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Formulation and Evaluation of sustained release Pellets of Domperidone

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Abstract:
The present research was engrossed on the development and evaluation of sustained release pellets of Domperidone with different grades of ethyl cellulose like ethyl cellulose N10, N7 and N20 by employing drug layering technology. Pellets were prepared and evaluated for loose bulk density, tapped bulk density, compressibility index and angle of repose, shows satisfactory results.Formulation was optimized on the basis of acceptable pellet properties (friability, drug content moisture content and loss on drying) and *in-vitro* drug release. The *in-vitro* release studies of pellets were carried out in 0.1N HCL for 2 hours and 6.8 PH phosphate buffer for 12 hours. The studies indicated that the drug release can be modulated by varying the concentration of the polymer. The formulations were further characterized to identify any possible interactions by FTIR spectroscopy and differential scanning calorimetry. The nature of the drug and the optimized formulation was determined by X-Ray diffraction. The surface morphology of the pellets was studied by scanning electron microscopy.

Keywords: Sustained release, Ethyl cellulose, Pellets, Domperidone

Introduction

Multiparticulate drug delivery systems are the utmost accepted and widely used dosage form as they offer so many benefits over unit dosage forms like improved bioavailability because of increased surface area, reduced inter subject variation and transportation and reduced chances of dose dumping. Pelletization is one of the most promising techniques for the multi particulate drug delivery systems[1].

The current investigation focuses on the pelletized form of multiple units where coating of sugar spheres with drug and further coatings were given to seal the drug and obtain sustain release, by a process pelletization which is stated to as a size widening process and the final product obtained is called pellets. The word 'pellet' has been used to define a variety of methodically produced, geometrically defined agglomerates attained from varied starting materials employing different processing conditions. These are oral dosage forms containing multiplicity of small discrete units, each revealing some desired characteristics[2-3].

Pellets provide a decrease in the dosage regimen and gastrointestinal irritation additionally controlling the drug release and increasing the absorption of the active ingredient. Also one of the beneficial properties of the pellet formulations is being a good candidate for the delivery of drug substances due to reducing the dose dumping effect. The reproducibility of the release characteristics from pellet formulations is also much better with respect to the single-unit dosage forms. They are suitable systems for film coating with respect to the low surface area- volume ratios. Also, resistance to the external factors such as moisture, air and light are the most advantageous properties of this dosage forms[4-7].

In the current study, pan coating and fluidized bed coater is employed for the preparation of Domperidone pellets. A core material is coated with the drug substance using pan coater following a barrier coating process in which drug loaded pellets were coated with HPMC E5 using fluidized bed coater following a sustained release process in which the release controlling polymer material is introduced[8-9]. The coating process for pellets is carried out mainly in order to alter the release of drug from the pelletized drug delivery systems. The some of the coating equipment used for the pan coating processes are standard coating pan and the perforated coating pan.

Domperidone, a peripheral dopamine2-receptor antagonist, regulates the motility of gastric and small intestinal smooth muscle and has been shown to have some effects on the motor function of the esophagus. It also has antiemetic activity as a result of blockade of dopamine receptors in the chemoreceptor trigger zone. It is a white to off-white free flowing crystalline powder, freely soluble in methanol and dimethyl formamide and very slightly soluble in water and alcohol. Domperidone is rapidly absorbed following oral administration and has the bioavailability of 15% only due to the first pass metabolism in the liver. It has the terminal elimination half-life of 7 hours and has the protein binding of about 91-93%[10].

The present research was mainly concentrated on the development and evaluation of controlled release pellets of Domperidone with different grades of ethyl cellulose like ethyl cellulose N10, N7 and N20 by employing pan coating technique. Different grades of ethyl cellulose were used in the present work and ethyl cellulose N7 was found to have a satisfactory drug release over other grades of ethyl cellulose. An attempt was made to optimize the composition of these different grades of ethyl cellulose to achieve the sustained release of drug from pellets. Low viscosity HPMC E5 was used as a binder and the film former in the present investigation[11-12].

EXPERIMENTAL SECTION

Materials: Domperidone was obtained as free sample from spansules formulation, Hyderabad. Sugar spheres, povidone, iso propyl alcohol, sun set yellow, HPMC E5, talc were obtained as gift samples from spansules formulations, Hyderabad. Methylene dichloride was obtained from triveniinterchemPvt Ltd, Gujarat. Ethyl cellulose of different grades like ethyl cellulose N10, N7 and N20 were obtained from alpha chemika, Mumbai.

Preparation of Domperidone pellets

Sugar spheres of weighed quantity are loaded into the coating pan, weighed quantities of blended drug was loaded on to the sugar spheres with continuous spraying of measured quantity of wetting solution (dissolve the required quantity of HPMC E5 and the PVP K30 in the measured quantity of iso propyl alcohol and mix with sun set yellow solution) by using 1.2mm spray gun nozzle. Pan was allowed to rotate for about 10 mins until uniform drug loading occurs. the coating pan was operated at a rpm of 15-20. The pellets were kept under rotation for 30 minutes to avoid sticking. The drug loaded pellets from the pan were spread on to the trays uniformly and dried at 60^0C temperature for 3 hours. After drying, the pellets were sifted by using vibro sifter to remove fines and the collected the uniform sized pellets.

The drug loaded pellets were loaded into the fluidized bed coater and coated with methylene dichloride and HPMC E5 polymer (1.5%) solution under specified conditions like inlet temperature, product temperature, exhaust temperature,

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atomization, spray rate, wurster height and rpm of the pump. The process parameters for sub coating using fluidized bed coater were given in table 1. Fluidized bed coater was allowed to coat the drug loaded pellets for 10 minutes until uniform coating was applied. The drug loaded pellets from the fluidized bed coater were spread on to the trays uniformly and dried at 60^0C temperature for 30 minutes.After drying, the pellets were sifted by using vibro sifter to remove fines and the collected the uniform sized pellets.

In the final step the sub coated/ barrier coated pellets (HPMC E5 coated pellets) were loaded into the fluidized bed coater and coated with the different grades of ethyl cellulose like N10, N7, and N20 with different concentrations (0.5%, 0.75%, 1%, 1.5%) and fluidized bed coater was allowed to coat barrier coated pellets with different grades of ethyl cellulose for 10 minutes until uniform coating was applied. Finally the coated pellets were dried at ambient conditions for 2 hours and sifted through vibro sifter to collect uniform sized pellets. The fluidized bed coater processing variables for final step were given in table2. Composition of various Domperidone sustained release pellets were given in the table 3, 4, 5.

Evaluation of physical and chemical parameters

Particle size determination

The average particle size of the pellet formulations of Domperidone were analyzed by simple sieve analysis method[13]. The particle size of various batches of pellets were given in the table 6.

Assay by UV

Standard preparation:

Transfer an accurately weighed quantity of about 100mg of Drug to 100ml volumetric flask. Add 20ml of DMF (dimethyl formamide) and sonicate to dissolve. Make up the volume to the mark with buffer solution of pH-1.2 and mix. Transfer 5ml of the above solution to 50ml volumetric flask and make up with buffer solution of pH-1.2

Sample preparation:

Weigh a quantity of pellets equivalent to 100mg of Domperidone and transfer 100ml volumetric flask. Add 20ml of DMF (dimethyl formamide) and sonicate to dissolve. Make up the volume to the mark with buffer solution of pH-1.2 and mix. Transfer 5ml of the above solution to 50ml volumetric flask and make up with buffer solution of pH-1.2

Procedure:

Measure the absorbance at the wave length of maximum at about 284nm using filtered portions of the solution under test, in comparison with the standard solution, using buffer solution of pH-1.2 as the blank and calculate as per the below formula. The assay of various batches of pellets was given in table 6

$$\text{Assay} = \frac{AT}{AS} \times \frac{WS}{100} \times \frac{5}{50} \times \frac{100}{WT} \times \frac{50}{5} \times P$$

Where,

AT = Absorbance of test solution

AS = Absorbance of standard solution

WS = Weight of working standard

WT = Weight of test sample

P = Potency of working standard

Friability test

The friability of the core pellets of Domperidone[14] was determined as % weight loss after 100 revolutions of 10g of pellets in a friabilator. The friability values of various pellets formulations were given in table 6.

$$\% \text{ Friability} = \frac{\text{Weight}_{\text{original}} - \text{Weight}_{\text{final}}}{\text{Weight}_{\text{original}}} \times 100$$

Moisture Content

Transfer about 25 ml Methanol into Karl Fischer titration vessel, titrate with Karl Fischer Reagent and determine the end point potentio-metrically.

Weigh accurately about 0.15g of disodium tartrate and transfer quantitatively into the Karl Fischer titration vessel. Titrate with Karl Fischer-reagent and determine the end point potentio-metrically. Note down the volume of Karl Fischer-reagent consumed. The strength of Karl Fischer-reagent is expressed as water equivalence(mg/ml).

$$\text{Water equivalence} = \frac{\text{Wt. of disodium tartrate x 15.66 x 1000}}{\text{100 x volume of KF reagent consumed}}$$

Standardization should be done at least in duplicate. If the values differ by more than 0.5%, third standardization as to be done.

Determination of Water:

Weigh accurately about 1.5g of sample such that a minimum of 5ml KF reagent should be consumed and transfer into the titration vessel containing, previously titrated methanol with KF reagent. Titrate with KF reagent and determine the end point potentio-metrically. The moisture content of various pellets formulations were given in the table 6.

$$\text{Water (\%)} = \frac{\text{Titre Value X water equivalence X 100}}{\text{1000 X Weight of sample}}$$

Loss on drying

The empty crucible was taken and it is dried for about 30 minutes and weighed(W1), place the sample of about 1gm and again crucible was weighed(W2), now the crucible was kept in furnace for about one hour which is maintained at a temperature of 250-300°C. Now the crucible is taken out from the furnace and kept for cooling in dessicator. After the crucible was cooled it is again weighed (W3). Now LOD is calculated in percentage using the following formula. The loss on drying of various pellets formulations were given in the table 6.

$$\text{LOD} = \frac{\text{W2-W3}}{\text{W2-W1}} \text{ X } 100$$

Where,

W1= weight of empty crucible

W2= weight of crucible+ weight of the sample

W3= weight of crucible+ weight of the sample (after drying)

***In-vitro* release study**

Dissolution studies for each formulation were performed in a calibrated 8 station dissolution test apparatus (LAB INDIA), equipped with paddles (USP apparatus II method) employing 900ml of 1.2 pH 0.1N HCL as a medium for first two hours and 6.8 pH phosphate buffer as a medium for 12 hours. The paddles were operated at 50 rpm and the temperature was maintained at 37 ± 0.5^{0}C throughout the experiment. Samples were withdrawn at regular intervals up to 12 hours and replaced with equal volume of dissolution medium to maintain the constant volume throughout the experiment. Samples withdrawn at various time intervals were suitably diluted with same dissolution medium and the amount of drug released was estimated by an ultraviolet visible spectrophotometer (Labindia, Mumbai, India) at 284nm. The dissolution studies on each formulation were conducted in three times.All the *in-vitro* dissolution parameters evaluated for various batches of pellet formulations were given in table 7.

Assessment of dissolution parameters

Pharmacokinetic parameters such as zero order, first order rate constant, Higuchi constant and peppas constants were calculated from the dissolution data obtained for various formulations

Characterization of pellets

Selected formulations were subjected to IR, XRD and DSC studies to identify the nature and possible interaction between drug and excipients.

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The surface and porosity characteristics of the powdered pellets were characterized by SEM analysis.

Stability studies

Stability studies of pharmaceutical products were done as per ICH guide lines[15]. These studies are designed to increase the rate of chemical or physical degradation of the drug substance or product by using exaggerated storage conditions.

Method:

Selected formulations were stored at different storage conditions at elevated temperatures such as 25^{0}C± 2^{0}C / 60% ± 5% RH, 30^{0}C ± 2^{0}C / 65% ±5% RH and 40^{0}C ± 2^{0}C / 75% ± 5% RH for 90 days. The samples were withdrawn at intervals of fifteen days and checked for physical changes.

Table 1: Fluidized bed coater process parameters for sub coating

Sl. No	Process Parameter	Range
1	Inlet temperature (°C)	45-50
2	Product temperature (°C)	40-45
3	Exhaust temperature (°C)	30-45
4	Atomization (barr)	2-4.5
5	spray rate (g/min)	60-120
6	Wurster height (mm)	20-50
7	Pump RPM	15-30

Table 2: Fluidized bed coater process parameters for functional coating

Sl. No	Process Parameter	Range
1	Inlet temperature (°C)	45-50
2	Product temperature (°C)	40-45
3	Exhaust temperature (°C)	30-45
4	Atomization (barr)	3-4.5
5	spray rate (g/min)	60-120
6	Wurster height (mm)	20-50
7	Pump RPM	15-30

Preparation of Domperidone sustained release pellets

Table 3: Drug loading stage

Sl. No	Ingredients	Quantity taken for 300 gms
1	Sugar spheres	190 gms
2	Domperidone	92.7 gms
3	PVP K30	6.62 gms
4	HPMC E5	1.325 gms
5	Talc	5.3 gms
6	Iso propyl alcohol	42.4 lts
7	Sunset yellow	0.53 gms

Table 4: Sub loading stage/ barrier loading stage

Sl. No	Ingredients	Quantity taken for 300 gms
1	Drug pellets	300 gms
2	HPMC E5 (1.5%)	4.95 gms
3	Iso propyl alchohol	50.5 lts
4	Methylene dichloride	12.7 lts
5	Sunset yellow	0.0053 gms

Table 5: Sustained release stage

Ingratiates	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13
Sub coated pellets	300 gms	300 gms	300 gms	300 gms	300 gms	300 gms	300 gms	300 gms	300 gms	300 gms	300 gms	300 gms	300 gms
Ethyl cellulose N_{10}	-	1.5 gms (0.5%)	2.25 gms (0.75%)	3 gms (1%)	4.5 gms (1.5%)	-	-	-	-	-	-	-	-
Ethyl cellulose N_7	-	-	-	-	-	1.5 gms (0.5%)	2.25 gms (0.75%)	3 gms (1%)	4.5 gms (1.5%)	-	-	-	-
Ethyl cellulose N_{20}	-	-	-	--	-	-	-	-	-	1.5 gms (0.5%)	2.25 gms (0.75%)	3 gms (1%)	4.5 gms (1.5%)
Iso propyl alchohol	-	34.5 lts	51.75 lts	69 lts	103.5 lts	34.5 lts	51.75 lts	69 lts	103.5 lts	34.5 lts	51.75 lts	69 lts	103.5 lts
Methulene dichloride	-	8.62 lts	12.93 lts	17.25 lts	25.87 lts	8.62 lts	12.93 lts	17.25 lts	25.87 lts	8.62 lts	12.93 lts	17.25 lts	25.87 lts
Diethyl phthalate	-	1.5 ml	2.25 ml	3.0 ml	4.5 ml	1.5 ml	2.25 ml	3.0 ml	4.5 ml	1.5 ml	2.25 ml	3.0 ml	4.5 ml

Table 6: Physical and chemical parameters of Domperidone sustained release pellets

Formulation	Particle size (µ)	Assay (%)	Friability (%)	Moisture content (%)	Loss on drying (%)
F1	1696±16	101.56	0.426	1.8	0.26
F2	1685±24	99.68	0.343	1.21	0.19
F3	1700±34	99.32	0.301	1.25	0.24
F4	1696±24	99.15	0.398	1.26	0.19
F5	1696±27	99.86	0.365	1.25	0.19
F6	1706±29	99.99	0.286	1.68	0.19
F7	1690±21	99.35	0.293	1.95	0.23
F8	1696±19	99.97	0.321	1.75	0.24
F9	1685±23	99.86	0.269	1.89	0.23
F10	1700±36	99.49	0.349	1.68	0.17
F11	1682±22	101.48	0.283	1.95	0.19
F12	1688±26	99.21	0.310	1.75	0.20
F13	1693±25	101.55	0.296	1.89	0.18

Table 7: *In-vitro* dissolution parameters of Domperidone sustained release pellets

Formulation code	Zero order R^2	First order R^2	Higuchi R^2	Peppas-model	
				R^2	Slope n
F1	1.000	1.000	1.000	1.000	0.0266
F2	0.9818	0.9182	0.9974	0.9967	0.4839
F3	0.9549	0.8467	0.9913	0.9938	0.7266
F4	0.9561	0.8422	0.9892	0.9927	0.8009
F5	0.9227	0.8426	0.9568	0.9848	0.8605
F6	0.8791	0.8149	0.9591	0.9847	0.4004
F7	0.9742	0.9116	0.9983	0.9976	0.4432
F8	0.9090	0.8262	0.9536	0.9691	0.4138
F9	0.9872	0.9352	0.9880	0.9907	0.4184
F10	0.9798	0.9311	0.9979	0.9935	0.3738
F11	0.9929	0.9387	0.9931	0.9933	0.4578
F12	0.9398	0.9318	0.9886	0.9931	0.4666
F13	0.9666	0.8992	0.9640	0.9812	0.5026

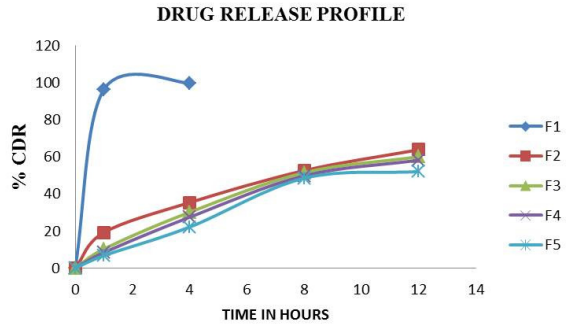

Figure 1: *In-Vitro* Dissolution Profile of F1 to F5 Formulations

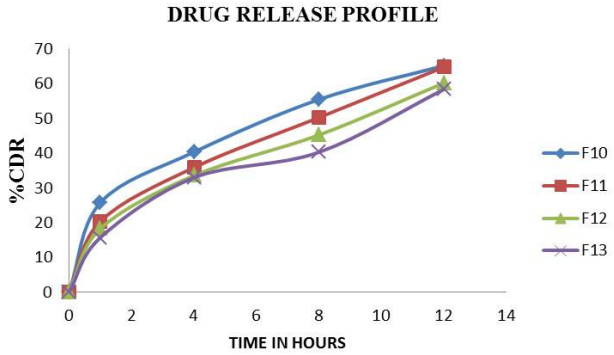

Figure 3: *In-Vitro*Dissolution Profile of F10 to F13 Formulations

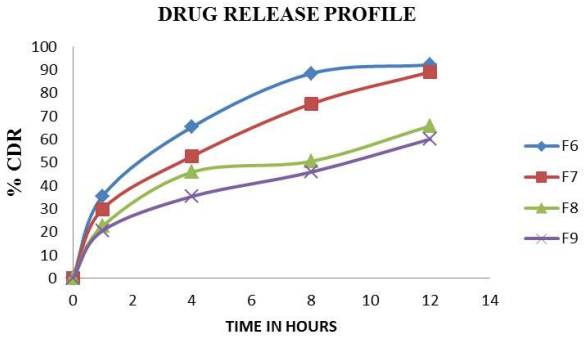

Figure 2: *In-Vitro*Dissolution Profile of F6 to F9 Formulations

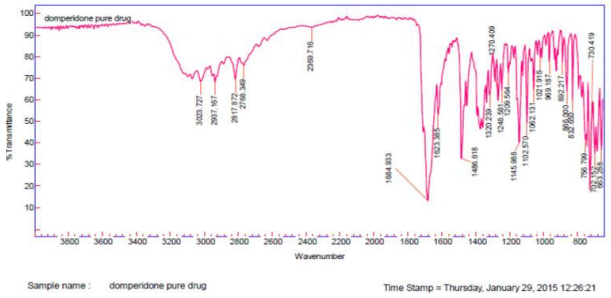

Figure 4: FTIR Spectroscopy of pure drug (Domperidone)

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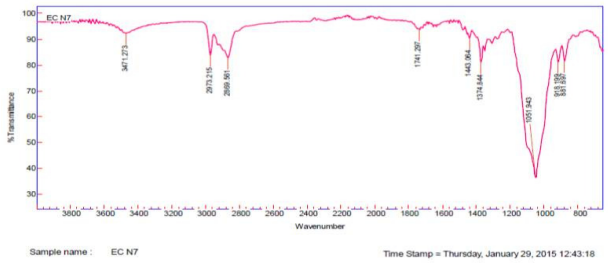

Figure 5: FTIR Spectroscopy of ethyl cellulose N7

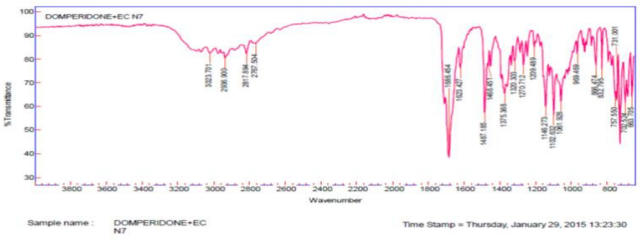

Figure 6: FTIR Spectroscopy of ethyl cellulose N7 + Domperidone

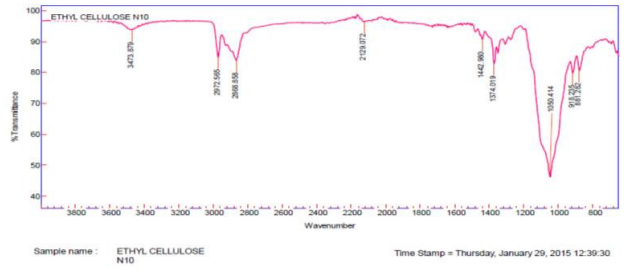

Figure 7: FTIR Spectroscopy of ethyl cellulose N10

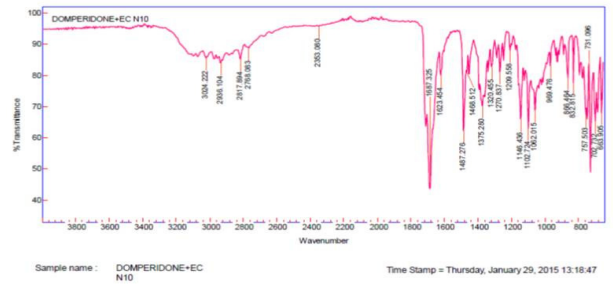

Figure 8: FTIR Spectroscopy of ethyl cellulose N10+ Domperidone

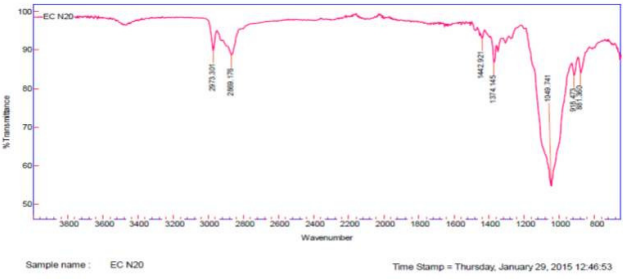

Figure 9: FTIR Spectroscopy of ethyl cellulose N20

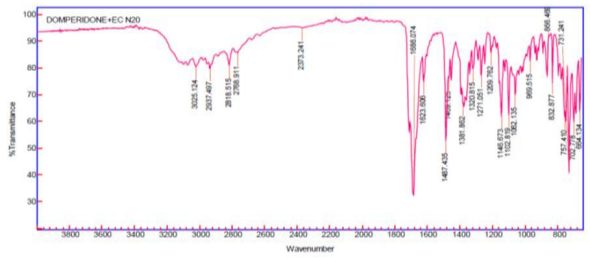

Figure 10: FTIR Spectroscopy of ethyl cellulose N20 + Domperidone

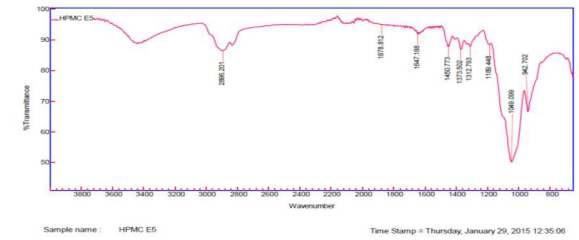

Figure 11: FTIR Spectroscopy of HPMC E5

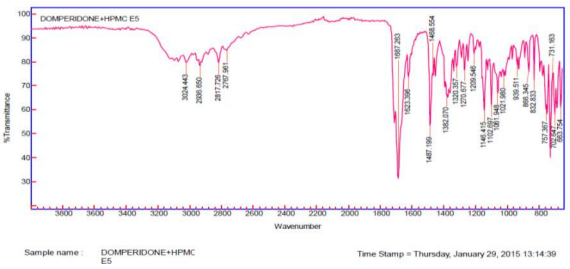

Figure 12: FTIR Spectroscopy of HPMC E5 + Domperidone

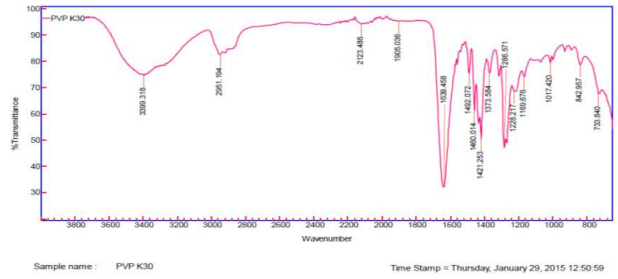

Figure 13: FTIR Spectroscopy of PVP K30

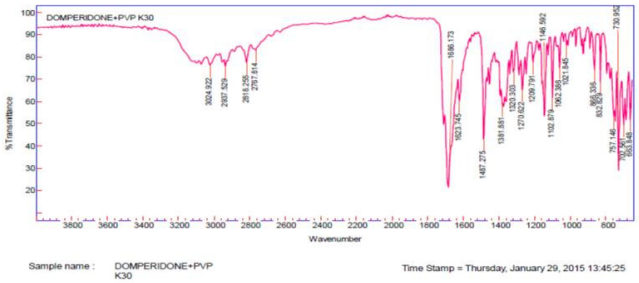

Figure 14: FTIR Spectroscopy of PVP K30 + Domperidone

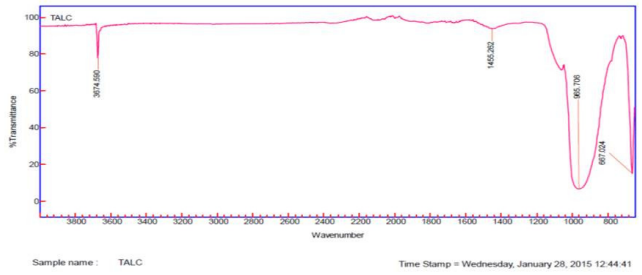

Figure 15: FTIR Spectroscopy of Talc

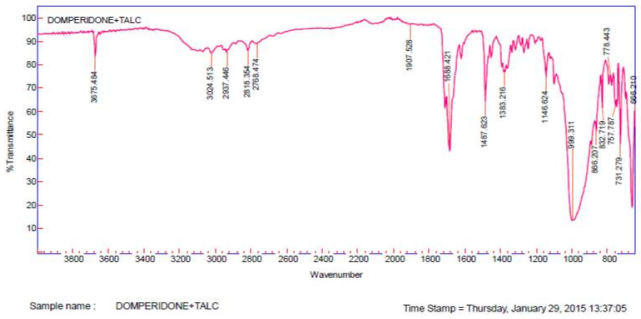

Figure 16: FTIR Spectroscopy of Talc + Domperidone

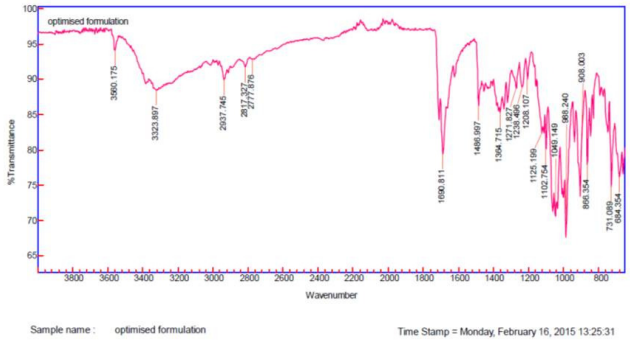

Figure 17: FTIR Spectroscopy of Optimised Formulation F7

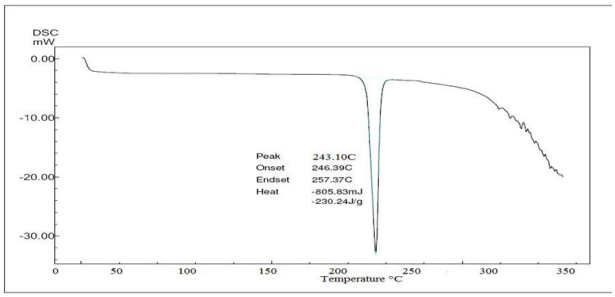

Figure 18: DSC Graph of Pure Drug Domperidone

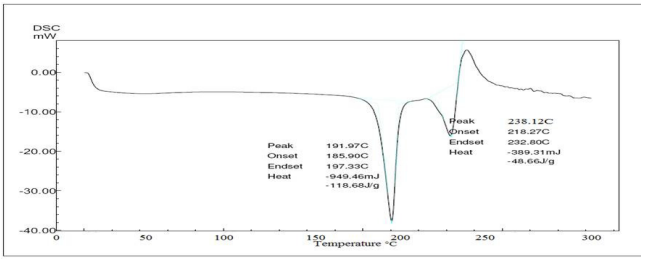

Figure 19: DSC Graph of Domperidone pellet Formulation F7

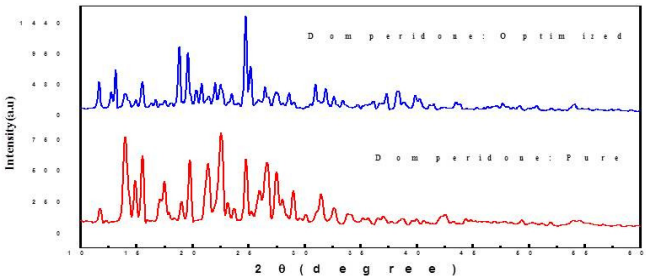

Figure 20: X-RAY Diffraction of Domperidone pure drug and optimised formulation F7

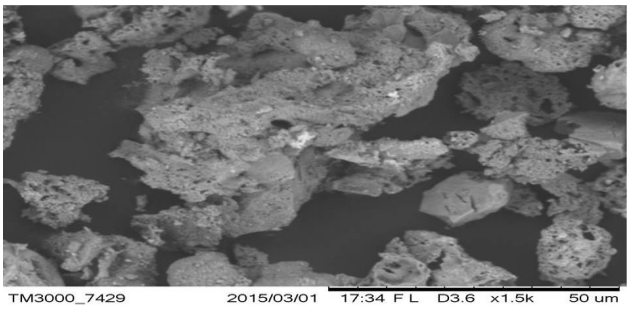

Figure 21: SEM Photograph of Powdered Domperidone pellet Formulation F7 at 2nd Hour

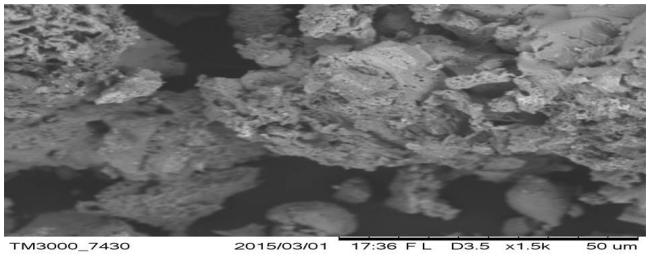

Figure 22: SEM Photograph of Powdered Domperidone pellet Formulation F7 at 6thHour

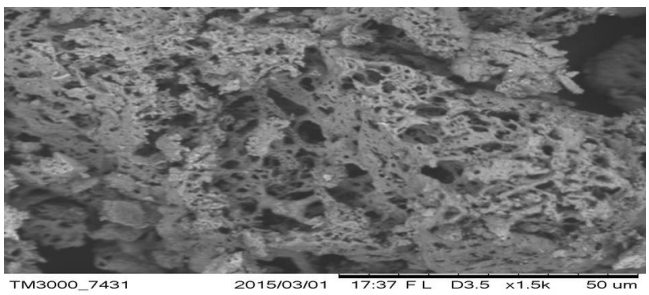

Figure 23: SEM Photograph of Powdered Domperidone pellet Formulation F7 at 12thHour

RESULTS AND DISCUSSION

Domperidone sustained release pellets were prepared by drug layering technology. Non pariel sugar spheres were used to coat the Domperidone. The drug layer was further coated with HPMC E5 at the concentration of 1.5% and finally the spheres were coated with different grades of ethyl cellulose like N10, N7, N20 at different concentrations like 0.5%, 0.75%, 1%, 1.5%. Ethyl cellulose a sustained release polymer was mainly used as coating agent for regulating the drug release from pellets. An attempt was made to optimize the composition of these different grades of ethyl cellulose to achieve the controlled release of drug from the pellets. HPMC E5 was used as a film former in the present investigation. Povidone was used as binder to achieve uniform drug layering in the current research work. Methylene dichloride and diethyl phthalate were used as co-solvent and plasticizer in the present investigation. All the batches of pellet formulations were formulated under identical conditions by maintaining specific process parameters which were given in the table 1, 2. The composition of various pellet formulations from drug loading stage to sustained release stage was given in the table 3, 4, 5.

All the pellet formulations were evaluated for physical and chemical parameters like particle size, friability, assay, moisture content and loss on drying. Particle size of all the batches of pellets was in the range of 1685-1706 microns determined by sieve analysis. The friability loss of the all batches was in the range of 0.2-0.4% and the percentage of drug present in the various formulations was found to be in the range of 99-101%. The moisture content and the loss on drying of all the batches of pellets were in the range of 1.2-1.9 and 0.1-0.2% respectively. All the physical and chemical parameters evaluated for various formulations of pellets were given in table 6. Dissolution studies were performed on all the sustained release pellets by using USP paddle method (Apparatus II). The drug release from the pellet formulations were extended up to 12 hours and were shown in the figure 1, 2, 3. The formulation F7 was found to release 89.14% of drug over extended period of time i.e., up to 12 hours. The drug release rate increased as the concentration of ethyl cellulose N7 polymer increased but up to 0.75% concentration further increase in the concentration of ethyl cellulose N7, the drug release was found to be decreased. The release data was fitted to various mathematical models to evaluate the kinetics and mechanism of drug release. The kinetic data of all formulations F-1 to F-13 could be best expressed by zero order equation as the plots showed highest linearity (R^2: 0.879 to 0.992), than first order release kinetics (R^2: 0.814 to 0.938).The 'n' values obtained from KorsmeyerPeppas plots range from (0.373 to 0.860) indicate that mechanism of release of formulations F-6 to F-10 was Quasi-Fickian diffusion, whereas the mechanism of drug release of formulations F2 to F5 and F11, F12 was Anomalous (non-fickian) diffusion. The mechanism of drug release from the formulation F13 was found to be fickian diffusion. All the *in-vitro* dissolution parameters evaluated for the various batches of pellet formulations were given in the table 7.

FTIR spectrum of Domperidone showed in scan at Figure 4. FTIR spectra of polymers like ethyl cellulose N_7, ethyl cellulose N_{10}, ethyl cellulose N_{20} and excipients like HPMC E5, PVP K30 and talc and physical mixture of drug, polymers and excipients are shown in figures (4-17). The

characteristic peaks of the drug were observed in the spectra of mixture of drug and polymer mixture, however the intensity of the peaks were reduced this might be due to very low concentration of drug in the mixture this indicates that there is no interaction between the drug and polymer mixtures.The FT-IR of pure drug was characterized by N-H stretching at 3122 cm^{-1} and C = O stretching at 1714.60 cm^{-1}, indicating the presence of –CONH group, asymmetric C-H stretching at 2937.38 cm^{-1}, symmetric C-H stretching at 2817.81 cm^{-1}, N-H deformation at 1693.38 cm^{-1}, aromatic C-H stretching at 3024.18 cm^{-1} and C = C at 1622.02 cm^{-1} shown in the Figure 4. FTIR Characterization of optimized formulation is shown in Figure 17. The peaks observed at 2973.74 cm^{-1} reveals asymmetric C-H stretching and peak observed at 2817.32 cm^{-1} reveals symmetric C-H stretching and peak observed at 1690.81cm^{-1} reveals C=C stretching.In all the mixtures of Domperidone with polymers and excipients the prominent and characteristics peaks of Domperidone are appeared indicating intactness of drug in mixtures. Hence these release retarding materials were selected for formulation of sustained release pellets. The DSC thermogram for Domperidone was observed at 243.10^{0}C and the melting peak of optimized formulation is at 238.12^{0}C was observed in the Figure 18 and 19 respectively. Change in temperature is due to various concentrations of drug and other excipients in physical mixture. This shows that there is no interaction between drug and optimized formulation. DSC studies revealed that there was no much shift in the melting point of the drug in the physical mixture compared to the pure drug; this indicates that there is no interaction between drug and other excipients. The diffraction spectrum of Domperidone pure drug and optimised formulation is shown in the Figure 20 which indicates the nature of Domperidone drug and the compatability of Domperidone and the excipients.

The diffraction of Domperidone pure drug was found at intensity of 750 a.u. whereas the diffraction of the optimised formulation was found to be increased to 1440 a.u. The increased in intensity of the optimised formulation is due to the various concentration of drug and other excipients in physical mixture. The intensity of pure Domperidone drug and the optimised formulation has changed but lies in the almost same plane. This shows that there is no interaction between drug and optimized formulation. XRD studies revealed that Domperidone is crystalline in nature as the XRD peak of Domperidone is sharp. SEM analysis was performed for the powdered pellets prepared by drug layering technique. From the SEM images it was observed that the prepared pellets were having wide pores on its surface. The SEM images of powdered Domperidone pellets taken at 2nd 6th and 12th hours were shown in the figure 21, 22, 23. The stability studies indicated that there was no visible and physical changes observed in the pellets after storage. Stability studies were carried out on selected formulation F-7 as per ICH guidelines. There was not much variation in the integrity of the pellets at all the temperature conditions. There was no significant changes in drug content , physical stability, moisture content, friability, and drug releasefor the selected formulation F-7 after 90 days at 25^{o}C± 2^{0}C / 60% ± 5% RH, 30^{0}C ± 2^{0}C / 65% ±5% RH and 40^{0}C ± 20 / 75% ± 5% RH.

Conclusion

The multiunit dosage form, pellets that were formulated by drug layering technique showed optimized sustained release of the drug Domperidone for extending the drug release for a prolonged period of time. Drug loaded pellets were coated with different grades of ethyl cellulose like N10, N7 and N20. The pellets gave a more controlled fashion of drug release than sustained matrix formulations

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