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FORMULATION AND EVALUATION OF ELEMENTARY OSMOTIC PUMP OF METOCLOPRAMIDE HCL

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ABSTRACT

Metoclopramide Hydrochloride belongs to the class of antidopaminergic and gastrointestinal agents that exerts preventive action against emesis. It exhibits burst effect owing to its high solubility causing fluctuations in the plasma level. The drug shows extrapyramidal side effects on account of its short half-life and frequent dosing. The objective of this study was to develop an elementary osmotic pump of the drug for slow-constant and pH independent release. Metoclopramide core tablets were prepared by direct compression method consisting of osmogens and hydroxypropyl methylcellulose (HPMC K100M) in varying concentrations. It was followed by dip coating with cellulose acetate coating polymer, drilling of the orifice to produce osmotic tablets and were evaluated for various parameters. From the data obtained, all the formulations showed the weight gain of about 5-7% and approximately 0.2 mm increase in thickness was observed after coating of tablets. F3 formulation exhibited the highest drug release of about 91.90% up to 20 h. Amount of osmogen and concentration of hydroxypropyl methylcellulose effected the drug release. Scanning electron microscopy revealed that the coat was intact and devoid of pores after the dissolution and diameter of the orifice was found to be 0.3 mm. The optimized formulation exhibited zero order release showing non-Fickian diffusion which was evident from the kinetic modelling. Once a day elementary osmotic tablets of Metoclopramide HCl thus formulated produces constant drug delivery with zero order kinetics which could be an effective way of surmounting the disadvantages of conventional forms.

KEYWORDS: Metoclopramide Hydrochloride, Osmotic system, Elementary osmotic pump, Osmogens, Cellulose acetate, Scanning electron microscopy, Zero order.

INTRODUCTION

Oral drug delivery is the most traditional way of administration of an extensive range of drug substances prevailing across the globe. It is considered to be firmly entrenched system in terms of targeting of drug molecules into systemic circulation owing to its convenience, non-invasiveness, cost effective and compliance to the patient. However, conventional route of administration exhibits a large extent of fluctuation in the blood stream leading to undesirable toxicity with reduced efficiency.[1] Further, unpredictable absorption and frequent dosing has paved the way for designing of controlled delivery systems.[2]

Investigations are being constantly carried out to encounter the optimized products over existing drugs that may help in exploring of an improved approach towards targeting the intended site.[3] Osmotic drug delivery system (ODDS) is a type of novel drug delivery system that promotes slow-constant release of the drug from the dosage form which is nominally affected by the gastric contents of the body. These are the most promising controlled release systems which can be efficiently utilized for the administration of drugs by both orally and implantation.[4] Drug release from these systems is negligibly affected by the changes in hydrodynamics of the release media and drug concentration lies within the perimeter of therapeutic window.[5] Different types of osmotic systems are available like Rose and Nelson pump, Higuchi Theeuwes pump, Alzet Mini osmotic pump, Elementary osmotic pump (EOP), Push pull osmotic pump, Controlled Porosity osmotic pump (CPOP) etc.[6] Among the various types of osmotic systems available, Elementary osmotic pump (EOP) requires a simple technique and economically most significant with regard to industrial development.[7] EOP's render several advantages like they (i) are simple in structure and easy to design, (ii) provides patient compliance, (iii) provides zero order kinetics and (iv) *in vitro in vivo* correlation can be achieved at a higher degree.[8]

Metoclopramide HCl (MCH) is a dopamine D2 antagonist which is primarily used as an anti-emetic drug.[9,10] MCH is a freely soluble drug which is rapidly and well absorbed from the GIT with a short half life of 5-6 hours. The dosing frequency is 3-4 times daily which may lead to non-compliance of the patient. High solubility of drug in water gives rise to burst effect that may lead to elevated peaks in blood. Conventionally available Metoclopramide preparations show side effects related to dose like irregular heartbeat, abdominal pain,

headache, dizziness etc. Although many works have been proposed related to sustained release formulations of Metoclopramide, but a few outcomes reported that the drug showed optimum level of sustained effect only at the higher pH as compared to the gastric pH.[11] Sometimes, the cross linking of polymers in sustained release matrix tablets decreases the drug release and it also depends on the polymer concentration.[12] Marketed oral controlled released capsule has the disadvantages of dose dumping and limitations like unpredictable gastric residence time (GRT) and reduced potential for accurate dose adjustment. Orally disintegrating tablet is yet another marketed formulation, but sustained effect is not achieved and it does not reduce the dosing frequency. Moreover, oral disintegrating tablets are hygroscopic in nature hence problems related to mechanical strength and stability are the major drawbacks.

The present work is to formulate once a day elementary osmotic pump of Metoclopramide HCl having pH independent and slow-constant release that can be an effective formulation with improved efficacy over conventional dosage forms.

MATERIALS AND METHODS

Materials

Metoclopramide HCl was procured from Yarrow Chem Products (Mumbai, India). Sodium chloride was obtained from Hi-Media Laboratories Pvt. Ltd., (Mumbai, India). Mannitol was procured from Ranbaxy Fine-Chem. Ltd., (New Delhi). Hydroxypropyl methylcellulose (HPMC K100M) was obtained from Otto Chemie Pvt. Ltd., (Mumbai, India). Avicel PH 102 was purchased from Yarrow Chem Products (Mumbai, India). Cellulose acetate was obtained from Sigma Aldrich Chemicals (Bangalore, India). PEG 400, acetone and methanol was purchased from Merck (India).

Methods

Compatibility studies for the drug-excipients using FT-IR

The FTIR[13] for the API as well the required polymers was carried out to ascertain the various functional groups along with the physical or chemical interactions involved. The individual polymers and the physical mixture containing drug were mixed separately with potassium bromide and were loaded into the pellets of FT-IR. The samples were scanned from 4000 to 400 cm^{-1} to obtain the characteristic peaks.

Preparation of core Tablets

Required quantities of excipients were weighed separately. Drug was passed through sieve number 60 followed by hydroxypropyl methylcellulose (HPMC K100M) and were triturated together in mortar and pestle. Later, osmogens (Sodium chloride and mannitol in variable quantities for different batches) were passed through the sieve and further trituration was done, followed by addition of Avicel pH 102. All the ingredients were then together triturated to obtain a homogenous mixture. This powder blend was used to determine flow properties. Further, magnesium stearate and talc were added as lubricant and glidants respectively. This mixture was compressed using 10 station compression machine (Rimek Mini Press I) by direct compression method in a batch of 30 tablets each using 8mm punch and the total weight of each tablet was 250 mg. The formulation for the core tablets is given in the Table 1.

Table 1: Formulation composition of core tablets.

Ingredients (mg)	Formulation Codes											
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Metoclopramide HCl	30	30	30	30	30	30	30	30	30	30	30	30
Sodium Chloride	25	50	75	25	50	75	-	-	-	-	-	-
Mannitol	-	-	-	-	-	-	25	50	75	25	50	75
Hydroxypropyl Methycellulose (HPMCK100M)	37.5	37.5	37.5	62.5	62.5	62.5	37.5	37.5	37.5	62.5	62.5	62.5
Avicel pH 102	154.5	129.5	104.5	129.5	104.5	79.5	154.5	129.5	104.5	129.5	104.5	79.5
Talc	1	1	1	1	1	1	1	1	1	1	1	1
Magnesium Stearate	2	2	2	2	2	2	2	2	2	2	2	2
Total	250	250	250	250	250	250	250	250	250	250	250	250

Preparation of Coating Material[14]

5% w/v of cellulose acetate was weighed accurately and was mixed gradually in 90 ml of acetone using magnetic stirrer. After thorough mixing of cellulose acetate required amount of plasticizer (PEG 400) was dissolved in methanol and this mixture was dissolved in the previous cellulose acetate mixture and further stirring was continued for 75 minutes. The coating solution was prepared according to the formulation coat B and the same was employed for coating the core tablets using Dip coating technique.[15] A medium sized copper wire was coiled in such a way that the two ends of the wire would act as a holder forming a grip to hold the tablet without dropping the tablet into the dipping solution. The tablets were dipped for 4 times until 5-7% of weight gain was achieved. The coated tablets were air dried and were mechanically drilled for the orifice using micro-needle of size 0.25 mm before subjecting them for further evaluations. The formulation for coating solution is given in the Table 2.

Table 2: Coating solution formulation.

Excipients	Quantities		
	Coat A	Coat B	Coat C
Cellulose Acetate (gm)	5	5	5
PEG 400 (gm)	0	0.5	0.75
Methanol (ml)	10	10	10
Acetone (ml)	90	90	90

EVALUATION OF FORMULATIONS

Precompression test for powders

The tests are performed to determine the flow property of the powder. The various test performed for powder before compression are bulk density, tapped density,[16] Carr's index, Hausner's ratio[17] and angle of repose.[18] All the tests were performed in triplicates.

Post compression tests for uncoated and coated tablets

Post compression tests were carried out for uncoated and coated tablets by considering various parameters like weight variation,[19] friability (Roche Friability Apparatus),[20] thickness of the tablets (Vernier Caliper) using 10 tablets of each batch and hardness (Monsanto Hardness Tester) was tested for 6 tablets of each formulation. Percentage weight gain of coated tablets was determined for 10 tablets of each batch.

Drug Content

10 tablets were crushed and an equivalent weight of 250 mg was taken and dissolved in 100 ml of 1.2 pH buffer in a 100 ml volumetric flask. The above solution was sonicated for 30 minutes. From this 1 ml was taken and further diluted to 100 ml of 1.2 pH buffer and then filtered using Whatmann filter paper. Absorbance was recorded in triplicate at 272 nm by spectrophotometrically to find out the drug content uniformity.

In vitro drug release

The *in vitro* drug release[21] was performed using 1.2 pH buffer for 2 hours followed by 6.8 buffer for 18 hrs in USP Type II apparatus at 50 rpm speed and a constant temperature of 37±0.5ºC. The samples were withdrawn at predetermined time periods and a sink condition was maintained by adding the respective buffer solutions. The samples were analysed using UV-Spectrophotometer at 272 nm in triplicate.

Effect of Level of Plasticizer

The effect of plasticizer[22] on the drug release was investigated by varying the concentration of PEG 400 in the coating solution. After selecting the optimized formulation, Coat A and Coat C was employed separately and were drilled for orifice. No plasticizer was incorporated in Coat A whereas Coat C consisted of 0.75gm of PEG 400. *In vitro* study was carried out for these formulations for 2 hours in 1.2 pH buffer followed by 8 hours in 6.8 buffer and compared with the drug release of optimized formulation where Coat B was applied. Experiment was carried out in triplicate and recorded.

Release Kinetics

The release kinetics of the formulation was determined by fitting the results for the *in vitro* drug release in various mathematical models (zero-order, first-order plot, Hixson Crowell, Higuchi Plot, Peppas plot) by using PCP v3 Disso software (version 3 Bharthi Vidyapeeth, Pune). The best fit model was obtained by obtaining the r^2 value.

Scanning electron microscopy

The optimized formulation was selected and the coating layer was carefully removed after the dissolution study and dried at 45ºC in the hot air oven for about 12 hours. Further, the coating layer was observed for the orifice size using JSM-6360 LV SEM apparatus after dissolution at 100x magnification.

Stability Test

Short term stability studies were carried out for optimized formulation at room temperature (25±2°C & 60±5% RH) and at an accelerated temperature (40±2°C & 75±5% RH) for 1 month. Samples were loaded in amber colored glass containers and stored in the stability chamber. The samples were analyzed for physical appearance, hardness, % friability, drug content and % drug release for 15th day and 30th day to investigate the stability of prepared tablets.

RESULTS AND DISCUSSION

FTIR Spectrum analysis

Using FTIR Spectrophotometer, the spectrum for the drug as well various ingredients used in the formulation were obtained along with the physical mixture of the combination of all components and the spectrum obtained was investigated for any change in the peak showing physical and chemical changes. The drug showed the peaks at specified regions which

indicated the presence of required functional groups in the drug. No such significant shifts in the peak were seen with the influence of polymers in both the physical mixtures 1 and 2. The observed frequencies for the drug along with the physical mixture is given in the Table 3 and the spectrums are shown in the Fig. 1, Fig. 2 and Fig. 3.

Table 3: Compatibility of drug and excipients by FT-IR studies.

Functional Group	Reported Frequency (cm^{-1})	Observed Frequency for Pure Drug (cm^{-1})	Observed Frequencies for Physical Mixture (cm^{-1})	
			Including Sodium chloride	Including Mannitol
N-H	3300-3500	3394.72	3394.72	3392.79
C-H (Aromatic)	2900-3100	3003.17	3003.17	2983.88
C-H (Alkyl)	2850-2960	2943.37	2941.44	2947.23
C=O	1660-1790	1660.71	1661.78	1669.64
C=C	1590-1680	1595.13	1595.13	1629.85
C-O	1050-1160	1157.29	1157.29	1157.29
C-N	1030-1230	1211.30	1211.30	1209.37
C-Cl	600-800	680.87	680.87	700.16

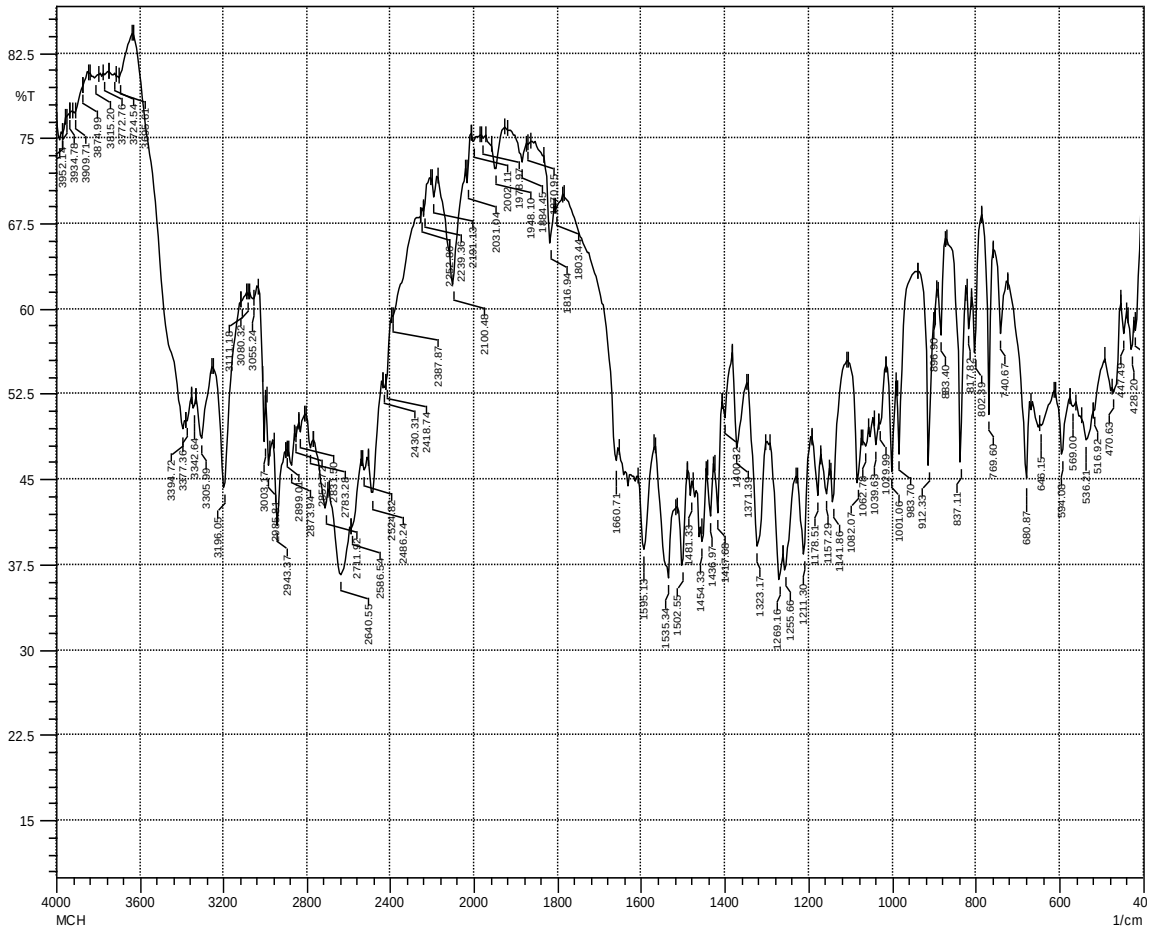

Fig. 1: Fourier-transform spectroscopy of pure Metoclopramide HCl.

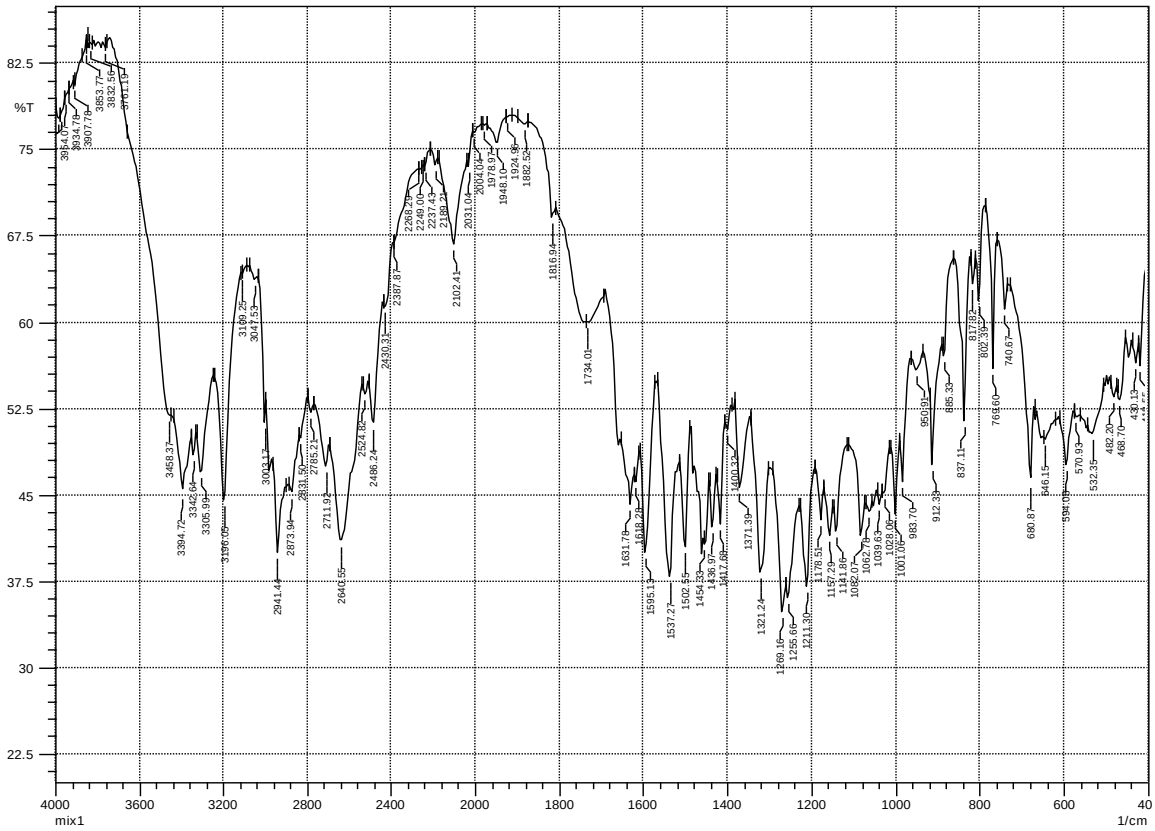

Fig. 2: Fourier-transform spectroscopy of physical mixture 1 containing Sodium chloride.

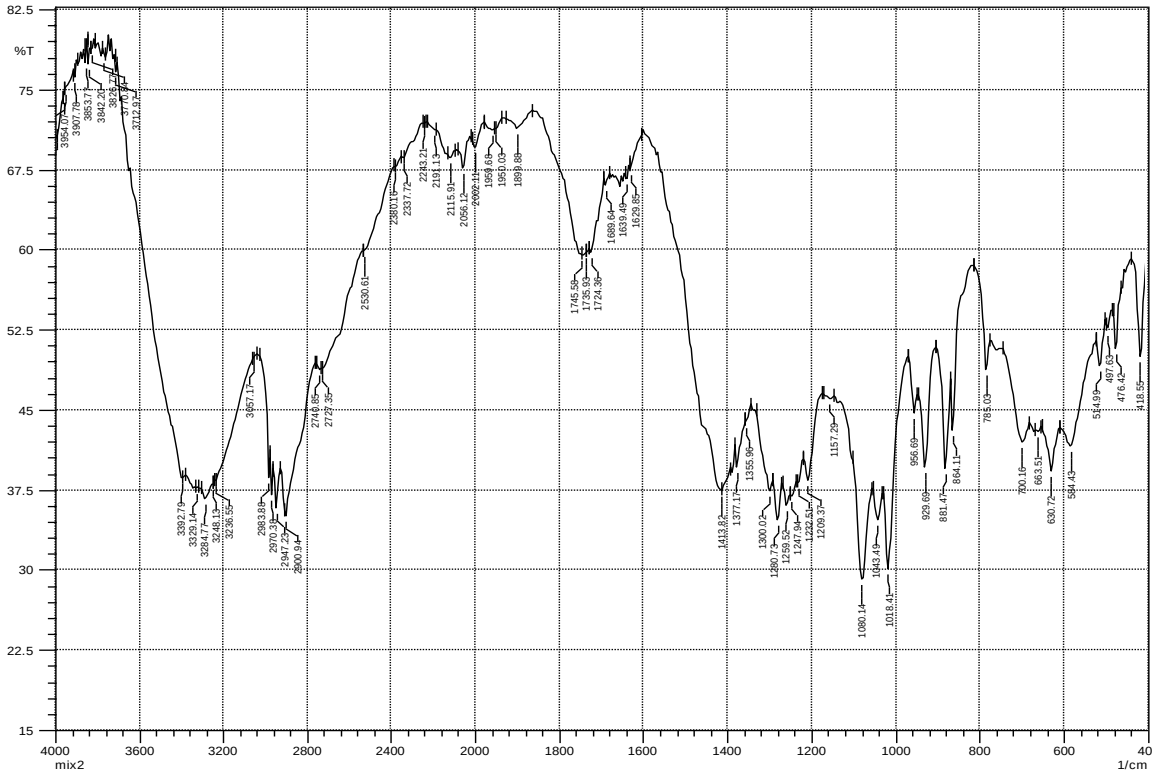

Fig. 3: Fourier-transform spectroscopy of physical mixture 2 containing Mannitol./

Precompression test for powders

The results of the various tests performed for the powder blend before compression were found to be in the acceptable limits. Bulk density of the formulations F1 to F12 was found to be in the range of 0.415±0.002 to 0.460±0.31 gm/cm^3 and tapped density was found between 0.473±0.001 to 0.520±0.002 gm/cm^3. The results of the Carr's index were found to be in the range of 11.24±0.27% to 16.6±0.33% and Hausner's ratio lies within 1.12±0.005 to 1.20±0.06 which indicates good powder flow property. Angle of repose (θ) for the formulations F1 to F12 were found to be in the range of 26.26±0.76 to 31.01±0.05 which ensured good flow of the powder blend.

Post compression tests for uncoated and coated tablets

Weight variation, thickness, hardness and friability were evaluated for uncoated and coated tablets. All the results obtained were found to be in accordance with the requirements of I.P. Further, percentage weight gain and drug content were evaluated for the coated tablets. The thickness of the tablets was increased by 0.2 mm approximately after the coating of core tablets. Post compression data for uncoated and coated tablets are tabulated in the Table 4 and Table 5 respectively.

Table 4: Post compression data for uncoated tablets.

Batch code	Weight variation (mg)	Hardness (Kg/cm^2)	Thickness (mm)	Friability (%)
F1	236.67±0.99	3.62±0.13	3.68±0.02	0.71±0.01
F2	238.52±0.56	3.91±0.12	3.73±0.025	0.67±0.05
F3	241.09±1.31	4.33±0.129	3.81±0.041	0.58±0.01
F4	242.28±1.89	3.79±0.188	3.98±0.025	0.53±0.011
F5	239.87±0.83	4.12±0.13	3.99±0.028	0.54±0.005
F6	240.92±0.80	4.37±0.14	4.02±0.026	0.49±0.011
F7	244.93±1.43	4.62±0.13	3.97±0.034	0.40±0.01
F8	249.2±1.13	4.75±0.22	4.05±0.033	0.24±0.005
F9	248.54±1.24	5.0±0.22	4.13±0.025	0.36±0.001
F10	247.8±1.37	5.29±0.18	4.22±0.013	0.28±0.03
F11	244.72±1.63	5.45±0.10	4.33±0.02	0.45±0.01
F12	243.86±1.99	5.25±0.22	4.27±0.026	0.32±0.006

All the data expressed are average of triplicate (n=3 ± SD)

Table 5: Post compression data for coated tablets.

Formulation Code	Weight variation (mg)	Weight gain	Hardness (Kg/cm^2)	Thickness (mm)	Friability (%)	Drug content (%)
F1	249.88±1.06	5.57±0.30	5.37±0.38	3.88±0.028	0.08±0.001	89.78±0.51
F2	252.7±2.07	5.94±0.25	5.58±0.43	3.95±0.057	0.11±0.003	87.06±0.31
F3	253.47±3.34	5.13±0.13	6.16±0.14	4.02±0.02	0.07±0.002	92.77±0.5
F4	255.62±4.35	5.50±0.08	5.54±0.43	4.19±0.03	0.11±0.001	89.46±0.53
F5	254.99±1.81	6.30±0.36	5.95±0.14	4.20±0.05	0.03±0.005	92.46±0.42
F6	253.6±2.49	5.26±0.13	6.25±0.28	4.23±0.03	0.15±0.002	96.97±0.37
F7	260.39±3.30	6.31±0.09	6.5±0.10	4.17±0.028	0.11±0.001	91.26±0.62
F8	263.29±2.99	5.65±0.30	6.41±0.40	4.25±0.05	0.18±0.007	93.07±0.27
F9	263.48±1.85	6.01±0.40	6.87±0.25	4.33±0.01	0.15±0.005	94.56±0.64
F10	265.17±3.93	6.66±0.22	7.29±0.20	4.42±0.03	0.07±0.003	90.96±0.58
F11	257.98±5.27	5.42±0.30	7.41±0.05	4.53±0.05	0.16±0.001	90.69±0.04
F12	258.83±4.13	6.14±0.23	7.30±0.25	4.47±0.03	0.03±0.002	94.86±0.36

All the data expressed are average of triplicate (n=3 ± SD)

In vitro drug release

In vitro drug release was performed for all the batches in triplicate where the release data was analysed for 2 hours in 1.2 pH buffer and for next 18 hours in 6.8 pH buffer. Drug release for all the formulations were in the range of 49.13±0.27% to 91.90±0.21%. The formulation F10 showed the lowest drug release which consisted of high concentration of hydroxypropyl methylcellulose as rate controlling polymer and mannitol as osmogen. On the other hand, the formulation F3 exhibited the highest drug release which consisted of sodium chloride as osmogen. Formulation F3 was considered as the optimized formulation out of all the batches and the same was considered for the further evaluation. The drug release is shown in the Fig 4 and Fig 5.

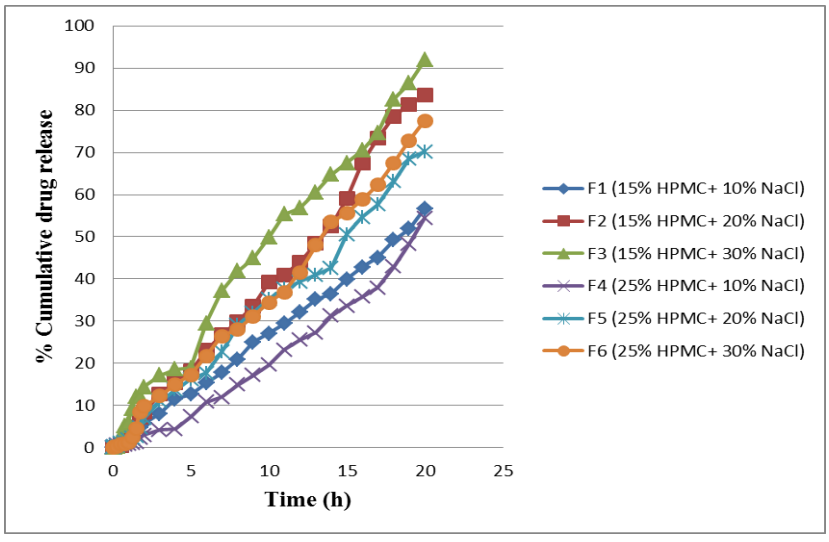

Fig. 4: Dissolution profile of formulations F1-F6.

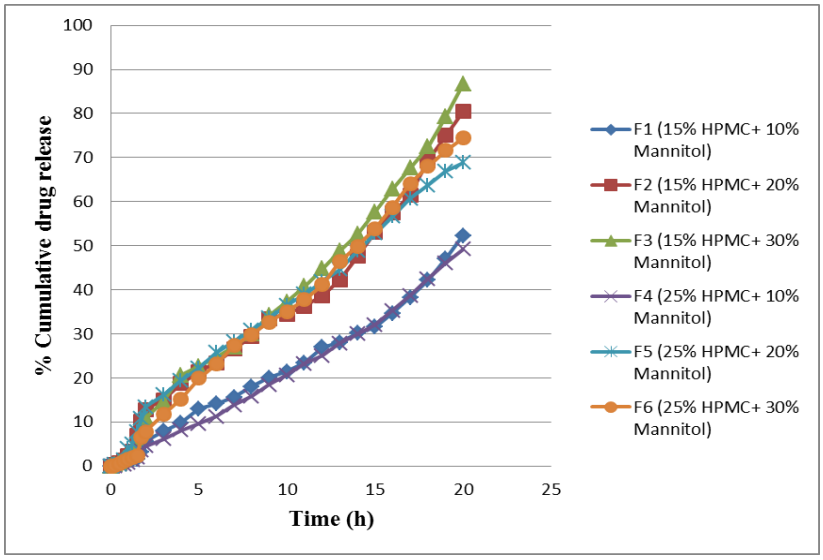

Fig. 5: Dissolution profile of formulations F7-F12.

Effect of hydrophilic polymer and osmogen concentration on drug release

From the obtained dissolution profile, it is evident that the formulations with high content of hydrophilic polymer showed decreased drug release where the cumulative values ranged from 49.76±0.27 % to 77.53±0.56 %. The formulations F4 to F6 and F10 to F12 consists of 25% of hydroxypropyl methylcellulose (HPMC K100 M) which is the possible cause for decreased drug release. Increased tortuosity would lead to lower drug release through diffusion. The formulations F1 to F3 and F7 to F9 consists of 15% of HPMC K 100M which showed relatively greater release rate that ranged from 52.27±0.24% to 91.90±0.21 %. It can be predicted that the addition of hydrophilic polymers in optimum concentration could control the release of drugs with high solubility from osmotic systems which complies with the report published by Suresh PV *et al*.[23]

Further, the drug release is also affected by the osmogen concentration and their osmotic property. The formulations containing high amount of osmogen showed drug release to a greater extent than those which contained low concentration of osmogen. The optimized formulation F3 with 30% of NaCl showed the highest drug release. Apart from the concentration, the osmotic pressure also affects the drug release in which the formulations containing sodium chloride having osmotic pressure of 365 atm showed higher release rate where as the formulations prepared out of mannitol having osmotic pressure of 38 atm showed lower drug release comparatively. It was in compliance with the study performed by Arjun N *et al*.[24]

Effect of level of Plasticizer on drug release

To investigate the effect of plasticizer used in the coating material, the core tablets of the optimized formulation F3 were coated with Coat A and Coat C containing 0% and 15% w/w of PEG 400 respectively and is compared with the formulation coated with Coat B (10% w/w of PEG 400). Dissolution was carried out in triplicate for 10 hours (initially 2 hours in 1.2 pH and next 8 hours in 6.8 pH) to assess the effect of PEG 400 on *in vitro* drug release. The formulation with no plasticizer showed decreased drug release due to slow imbibition of water through the semipermeable membrane. With the increasing level of plasticizer, the membrane porosity also increases due to the solubilisation of PEG 400 and as a result the release of the drug is also increased. The formulation coated with Coat C showed higher release rate and this complies with the work of Pramod Kumar *et al*.[25] The drug release of three different formulations is given the Fig. 6.

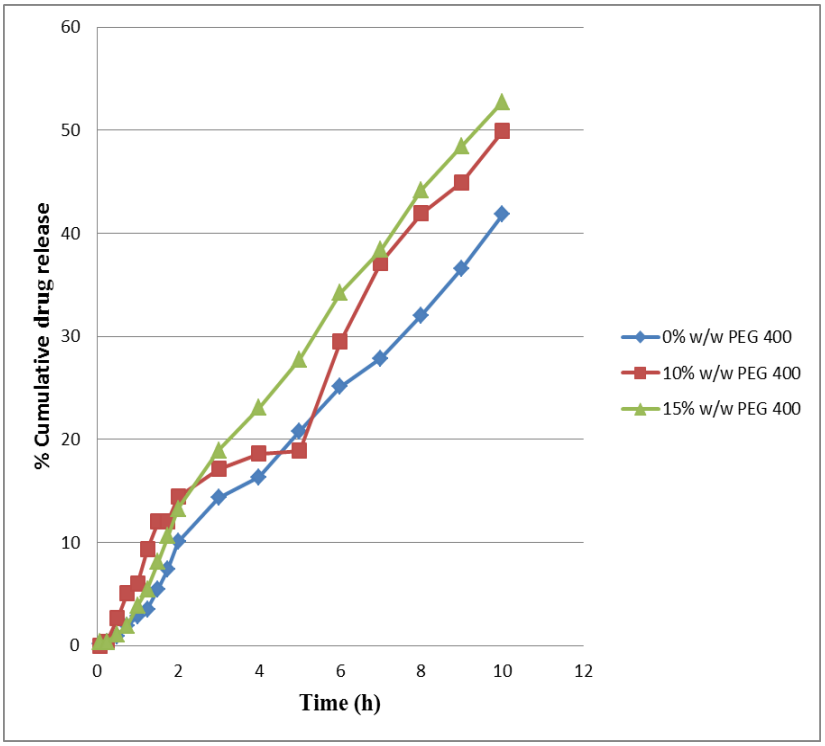

Fig. 6: Effect of plasticizer on drug release.

Release Kinetics

The release kinetics was assessed by using PCP v3 Disso software in which release profile was fitted to different kinetic models. The results showed that most of the formulations were best fit to zero order kinetics. The optimized formulation F3 exhibited zero order release with *n* value = 0.8922 and k value = 4.603 which states that drug is released by non-Fickian diffusion mechanism. The kinetic data is given in the Table 6.

Table 6: Release kinetics of formulations F1-F12.

Formulation Code	First Order R^2	Zero Order R^2	Higuchi Matrix R^2	Korsmeyer Peppas R^2	Hixon Crowell R^2	Best Fit Model
F1	0.9830	0.9986	0.9157	0.9985	0.9906	Zero Order
F2	0.9269	0.9933	0.8962	0.9925	0.9572	Zero Order
F3	0.9347	0.9939	0.9373	0.9905	0.9741	Zero Order
F4	0.9470	0.9784	0.8550	0.9964	0.9593	Peppas
F5	0.9535	0.9842	0.8735	0.9949	0.9665	Peppas
F6	0.9541	0.9966	0.9092	0.9700	0.9749	Zero Order
F7	0.9669	0.9899	0.9017	0.9749	0.9767	Zero Order
F8	0.9259	0.9872	0.9090	0.9693	0.9553	Zero Order
F9	0.9360	0.9948	0.9161	0.9863	0.9656	Zero Order
F10	0.9710	0.9918	0.8871	0.9846	0.9794	Zero Order
F11	0.9842	0.9902	0.9500	0.9860	0.9923	Hixon-Crowell
F12	0.9636	0.9978	0.9179	09829	0.9810	Zero Order

Scanning Electron Microscopy (SEM):

SEM was performed to find out the size of the delivery orifice and to elucidate the changes in the membrane surface of the coat while dissolution study. The size of the orifice was found to be 0.3 mm under the magnification of 100 x. The membrane was found to be intact and there were no visible pores formed on the surface before and after the dissolution. The SEM photographs are shown in the Fig. 7 and Fig. 8.

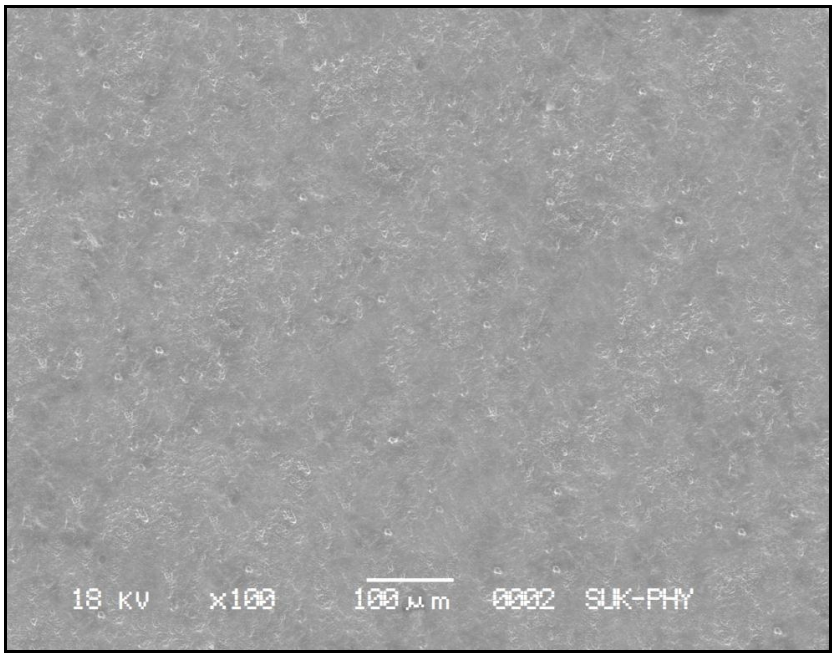

Fig. 7: Scanning electron microscopic image of coating membrane before dissolution.

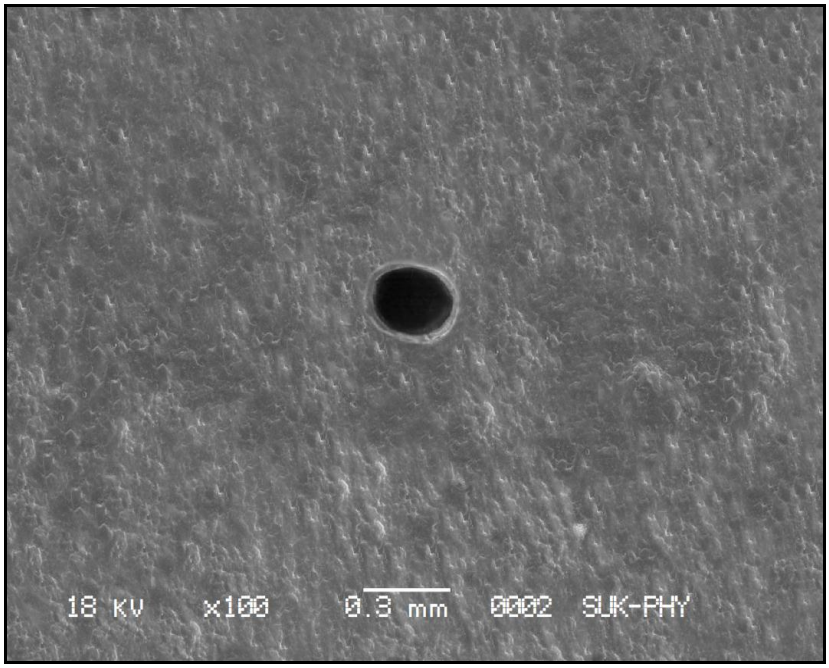

Fig. 8: Scanning electron microscopic image of delivery orifice after dissolution.

Stability studies

The tablets were evaluated on the 15th day and 30th day for a period of one month for the assessment of drug content, hardness, friability and *in vitro* drug release. From the preliminary observation, it was found that the membrane did not show any visible change in colour or appearance and the values in the Table 7 shows the obtained results are within the permissible range. The formulations were found to be stable at room temperature (25°C±2°C & 60±5% RH) and at accelerated conditions (25°C ±2°C & 60 ± 5% RH).

Table 7: Stability study data of optimized formulation.

Parameters	Initial	15 days 25°C/60%RH (Short term)	15 days 40°C/75% RH (Accelerated)	30 days 25°C/60%RH (Short term)	30 days 40°C/75% RH (Accelerated)
Physical appearance	White colour	No change	No change	No change	No change
Hardness	6.25±0.27	6.25±0.31	6.0±0.18	6.1±0.36	6.0±0.22
% Friability	0.07±0.02	0.08±0.05	0.08±0.001	0.09±0.03	0.08±0.06
Weight variation	253.47±0.02	253.21±0.13	253.26±0.08	253.10±0.05	253.07±0.07
Drug content	92.77±0.06	92.13±0.02	92.17±0.16	91.98±0.32	91.02±0.11
% Drug release	91.90±0.21	91.45±0.07	91.39±0.21	91.27±0.45	91.1±0.17

All the data expressed are average of triplicate (n=3 ± SD)

CONCLUSION

Elementary osmotic tablets of Metoclopramide HCl were successfully prepared and from the obtained results, it can be concluded that pre-compression parameters were found to be in the optimum range as per IP standards. Hardness was found to be 3.62±0.13 Kg/cm^2 to 5.45±0.10 Kg/cm^2 prior to coating and it ranged from 5.37±0.38 Kg/cm^2 to 7.41±0.005 Kg/cm^2 after the coating. Before coating, thickness varied from 3.68±0.02 mm to 4.33±0.026 mm and found to be 3.88±0.028 to 4.53±0.05 mm after the application of coat. Percentage weight gain after the coating of the tablets was found to be in the range of 5.13±0.13 % to 6.66±0.22 %. All the formulations had the drug content in the acceptable range between 87.06±0.31% to 96.97±0.37 % which assured uniformity of the dose.

The cumulative % drug release of the prepared formulations ranged from 54.50±0.08% to 91.90±0.21% at the end of 20 hours. Formulation F3 showed the highest drug release which contained sodium chloride as osmogen and formulation F10 exhibited lowest release rate where it consisted of mannitol in the same concentration. Kinetic model study revealed that the optimized formulation F3 exhibited zero order kinetics as the best fit model and with a 'n' value of 0.8922 showed non-Fickian diffusion mechanism. The optimized formulation F3 after short term stability study at room temperature (25ºC/ 60% RH) and at accelerated temperature (40ºC/ 75% RH) was found to be stable after a period of 30 days. The obtained results indicated that elementary osmotic pumps of Metoclopramide HCl can be efficiently formulated to achieve slow, constant and pH independent release.

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Conflict of interest

There are no conflicts of interest.

REFERENCES

1. Kushal M, Monali M, Durgavati M, Mittal P, Umesh S, Pragna S. Oral controlled release drug delivery system: an overview. Int. Res. J. Pharm., 2013; 4(3): 70-6.

2. Tanmoy G, Amitava G. Drug delivery through osmotic systems- an overview. J. Appl. Pharm. Sci., 2011; 1(2): 38–49.
3. Rajan KV, Sanjay G. Current status of drug delivery technologies and future direction. Pharm. Technol., 2001; 25(2): 1-14.
4. Kashmir S, Manpreet KW, Geeta Agarwal G, Harikumar SL. Osmotic pump drug delivery system: a novel approach. J. Drug. Deliv. Ther., 2013; 3(5): 156–62.
5. Chinmaya KS, Ram Mohan RS, Sudhakar M, Nalini KS. Advances in osmotic drug delivery system. J. Chem. Pharm. Res., 2015; 7(7): 252-73.
6. Rajesh AK, Chirag P, Pranav P, Vipul K, Tejal GS, Rajnikant CP et al. Osmotic drug delivery system as a part of modified release dosage form. ISRN Pharm., 2012; 2012: 1-9.
7. Theewes F. Elementary osmotic pump. J. Pharm. Sci., 1975; 4(12): 1987–91.
8. Brahma PG, Navneet T, Nishi PJ, Jitendra B, Surendra J. Osmotically controlled drug delivery system with associated drugs. J. Pharm. Pharmaceut. Sci., 2010; 13(3): 571-88.
9. Tripathi KD. Essentials of Medical pharmacology. 6th Ed. New Delhi: Jaypee Brothers Medical publishers (p) Ltd., 2008; 664-5.
10. https://www.drugbank.ca/drugs/DB01233 “Accessed on 7 April 2020”.
11. Ayhan S, Cetin T, Ziya B, Cansel KO, Yalcin O. Effect of different polymers and their combinations on the release of Metoclopramide HCl from sustained-release hydrophilic matrix tablets. Pharm. Dev. Technol., 2013; 18(5): 1122-30.
12. Paloma F, Cristina P, Jose LL, Gloria F. In Vitro Release of Metoclopramide from Hydrophobic Matrix Tablets. Influence of Hydrodynamic Conditions on Kinetic Release Parameters. Chem. Pharm. Bull., 2001; 49(10): 1267-71.
13. Faix O. Fourier transform infrared spectroscopy. In: Lin SY, Dence CW, editors. Methods in Lignin chemistry. Berlin: Springer-Verlag, 1992; 83–109.
14. Derakshandeh K, Ghasemnejad BM. Development and optimization of buspirone oral osmotic pump tablet. Res. Pharm. Sci., 2014; 9(4): 233-41.
15. Puetz J. Dip Coating Technique. In: Michel AG, Martin M, editors. Sol-Gel Technologies for Glass Producers and users. New York: Springer Science + Business Media., 2004; 37-8.
16. Silva JP, Splendor D, Gonclaves MB, Costa P, Lobo JM. Note on the Measurement of Bulk Density and Tapped Density of Powders According to the European Pharmacopeia. AAPS Pharm Sci Tech., 2013; 14(3): 1098-1100.
17. Rakhi BS, Mobin AT, Mansoor AK. Comparative Evaluation of Flow for Pharmaceutical Powders and Granules. AAPS Pharm Sci Tech., 2008; 9(1): 250-8.

18. Hamzah MB, Omar SB. A review on the angle of repose of granular materials. Powder Technology, 2018; 330: 397-417.
19. Lachman L, Lieberman AH, Kaning LJ. The theory and practice of industrial pharmacy. 3rd ed. Bombay: Indian Varghese Publishing House, 1987; 300.
20. Saleem M, Shahin M, Srinivas B, Ashraf B. Evaluation of tablets by friability apparatus. Int. J. Res., 2014; 4(4): 837-40.
21. Ramakrishna N, Mishra B. Development and evaluation of osmotic pump tablets of Naproxen sodium. Pharmazie, 2001; 56(12): 958-62.
22. Javad S, Mahbobeh S, Parinaz AR. Factors affecting the release of nifedipine from a Swellable elementary osmotic pump (SEOP). Drug. Deliv, 2008; 15(1): 43-8.
23. Prabakaran D, Paramjit S, Parijat K, Suresh PV. Effect of hydrophilic polymers on the release of diltiazem hydrochloride from elementary osmotic pumps. Int. J. Pharm., 2003; 259(1-2): 173-9.
24. Arjun N, Narendar D, Sunitha K, Harika K, Nagaraj B. Development, evaluation and influence of formulation and process variables on in vitro performance of oral elementary osmotic device of atenolol. Int. J. Pharm. Investig, 2016; 6(4): 238-46.
25. Pramod K, Sanjay S, Brahmeshwar M. Development and Evaluation of Elementary Osmotic Pump of Highly Water Soluble Drug: Tramadol Hydrochloride. Curr. Drug. Deliv, 2009; 6(1): 130-9.