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Formulation Development and Evaluation of Domperidone Sustained Release Matrix Tablets by Two Different Methods Using Guar Gum as a Sustaining Agent

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ABSTRACT: The aim of this study was to develop and evaluate sustained release matrix tablets of domperidone using natural gum (guar gum) as a sustaining agent in different drug to polymer ratios and prepared by two different techniques i.e. by wet granulation and solvent evaporation method and evaluating the effect on drug release profile by changing the preparation technique. Guar gum is a natural polymer and used along with other excipients to develop a formulation which enhance and prolong the anti-emetic effect of domperidone matrix tablets as these polymers are easily available and more effective than other synthetic retarding agent by forming a thick gel layer on exposure to water. Domperidone is an anti emetic agent and used in the treatment of upper GIT motility by antagonistic effect on D2 receptors at CTZ, after oral administration it is eliminated from the body after few hours due to its short half life. To enhance the patient compliance and to reduce the frequency of drug administration various formulations were prepared using guar gum as a sustaining agent. Formulation F.W.G.G3 prepared by wet granulation method in which the drug to polymer ratio was 1:2 showed a prolonged effect up to 20 hours. Similarly formulations F.C.G.G3 prepared by solvent evaporation technique prolong the effect more than 18 hours which shows that the sustaining effect of the guar gum was directly proportional to the concentration of the polymer used. It was also experienced that by changing the method of preparation from wet granulation to solvent evaporation the drug release becomes constant and no fluctuation was observed as compared to wet granulation method the drug release pattern shows little bit fluctuation due to uneven distribution of the drug and polymer. Different models for kinetic study were applied like zero order, first order, Higuchi, Hixson Crowell and Korsmeyer to study the release pattern and mechanism.

Key words: Sustained Release Matrix Tablets · Domperidone · Guar Gum · Wet Granulation Technique · Solvent Evaporation Technique

INTRODUCTION

Sustained release (SR) oral drug delivery systems are useful for maintaining optimal concentration of drugs having narrow therapeutic range and short half life. In sustained release matrix tablets plasma drug levels are achieved by immediate release of initial dose which is then sustained by maintenance dose for a predetermined time. Sustained release matrix tablets are commonly prepared to prolong the effect of the drug, decrease the frequency and to enhance patient compliance and clinical efficacy. The main objective of designing sustained release oral drug delivery system is to prolong the drug release from the dosage form for several hours and to achieve and maintain constant blood level. The drugs having short elimination half life prepared by conventional method needs frequent intervals to maintain blood concentration within therapeutic range which is in most cases responsible for patient non compliance as well as increases side effects [1].

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Hydrophilic matrix systems are frequently used for sustained release oral drug delivery system because they are easy to manufacture, cost effective and decreased the chances of systemic toxicity [2].Drug release from matrix systems using natural gums involves various process to release the drug, like fluid penetration, gel formation, diffusion of drug from the thick gel, nature and concentration of the polymer used and erosion of the layer [3,4].

Nowadays natural gums and especially the polysaccharide gums are the prime focus of the formulation developers and preferred over synthetic polymers because they are easily available, biodegradable and shows least immunogenic and biocompatibility [5,6].

Guar gum is a hydrophilic natural gum. Guar gum is also known as guran, an endosperm of guar beans. Guar gum is a polysaccharide having high molecular weight and can be used as a sustaining material in the development of sustained release matrix tablets. Guar gum prolonged the drug release from matrix tablets by forming a thick gel layer on exposure to aqueous medium and the drug release from the thick matrix is either by diffusion or by erosion of the matrix [7,8].

Domperidone shows gastro prokinetic and anti-emetic activity and used in the management of upper GIT motility and gastro paresis by blocking Dopamine (D_2) receptors at chemoreceptor trigger zone in postrema and also at the gastric region [9].

Domperidone when administered as conventional tablet dosage form, its onset of action is about 30 minutes and the drug produces its effect for 4-7 hours. Drug release studies of these immediate release tablet dosage forms in healthy subjects that Domperidone were not measurable in blood after few hours of oral administration and eliminated in 5-7 hours from the body [10].

The aim of our study was to prepare sustained release domperidone matrix tablets using natural polymer like guar gum to reduce the frequency of conventional dosage form, side effects. Comparative study of all the formulations prepared by two different methods i.e. by wet granulation method and solvent evaporation method and also the effect of concentration of polymers used on release kinetics for the matrix tablet.

MATERIALS AND METHODS

Materials: Domperidone was purchased from Polyfine Pharma. Pvt. Ltd. Peshawar, Pakistan, Guar gum was purchased from Hizat Pharma. Pvt. Ltd. Peshawar, Pakistan, Lactose (The Lactose Newzeland Company, Newzeland), Talc, Magnesium Stearate, ethanol were gifted from Sarhad University of Science and Information Technology, Peshawar, Pakistan. All other materials used were of analytical grade and used as received.

Equipments: Oscillating granulator (F. D & C Karachi, Pakistan), Rotary evaporator (Heidolph, Germany), EZ stirrer, ZP19 Rotary Tablet Press (STC, Shanghi, China), Tablet Hardness Tester (Pharma tester, Germany), Dissolution test Apparatus, Friabilator (Erweka, Germany), UV/Visible spectrophotometer (Model No: CT 06484-4794.U.S.A.Perkin Elmer) was used in this study.

METHODOLOGY: Before compression, granules were prepared by two different methods i.e. by wet granulation and by solvent evaporation technique which is as follows Preparation of Granules

I) By Wet Granulation Method: Various formulations were prepared of Domperidone matrix tablets by wet granulation technique as shown in the table 1. The active ingredient (Domperidone), bio-polymer (Guar gum), diluents and fillers except lubricants and glidents were mixed properly in a laboratory scale ribbon mixer for 15 minutes after passing them through a suitable mesh until a uniform mixture was obtained. Then water was slowly added at a steady rate to the blended material and mixed well to get a uniform wet mass, that was passed through mesh number 8 using an oscillating granulator and dried in a tray dryer at 45-60 ^{0}C for 1 hour. The dried granules were then passed through the oscillating granulator equipped with mesh number 12. The dried granules were lubricated with magnesium Sterate and talcum by mixing in a polythene bag.

ii) by Solvent Evaporation Method: Various formulations of Domperidone co-evaporates were prepared by the solvent evaporation method with different ratios of sustaining materials as shown in various formulations in table 1. In this method the Domperidone was dissolved in organic solvent (isopropyl alcohol) using EZ Stirrer. Then the drug solution was added in the form of thin stream to the polymer solution with continuous stirring using the same stirrer. The entire solvent was completely evaporated under reduced pressure, at 40 °C using Rota vapor (Heidolph, Germany) with solvent recovery. The recovered solvent was used for next batch. The solid dispersion so obtained was dried at 60 °C in oven for 24 hours. The dried material obtained was passed through mesh #. 12, then talc and magnesium sterate were added as glident and lubricant respectively, lactose was added as diluent and mixed in lab scale mixer for 5 minutes.

Co-evaporates were evaluated for different physical properties like angle of repose, lose bulk density, taped bulk density, compressibility Index and content of active ingredients.

Preparation of Tablets: Finally, granules and co-evaporates were compressed at a compression force of 6500-7500 Newton by ZP 19 Rotary tablet compression machine using 6.0 mm diameter, beveled edge punches.

Evaluation of Physical Properties: Different tests have been followed for the evaluation of physical properties of granules and co-evaporates like angle of repose, bulk density, compressibility index and drug content was determined, similarly for matrix tablets twenty tablets from each formulation were selected randomly and hardness, friability, weight variation, thickness and content of uniformity were determined by fulfilling all the official parameters which are represented in table 2. [11-13].

***In vitro* Drug Release Study:** The drug release characteristics of Domperidone sustained release matrix tablets were determined according to official method by using type II dissolution apparatus (paddle type) in which HCl Buffer of pH 1.2 for first two hours and phosphate buffer pH 6.8 for remaining time at a rotation speed of 100 rpm and a temperature of the bath was maintained at 37.0± 0.5°C. The volume of the dissolution medium were kept 900 ml and after a specified period of time 5ml of sample were taken and filtered, after filtration diluted with 50 ml of dissolution medium than analyzed quickly in UV double beam spectrophotometer at 285 nm. After each withdrawal same amount of dissolution medium was added to maintain the volume of the bath up to 900ml and continued the process further with same procedure [14,15].

Drug Release Kinetic Study: The release kinetics of the drug was studied by putting the data obtained from the *in vitro* drug release in various models like:

***Zero Order* ($Qt = k_0 t$):** The zero-order kinetic explains the system as a one in which the drug-release rate is independent of its concentration. It is the cumulative amount of drug release vs. time and mathematically it is represented as $Qt = k_0 t$. where, Qt is the amount of drug release at time t, k_0 is the zero order rate constant an t is time in hours [16,17].

***First Order* (log Q=log Q_0 - kt/2.303):** According to first-order rate of drug release is dependent on the concentration. First order equation represents log cumulative percentage of drug remaining vs. time and mathematically it is written as log Q=log Q_0 - kt/2.303. Where, k *is the first order rate constant,* Q_0 is the initial concentration of the drug and t is time in hours [16,17].

***Higuchi Equation* ($Qt = K t^{1/2}$):** Higuchi model describes release of drugs from an insoluble matrix as a square root of time dependent process based on Fickian diffusion. Higuchi model is the cumulative % drug release vs. square root of time and its equation can be written as $Qt = K t^{1/2}$ Where K is the diffusion rate constant Qt is the amount of drug released at time t and t is the time in hours [16,17].

***Hixson Crowell Cube Root Law* ($W_0^{1/3} - W_t^{1/3t} = Kh_c t$):** The Hixson-Crowell cube root law explains the drug release from dosage form in which there is a change in the surface area and the diameter of the particles present in the tablet. This model shows the cube root of drug % remaining in matrix vs. time and its equation is represented as $W_0^{1/3} - W_t^{1/3t} = Kh_c t$. where Kh_c is the Hixson Crowell rate constant, W_t is the amount of drug released at time t and W_0 is the initial concentration of drug in the tablet [16,17].

***Korsmeyer and Peppas Equation* (Log (Q t / Q f) = Log k + n Log t):** Korsmeyer model shows a simple relationship between log cumulative % drug release vs. log time and mechanism of drug release was also described by a simple equation that $Mt / M8 = K t^n$. Where K is the rate constant, $Mt / M8$ is the amount of drug released at time interval t and n value determine the mechanism of drug release as shown in the table [16, 17].

RESULTS AND DISCUSION

Sustained release matrix tablets of domperidone using guar gum was prepared by incorporating drug, sustaining agent and other excipients in different ratios and hence six different formulations were prepared as shown in table 1. Three formulations were prepared by wet granulation method and other three formulations were prepared by solvent evaporation method. All these formulations were than treated with different official test to check the physicochemical properties of these matrix tablet formulations. After the preparation of granules and co-evaporates angle of repose, loose and tapped bulked

Table 1: Composition of 30 mg Domperidone matrix tablets in which each formulation drug to polymer ratio is represented as: F.W.G.G1= guar gum (1:1) by wet granulation, F.W.G.G2=guar gum (1:1.5) by wet granulation, F.W.G.G3=guar gum (1:2) by wet granulation. F.C.G.G1= guar gum (1:1) by solvent evaporation, F.C.G.G2=guar gum (1:1.5) by solvent evaporation, F.C.G.G3=guar gum (1:2) by solvent evaporation.

S.No	Formulation Code	Lactose (mg)	Guar gum (mg)	Magnesium Sterate (mg)	Talcum (mg)
			(By Wet Granulation Technique)		
1	F.W.G.G1	60.5	30	3.0	1.5
2	F.W.G.G2	45.5	45	3.0	1.5
3	F.W.G.G3	30.5	60	3.0	1.5
			(By Solvent Evaporation Technique)		
4	F.C.G.G1	60.5	30	3.0	1.5
5	F.C.G.G2	45.5	45	3.0	1.5
6	F.C.G.G3	30.5	60	3.0	1.5

Table2: Physicochemical properties of granules (Mean±SD)

	Formulations(by Wet granulation)		
Physicochemical Properties (Granules)	F.W.G.G1	F.W.G.G2	F.W.G.G3
Angle of Repose	24.53±0.7	26.96±0.7	25.81±0.8
Loose bulk density(LBD g/ml)	0.50±0.01	0.51±0.01	0.52±0.01
Tapped bulk density (TBD g/ml)	0.518±.02	0.553±.02	0.572±.03
Compressibility index (%)	12.37±0.5	11.56±0.4	10.44±0.5
Drug content (%)	98.6±2.8	99.1±2.7	98.8±2.6
	Formulations (by Solvent evaporation)		
Physicochemical Properties (Granules)	F.C.G.G1	F.C.G.G2	F.C.G.G3
Angle of Repose	25.03±0.6	27.36±0.7	27.90±0.8
Loose bulk density(LBD g/ml)	0.51±0.02	0.53±0.01	0.55±0.01
Tapped bulk density (TBD g/ml)	0.522±.02	0.571±.02	0.583±.03
Compressibility index (%)	12.10±0.4	11.01±0.5	10.24±0.5
Drug content (%)	98.8±2.7	98.97±2.5	99.55±2.6

densities, compressibility index and drug content were determined and all were in official limits and were acceptable as shown in table 2. Angle of repose of the granules prepared with all formulations was between 24.53±0.7 to 26.96±0.7 while for solvent evaporation it ranges from 25.03± 0.6 to 27.90± 0.8 that indicates good flowability [18]. The compressibility index values were in the range of 10.44 ± 0.5 % to 12.37 ± 0.5% for all the formulations prepared by wet granulation method and it ranges from 10.24 ± 0.5 to 12.10 ± 0.4 for formulations prepared by solvent evaporation method, thus predict good flow characteristics. The drug content in the granules and co-evaporates was between 98.60 ± 2.8 % to 99.55 ± 2.6% it indicates the uniform distribution of drug. Granulation is a basic process which play a very important role in manufacturing of many dosage forms such as controlled release of a drug from coated or matrix-type particles. Physical properties of granules such as surface area, shape, hardness, surface characteristics and size can directly affect the dissolution rate of drugs contained in the dosage forms [19].

Similarly after the preparation of tablets, randomly selected samples from all the formulations were tested for hardness, friability, thickness and weight variation according to official procedure. The thickness of the tablets was in the range of 2.99 ±.026 to 3.15±.024 mm for formulations prepared by wet granulation method while 2.03 ±.024 to 2.09±.024 mm was found for the tablet formulations prepared by solvent evaporation method. In a weight variation test, the average percentage deviation of all batches was found to be within the range as per official requirements of USP 32 as shown in table 3. The drug content in the tablet was between 98.1 ± 2.0% to 99.2 ± 2.4% it indicates the uniform distribution of drug in tablets. Formulations prepared by wet granulation method showed hardness for matrix tablets in the range of 83.45±1.2 to 86.25±1.2 Newton while for formulations prepared by solvent evaporation it ranges from 84.12±1.1 to 87.21±1.3 Newton and the percent friability for all the formulations was in the range of 0.40±0.04% to 0.49 + 0.04%, showing that the tablets have good physical properties [20].

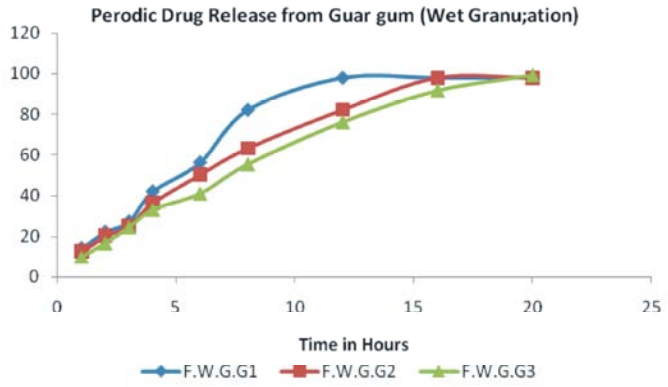

Fig. 1: Cumulative percentage (mean±SD) of Domperidone released from SR matrix tablets using Guar gum by wet granulation

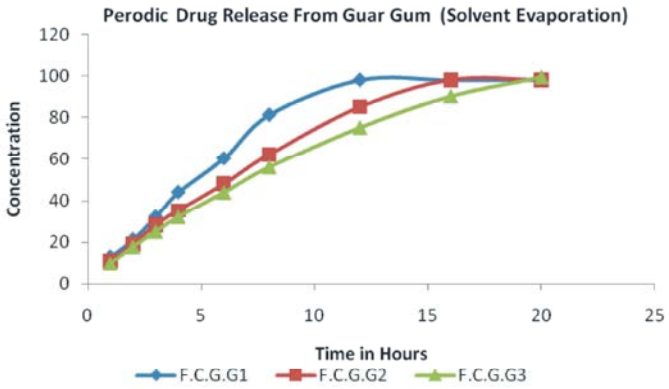

Fig. 2: Cumulative percentage (mean±SD) of Domperidone released from SR matrix tablets using Guar gum by solvent evaporation

***In vitro* Drug Release Studies:** Figure 1 represents the drug release pattern of six different formulations in which guar gum was used as a retarding material in different proportions that is drug to polymer ratio 1:1, 1:1.5. 1:2. The formulation F.W.G.G1 releases 27.17 % in first three hours, 56.22 % after 6 hours and 98 % upto12 hours. Whereas formulation F.W.G.G2 releases 25.07% in first three hours, 50.23% after 6 hours, 82.2% after 12 hours and 99% upto16 hours. Similarly the F.W.G.G3 formulation releases 24.53%, 40.97% and 76.22% in 3, 6 and 12 hours respectively and retards the release up to 20 hours as shown in the Figure 1. Generally as the concentration of the gums were increases the release rate was decreased in all the cases as shown.

Similarly the formulation F.C.G.G1 releases 32.09% in first three hours, 60.31% after 6 hours and 98% upto12 hours. Whereas formulation F.C.G.G2 releases 28.22% in first three hours, 48.03% after 6 hours, 85.00% after 12 hours and 98% upto16 hours. Similarly the F.C.G.G3 formulation releases 25.16%, 44.03% and 75.11% in 3, 6 and 12 hours respectively and retards the release up to 20 hours as shown in the Figure2.

The release of drug not only depends upon the nature of matrix but also depends upon the drug polymer ratio. As the percentage of polymer in a formulation was increased, the release rate was decreased. This might be due to structural reorganization of hydrophilic polymer. Increase in concentration of the polymer might result in increase in the tortuosity or gel layer of the polymer. When bio-polymers exposed to aqueous medium, it undergoes rapid hydration and chain relaxation to form viscous gelatinous layer (gel layer). So the reason was that as the amount of gum in the matrix was increased there would be high degree of gum hydration with simultaneous swelling this would result in a corresponding lengthening of the drug diffusion pathway and decrease in drug release rate[21].

Drug Release Kinetics: In order to study the release kinetics the data obtained from *in vitro* drug release profile were plotted in various models using regression coefficient analysis [22] as shown in Table 6. The cumulative amount of drug release from the matrix tablets of all the formulations at different intervals of time was

plotted according to zero-order, first order, Higuchi model, Hixson-Crowell model and the Korsmeyer model in order to scrutinize the release mechanism of the drug from different formulations. Higher correlation coefficient were found when the data was fitted to zero-order kinetics (R^2: 0.9717-0.9818), as compared to first order kinetics (R^2: 0.8194-0.8893), which indicates that the drug release from all the formulations followed zero-order kinetics as shown in table 6. Release of the drug from the matrix tablets formulations containing hydrophilic polymers/ gums usually involves the factors of diffusion. Diffusion is the movement of the drug from the matrix to the release medium, which depends on the concentration. According to Higuchi when the drug is released from the matrix, the distance for diffusion increases and the rate of drug release decreases [23]. The dissolution profiles of drug from all the formulations could be expressed by Higuchi's model, as the plots also showed linearity with regression values (R^2: 0.9700 to 0.9966),But this model also fail to explain the release mechanism of the drug from the matrix tablets because of swelling upon hydration along with gradual erosion of the matrix tablets. If the data is plotted according to Hixson-Crowell model the regression values R^2 was found in the range of 0.9703 to 0.9820.

In order to explain the release exponent for all the formulation of matrix tablet, the log value of percent drug dissolved was plotted vs. log time for each batch of formulations according to the Korsmeyer equation. The correlation coefficient values showed higher linearity in all group of formulations (R^2: 0.9810to 0.9976). As the value of $n = 0.5$ indicates Fickian (case I) release; $0.5 < n < 1$ for non-Fickian (anomalous) release; and 1.0 indicates super case II type of release. Case II generally refers to the erosion of the polymeric chain and anomalous transport (Non-Fickian) refers to a combination of both diffusion and erosion controlled-drug release [24]. As shown in the Table 6, the (n) values for all the formulations were from 0.7714to 0.8557 which were less than 0.89 and more than 0.45 it means that all the formulations followed non-Fickian release mechanism ($0.5 < n < 1$), which shows a coupling of diffusion and erosion mechanism of drug release- so called anomalous diffusion. The relative complexity of these formulations and their components may show that the release of drug was controlled by more than one process. Therefore, diffusion along with erosion may be the mechanism of drug release from these formulations [25].

Comparative Studies of Wet Granulation Method Versus Solvent Evaporation Method for Domperidone Matrix Tablets: For the comparison studies of both wet granulation method and solvent evaporation method the evaluation of various physical properties of granules and tablets were carried out by comparing the physical data obtained from granules and tablets prepared by both of these methods. It was observed that there was a slight difference among the various parameters that ultimately affect the drug release kinetics.

The lose bulk density and taped bulk density values obtained from solvent evaporation method were slightly greater than the values obtained from wet granulation method as given in their respective tables. Similarly the values for angle of repose were also found slightly higher as shown in Table 2.

Table 3: Physicochemical properties of Tablets (Mean±SD, n=20)

	Formulations (by Wet Granulation)		
Physicochemical properties (Tablets)	F.W.G.G1	F.W.G.G2	F.W.G.G3
Thickness (mm)	3.01±.025	2.99±.026	3.15±.024
Weight (mg)	125.15	124.94	126.0
Friability (%)	0.49±0.04	0.45±0.03	0.42±0.03
Hardness (N)	83.45±1.2	84.10±1.4	86.25±1.2
Drug content (%)	98.4±2.6	99.2±2.4	98.5±2.1
	Formulations (by Solvent Evaporation)		
Physicochemical properties (Tablets)	F.C.G.G1	F.C.G.G2	F.C.G.G3
Thickness (mm)	2.03±.024	2.09±.025	2.09±.024
Weight (mg)	126.26	126.65	126.24
Friability (%)	0.46±0.03	0.42±0.04	0.40±0.04
Hardness (N)	84.12±1.1	85.08±1.3	87.21±1.3
Drug content (%)	98.2±2.4	99.0±2.1	98.1±2.0

Table 4: Diffusion exponent and drug release mechanism by Korsmeyer

Diffusion exponent (n)	Overall drug release mechanism
0.45	Fickian diffusion
0.45 < n < 0.89	Anomalous(non-Fickian) diffusion
0.89	Case-II transport
n > 0.89	Super case-II transport

Table 5: Comparative % drug release from various formulations of Domperidone matrix tablets

	Formulations (by Wet Granulation)			Formulations (by Solvent Evaporation)		
Time (hr)	F.W.G.G1	F.W.G.G2	F.W.G.G3	F.C.G.G1	F.C.G.G2	F.C.G.G3
1	14.2677	12.4724	10.0472	12.97638	10.92913	9.984252
2	22.1102	20.2205	16.9449	21.25984	19.27559	17.88976
3	27.1811	25.0709	24.5354	32.09449	28.22047	25.16535
4	41.8583	36.2835	33.0394	44.06299	35.33858	32.09449
6	56.2205	50.2362	40.9764	60.31496	48.0315	44.0315
8	82.1417	63.3071	55.4646	81.22835	62.23622	56.09449
12	98.0157	82.2677	76.2205	98.01575	85.00787	75.11811
16	98.0157	98.0787	91.7795	98.01575	98.07874	90.11024
20	98.0157	98.0787	99.3701	98.01575	98.07874	99.37008

Table 6: Mathematical modeling and assessment of release kinetics of various formulations of domperidone

	Zero Order	First Order	Higuchi	Hixson Crowell	Korsmeyer		
Formulation By	----------	----------	--------	----------	----------		
wet Granulation	R^2	R^2	R^2	R^2	R^2	n	Drug Release Mechanism
F.W.G.G1	0.9717	0.8893	0.9700	0.9703	0.9810	0.8245	Non-Fickian
F.W.G.G2	0.9804	0.854	0.9928	0.9735	0.9938	0.7714	Non-Fickian
F.W.G.G3	0.9742	0.8281	0.9924	0.9777	0.9956	0.7875	Non-Fickian
	Zero Order	First Order	Higuchi	Hixson Crowell	Korsmeyer		
Formulation By	----------	----------	--------	----------	----------		
Solvent evaporation	R^2	R^2	R^2	R^2	R^2	n	Drug Release Mechanism
F.C.G.G1	0.9718	0.8497	0.9878	0.9820	0.9927	0.8557	Non-Fickian
F.C.G.G2	0.9818	0.837	0.9942	0.9792	0.9976	0.8053	Non-Fickian
F.C.G.G3	0.9747	0.8194	0.9966	0.9731	0.9964	0.7786	Non-Fickian

Whereas by comparing the hardness of the tablets prepared by these two methods it was seemed that the hardness of the tablets prepared by solvent evaporation method were greater than the tablets prepared by wet granulation method, whereas the friability of the tablets by wet granulation method were greater as compared to the tablets prepared by solvent evaporation method as shown in Table 3, which may be due to the high binding forces between the molecules of drug and polymers because in solvent evaporation method both the drug and polymers are dissolve in the solution forms in one solvent or in separate solvents and then incorporated due to which both the drug and polymer combine together at the molecular level, while in case of wet granulation method the drug and the polymer are mixed which give a physical mixture that have no capacity to comes in contact at the molecular level this was the reason that the matrix tablets prepared by solvent evaporation method shows high densities, angle of repose, greater hardness and low friability values as compared to wet granulation method. However, it was observed that by changing the method of preparation the drug contents in both the granules and tablets and similarly the thickness and weight of the tablets were approximately the same as shown in Tables 2 and 3.

Comparison of drug release from the matrix tablets prepared by both of the methods was carried out and generally it was observed that the release pattern from the formulations prepared by wet granulation method show slight fluctuation and showed an irregular release pattern, while the formulations prepared by solvent evaporation method show uniform release pattern as shown in Table 5. Details of the drug release offered by various formulations are discussed below.

By comparing the drug release study from the tablet prepared by these two different methods it was observed that there was a slight fluctuation in the release pattern for formulation prepared by wet granulation technique. In case of tablets using guar gum as a sustaining material by comparing the drug release, the formulations F.W.G.G2 and F.W.G.G3 shows uneven release pattern as showed in Figure 1, whereas constant release pattern was seen in the formulations containing the same drug to polymer ratio prepared by solvent evaporation method as depicted in Figure 2.

Similarly by comparing the Figures 1 and 2 it is cleared that all the formulations prepared by solvent evaporation method showed constant release where as formulations prepared by wet granulation method showed little fluctuation or uneven release pattern.

CONCLUSION

From the present study it is concluded that guar gum is a suitable candidates for sustaining the drug release from matrix tablets and among various formulations prepared it was cleared that as the polymer concentration increases the drug release was retarded and formulation in which the drug to polymer ratio was 1:2 retards the drug release more than 20 hours and can be used as sustained release domperidone matrix tablet once a day. So in the light of the above discussion it was confirmed that there was a difference in physical parameters of the granules and tablets and all these parameters such as loose bulk density, taped bulk density, angle of repose, hardness and friability that have direct effect on the release rate of the drug form matrix tablets and it is recommended that as from the results of all the formulations prepared by solvent evaporation technique shows constant release throughout whereas drug release from the formulations prepared by wet granulation method shows fluctuation in majority of the cases and produced uneven release pattern therefore for constant release to achieve steady state concentration in blood, solvent evaporation method may be preferred over wet granulation method.

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