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FORMULATION ANDIN-*VITRO / IN-VIVO* ESTIMATION OF SUSTAINED RELEASE MUCOADHESIVE TABLETS OF ITOPRIDE HYDROCHLORIDE

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Abstract

Mucoadhesive tablets of Itopride HCl were formulated with a view toenhance bioavailability, extend the drugrelease and also decrease the recurrence of dose administration.

Methods: The mucoadhesive tablets were formulated by direct compression method using carboxymethyl cellulose blending with carboxymethyl cellulose and Polycarbophil.

Results: Tablets showed good mucoadhesive characteristic in the *in vitro* test and detected that carboxymethyl cellulosehad greater mucoadhesive force than that of Polycarbophil. ItoprideHCl release from this mucoadhesive tablets was slow and showed sustained release. Bioavalibility study of optimized formula was carried out and results revealed that the mucoadhesive tablets showed bioequivalence with a commercial immediate release tablet with higher mean AUC $_{(0-\infty)}$ and C_{max} and longer T_{max}.

Conclusion: The results confirm thatthe prepared Mucoadhesive tablets of ITO HCl could be a promising drug delivery system with sustained-release action and enhanced drug bioavailability.

Introduction

The drug administration via oral route considered the preferred ways of drug delivery to systemic circulation of body,[1]and considered the most common route because it is safer, convenient, economical, usually good absorption and no need for sterilization. Non-ulcer dyspepsia (NUD), gastro-esophageal reflux disease (GERD), gastritis, diabetic gastroparesis and functional dyspepsia are troubles of gastric motility in clinical performance. An acetylcholinesterase blocker (often abbreviated AChEI) or anti-cholinesterase acts a new gastro prokinetc agent which prohibits the enzyme acetylcholine esterase (AChE) responsible for Acetylcholine degradation. Itopride hydrochloride is an optional drug for Gastro esophageal reflux disease (GERD) and other gastric motilitydisorders.[2,3]There is evidence that Itopride may have prokinetic effects throughout the gastrointestinal tract from the stomach to the end of the colon.[4]ItoprideHCl has half-life of 5-6 hours and needs recurrent administration of dose.[5] So it is requisite to formulate sustained release preparation to defeat this draw back.

Mucoadhesive is considered a significant section of drug delivery systems by efficient carrier capacity. Mucoadhesive tablets are the transporter related drug delivery system through possess a core of drug and completely outer layers of polymers as coating material.[6] However, the accommodation of these techniques is due to their appropriate to possess means for close contact of the drug with the absorbing membrane.[7]This can be achieved through adding bioadhesive polymers to formulations. The choice of matrices mainly depends on sustainability of drug release, safety profile, the matrixstability, and release patternof the drug, biodegradability and biocompatibility of the matrix components.[8]

Mucoadhesive tablets have characteristics such as effective absorption and enhanced the drug bioavailability through contacting with the mucosal layer and drug targeting to the absorption site.[9]The objective of the research was to enhance the drugbioavailability in attempt to reduce the daily dose required for the drug, also to formulate

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extended-release tablet formula. An in vivo study was also conducted on rabbits to calculate the pharmacokinetic parameters for the selected mucoadhesive tablet formula and to estimate the absolute bioavailability in comparison to commercial tablet formula of itoprideHCl (**Ganaton**®).

Materials and methods

Materials

ITO HCl was purchased from Hangzhou Uniwise International Co, China. Hydroxypropyl methylcellulose, polycarbophilw obtained from (Aldrich Chemical Company, USA). Ethylcellulose (EC) was supplied from (Merck, Germany). Microcrystalline cellulose (Avicel ph. 101) was purchased from (FMC international Co., Belfast, Ireland). EudragitRSpm was obtained from (Rhompharma, GMBH, Darmstadt, Germany). Sodiumcarboxymethylcellulosewas purchased from (Pharmazell, Germany).Carbopol 934p was received from (Merck, Germany).carboxymethyl cellulosewas obtained from (Al Gomhoria Co, Egypt).Magnesium stearate was bought from (Alba Chemical Company, USA). Commercial immediate release ItoprideHCl tablets Ganaton®, were obtained from ABBOTT Company, Egypt.All chemicals were used as received.

Methods

Preparation of mucoadhesive tablets

Mucoadhesive tablets of various polymers were formulated by direct compression technique. All the tablet components were mixed to get uniform blending. The tablets were formulated by using a single die punch tablet machine (Korsch – Berlin, EK/0, Frankfort, Germany), fitted with 8 mm flat -faced punches. Contents of the prepared tablets are indicated in Table (1.

Micromeritic Properties

The bulk and tapped density of powders were measured in 10 ml of graduated cylinder. Weighed quantities of powders were placed into a 10 ml of measuring cylinder.[10] After noting the initial volume, the sample present in the measure was tapped mechanically onto a hard surface. The tapping was done for 100 times. The initial bulk volume and tapped volume were noted from which, their respective densities were calculated. The bulk and tapped density were determined by the following relation:

Bulk density = (weight of powder / Volume of powder) x 100

Tapped density= (weight of powder / tapped Volume of powder) x 100

Compressibility Index

Compressibility index of all formulations was calculated by the next formula:
Compressibility index = (Tapped density –Bulk density / Tapped density) x 100

Hausner's Ratio

Hausner's ratio was also calculated by using following equation:
Hausner's ratio= (Tapped density / Bulk density) x 100

Angle of Repose

The angle of repose was estimated by the fixed funnel technique. Accurately weighed powder mixtures were placed in funnel. The funnel height was fitted in this a manner so as the funneltip touched to top of the powders. The powder was left to flow freely through the funnel onto the surface. The diameter of cone was measured. The Angle of repose was determined through the following equation:
$\tan \Theta = 2h/d$
Where, θ = Angle of repose, h = height of funnel and d = radius of funnel

Evaluation of mucoadhesive tablets The formulated tablets of all sustained release mucoadhesive polymers were estimated for the official characters including Hardness, friability, thickness and weight variation.

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1- Hardness study:
The prepared tablet was objected between two anvils of hardness tester(Erweka-type TBT, G.M.B.H, Germany), and force (kg) was progressively increased for obtaining accurate result. The reading at the apparent scale was scored for the pressure that was needed to fracture the tablets.

2-Friability:
Twenty prepared mucoadhesive tablets were weighed and objected in the Roche friabilator (Erwekafriabilator apparatus, G.m.b.H, Germany), and the equipment was rounded at 25 rpm for 4 minutes. After rotations, the formulated mucoadhesive tablets were dedusted and weighed again. The recorded data has not been exceed than 1%.The friability percent was confirmed through the following equation.[11]

$$\% F = \{1-(Wt/W)\} \times 100$$

Where, % F = Percentage friability, W = initial tablets weight, Wt = tablets weight after rotation.

3- Drug content:
Five tablets of each formula were taken and grinded. Amount of triturate equal to 100 mg of the drug was weighed and placed into 100 ml volumetric flask and HCl (0.1N) was added and the flask was hand shaken for 5 minutes and 0.1N HCl was added to prepare volume up to 100 ml. The solution was sonicated for 15 minutes then filtered by what manfilter paper. Lastly a solution was diluted and the absorbance was calculated spectrophotometrically at 258 nm against 0.1N HCl blank.[12]

4- Weight variation:
Twenty prepared tablets were selected at random method from each batch and weighed individually by an electronic balance. The mean weight and standard deviation of 20 prepared tablets was determined.

Determination of mucoadhesive strength
Mucoadhesive strength measurement is carried out to estimate capability of the formulae to bind to stomach mucosa for long time.[13]The adhesion forces of the tablets were determined by mucoadhesive measurement tooldisplayed in Figure 1. The sheep fundus tissues pieces were frosted in saline solution and exposed to room temperature before using. At testing time a piece of tissue (c) was confirmed on the top of glass vial (b)keeping the side of mucosa out by a rubber tape and aluminum cover,. The diameter of mucosal layer was 1 cm. The vial with the fundus tissue (c) was kept at 37^{O}C for 10 min. Then the vial with piece of tissue (c) was joined to the balance (a) and other vial was fixed on height adjustable pan (e). To a lower vial a prepared tablet (d) was firmed using cello tape. The height of the lower vial was adjusted so that a tablet could adhere to the mucosal tissue on the upper vial. A pressure was applied on the upper vial for 2 minutes then the upper vial was connected to the balance. The weight on the right side of the pan was quietly inserted with an increase of 0.5 g until the two vials separated. The overall weight (gm) needed to separate two vials was calculated as a measure of mucoadhesive strength. The adhesion force was calculated by the following equation:

Adhesionforce (N) = Mucoadhesive strength X 9.81/100

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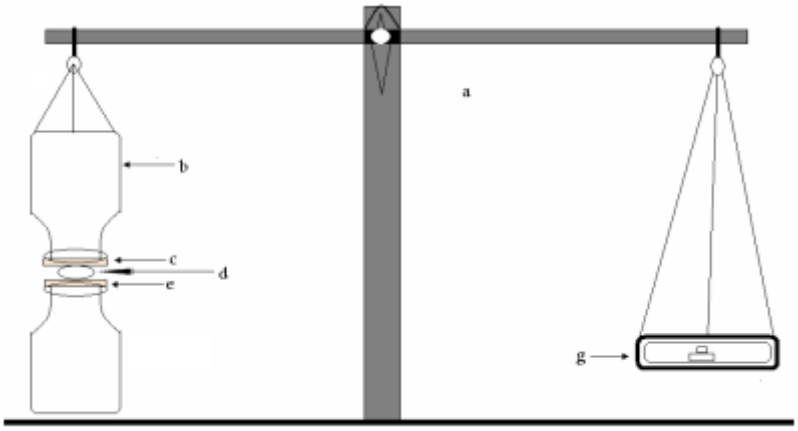

Fig. 1: Modified physical balance(a) Balance, (b) Upper glass vial, (c) Section of tissue, (d) Tablet, (e) Another vial was fixed on height adjustable pan and (g) gram.

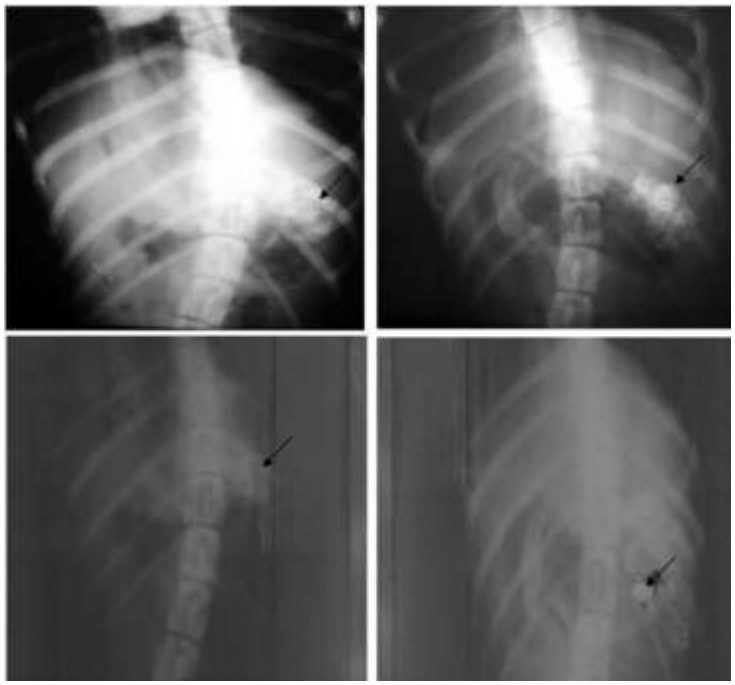

Figure (2):In vivo mucoadhesive study

Table (1): Formulation of Itopride HCl mucoadhesive tablets (F_1- F_{10})

No. of formulae	Content (mg)							
	ITO	carboxymethyl cellulose	Na-CMC	polycarbophil	Eudragit RSpm	Avicel	Mg.St.	Total weight
F_1	150	100	--	--	--	95	5	350
F_2	150	125	--	--	--	70	5	350
F_3	150	150	--	--	--	45	5	350

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F_4	150	--	100	--	--	95	5	350
F_5	150	--	125	--	--	70	5	350
F_6	150	--	150	--	--	45	5	350
F_7	150	--	--	100	--	95	5	350
F_8	150	--	--	125	--	70	5	350
F_9	150	--	--	150	--	45	5	350
F_{10}	150	50	--	--	100	95	5	350

Table (2): Evaluation of precompression parameters

Formulation code	Angle of repose (θ)	Compressibility (%)	Hausner's ratio
Plain ItopridеHCl	46.03° ± 0.18	33.33 ± 0.11	1.84± 0.01
F_1	25.01° ± 0.32	14.92± 0.18	1.17± 0.11
F_2	25.01 ° ± 0.25	14.36± 0.11	1.29± 0.03
F_3	25.62 ° ± 0.10	15.06± 0.19	1.11± 0.01
F_4	26.26 ° ± 0.13	14.47± 0.22	1.29± 0.31
F_5	26.28 ° ± 0.39	14.92± 0.34	1.12± 0.26
F_6	25.96 ° ± 0.14	15.36± 0.45	1.14± 0.01
F_7	25.62 ° ± 0.16	15.22± 0.11	1.13± 0.07
F_8	27.42 ° ± 0.34	15.03± 0.28	1.22± 0.01
F_9	26.07 ° ± 0.22	14.91± 0.31	1.11± 0.21
F_{10}	24.11 ° ± 0.12	14.22± 0.13	1.19± 0.21

All values are expressed as mean ± SD

Table 3: Physical parameters of the mucoadhesive tablets(F_1-F_{10})

Property / Formula	**Mean weight (mg ±SD) n =20**	**Mean thickness (mm±SD) n =20**	**Friability (% Loss) n =10**	**Mean hardness (Kg±SD) n =10**	**Drug content (mg %±SD) n =10**
F_1	350.07 (±1.1)	3.4 (±0.01)	0.51	5.2 (±0.11)	99.93
F_2	350.09 (±1.3)	3.4 (±0.02)	0.18	5.3 (±0.16)	98.45
F_3	350.03 (±1.3)	3.5 (±0.11)	0.12	6.1 (±0.17)	100.09
F_4	350.21 (±1.9)	3.4(±0.11)	0.19	5.7 (±0.16)	99.30
F_5	349.95 (±1.1)	3.4 (±0.14)	0.14	5.5 (±1.28)	100.26
F_6	350.98 (±0.8)	3.6 (±0.21)	0.61	6.2 (±0.15)	99.21
F_7	350.71 (±0.5)	3.5 (±0.13)	0.12	7.0 (±0.61)	98.30
F_8	351.06 (±0.3)	3.4(±0.11)	0.19	6.7 (±0.85)	100.06
F_9	350.45 (±1.2)	3.6 (±0.14)	0.14	7.0 (±0.11)	96.66
F_{10}	350.09(±0.7)	3.5 (±0.19)	0.16	6.6 (±0.12)	99.90

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Table (4): In vitro mucoadhesive strength study of prepared mucoadhesive tablets (F_1- F_{10})

Formulation code	mucoadhesive strength	mucoadhesive force
F_1	18.5 ± 0.06	1.813
F_2	25.5± 0.50	2.205
F_3	23.5 ± 1.60	2.303
F_4	14.5 ± 0.50	1.421
F_5	15.5 ± 0.23	1.519
F_6	17.5 ± 0.45	1.715
F_7	13.5 ± 0.19	1.323
F_8	14 ± 0.17	1.372
F_9	14.5 ± 0.50	1.421
F_{10}	13 ± 1.52	1.294

In vitro drug release study

The dissolution studies of mucoadhesive tablets were estimated through USP dissolution apparatus II at a rotation speed of 100 rpm in 500ml medium at 37±0.5 °C.The tablets transferred to dissolution medium 0.1 N HCl and samples were taken at selected time intervals, filtered through Whatmann filter paper no. 41 and tested by UV spectrophotometer at 258 nm. The result of the drug release was treated with different kinetics equations like zero order, first order and Higuchi diffusion model.

Table (5): Percent of ITO HCl released from the prepared mucoadhesive tablets

Time (h)	% of ITO HCl Released									
	F_1	**F_2**	**F_3**	**F_4**	**F_5**	**F_6**	**F_7**	**F_8**	**F_9**	**F_{10}**
0	0	0	0	0	0	0	0	0	0	0
1	12.12 ± 1.27	11.75 ±1.19	10.63 ±1.29	48.83± 1.48	44.18± 2.88	35.34± 0.76	48.09±1. 57	28.01±1. 84	11.78± 1.42	4.47±2. 86
2	23.68 ± 2.24	22.49 ±0.76	21.78 ±0.56	78.27± 0.83	66.5±0 .89	52.86± 2.78	64.56±0. 96	37.52±1. 46	21.51± 1.24	9.64±2. 69
3	48.98 ± 2.31	38.19 ±1.53	36.41 ±0.32	84.72± 0.78	76.27± 1.46	69.23± 2.34	77.11±0. 65	42.12±0. 96	30.67± 0.76	18.43± 3.58
4	59.36 ± 0.62	46.43 ±2.81	45.21 ±1.83	88.08± 2.78	82.34± 1.44	79.71± 0.89	84.46±0. 67	45.61±0. 76	38.24± 1.53	23.64± 3.45
6	76.66 ± 0.85	60.77 ±0.94	59.05 ±2.96	94.61± 1.47	89.54± 1.86	87.46± 0.54	99.76±0. 71	60.23±3. 21	52.56± 2.63	40.49± 1.44
8	95.42 ± 1.48	75.93 ±3.75	72.75 ±3.59		92.11± 0.65	89.52± 0.92		72.41±3. 75	64.49± 0.94	57.36± 0.57
10		91.17±1 .98	86.13 ±2.18			96.72± 1.13		95.34±0. 52	80.2±0. 95	73.11± 0.55
12			95.37 ±3.49						93.23± 3.41	87.38± 3.36
16										94.98± 0.57

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24										99.64± 0.55

Table (6): Kinetic treatment of the dissolution data for ItoprideHCl mucoadhesive tablets (F_1- F_{11})

Formulae	Zero order			First order			Higuchi-diffusion model		
	r	K0	Intercept	r	K1	Intercept	r	Kh	Intercept
F_1	0.9848	12.9251	1.28826	-0.8943	-0.2500	2.3171	0.9929	35.6190	-12.9559
F_2	0.9847	8.9728	5.2067	-0.9702	-0.0975	2.0739	0.9921	30.4341	-11.9160
F_3	0.9880	8.5500	5.1572	-0.9869	-0.0820	2.0459	0.9881	29.7023	-12.0895
F_4	0.8436	14.0350	28.325	-0.9773	-0.2059	1.8887	0.9957	40.4248	7.8390
F_5	0.9076	9.7117	31.1225	-0.9721	-0.1348	1.8639	0.9746	33.4091	9.9864
F_6	0.8748	8.2414	28.8290	-0.9855	-0.1359	1.9419	0.9858	31.2383	6.9898
F_7	0.9139	14.8997	22.5974	-0.9165	-0.3963	2.2563	0.9951	40.8255	3.8434
F_8	0.9597	7.7281	13.5143	-0.8781	-0.1035	2.0628	0.9808	27.5462	-2.5692
F_9	0.9922	8.9834	6.3828	-09849	-0.0658	2.0293	0.9965	27.7585	-12.0410
F_{10}	0.9817	6.8032	4.2288	-0.9982	-0.0492	2.0063	0.9558	26.7220	-19.9665

In vivo mucoadhesionstudy

In-vivo estimation of mucoadhesive characters of formulated tablets was carried outon dogs by X-ray studies. Tablets containing barium sulphate (instead ofitoprideHCl) were prepared usingcarboxymethyl cellulose and avicel as matrix components. These prepared tablets were administered to dogs about 10kg with aglassful of water after fastingovernight. X-rayphotographs were taken at time intervals (2, 6, 12 and 24hr) and observed for the tablets position.

In vivo evaluation of a selectedmuco adhesive formula by Comparative bioavailability study

1-Treatment protocol and sample analysis

The selected mucoadhesive formula containing 150 mg of ITO was compared with commercial immediate release ItoprideHCl tablets Ganaton®.The study was carried out using three groups of Newzeland rabbits (2.5 kg) each group consists of 3 rabbits. Group I (Control group) was starved and only water was allowed. Group II was administered mucoadhesive tablet formula F_{10}Group III was administered commercial tablets (Ganaton®).The rabbit groups II and III were starved overnight before drug administration and continued fasting until 4 hr post dose, with free access to water. Each group was given a drug dose of 15 mg /Kg from the tested preparations **F_{10}** and Ganaton®. The study was conducted as single doses cross over design, with 7-days washout period. Blood samples (1 ml) were withdrawn transferred to heparinized tubes at these time intervals 0, 0.5, 1.0, 2.0, 4.0, 6.0, 8.0, 12.0, 18.0 and 24.0 hr after drug administration. Plasma was directly separated by centrifugation and was stored at -20° C until used for analysis. Before drug administration, blood samples were collected and plain plasma was separated by centrifugation and used for the calibration curve construction.

2-Calculation and statistical treatment of pharmacokinetic parameters

The pharmacokinetic parameters were calculated from theplasma level data obtained for the individual rabbits and presented as mean ± SD. From the data of plasma concentration, the maximum plasma concentration (C_{max} µg /ml) and the corresponding time (T_{max}hr) were directly extracted for the two treatments in each individual animal. A plot of the mean plasma concentration versus time has been constructed for each treatment. The area under the plasma concentration-time curve from time zero to 24 h (AUC_{0-24} µg.hr/ml) was obtained by applying the trapezoidal rule. AUC_{24} was estimated by adding the area under the tail to AUC_{0-24} h .The area under the tail was calculated by dividing the measurable concentration by the elimination rate constant obtained by linear regression of the elimination phase of the plasma concentration versus time curve. The mean residence time MRT (hr) which is a non-compartmental pharmacokinetic parameter was obtained using the suitable equation[11].After the calculation of the area under the first-moment curve ($AUC_{0-\infty}$ µg.hr/ml). The relative bioavailability (F_R) of the tested formula compared with the reference product was calculated as:

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$$F_R\ (\%) = \frac{AUC_{0\text{-}24\ hr}(\text{tested formula})}{AUC_{0\text{-}24\ hr}(\text{Commercial product})} X\ 100$$

The significance of the difference between the two treatments was evaluated by one-way analysis of variance (ANOVA) usingstatistical computer package (SPSS version 13.0). Differences were considered significant at $P<0.05$.

Statistical analysis

All experiments were performed in triplicate. The differences were estimated for statistical significance by student's t-test.

Result and discussion

The study was achieved to evaluate the in vitro mucoadhesive force of different polymers such as carboxymethyl cellulose, Carboxy methyl cellulose Hydroxypropyl methylcellulose, and EudragitRSpm. All tablet formulations were estimated for the physical characteristics. The tablet hardness[2, 3] is in the average of 5.2 – 7kg/cm^2.The friability Percent was less than 0.6% in all the prepared formulations with the thickness in the range of 3.4-3.6mm. The in vitro mucoadhesive force was measured on the adjusted balance to determine the strength of adhesion needed to separate the tablet. The mucoadhesive strength of the polymers is 25.5 based on their composition and other physicochemical characters. The adhesion force of various polymers was arranged as EudragitRSpm (1.294) <Polycarbophil (1.323) < Sodium carboxy methylcellulose (1.519) <carboxymethyl cellulose (2.205). EudragitRSpm and carboxymethyl cellulose showed the lowest and highest adhesion force respectively.

Optimized batch **F_{10}** was still adhering until 8 hours. Mucoadhesive tablets are taking up water from the mucosal tissue by absorbing[4] and swelling leading to considerable stronger adhesion. From the adhesion force estimation it was indicated that carboxymethyl cellulose had greater mucoadhesive force than that of Polycarbophil. carboxymethyl cellulose possesses various carboxyl groups, when move at the wetted mucosal surface, they orientate this mucoadhesive site towards mucosa and interact through hydrogen bonding. Also greater swelling rate of carboxymethyl cellulose causing a large surface of polymer that is expand to the mucosal membrane lead to increase in number of hydrogen bonding between the polymer and mucosal membrane, thus increase the mucoadhesive strength of polymer. Graphical representation is shown in (**Figure 2**).

The formula **F_{10}** containing carboxymethyl cellulose along with EudragitRSpm sustained the release of itopride hydrochloride up to 24 hrs found to be 99.64±0.55. The formulation **F_1** and **F_2** containing carboxymethyl cellulose also showed sustained release of 95.42 ± 148 and 91.17 ± 198 with increase in polymer ratio at the end of 24 hr. It is due to the fact that carboxymethyl cellulosehydrated faster under acidic medium and made the diffusion barrier rapidly resulting in slower release in the acidic phase[5]. As the polymer to the drug ratio was increased the drug release decreases. The decrease in the release of the drug is due to the higher density of polymer matrix that produce increasing in diffusion pathway extent. The release would depend on diffusion of Itopride hydrochloride through the insoluble matrix of carboxymethyl cellulose polymer in 0.1N HCl and a sustained drug release behavior was observed.

The formulation coded **F_{10}** were chosen for bioavailability studies. The bioavailability of formulation is a significant factor to determine the efficacy of dosage form[12]. The bioavailability result did not indicate any significant change in efficiency. Fig.7 shows the change in plasma concentration of ITO with time after oral administration of the reference standard, and the mucoadhesive tablet to rabbits. Table 6 includes the pharmacokinetic parameters (± SD) generated from the analysis of the individual data[13]. The C_{max} was found to be 5.985 µg/ml for mucoadhesive tablets and the corresponding **T_{max}**was5.00 h. It is obvious that the mucoadhesive tablets exhibited delayed **T_{max}**.

The **$t_{(1/2)}$** were 1.365 h for the mucoadhesive formula, the value of the MRT, which is the non-compartmental analogue of **$t_{(1/2)}$** were also parallel to those of **$t_{(1/2)}$**. The tested formula showed a slightly higher MRT (14.434 h).

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AUC $_{0-\infty}$ = 116.615 (µg.hr/ml) for the mucoadhesive formula, the relative bioavailability was 238.8198 %. ITO is considered an example of drugs with high pharmacokinetic variability[14]. The pharmacokinetic data presented here did not show extraordinary variability when compared with most published bioavailability studies. The maximum RSD % was 3.950 %. The floating tablet showed more sustained release characteristics.

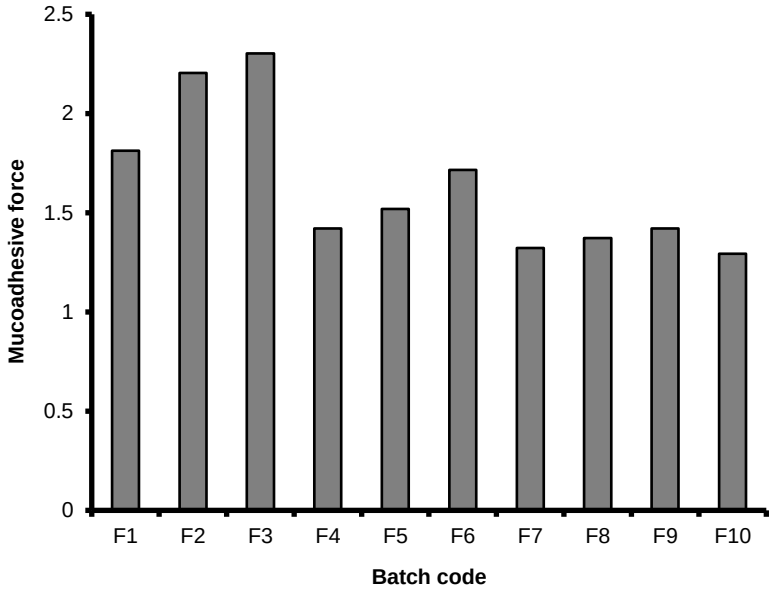

Figure (3) Comparison of bioadhesive strength for mucoadhesive oral tablets (F_1- F_{10})

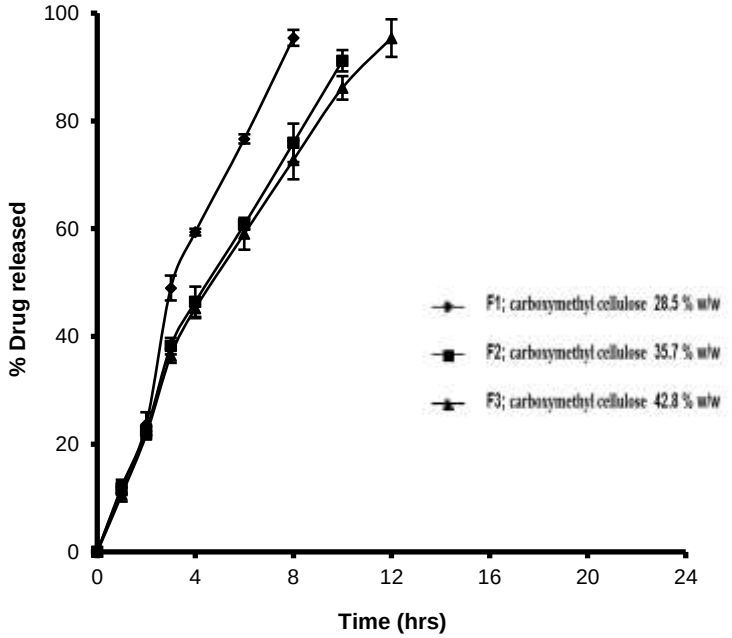

Figure (4): Release profile of ItoprideHCL tablets containing different percent of carboxymethyl cellulose

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Indian Journal of Medical Research and Pharmaceutical Sciences
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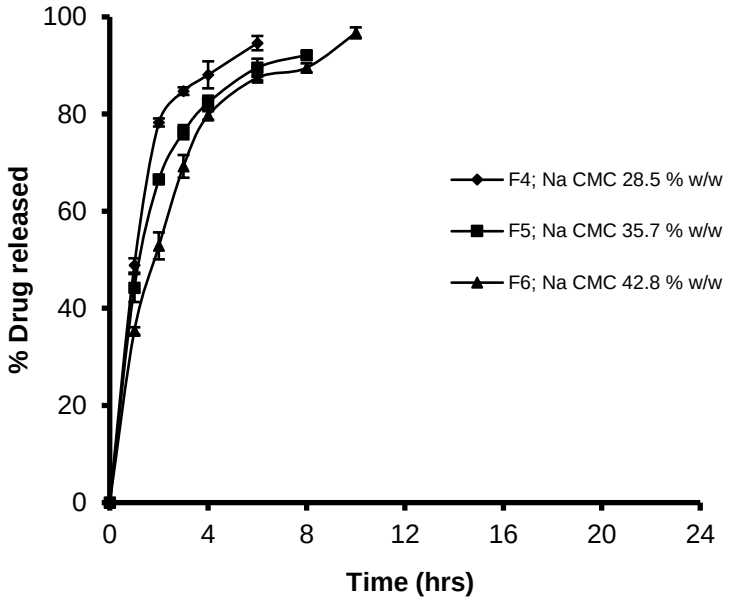
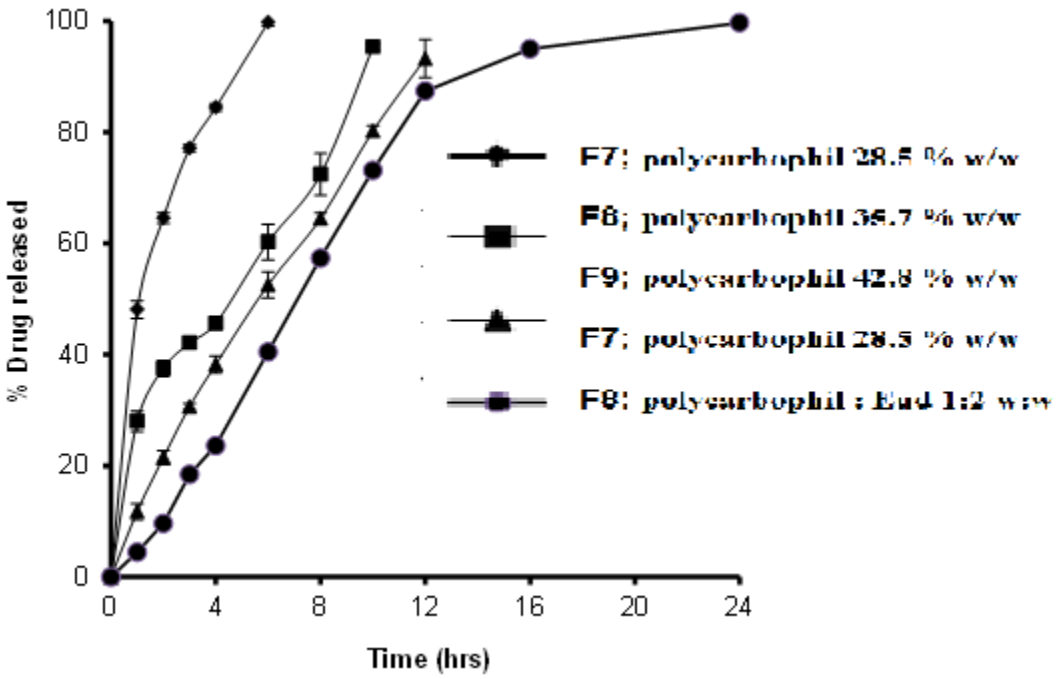


Figure (5): Release profile of Itopride HCL tablets containing different percent of Na CMC



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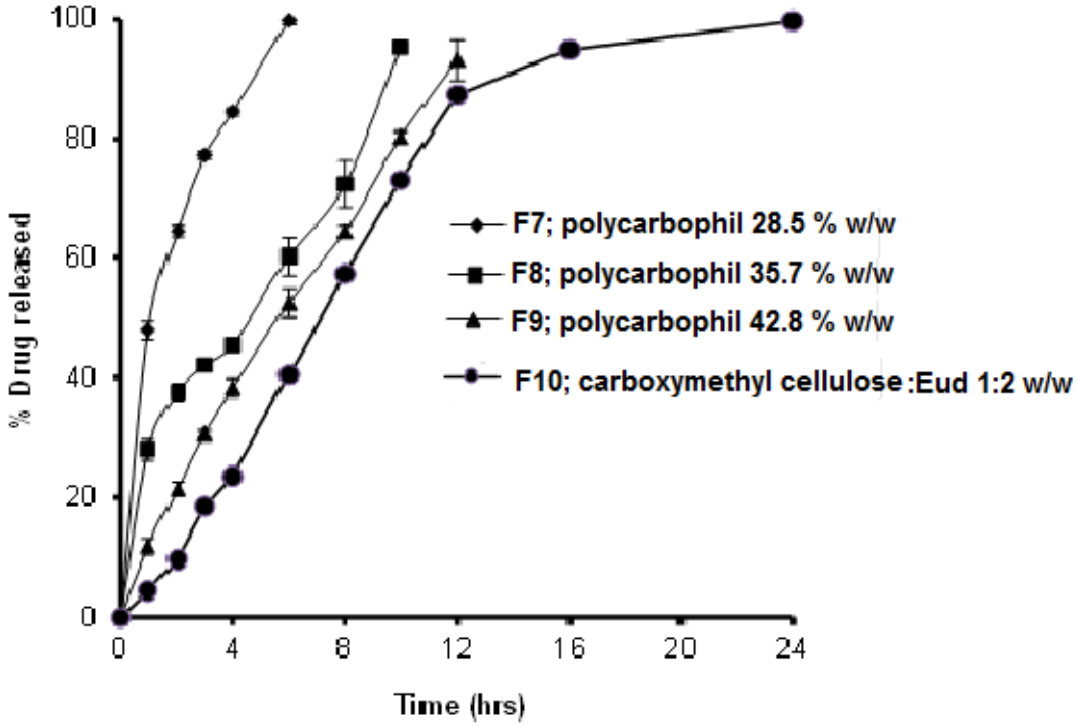

Figure (6): Release profile of Itopride HCL tablets containing different percent of polycarbophil.

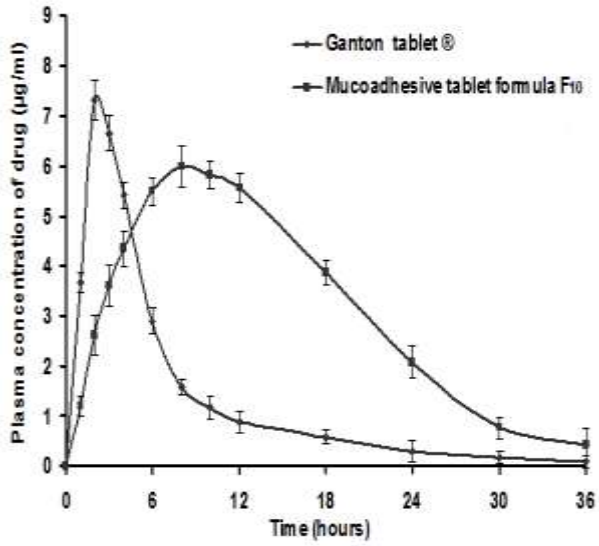

Fig. (1): Plasma concentrations of ItopprideHCl after oral administration of the commercial tablets (Ganaton®) and the prepared ItopprideHCl sustained release tablet formula F_{10}.

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Table 7: Pharmacokinetic parameters of ItoprideHCl following oral administration of the prepared ItoprideHCl sustained release tablets formula F_{25} in comparison with the commercial immediate release tablets, Ganaton®.

Pharmacokinetic parameter	Ganaton®	Formula (F_{10})	Significance
T_{max} (hr)	2	8	S
C_{max} (µg/ml)	7.299	5.985	S
K_{ab} (hr^{-1})	0.705	0.507	S
$t_{(1/2)\ ab}$ (hr)	0.982	1.365	S
K_{el} (hr^{-1})	0.107	0.103	N.S
$t_{(1/2)el}$ (hr)	6.485	6.672	N.S
V_d(Liters)	1.016	0.935	S
AUC $_{0\text{-}24}$ (µg.hr/ml)	47.052	112.369	S
AUC $_{0\text{-}\infty}$ (µg.hr/ml)	49.894	116.615	S
$AUMC_{0\text{-}24\ hr}$ ($\mu g.hr^2/ml$)	340.065	1489.545	S.
$AUMC_{(0\text{-}\infty)}$(μ g.hr^2/ml)	436.324	1683.275	S.
MRT(hr)	8.745	14.434	S.
Cl_T (ml/min)	5.010	2.1437	S.
F_R (%)	---------	238.8198	--------

*S. = statistically significant ($p < 0.05$).
N.S= statistically non-significant ($p > 0.05$).

Conclusion

The formulation of mucoadhesive tablets had been made probable by the different convenient polymers to sustain the release of the drug. In the recent years the attention is increasing to improve a drug delivery mode using a mucoadhesive polymer which will contact to the membrane or to the exterior surface covering the membrane for targeting to different absorptive mucosal membrane like optical, rhinal, pulmonary, buccal, gastric, vaginal etc. Thus, in the current research a trial was achieved to investigate the mucoadhesive strength of the various sustained release mucoadhesive polymers by simple method. The force of adhesion of various polymers was established and arranged as EudragitRSpm<Polycarbophil< Sodium carboxy methylcellulose <carboxymethyl cellulose. These sustained release mucoadhesive polymers can be hard done in the effective formulation of mucoadhesive targeting drug delivery methods.

Disclosure

The authors report no conflicts of interest in this work.

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