WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.074
Volume 7, Issue 09, 1-7. Conference Article ISSN 2277–7105

FORMULATION AND EVALUATION OF FLOATING TABLETS OF GABAPENTIN

Abhijit Satpathy*, K. C. Panigrahi, Soumyastuti Patnaik and Ch. Niranjan Patra

Department of Pharmaceutics, Roland Institute of Pharmaceutical Sciences, Brahmapur-760010, Ganjam.

Article Received on
18 March 2018,
Revised on 08 April 2018,
Accepted on 29 April 2018
DOI: 10.20959/wjpr20189-12072

***Corresponding Author**
Abhijit Satpathy
Department of Pharmaceutics, Roland Institute of Pharmaceutical Sciences, Brahmapur-760010, Ganjam.

ABSTRACT

Gabapentin is used as anticonvulsant drug belongs to BCS class III. It has high aqueous solubility and less permeability. It exhibits low oral bioavailability i.e. 27% only. The primary objective of the present research was to improve the gastric residence time and bioavailability of gabapentin using different polymer HPMC K 100M and HPMC K4M and also to study the effect of various excipients on the solubility and rate of dissolution as secondary objective. The FTIR study of the optimized formulation, blank physical mixture and drug loaded physical mixture revealed no interaction with drug and polymer. The DSC study of the formulation and physical mixture also confirmed there was no any interaction with drug and polymer. The floating tablets of drug was prepared using HPMC K100M and HPMC K4M as polymer and other excipients in different drug, polymer and excipients ratios by direct compression method. The flow properties of formulation found to be better as compared to the drug alone and also to the physical mixture. In vitro dissolution study of all formulations were carried out using USP II apparatus and found formulation F5 has better dissolution rate and solubility as compared to other formulations.

KEYWORDS: Gabapentin, HPMC K100M, HPMC K4M, direct compression.

INTRODUCTION

The primary aim of oral controlled drug delivery system is to achieve better bioavailability and release of drug from the system, which should be predictable and reproducible. But this is difficult due to number of physiological problems such as fluctuation in the gastric

emptying process, narrow absorption window and stability problem in the intestine. This can be overcome by altering the physiological state and designing the formulations, by which gastric emptying process can be extended from few minutes to 12 h. Prolonged gastric retention increases bioavailability, decreases wastage of drugs, increases solubility of drugs, which are less soluble in alkaline pH. These dosage forms prolongs the gastric residence time enabling an extended absorption phase for the local treatment of drugs and better bioavailability for the drugs that are unstable in intestinal or colonic environment. Gastric retention can be achieved by mucoadhesion or bio adhesion systems, expansion systems, high density systems, magnetic systems, super porous hydrogels, raft forming systems, low density systems, and floating ion exchange resins.

Gabapentin has a short elimination half life and limited absorption due to a saturable L-amino acid transport system, which is expressed predominantly in the proximal small intestine. Hence, the original immediate-release gabapentin formulation (gabapentin TID) must usually be taken three times a day for optimal efficacy. Gabapentin TID is also associated with a high incidence of dizziness and somnolence and some patients are unable to tolerate the doses required for maximum pain relief. A once-daily, gastro retentive formulation of gabapentin was recently approved by the US Food and Drug Administration (FDA) for the management of post herpetic neuralgia. This Gabapentin belongs to BCS class III. It has high aqueous solubility and low permeability. It also exhibits low oral bioavailability i.e. 27 % only and low biological half life i.e. 5 to 7 h. Hence this drug was used as a model drug for the formulation of floating tablets.

MATERIALS USED

Gabapentin was obtained as gift sample from Aurobindo Pharma, Hyderabad. HPMC K100 M and HPMC K4M were obtained as gift sample from Colorcon, Goa. Sodium Bicarbonate, Microcrystalline Cellulose PH 102 was purchased from Himedia, India. All other chemicals and reagents used were of analytical grade.

METHOD

Preparation of Floating Tablets

Floating tablets of gabapentin were prepared by direct compression method. The required quantity of drug, HPMC K100M and HPMC K4M as hydrophilic polymer, sodium bicarbonate as gas generating agent and microcrystalline cellulose as binder were mixed in a polythene bag. Finally lubricant talc was added to the above premix and mixed for 2 minutes.

Table 1: Composition of Floating Tablets of Gabapentin.

	F1	F2	F3	F4	F5	F6
Gabapentin	300	300	300	300	300	300
HPMC K100M	60	120	180	-	-	-
HPMCK 4M	-	-	-	60	120	180
Sodium Bicarbonate	30	30	30	30	30	30
Microcrystalline Cellulose	205	145	85	205	145	85
Talc	5	5	5	5	5	5
Total weight	600	600	600	600	600	600

CHARACTERIZATION

1. Micromeritics Properties

- **Bulk density**

The prepared powder formulations of gabapentin were filled into a 10 ml measuring cylinder and the volume was noted down.

It is determined by the following formula.

Bulk density= Mass / Bulk Volume

- **Tapped density**

The formulation was applied to a mechanical tapping apparatus and for 50 tapings. This process was continued till a constant volume was obtained. After getting a constant value the volume was noted down.

It is determined by the following formula.

Tapped density= Mass/ Tapped volume

- **Carr's index:** It is determined by the following formula.

Carr's index= (Tapped density-Bulk density/ Tapped density) ×100

- **Hausner's ratio:** It is determined by the following formula.

Hausner's ratio=Tapped density/Bulk density

2. Fourier Transform Infrared (FT-IR) spectroscopy

Fourier Transform Infrared spectroscopy has been used to study the physical and chemical interaction between gabapentin and HPMC K100M. [Figure 1].

3. Differential scanning Calorimetry (DSC)

DSC analysis measures the amount of energy absorbed or released by a sample when it is heated or cooled, providing quantitative and qualitative data on endothermic (heat absorption) and exothermic (heat evolution) processes.DSC was performed using DSC 60 (SHIMADZU, TOKYO, JAPAN) calorimeter to study the thermal behaviours of gabapentin alone and mixture of gabapentin and HPMC K100M.[Figure 2]

4. In vitro buoyancy

Buoyancy lag time and duration of buoyancy were determined in the USP dissolution apparatus II (USP, 2008) with simulated gastric fluid (without enzyme). The time between the floating tablet introduction into the medium and its buoyancy in the medium was taken as the buoyancy lag time and the duration of the tablet remaining buoyant was observed visually.[Table 3]

5. In-vitro Dissolution Test

In vitro dissolution studies were performed using USP dissolution apparatus II. The dissolution test for the prepared tablets was carried out in 900 mL of 0.1N HCl at 37°C and 50 rpm for 12 h. At specific time intervals 5 mL of samples were withdrawn, filtered and analyzed for their concentration using UV spectrophotometer at 235 nm. The withdrawn samples were replaced by equal amounts of the dissolution media to maintain constant volume.[Figure 3]

Table 2: Micromeritic properties of pre-mix powders.

PARAMETERS	F_1	F_2	F_3	F_4	F_5	F_6
Carr's Index	19	20	18.98	21.22	18.14	18.57
Hausner's Ratio	1.15	1.14	1.05	1.19	1.03	1.07
Angle of repose	31.12	32.22	28.11	33.25	25.85	29.54

Table 3: Quality control tests and buoyancy test for Floating tablets.

PARAMETERS	F_1	F_2	F_3	F_4	F_5	F_6
Thickness (mm)	3.2	3.2	3.2	3.3	3.2	3.3
Hardness (Kg/cm^2)	7.2	8.4	8.7	7.2	6.3	6.2
Friability (%)	0.16%	0.83%	0.66%	0.33%	0.33%	0.5%
Disintegration time	Not disintegrated during 30 m in of disintegration study					
Floating Lag Time (sec)	26	27	18	21	20	40
Floating duration (h)	24	24	24	24	24	24

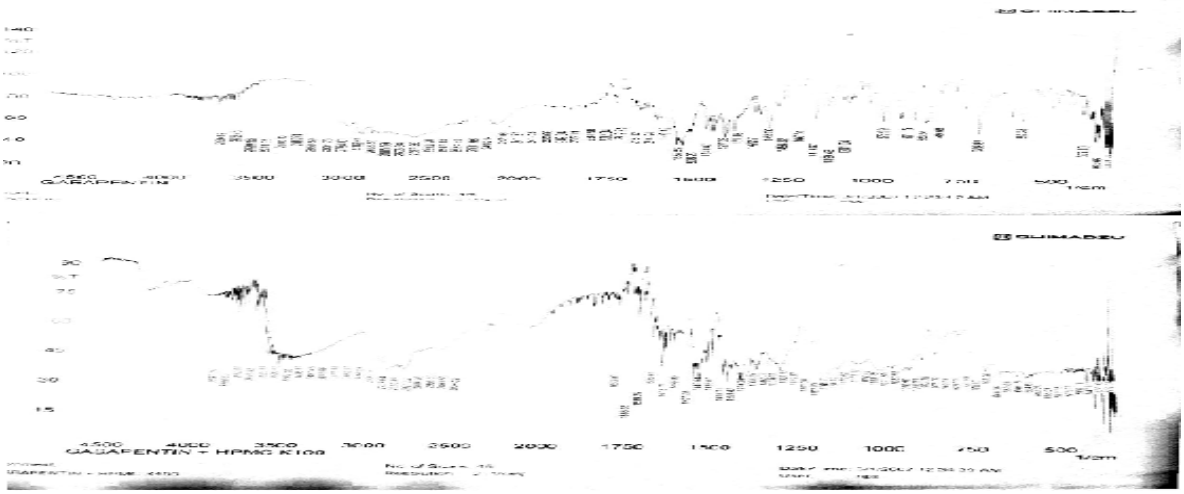

Figure 1: FT-IR spectra for gabapentin and HPMC.

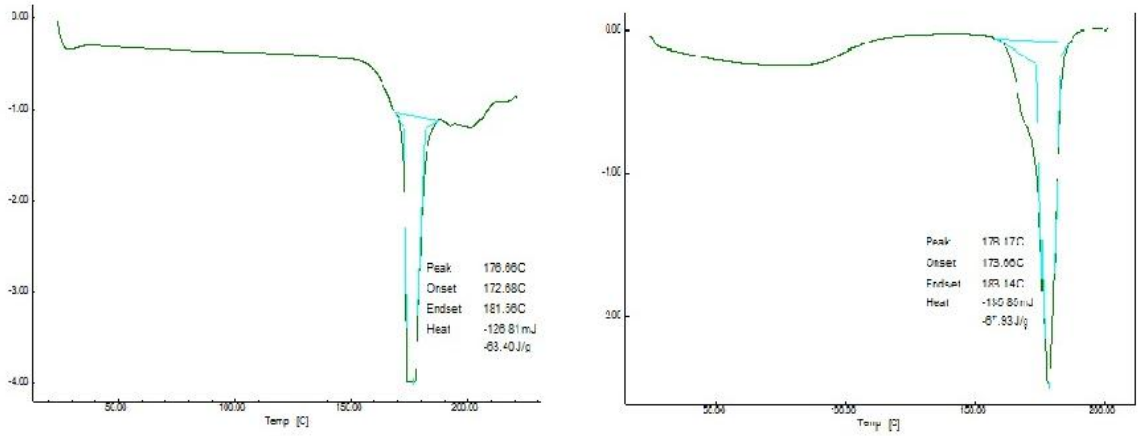

Figure 2: DSC thermogram for gabapentin and HPMC.

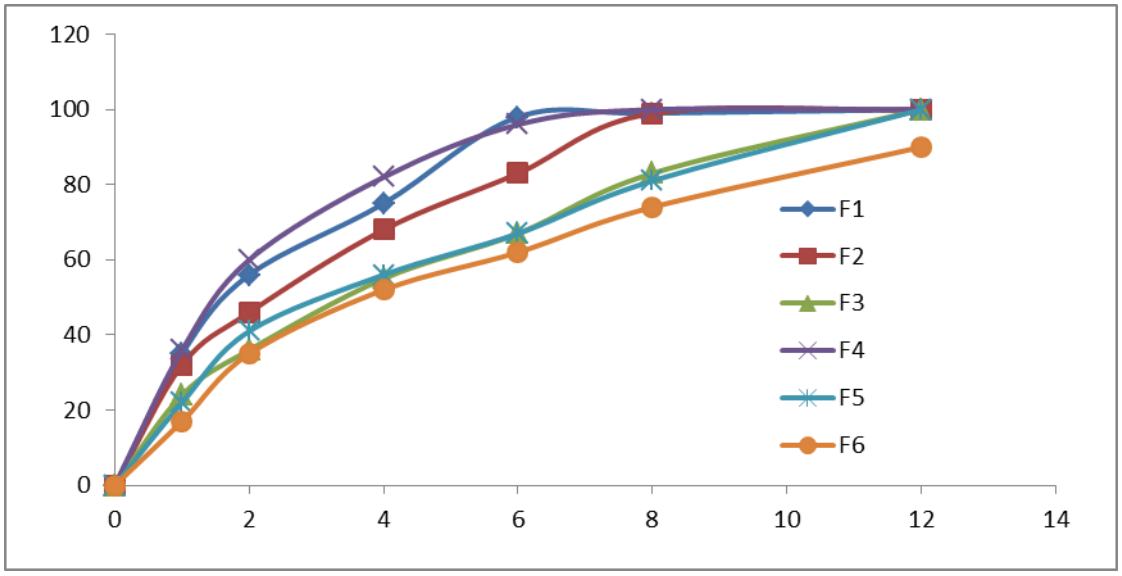

Figure 3: Comparative Dissolution Data of different formulations GABAPENTIN.

Table 4: Kinetic Release of Dissolution.

FORMULATIONS	CORRELATION COEFFICIENT			SLOPE
	ZERO ORDER	FIRST ORDER	HIGUCHI EQUATION	KORSMEYER & PEPPERS RELEASE EXPONENT (n)
F1	0.976	0.997	0.998	0.552
F2	0.968	0.998	0.997	0.518
F3	0.975	0.995	0.998	0.502
F4	0.974	0.996	0.998	0.518
F5	0.968	0.997	0.999	0.520
F6	0.924	0.997	0.997	0.512

RESULT AND DISCUSSION

Pure drug gabapentin showed poor flow however the pre-mix for the direct compression showed desirable flowability and compressibility as observed from the angle of repose, carr's index and hausner's ratio.

FT-IR study for the pure drug gabapentin showed the presence of following functional groups at corresponding wave numbers. A distinct peak at 1557 cm^{-1} and 1660 cm^{-1} suggests the presence of ketone group, presence of primary amine group was confirmed due to the presence of peak at 3059 cm^{-1}. Bending and stretching vibration for presence of –OH group was confirmed due to peaks at 3620 cm^{-1} and 1300 respectively. All the peaks were also observed incase of formulation prepared with HPMC K4M and HPMC K100 M. Hence drug and HPMC are compatible with each other. [Sharma et al., 2015].

DSC study for the pure drug gabapentin showed a sharp endothermic peak at 176 ^{0}C with onset and end set temperature of 172^{0}C to 181^{0}C respectively. The physical mixture of drug with HPMC showed a melting endotherm at 176 ^{0}C. Hence there is interaction between drug and HPMC. [Sharma et al., 2015].

Floating lag time was less than 1 min for all the formulations which indicates that the amount of sodium carbonate used was optimum for attaining quick floating. The duration of floating for all formulations was more than 24 h due to the higher viscosity grades of HPMC K4M and K100M which helps in maintaining matrix integrity. [Dul *et al*] In vitro dissolution study revealed that HPMCK100M based formulations F1 and F2 could not sustain release of drug for 12 h whereas F3 exhibited drug release up to 12 h. In case of HPMCK4M based matrix tablets formulation F4 could not sustain drug release for 12 h whereas formulation F5 and F6 showed sustain drug release for 12 h. However keeping in view, the minimum amount of polymer for F5 was selected as the optimized formulation. It was concluded that diffusion of

drug through the hydrated gel layer was the predominant drug release mechanism for most of the formulations studied. The dissolution shows higher correlation to 1st order equation. Hence drug release followed 1st order kinetics. High correlation for Higuchi equation suggests that drug release was primarily by diffusion mechanism. The values of drug release exponent for all formulation were nearly equal to 0.5. Hence the drug release mechanism was found to be Fickian diffusion type. [Table 4] [KP Gharti *et al.* 2012].

CONCLUSION

From the above research it was concluded that floating tablets for gabapentin can be prepared successfully using sodium carbonate as gas generating agent and HPMCK100M and HPMCK4M as release retardant.

REFERENCES

1. Natasha Sharma, Dilip Agarwal, M.K. Gupta and Mahaveer Pr. Khinchi A Comprehensive Review on Floating Drug Delivery System. International Journal of Research in Pharmaceutical and Biomedical Sciences ISSN: 2229-3701.
2. J Young Pharm. 2012 Oct-Dec; 4(4): 201–208.PMCID: PMC3573371.Formulation and *in vitro* evaluation of floating tablets of hydroxypropyl methylcellulose and polyethylene oxide using ranitidine hydrochloride as a model drug KP Gharti, P Thapa, U Budhathoki, and A Bhargava.
3. Asian Pac. J. Health Sci, 2015; 2(1): 133-147 e-ISSN: 2349-0659, p-ISSN: 2350-0964 Sharma and Goyal Formulation, development and optimization of gastroretentive floating drug delivery system of Olmesartan Medxomil Anjali Sharma, Naveen Goyal.
4. Int. Res J Pharm. App Sci, 2014; 4(2): 14-24 ISSN: 2277-4149 K. P. R. Chowdary et al., 2014 14 International Research Journal of Pharmaceutical and appliedsciences (IRJPAS) FLOATING DRUG DELIVERY SYSTEMS- A REVIEW OF RECENT RESEARCH K.P.R.Chowdary*, K.Ravi Shankar and Vijay Teeda.
5. ejpmr, 2017; 4(2): 347-365 ISSN 2394-3211 FORMULATION, OPTIMIZATION AND INVITRO EVALUATION OF GASTRO RETENTIVE SUMATRIPTAN SUCCINATE TABLETS G. Pratap Kumar*, Venkata Naga Swetha M. and T. Murali Krishna.
6. Dul *et al.* World journal of pharmacy and pharmaceutical sciences formulation and evaluation of floating matrixtablets of valsartan using peanut husk powder by non-effervescent method dr. A. Abdul hasan sathali* and s. Vanitha, 4(06): 1007-1021. Research Article ISSN 2278–4357.