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Development and *in Vitro* Evaluation of Paliperidone Floating Tablets Using Natural Polymers

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KEYWORDS

Paliperidone;

Gaurgum,

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and

Floating drug delivery system

ABSTRACT

Aim: the aim of the present study was formulation and evaluation of the floating tablets of Paliperidone with natural polymers

Method: The floating drug delivery system of Paliperidone tablets were prepared by direct physical compression method using Guar Gum and Xanthan gum as Natural polymers and Sodium bicarbonates as a gas generating agent. All the formulations were evaluated for physicochemical parameters, *in vitro* buoyancy, drug content, in vitro dissolution, Kinetic models, drug stability studies.

Results: the results were found within the limits for all formulations. Among all the formulation F4 showed the better buoyancy, drug release profiles. The release of drug from the prepared formulations (F4) was found to follows Higuchi kinetics., and it was more stable at various storage conditions.

Conclusion: Paliperidone floating tablets were successfully developed by natural polymers and was stable for three months.

Introduction

The drug delivery system of oral route has been widely used routes of drug administrations. This is well known and easy administration [1]. The method of Gastro retentive system of drug delivery (GRDDS), is the system in which the tablet is going to be long time retained and more absorbed in the stomach, so that we can enhance the bioavailability of drugs [2].

There are many methods has been used to prolonging the drug retentions in stomach, which includes floating systems [3], muco-adhesive systems [4], magnetic systems [5] and swelling system [6], high density-systems [7-8].

Paliperidone is a atypical antipsychotic agent and is used for the treatment of schizophrenia disease and schizoaffective disorder. But the problem occurred with this drug is low oral bioavailability. Paliperidone is degraded by the cytochrome P450-3A4 (CYP3A4) [9] and this drug was not stable in alkaline condition [10]. Paliperidone solubility is more at low acidic pH and less soluble in basic pH [11]. Tshis drug shows its primary absorption in stomach [12-15] and it has a short t1/2 (3-5 hr). So that Paliperidone is a suitable drug in this study.

MATERIAL AND METHODOLOGY

Paliperidone was purchased from MSN Laboratory, India. Xanthan gum, Guar gum were received from Parag Fine Organics, Mumbai¸India. Crospovidone, PVP k-30, Sod. bicarbonate, Mg.stearate, Dicalcium phosphate are obtained from S.D. Fine-Chemicals, India.

Formulation development of Paliperidone floating tablets: take the required quantity of drug Paliperidone and other excipients then passed individually by using sieve no ≠ 40. The ingredients were thoroughly mixed by triturating method and with a suitable lubricant as talc powder up to the time of 15 min. The tablets are made by direct physical compression method was adopted, using with 6mm punch. The different formulation compositions were shown in table 1.

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Table 1: Composition of the Paliperidone floating tablets.

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Paliperidone	6	6	6	6	6	6	6	6	6	6
Guar gum	20	30	40	50	60	-	-	-	-	-
Xanthan gum	-	-	-	-	-	20	30	40	50	60
$NaHCO_3$	20	20	20	20	20	20	20	20	20	20
DCP	60	50	40	30	20	60	50	40	30	20
Crospovidone	30	30	30	30	30	30	30	30	30	30
Mg.Stearate	4	4	4	4	4	4	4	4	4	4
PVP K-30	10	10	10	10	10	10	10	10	10	10
Total tablet weight (mg)	150	150	150	150	150	150	150	150	150	150

The drug compatibility study (Drug-and Excipient): The studies of drug excipient compatibility were conducted using with Calorimetry of Differential Scanning (DSC) analysis. The DSC grams are determined for pure drug and for drug with other excipients.

Physico-chemical properties Evaluations: The developed tablets were subjected for *in vitro* characterization which includes variations of weight, hardness, thickness, friability, stability study, in *vitro* drug release studies, *studies of* Floating Lag Time (FLT) and Total Floating Time (TFT).

To study the weight variation: In this study, taken the twenty tablets and determined the individual weights and weights of collectively on a digital weighing balance. The mean and deviations were calculated.

Hardness test: The tablets hardness is determined by using with Monsanto hardness tester. Mean and SD were determined.

Thickness: Take randomly selected ten tablets and calculated the tablets thickness with the help of vernier calipers..

Friability: This test was conducted by using Roche friabilator. Taken and weighed the 10 tablets randomly and placed in the friabilator apparatus, during the friabilation it rotates hundred totetions (25 rpm /4 min), So the tablets were re-weighed with dedusted and to calculate the weight of tablets after friability test.

Assay: Assay procedure: randomly collected **t**en tablets weighed and crushed into powder and taken the powder weight up to 10 mg of paliperidone in the base of 100 ml volumetric flask, and Added 0.1N Hydrochloric acid (HCl) few ml and sonicated it for 15 minutes. The final volumes were made by 0.1N HCl up to to the mark of 100ml. 1 ml of final solution was taken and diluted with 0.1 N HCl, then absorbance was measured using with UV/Visible spectrophotometer at 283 nm.

Buoyancy study: The floating behavior of tablets were studied by placing them in a beaker which is containing 250 ml of 0.1N HCl., The time taken by the tablet to ascend on to the surface for floating was considered as the floating lag time (FLT) and how long the tablet remains buoyant was considered as total floating time (TFT).

Studies of Drug releases: Dissolution studies were performed for the developed Paliperidone floating tablets by using with USP type-II (Paddle) dissolution apparatus. (Temp at: 37±0.5ºC; 50 rpm; 900 ml of 0.1N HCl as dissolution medium). At definite time period, 5 ml of drug sample was collected and analyse the sample with UV spectrophotometer at 283 nm.

Drug release kinetics :

To study the drug release kinetics as following models: Higuchi, zero-order and first-order[16] and Peppas kineticls [16-17]. They considered the best fitting one model with the high correlation coefficients.

Study of Tablets Physical stabilities: The physical stability of tablets were conducted on the best formulation tablets by placing in a desiccator (40^0C/75% RH). After 3 months, for determined the drug quantity and percentage of drug releases.

RESULTS & DISCUSSION

Paliperidone showed the pH dependent solubility pattern in various media. The results shown the highest solubility in acidic pH and solubility was decreased with the increase of pH.

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Drug-Excipient compatibility study: DSC studies results revealed to shown that Paliperidone endothermic peaks at the 158-160°C., which represents in Fig.1., No deviations were found in this peak, which is obtained with drug and excipient mixture when compared to the pure drug peak (Fig.2). So there are no drug excipient interactions.

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Paliperidone floating tablets *in vitro* characterisations:

The Paliperidone floating tablets were developed by the method of direct physical compressions with xanthan gum and guar gum., the data was represented in table 2. All the ten formulations were showed in the acceptable pharmacopoeial specifications. Thicknesses were found to be in the range of 2.51mm to 3.11mm. Hardness and friability's were obtained to be 4.8-5.2kg/cm^2 and 0.12-0.37%., which indicates the tablets have been adequate mechanical strength and within the specified weight vatiation limits and all formulations of drug content range found as 98.28-99.56%, it indicating that there is a acceptable amount of drug was found in all the formulations [20-21].

The *in vitro* buoyancy, study was conducted for paliperidone floating tablets with the agent of gas generating such as sodium bicarbonate which is to facilitate the floating property of tablets. The buoyant period for all the formulations were remained above 12 h (Table 2 & Fig 5)., and were floated within less than one minute. Floating lag time development in formulations of F1-F5 with various concentrations of guar gum and sodium bicarbonate in equal quantity and ratios, it found the range of 15 to 35 sec, while the formulations of F6-F10 was developed with xanthan gum, was found to be in the range of 37-62 sec. It showed that the FLT is decreased for all the formulations and simultaneously TFT is increased with increasing of polymers concentrations and FLT is not statistical significant.

The study of drug releases were conducted for Paliperidone tablets in 0.1 N HCl., The 12 hours study was conducted and calculated the cumulative drug releases for F1-F5 formulations (guar gum) and F6-F10 formulations (xanthan gum). The dissolution profiles for the formulations F1-F5 results in Fig5. The effects of various concentrations of guar gum on drug release are evaluated. It reveals that as the concentrations of guar gum was increased; the drug release profile from the floating tablets was significantly decreased [22].

The dissolution studies stated that the release of F1-F3 formulation tablets as 92.4, 95.2 and 96.7 %, respectively, in 6, 8, 10 h (Fig 3) whereas, the Formulation F4 shown a maximum drug releasing of 98.5 % in 12 hours. The differences in drug releasing properties due to various concentrations of polymer used in formulations. Here the F1-F3 Formulations were not able to release the drug for the required of time period, whereas the formulation F4 released the drug for up to 12 hours and with a floating of lag time of 18 sec., the F5 formulation is failed to release the necessary drug profile. F4 Formulation is selected as the optimized formulation.(Fig 3).

The dissolution profiles for F6-F10 formulations developed with xanthan gum were shown in Fig.4. F6-F8 formulations showed the drug release concentrations of 86.8, 84.3 and 87.3, respectively, in 6, 8,10hours. There are various drug release profiles due to concentrations differences in polymer. From this series of formulations, the better released formulation of F9 is selected as the optimized formulation.(Fig 4). The *in vitro* drug release profile data is fitted with kinetic models and optimized formulation follows Higuchi model (Table 3).

Stability study:

The selected best formulation F4 from the above studies and it was subjected for stability study for the three months period. After three months evaluated the tablets physical appearance, drug content and drug release studies. The results of color, drug release and drug content of the tablets found that there is no significant change (Table 4).for a period of three months study under various conditions of storage and it considered the formulation F4 is more stable.

CONCLUSION

Paliperidone gastro retentive floating tablets were developed using with floating method. the *in vitro* buoyancy study and drug release studies, the F4 formulation was selected as optimized best. F4 givesn the drug release (98.47±0.71%) up to 12 h and remained buoyant for more than 12 h. and this F4 formulation was stable for three months in various storages, as there is no change in the color and appearance, floating properties , drug content and drug releases.

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Table 2: Physical parameters of floating tablets of Paliperidone

Formulation	Weight variation (mg)	Hardness (kg/cm^2)	Thickness (mm)	Friability (%)	Drug content (%)	FLT (sec)	TFT (h)	Drug release (%)
F1	152	4.9 ±0.11	2.5± 0.05	0.22	98.28	15 ± 1	> 12	99.56
F2	151	5.2 ±0.21	2.8± 0.08	0.36	99.52	23 ± 3	> 12	97.95
F3	149	5.1 ±0.30	2.6± 0.05	0.25	99.04	27 ± 5	> 12	80.05
F4	150	5.0 ±0.27	2.5± 0.08	0.33	99.56	18 ± 4	> 12	99.96
F5	151	4.8 ±0.15	2.9± 0.05	0.26	99.41	35 ± 2	> 12	97.98
F6	153	5.2 ±0.23	2.7± 0.05	0.37	99.84	45 ± 7	> 12	89.20
F7	152	4.8 ±0.10	2.8± 0.01	0.12	98.28	47 ± 8	> 12	70.98
F8	149	5.1 ±0.22	3.1± 0.03	0.14	99.52	62 ± 2	> 12	66.65
F9	151	5.2 ±0.25	2.5± 0.04	0.19	99.04	37 ± 4	> 12	96.32
F10	152	5.20 ±0.28	2.7± 0.08	0.28	98.56	49 ± 9	> 12	84.19

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Table 3: The correlation coefficient (R2) values for optimized formulation

Zero order	First order	Higuchi	Peppas
0.9815	0.7027	0.9953	0.8928

Table 4: Stability studies optimized batch

Parameters	Storage conditions		
	At 2-8°C	**Room temperature**	**At 40°C**
% Cumulative Drug Release	95.10%	98.82	94.73%
Drug Content Uniformity	99.13%	99.35%	98.46%
Color Change	No	No	No

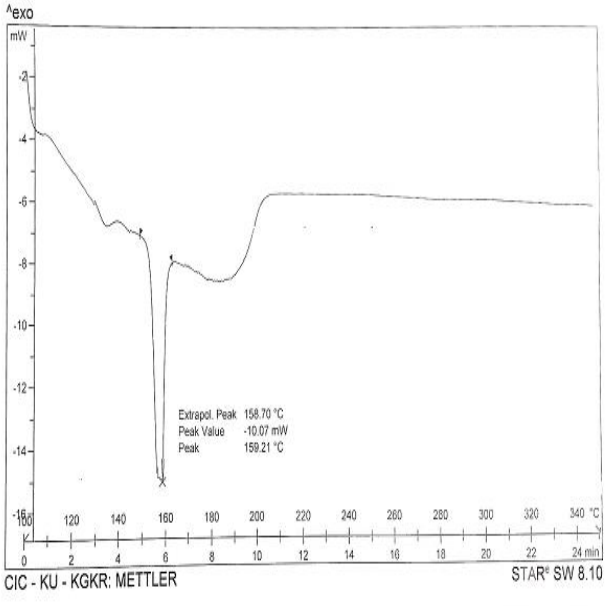

Fig 1: DSC spectra for pure drug

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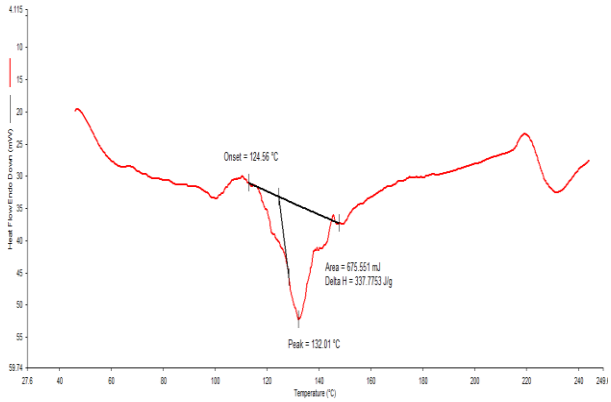

Fig 2: DSC spectra for Drug +Excipients

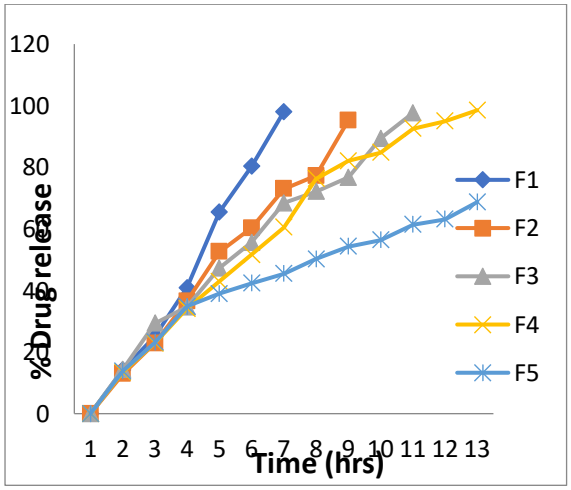

Fig 3: Drug release profiles of Paliperidone floating tablets composed of guar gum

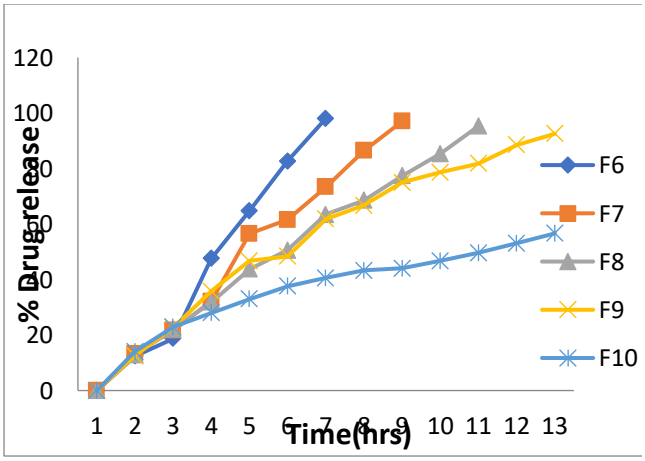

Fig 4: Drug release profiles of Paliperidone floating tablets composed of xanthan gum

Fig.5:Floating characteristics of Paliperidone floating tablets.

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CONFLICT OF INTEREST

Authors have no conflict of interest.

AUTHOR CONTRIBUTIONS

The author are involved in working research and writing of the manuscript. The corresponding author is suggested the work and framing up the research design. The research profile of the authors can be verified from their ORCID ids, given below:

REFERENCES

1. A. Streube , J Siepmann, R Bodmeier Gastroretentive drug delivery systems Expert Opin. Drug Deliv. 2006; 3 (2): 217-233. doi: 10.4274/tjps.galenos.2021.44959
2. A. Streubel, J. Siepmann., R Bodmeier, Drug delivery to the upper small intestine window using gastroretentive technologies. Curr. Opin. Pharmacol. 2006; 6: 501-508. DOI: 10.1016/j.coph.2006.04.007
3. R.Groning,, G Heun,. Oral dosage forms with controlled gastrointestinal transit. Drug Develop. Indust. Pharm. 1984; 1: 527-539. DOI: 10.5958/2231-5659.2019.00014.6
4. J .Fujimori, Y Machida, S .Tanaka, T.Nagai, Effect of magnetically controlled gastric residence of sustained release tablets on bioavailability of acetaminophen. Int. J.

Pharm. 1995; 119: 47-55. doi: 10.3390/pharmaceutics13101591

5. S.Dhaliwal, S Jain, H.P Singh, A.K Tiwar. Mucoadhesive microspheres for gastroretentive delivery of acyclovir. In vitro and in vivo evaluation. AAPS J. 2008; 10: 322-330. DOI: 10.1208/s12248-008-9039-2
6. A.A Deshpande, N.H. Shah, C.T Rhodes, W Malick. Development of a novel controlled-release system for gastric retention. Pharm. Res. 1997; 14: 815-819. DOI: 10.1023/a:1012171010492
7. S .Baumgartner, J .Kristl, F Vrečer, P Vodopivec, B .Zorko. Optimisation of floating matrix tablets and evaluation of their gastric residence time. Int. J. Pharm. 2000;195: 125-135. DOI: 10.1016/s0378-5173(99)00378-6
8. J.E Devereux,, J.M Newton., M.B Short,. The influence of density on the gastrointestinal transit of pellets. J. Pharm. Pharmacol. 1990;42: 500-501. DOI: 10.1111/j.2042-7158.1990.tb06604.x
9. PJ .Pistell, S .Gupta, AG .Knight, M .Domingue, RM Uranga, DK Ingram, I Kheterpal, Ruiz C, Keller JN, Bruce-Keller AJ, Metabolic and neurologic consequences of chronic lopinavir/ritonavir administration to C57BL/6 mice, Antiviral Research. 2010;88: 334-342. DOI: 10.1016/j.antiviral.2010.10.006
10. D .Law, EA .Schmitt, KC .Marsh, EA .Everitt, Wang W, Fort JJ, Krill SL, Qiu Y, Ritonavir-PEG 8000 Amorphous Solid Dispersions: In Vitro and In Vivo Evaluations, J Pharm Sci. 2004; 93: 563-570. https://doi.org/10.1002/jps.10566
11. D .Law, SL Krill, EA Schmitt, JJ Fort, Y Qiu, W Wang, WR Porter, Physicochemical Consideration in the preparation of Amorphous Ritonavir- Poly(ethylene glycol) 8000 Solid Dispersions, J Pharm Sci 2001;90:1015-1026. DOI: 10.1002/jps.1054
12. GC. Williams , PJ Sinko, Oral absorption of the HIV protease inhibitors: a current update, Adv Drug Del Rev. 1999; 39: 211-238. DOI: 10.1016/s0169-409x(99)00027-7
13. RB Kim, MF From, Wandel , Leake B, Wood AJJ, Roden DM, The drug transporter P-Glycoprotein limits oral absorption and brain entry of HIV-1 Protease Inhibitors, J Clin Invest. 1998; 101: 289-294. doi: 10.1172/JCI1269
14. BJ. Aungst ., P-glycoprotein, secretory transport, and other barriers to the oral delivery of anti-HIV drugs, Adv Drug Del Rev. 1999; 39: 105-116. DOI: 10.1016/s0169-409x(99)00022-8
15. T. Higuchi, Mechanism of sustained action medication, J. Pharm. Sci. 1963; 52: 1145-1149. DOI: 10.1002/jps.2600521210
16. R.W. Korsmeyer, R. Gurny, E. Docler, P. Buri, N.A. Peppas, Mechanism of solute release from porous hydrophilic polymers, Int. J. Pharm. 1983; 15: 25-35. https://doi.org/10.1016/0378-5173(83)90064-9
17. BR Mathews. Regulatory aspects of stability testing in Europe. Drug Dev. Ind. Pharm. 1999; 25: 831-856. DOI: 10.1081/ddc-100102245
18. M.N. Gambhire, K.W. Ambade, S.D. Kurmi, V.J. Kadam, K.R. Jadhav, Development and in vitro evaluation of an oral floating matrix tablet formulation of diltiazem hydrochloride, AAPS PharmSciTech. 2007; 8 (3): E1–E9 (Article 73). DOI: 10.1208/pt0803073

Books

19. United States Pharmacopeia 27 and National Formulary 22, Asian Edition, United States Pharmacopeial convention, Inc., Rockville, 2004 (electronic version).
20. United States Pharmacopoeia. US Pharmacopoeial Convention. Inc. Rockville MD. Asian ed; XXXI: pp. 2008; 3200-3201.
21.
22. NS Brahma, HK Know. Floating drug delivery systems: an approach to oral controlled drug delivery via gastric retention. J. Control. Release 2000; 63(1-2): 235-259. DOI: 10.1016/s0168-3659(99)00204-7
23. LLWS Cheong, PWS Heng, LF Wong. Relationship between polymer viscosity and drug release from a matrix system. Pharm. Res. 1992; 9(11): 1510-1514. DOI: 10.1023/a:1015883501871