcium silicate solution was stirred on a magnetic stirrer with a rotation speed of 500rpm. The drug solution was added drop by drop into calcium silicate dispersion. The dispersion was allowed to stir on magnetic stirrer for 20 min. Later the dispersion is subjected to cold ultra sonication for 10 min and filtered. The filtered sample was subjected to drying for 24h in order to obtain drug loaded calcium silicate pellets.[9] The composition of Itopride absorbed calcium silicate formulations was given in table 1.

Evaluation of Itopride Pellets

The prepared Itopride absorbed Calcium Silicate pellets were subjected for testing % yield, drug entrapment efficiency, drug content uniformity and drug release studies.[10] The results were given in table 2.

In vitro Dissolution Studies of Itopride Absorbed Calcium Silicate

A calibrated eight-station dissolution test apparatus with paddles (USP apparatus II method) was used to conduct dissolution tests for all Itopride-absorbed calcium silicate pellets. 900 milliliters of distilled water were used as the dissolving medium, and the temperature was maintained at 37±1ºC at 50 rpm. To maintain sink conditions throughout the experiment, the samples were removed at 5, 10, 15, 20, 30, 45, and 60 minutes and replaced with an equivalent volume of the same dissolution fluid. The same dissolution solution was used to dilute samples taken at different times, and the amount of drug dissolved was calculated using a double beam UV spectrophotometer set to 258 nm. The dissolution profiles for all formulations were shown in figure 1.

Preparation of Itopride Controlled Release Tablets

Direct compression was used to develop itopride controlled release tablets with different polymer concentrations.[11] MCC was used as diluent and cushioning agent. Increasing concentrations of controlled release polymers like xanthan gum, gum karaya and HPMC K4M were used. Pellets of optimized itopride-absorbed calcium silicate were weighed separately, put through sieve number 80, and then blended in a double cone blender for fifteen minutes. Post addition of 1% talc and magnesium stearate, tablets were made using a CLIT 10 station mini press. Formulations I1 to I5 were made utilizing itopride-absorbed calcium silicate pellets (IC3) and different gum karaya concentrations. Formulations I6 to I10 were made using Xanthan gum along with optimized Itopride absorbed calcium silicate pellets IC3. Formulations I11 to I15 were made using HPMC K4M along with optimized Itopride absorbed calcium silicate pellets IC3. Formulation I16 has equal amounts of xanthan gum and gum karaya, I17 has equal amounts of gum karaya and HPMC K4M, and I18 has equal amounts of xanthan gum and HPMC K4M. ID is made with only Itopride pure drug. IC contains only optimized Itopride absorbed calcium silicate pellets IC3 without any polymer. The compositions were given in tables 3 to 5.

Pre-compression Parameters Evaluation for Itopride Granules

The produced granules were assessed for a number of pre-compression metrics, including Hausner's ratio, Carr's index, and angle of repose.[12] The results were indicated in table 6.

Post Compression Parameters Evaluation for Prepared Itopride Tablets

For produced tablets, post-compression characteristics such drug content, hardness, friability, and weight uniformity were assessed.[13] The results were given in table 7.

In-vitro Dissolution Studies of Itopride Controlled Release Tablets

900 milliliters of distilled water were used as the dissolution medium in the USP Apparatus Type II dissolution test. At 0.5, 1, 2, 4, 6, and 8 hours, the samples were taken. Additionally, some formulations were dissolved for ten and twelve hours. The samples were diluted with the dissolving media if needed. The cumulative percentage of drug released was computed by measuring absorbance at 258nm. The dissolution profiles were depicted in figure 2.

Statistical Analysis

The outcomes were assessed statistically. For drug content and drug dissolution profiles, the mean and their standard deviations (S.D.) were computed because the procedures were carried out and the data were obtained in triplicate.

Characterization Studies

Itopride, xanthan gum, gum karaya, HPMC K4M, and optimized controlled release formulations were subjected to scanning electron microscopy (SEM) analysis to determine surface characteristics. Fourier transfer infrared (FTIR) studies were conducted to observe the drug–polymer interactions, and the optimized formulations were chosen based on the dissolution studies. The results were presented in figures 3 and 4.

RESULTS AND DISCUSSION

Preparation of Itopride Microspheres using Calcium Silicate

Itopride microspheres coded as IC1 to IC5 were made using calcium silicate in increasing concentrations of 1 to 5% w/w. The composition of the microspheres was given in table 1.

Table 1: Composition of Itopride Microspheres made using Calcium Silicate

S. No	Formulation	Itopride: % of Calcium Silicate used
1	IC1	1:1.0
2	IC2	1:2.0
3	IC3	1:3.0
4	IC4	1:4.0
5	IC5	1:5.0

**One part of Itopride is equivalent to 50mg*

Evaluation of Various Parameters of Itopride Absorbed Calcium Silicate

Itopride-absorbed calcium silicate pellet formulations were assessed for a number of factors, including drug content homogeneity, drug entrapment efficiency, and yield percentage. Table 2 shows the outcomes for different calcium silicate pellet formulations that were absorbed by itopride. According to the investigations, the formulations' yield ranged from 81.81 to 89.48%. These formulations had more than 95% of itopride. In vitro dissolution tests were conducted on these formulations.

Table 2: Various Parameters of Itopride absorbed Calcium Silicate Pellet Formulations

Formulation	% Yield	Drug Entrapment Efficiency (%) (Mean±S.D) *	Drug Content (mg) (Mean±S.D) *
I	--	--	49.79±0.72
IC1	83.52	96.63±1.12	50.10±0.59
IC2	89.48	98.95±1.10	49.95±0.98
IC3	89.32	99.02±1.04	50.04±0.55
IC4	87.31	99.77±1.14	49.98±0.77
IC5	81.81	98.28±0.99	50.25±0.65

**S.D indicates standard deviation (N=3)*

***Invitro* Dissolution Studies of Itopride Absorbed Calcium Silicate Pellets**

Dissolution studies were carried on Itopride absorbed calcium silicate pellets using USP paddle method (apparatus II) with distilled water as dissolution medium. The dissolution profiles were shown in figure 1. The pure drug Itopride exhibited drug release of 99.91% within 15min of dissolution. As Itopride is a BCS class I drug, the drug release is faster. Calcium silicate based pellets exhibited variations in drug release pattern. In IC1 to IC3 formulations made with 1 to 3%w/w of calcium silicate, the drug release was decreased from 91.14 to 78.08% within 60 min of dissolution. In IC4 and IC5 formulations made with 4 and 5%w/w calcium silicate, the drug release was retarded which is less than 50% even after 60 min of dissolution. This might be due to the increased binding effect of calcium silicate with drug. It inhibits the wettability of drug and thus resulted in decreased drug release. With its porous structure and large pore volume, calcium silicate causes controlled drug release through nano-porosity.[14] Formulation IC3 made with 3%w/w calcium silicate was found to be suitable for further preparation of controlled release tablets.

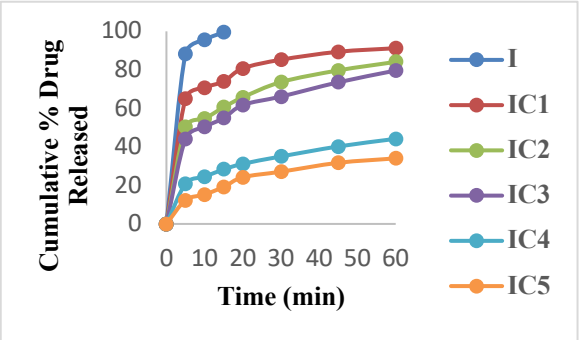


Figure 1: Drug Release Profiles of Itopride absorbed Calcium Silicate Pellets

Preparation of Itopride Controlled Release Tablets

The direct compression method was used to create all of the controlled release tablet formulations. In order to prepare the tablets using the direct compression method, known proportions of IC3 containing itopride made with 3%w/w calcium silicate equivalent to a 50 mg dose were blended with diluents and different concentrations of polymers. The mixture was then lubricated with 1% lubricant and glidant before being directly compressed into tablets. Tables 3 to 5 listed the composition of several Itopride controlled release tablets. Formulation ID was compressed without adding any polymer or calcium silicate absorbed formulation. Formulation IC was compressed with only IC3 without any polymer. Formulations I1 to I5 were prepared by using gum karaya (0.2 to 1 ratios equivalent to drug dose) along with optimized Itopride absorbed calcium silicate pellets IC3.

Table 3: Composition of Itopride Controlled Release Tablets (I1 – I5)

Ingredient (mg/tablet)	**Formulations**						
	ID	**IC**	**I1**	**I2**	**I3**	**I4**	**I5**
Itopride hydrochloride	50	--	--	--	--	--	--
IC3	--	144	144	144	144	144	144
Gum Karaya	--	--	7	14	21	28	35
Xanthan Gum	--	--	--	--	--	--	--
HPMC K4M	--	--	--	--	--	--	--
MCC PH 102	196.25	102.25	95.25	88.25	81.25	74.25	67.25
Sacchari n Sodium	1.25	1.25	1.25	1.25	1.25	1.25	1.25
Talc	1.25	1.25	1.25	1.25	1.25	1.25	1.25
Magnesium Stearate	1.25	1.25	1.25	1.25	1.25	1.25	1.25
Total Weight	250	250	250	250	250	250	250

Formulations I6 to I10 were made using Xanthan gum (0.2 to 1 ratios equivalent to drug dose) along with optimized Itopride absorbed calcium silicate pellets IC3. Formulations I11 to I15 were made using HPMC K4M (0.2 to 1 ratios equivalent to drug dose) along with optimized Itopride absorbed calcium silicate pellets IC3.

Table 4: Composition of Itopride Controlled Release Tablets (I6 – I15)

Ingredient (mg/tablet)	**Formulations**									
	I6	**I7**	**I8**	**I9**	**I10**	**I11**	**I12**	**I13**	**I14**	**I15**

Itopride hydrochloride	--	--	--	--	--	--	--	--	--	--
IC3	144	144	144	144	144	144	144	144	144	144
Gum Karaya	--	--	--	--	--	--	--	--	--	--
Xanthan Gum	7	14	21	28	35	--	--	--	--	--
HPMC K4M	--	--	--	--	--	7	14	21	28	35
MCC PH 102	95.25	88.25	81.25	74.25	67.25	95.25	88.25	81.25	74.25	67.25
Saccharin Sodium	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25
Talc	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2
	5	5	5	5	5	5	5	5	5	5
Magnesium Stearate	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25
Total Weight	250	250	250	250	250	250	250	250	250	250

Formulations I16 to I18 were made by combining the polymers used in the study. This evaluates the combined effect of various polymers on controlled release of Itopride. This also helps in detecting the combination of polymers to be incorporated for prolonged drug release formulation preparation. I16 contains equal amounts of xanthan gum and gum karaya, I17 contains equal amounts of gum karaya and HPMC K4M, and I18 contains equal amounts of xanthan gum and HPMC K4M. MCC used in the formulation itself acts as a cushioning agent.

Table 5: Composition of Itopride Controlled Release Tablets

Ingredient (mg/tablet)	**Formulations**			
	I6	**I16**	**I17**	**I18**
Itopride Dihydrochloride	--	--	--	--
IC3	144	144	144	144
Gum Karaya	--	17.50	17.50	--
Xanthan Gum	7	17.50	--	17.50
HPMC K4M	--	--	17.50	17.50
MCC PH 102	95.25	67.25	67.25	67.25
Saccharin Sodium	1.25	1.25	1.25	1.25
Talc	1.25	1.25	1.25	1.25

Magnesium Stearate	1.25	1.25	1.25	1.25
Total Weight	250	250	250	250

Evaluation of Itopride Controlled Release Tablets

Pre-Compression Parameters of Itopride Controlled Release Granules

Before the tablet blends were compressed into controlled release tablets, a number of pre-compression characteristics were assessed. For each of these tablet formulations, pre-compression metrics such as Hausner's ratio, Carr's index, and angle of repose were assessed. For the Itopride formulation ID without any polymer, the angle of repose, Carr's index, and Hausner's ratio were 32°, 22%, and 1.21, respectively. Several Itopride tablet formulations prepared with gum karaya, xanthan gum, and HPMC K4M had angle of repose values between 22 and 23^0, indicating that the formulations had good flow characteristics.

Table 6: Pre-Compression Parameters of Itopride Granules

S.No	Formulation	Angle of Repose (^{0})	Carr's Index (%)	Hausner's Ratio
1	ID	32	22	1.21
2	IC	23	18	1.22
3	I1	22	14	1.18
4	I2	23	14	1.16
5	I3	23	13	1.13
6	I4	22	12	1.14
7	I5	22	13	1.14
8	I6	23	14	1.14
9	I7	22	13	1.12
10	I8	22	13	1.14
11	I9	23	14	1.14
12	I10	22	12	1.12
13	I11	23	14	1.14
14	I12	22	13	1.14
15	I13	23	13	1.14
16	I14	23	14	1.14
17	I15	22	13	1.13
18	I16	22	13	1.12
19	I17	23	14	1.13
20	I18	22	13	1.13

Itopride tablet formulations had Carr's index values between 12 and 18%, indicating that they have good repacking ability under compression. Good flow characteristics were indicated by the Hausner's ratio, which was found to be between 1.12 and 1.22. Table 6 showed the Itopride formulations' pre-compression parameters.

Post Compression Parameters of Itopride Controlled Release Tablets

Physical characteristics of the compressed tablets, including weight uniformity, hardness, friability, swelling index, and drug content, were also assessed. All tablet formulations' weight homogeneity showed that the tablets met I.P. requirements. All formulations had hardness values between 3.2±0.10 and 3.3±0.15 kg/cm^2. All tablet formulations showed very little friability loss, indicating that they had all passed the friability test in accordance with I.P. criteria. Every tablet formulation's estimated drug content fell within a very consistent range. For different Itopride formulations, the swelling index ranged from 86 to 249%.

Among all the formulations, I18 exhibited highest swelling index of 249% which is due to the presence of combination of xanthan gum and HPMC K4M as polymers. This is due to the fact that the pores formed by calcium silicate were covered with polymers used in tablets.[15]

Also, the gums used in the preparation of tablets have swelling property when contacted with water and releases drug in sustained manner.[16] Post compression parameters of Itopride tablets were presented in table 7.

Table 7: Post Compression Parameters of Various Itopride Tablets

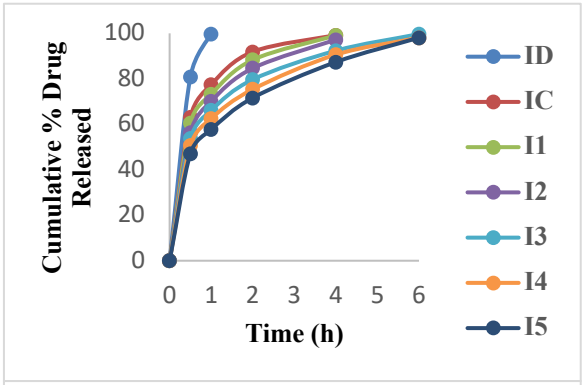
Formul	Weigh	Hard	Friab	Swel	Drug

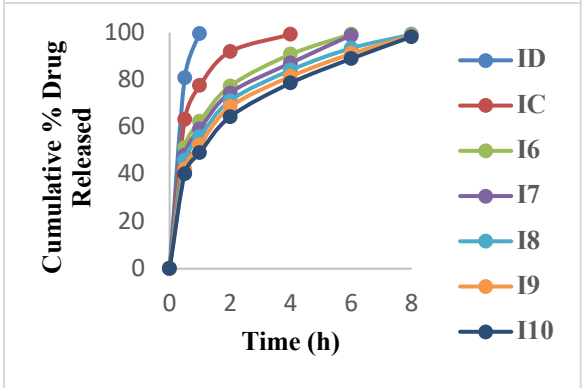
ation	t Uniformity (mg)	ness (Kg/cm^2)	ility (% loss)	ling Index (%)	Content (mg/tablet)
ID	249±1.14	3.2±0.10	0.4	--	50.11±1.01
IC	248±1.22	3.3±0.11	0.3	86	49.67±1.24
I1	250±1.11	3.2±0.15	0.2	94	50.05±1.10
I2	251±1.10	3.3±0.12	0.3	103	50.09±1.52
I3	249±1.24	3.2±0.10	0.2	110	50.91±1.06
I4	249±1.24	3.3±0.11	0.3	118	50.01±1.22
I5	251±1.08	3.2±0.12	0.2	129	49.64±1.01
I6	250±1.19	3.3±0.09	0.3	108	49.18±1.11
I7	249±1.10	3.3±0.12	0.3	120	50.22±1.03
I8	250±1.07	3.2±0.10	0.2	135	50.02±1.12
I9	248±1.14	3.3±0.15	0.3	149	49.95±1.10
I10	250±1.05	3.2±0.14	0.2	165	49.99±1.02
I11	249±1.11	3.3±0.11	0.2	118	50.01±1.11
I12	250±1.06	3.3±0.12	0.3	136	49.99±1.13
I13	249±1.40	3.3±0.15	0.3	170	50.05±0.98
I14	250±1.15	3.3±0.13	0.2	211	49.97±1.01
I15	250±1.20	3.2±0.13	0.2	245	50.10±1.04
I16	251±1.15	3.3±0.12	0.3	128	50.07±0.89
I17	251±1.22	3.3±0.15	0.2	178	50.04±1.05
I18	250±1.30	3.3±0.14	0.3	249	49.97±1.01

***In-vitro* Dissolution Studies of Itopride Controlled Release Tablets**

Dissolution investigations were carried on all the controlled release tablet formulations utilizing the U.S.P paddle method (apparatus II) in distilled water as dissolution medium by maintaining the bath temperature at 37+1ºC at 50rpm. The formulation ID prepared without using any polymer exhibited a drug release of 99.62% after 1h of dissolution. This is due to the high solubility and permeability nature of Itopride. Formulation IC having IC3 calcium silicate absorbed drug without any polymer exhibited 99.17% drug release after 4h of dissolution. The tablets I1 and I2 exhibited maximum drug release within 4h and I3 to I5 exhibited drug release of 98.01% to 99.68% after 6h of dissolution. This is due to the increase in concentration of gum karaya. The tablets I6 and T7 exhibited maximum drug release within 6h and I8 to I10 exhibited drug release of 98.27% to 99.21% after 8h of dissolution. This is due to the increase in concentration of xanthan gum. When natural gums

come into touch with water, they hydrate and swell. The drug must pass through the hydrated gel created by the water's slow penetration by dissolving and diffusing over the lengthening diffusional channel. When hydrogen-bonding forces preserve the integrity of the hydrophilic gum matrix and result in regulated drug release over an extended period of time, xanthan gum hydrates.[17] The tablets I11 and I12 exhibited maximum drug release within 8h and I13 to I15 exhibited drug release of 98.29% to 99.81% after 10h of dissolution. This is because the concentration of HPMC K4M increased; the rate of drug dissolution decreased as the concentration of polymer increased; the viscosity of HPMC was crucial in regulating the swelling and erosion profile; and the presence of HPMC caused the water uptake of these formulation matrices to occur very slowly for longer periods of time. Surface polymer of the matrices formed stronger gel immediately in contact with dissolution media which delayed further liquid permeation to the inner cores and subsequently slowed down swelling process.[18] The formulation I16 made with combination of xanthan gum and gum karaya exhibited drug release of 99.25% within 8h. Formulation I17 made with combination of gum karaya and HPMC K4M exhibited drug release of 99.32% within 10h. Formulation I18 made with combination of xanthan gum and HPMC K4M exhibited drug release of 99.29% within 12h. This might be attributed to the combined swelling effect of both the polymers used along with porous nature of calcium silicate that allows prolonged drug release.[19] The dissolution profiles of the controlled release tablets were presented in figure 2.





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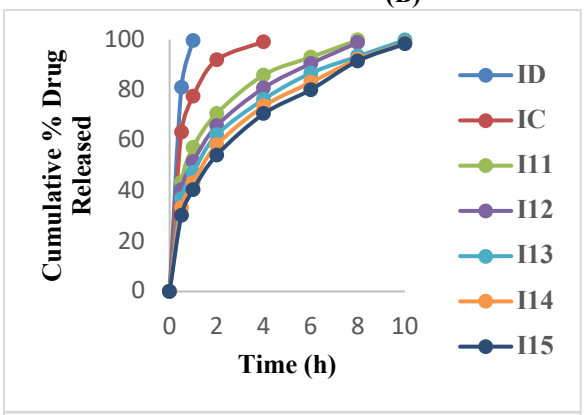
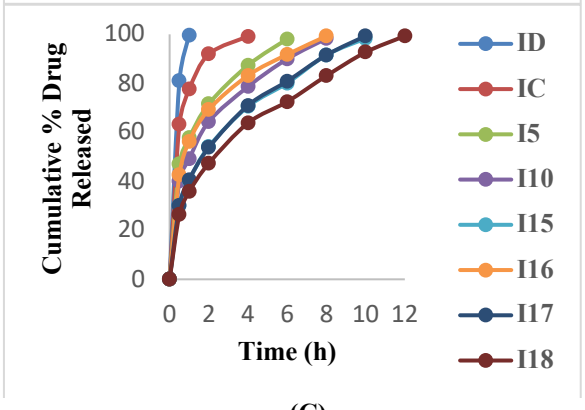




(C)

(D)

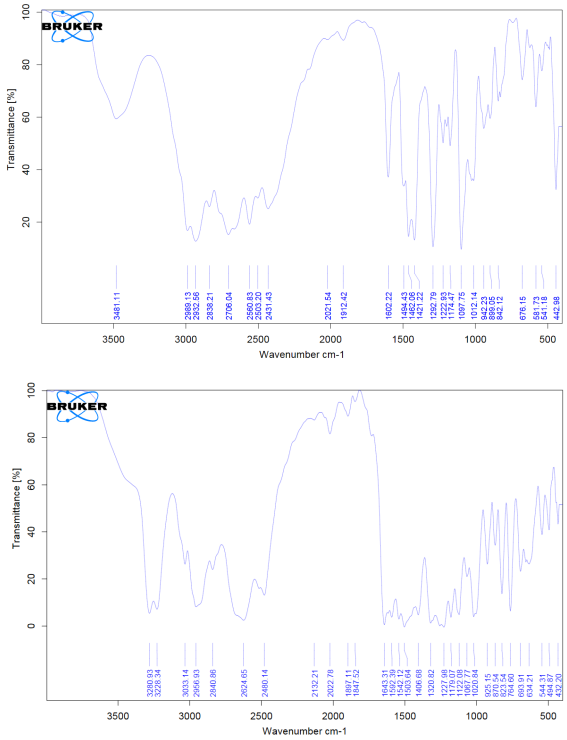
Figure 2: Drug Release Profiles of Itopride Controlled Release Tablets

Characterization Studies

The optimized formulations were chosen for characterization investigations based on the dissolution tests conducted on each formulation. Itopride pure drug, calcium silicate, HPMC K4M, xanthan gum, gum karaya, optimized formulations like IC3 pellets having Itopride and calcium silicate in 1:3 ratios, controlled release matrix tablets I16 with Itopride, gum karaya and xanthan gum, I17 with Itopride, gum karaya and HPMC K4M and I18 with Itopride, xanthan gum and HPMC K4M were selected for FTIR and SEM analysis.

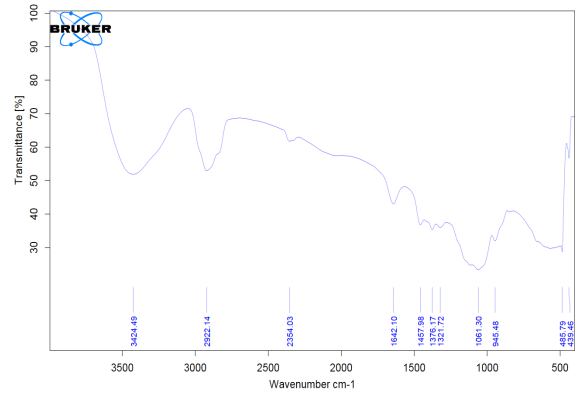
Fourier-Transform Infra Red (FT-IR) Spectroscopic Analysis

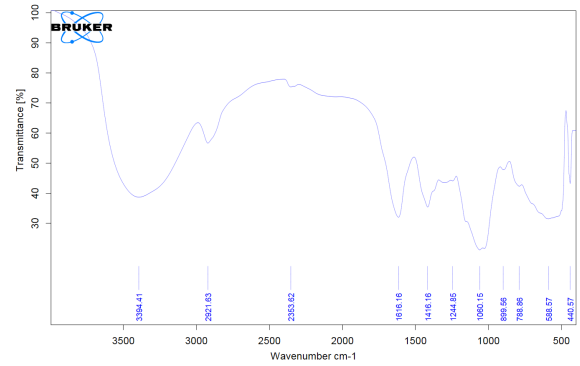
FTIR spectral investigations were conducted. Itopride exhibited sharp peaks at 3280 cm^{-1}, 3228 cm^{-1}, 2956 cm^{-1}, 1643 cm^{-1}, 1503 cm^{-1}, 1122 cm^{-1}, 925 cm^{-1} and 870 cm^{-1} indicating the presence of N-H stretching, C-H stretching, O-H stretching, C-C stretching, N-O asymmetrical stretching, C-O stretching, C-N stretching, O-H bending and aromatic C-H bending respectively. Calcium silicate exhibited sharp peaks at 2353 cm^{-1}, 1438 cm^{-1} and 879 cm^{-1} indicating C=N stretching, C-H bending and aromatic C-H bending. HPMC K4M exhibited sharp peaks at 2922 cm^{-1}, 2354 cm^{-1}, 1457 cm^{-1} and 1376 cm^{-1} indicating O-H stretching, C=N stretching, C-H bending and N-O symmetrical stretching. Xanthan gum exhibited sharp peaks at 2921 cm^{-1}, 2353 cm^{-1}, 1244 cm^{-1} and 899 cm^{-1} indicating O-H stretching, C=N stretching, C-O stretching and aromatic C-H bending. Gum karaya exhibited sharp peaks at 2928 cm^{-1}, 1421 cm^{-1} and 893 cm^{-1} indicating O-H stretching, C-H bending and aromatic C-H bending. IC3 pellets exhibited sharp peaks at 3279 cm^{-1}, 3229 cm^{-1}, 2959 cm^{-1}, 2356 cm^{-1}, 1642 cm^{-1}, 1502 cm^{-1}, 1227 cm^{-1}, 1127 cm^{-1}, 923 cm^{-1} and 876 cm^{-1} indicating the presence of N-H stretching, C-H stretching, O-H stretching, C=N stretching, C-C stretching, N-O asymmetrical stretching, C-O stretching, C-N stretching, O-H bending and aromatic C-H bending. This indicates that itopride was well combined with calcium silicate without any major interactions. I16 formulation exhibited sharp peaks at 3279 cm^{-1}, 3233 cm^{-1}, 2956 cm^{-1}, 2358 cm^{-1}, 1642 cm^{-1}, 1505 cm^{-1}, 1229 cm^{-1}, 1125 cm^{-1}, 925 cm^{-1} and 866 cm^{-1} indicating the presence of N-H stretching, C-H stretching, O-H stretching, C=N stretching, C-C stretching, N-O asymmetrical stretching, C-O stretching, C-N stretching, O-H bending and aromatic C-H bending. I17 formulation exhibited sharp peaks at 3284 cm^{-1}, 2916 cm^{-1}, 2355 cm^{-1}, 1470 cm^{-1}, 1372 cm^{-1}, 1117 cm^{-1}, 933 cm^{-1} and 879 cm^{-1} indicating the presence of N-H stretching, O-H stretching, C=N stretching, C-H bending, N-O symmetrical stretching, C-N stretching, O-H bending and aromatic C-H bending. I18 exhibited sharp peaks at 3274 cm^{-1}, 2916 cm^{-1}, 2356 cm^{-1}, 1473 cm^{-1}, 1375 cm^{-1}, 1119 cm^{-1}, 929 cm^{-1} and 877 cm^{-1} indicating the presence of N-H stretching, O-H stretching, C=N stretching, C-H bending, N-O symmetrical stretching, C-N stretching, O-H bending and aromatic C-H bending. There was no interaction between the drug and excipients because the remaining peaks remained unchanged. Figure 3 displayed the comprehensive spectral elucidation.



(A)

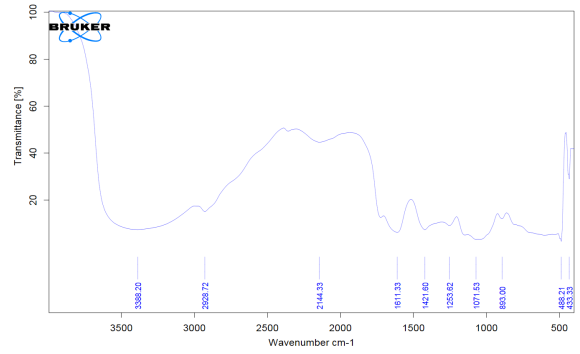
(B)

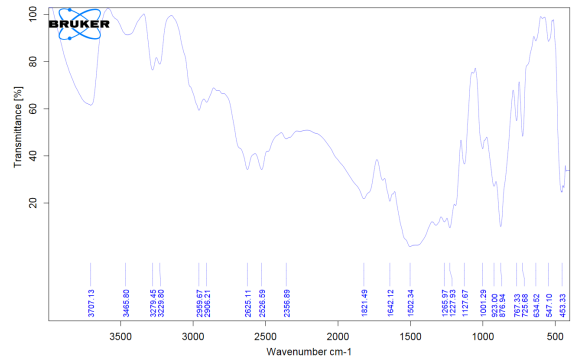




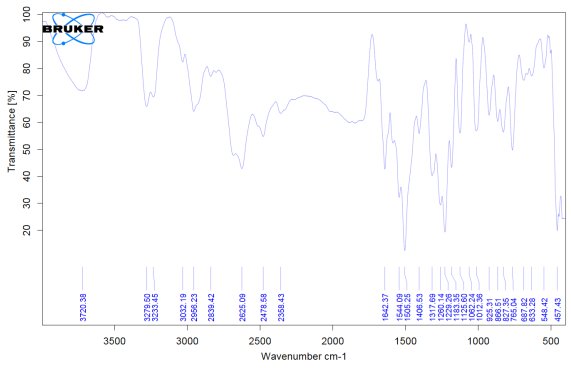
(C)

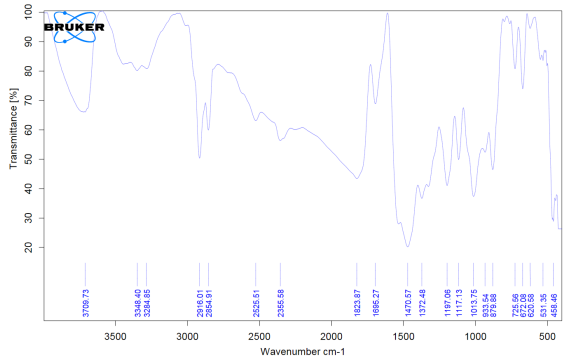
(D)



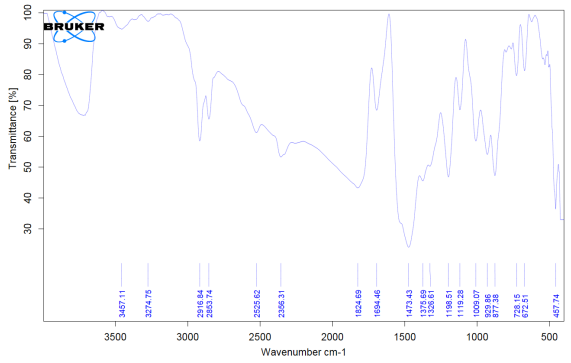


(E) **(F)**





(G) **(H)**

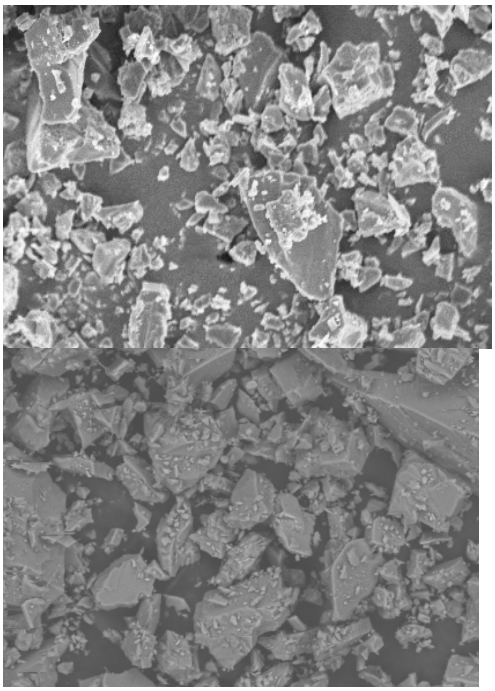


(I)

Figure 3: FTIR Spectra: (A) Itopride (B) Calcium Silicate (C) HPMC K4M (D) Xanthan Gum (E) Gum Karaya (F) IC3 pellets (G) I16 (H) I17 (I) I18

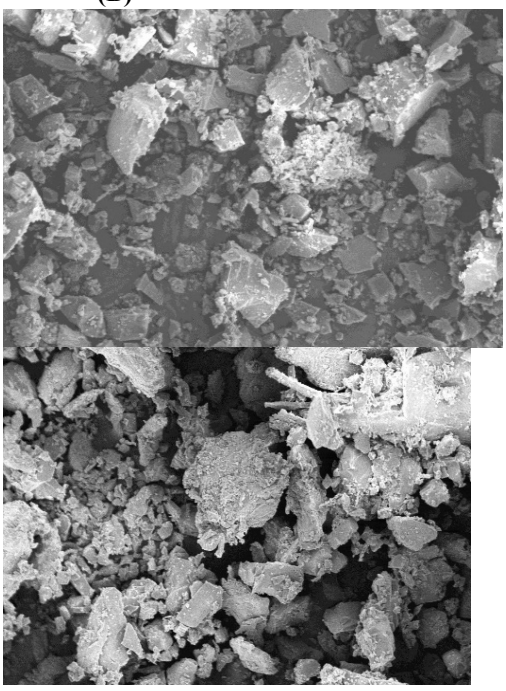
Scanning Electron Microscopy

SEM images of Itopride exhibited irregular, angular plate shaped particles with smooth surface. Calcium silicate exhibited angular and flaky particles with uneven surfaces. IC3 pellets exhibited irregular heterogenous angular particle morphology with agglomeration of drug with calcium silicate.



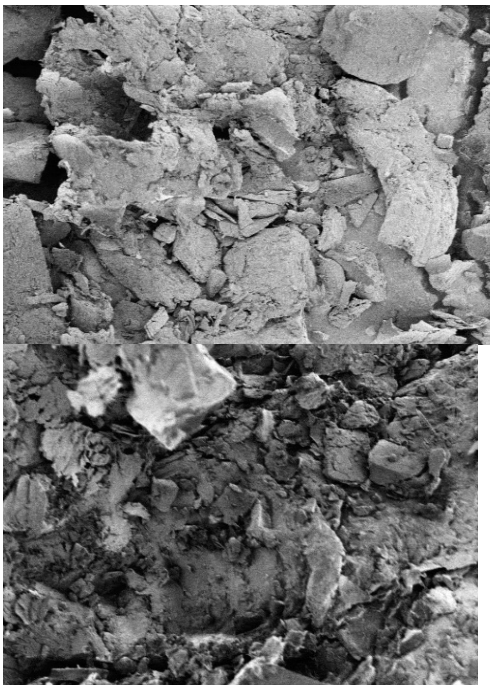
(A)

(B)



(C)

(D)



(E)

(F)

Figure 4: SEM Images: (A) Itopride (B) Calcium Silicate (C) IC3 pellets (D) I16 (E) I17 (F) I18

The SEM image of I16 formulation exhibited irregular, angular, flaky microstructures with moderate agglomeration. The SEM image of I17 exhibited large flaky, irregular granular, rough granular and uneven microstructures with moderate agglomeration. The SEM image of I18 irregular flaky fragmented, angular fractured heterogenous agglomerates. The SEM images were clearly shown in the figure 4.

CONCLUSION

Itopride absorbed calcium silicate pellets were made; IC3 made in 3%w/w calcium silicate demonstrated delayed drug release and was found to be suitable for further preparation of controlled release tablets. These studies revealed that the proportion of calcium silicate has influenced the dissolution parameters of various formulations. Itopride controlled release tablets were prepared using different concentrations of xanthan gum, gum karaya, and HPMC K4M and were subjected to in-vitro dissolution studies, which revealed that the proportion of gums as release retarding agents has affected the dissolution parameters of various formulations.

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