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Development and Characterization of Floating Matrix Tablets of Gabapentin

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Fauziya Husaini*[1], Nisha Thakre[1], Rama Shukla[1], Manu Singhai[2], A.K. Singhai[1]

[1]Department of Pharmaceutics, Lakshmi Narain College of Pharmacy, Bhopal, India

[2]ISF College of Pharmacy, Moga (Punjab)
Lakshmi Narain College of Pharmacy Bhopal

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ABSTRACT

Objective The objective of the present investigation was to increase the Gastro retention time of Gabapentin (GBPT). **Materials and Method** the floating matrix tablets of Gabapentin were prepared by direct compression method with free flowing powder by using selected drug and excipients authenticated by Fourier-transform infrared spectroscopy (FTIR) of HPMC K4, Lactose $NaHCO_3$, magnesium stearate and talc were used in variable concentration for different formulation (F-1 to F-9) .Floating matrix tablets were further characterized for drug content and *in vitro* drug release studies. **Results** Among various formulation, optimized formulation (F6) shown better *in-vitro* release patternie. 99.99% in 12 hrs. The results suggested that direct compression is a suitable method to formulate floating matrix tablet of Gabapentin and it can perform therapeutically better than conventional immediate release dosage form. **Conclusion**: The present study that the combined mix matrix system containing hydrophobic and hydrophilic polymer minimized the burst release of drug from the tablet.

INTRODUCTION

The objective of any drug delivery system is to afford therapeutic amount of drug to the proper site of action in the body to attain promptly and then maintain the desired drug concentration [1].

Controlled release (modified release) dosage forms are growing in popularity. These more sophisticated systems can be used as a means of altering the pharmacokinetic behavior of drugs in order to provide twice or once a day dosage. The commonly used and most convenient method of drug delivery is oral route of drug administration. Usually, once a day or twice a day preparations delivers the drug through GIT. [2] It is evident from the recent research and patent literature that an increased interest in novel dosage forms that are retained in the stomach for a prolonged and predictable period of time exists today.

Gabapentin:

Gabapentin (Neurontin) is a medication used as an anticonvulsant and analgesic. It was originally developed to treat epilepsy and is currently also used to relieve neuropathic pain. It is recommended as a first line agent for the treatment of neuropathic pain arising from diabetic neuropathy, post-herpetic neuralgia, and central neuropathic pain.

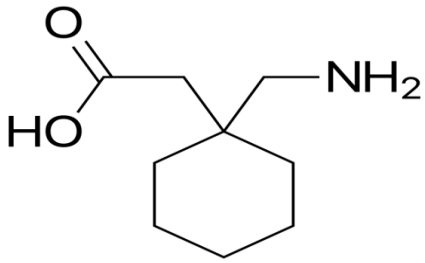

Figure No. 1: Structure of Gabapentin

Synonyms: Gabapentin GR, Gabapentine [INN-French], Gabapentinum [INN-Latin],

Categories: Anti-anxiety, Anti-convulsant, Anti-parkinson agent, Analgesic, Calcium Channel Blocker, Antimanic agent, Excitatory Amino Acid Antagonist

Molecular Weight: Average: 171.2368

Chemical formula: $C_9H_{17}NO_2$

Mechanism of action:

Gabapentin interacts with cortical neurons at Auxillary subunits of voltage-sensitive calcium channels. Gabapentin increases the synaptic concentration of GABA, enhances GABA responses at non-synaptic sites in neuronal tissues, and reduces the release of mono-amine neurotransmitters [6].

The present research investigation is planned with the following Objectives

- Formulation and development of floating matrix tablet of Gabapentin
- Evaluation of floating matrix tablet of Gabapentin
- *In-vitro* buoyancy studies and drug release studies

MATERIALS AND METHODS

Table No. 1: List of drug and Excipients used

S. No.	Materials Used	Sources
1.	Gabapentin	Alembic Pharma Vadodra.
2.	Ethyl Cellulose	Mapromax, Life sciences Pvt. Ltd., Dehradun.
3.	H.P.M.C. K4	
4.	Talc	
5.	Magnesium Stearate	
6.	Aerosil	
7.	Avicel	

***Pharma Grade**

Determination of λmax. of Gabapentin

The absorption maximum of Gabapentin was determined by running the spectrum of drug solution in double beam ultraviolet spectrophotometer.

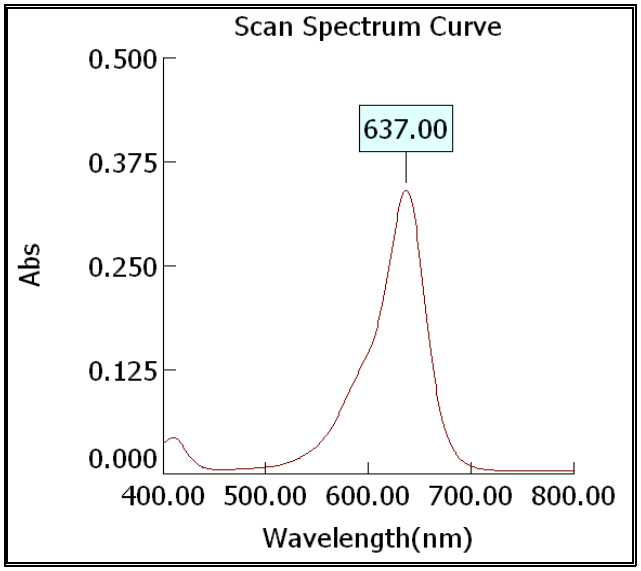

Figure No. 2: λmax. of Gabapentin

Procedure: 100mg Gabapentin was dissolved in 100 ml of distilled water in a volumetric flask. 5 ml of this solution was taken and diluted to 50 ml. The resulting solution was serially diluted to obtain drug concentrations of 5-25 µg/ml. To added 2 ml of standard solution, 1 ml of folin catechu reagent and Chloroform 3 ml was Pipetted out the colour layer and the absorbance of the solutions were measured against distilled water as blank at 637nm using the UV spectrophotometer. The plot of absorbance vs. concentration was plotted and the Beer's range was determined.

Table No. 2: Calibration Curve of Gabapentin at 637 nm

S. No.	Conc. (µg/ml)	Absorbance*			
		I	II	III	Average
1.	5	0.156	0.157	0.156	0.156
2.	10	0.312	0.315	0.313	0.313
3.	15	0.445	0.442	0.445	0.444
4.	20	0.615	0.612	0.614	0.614
5.	25	0.748	0.749	0.748	0.748

***(n=3)**

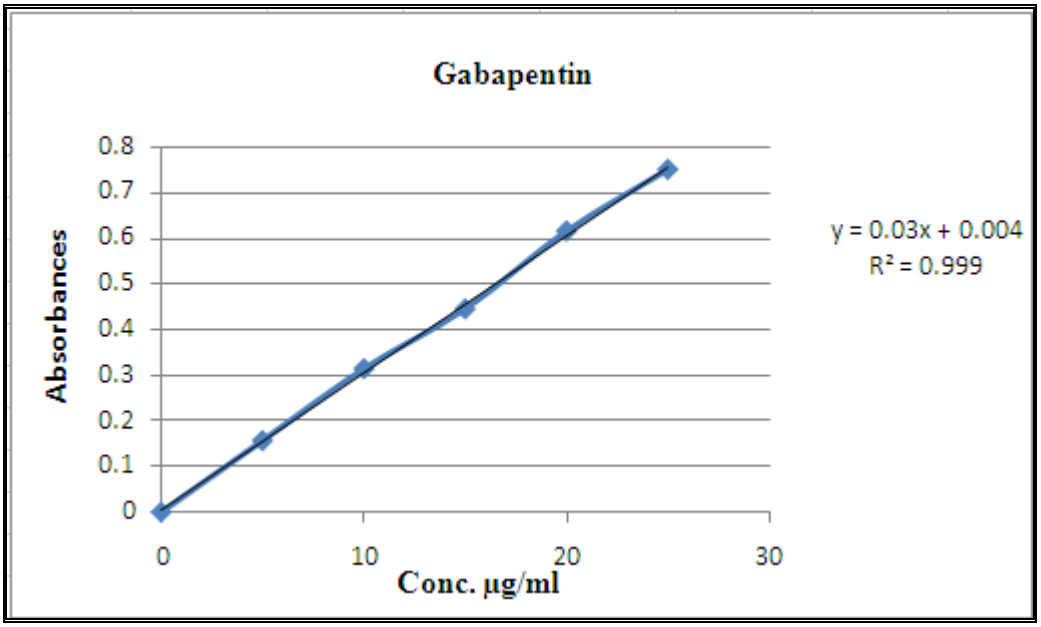

Figure No. 3: Calibration curve of Gabapentin at 637.0 nm

The linear regression analysis for calibration curve

The linear regression analysis was done on absorbance data points. The results are as follows:

Table No. 3: Calibration curve of Gabapentin at 637nm

Slope	0.030
The intercept	0.004
The correlation coefficient (R^2)	0.994

FORMULATION DEVELOPMENT

Preparation of Gabapentin Floating Matrix Tablets:-

Direct compression was followed to manufacture the floating matrix tablets of Gabapentin. All the polymers selected, drug and excipients were passed through sieve no. 40 before using in formulation.

Polymers selected for tablets are: - HPMC K15, HPMC K4

Excipients like Talc, Citric acid, Lactose, Magnesium Stearate were selected for the study.

Table No. 4: Various formulations of Gabapentin floating matrix Tablets

Excipients(mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Gabapentin	100	100	100	100	100	100	100	100	100
HPMC K 4	160	180	200	-	-	-	80	90	100
HPMC K 15	-	-	-	160	180	200	80	90	100
Lactose	45	25	05	45	25	05	45	25	05
$NaHCO_3$	10	10	10	10	10	10	10	10	10
Citric acid	05	05	05	05	05	05	05	05	05
Talc	05	05	05	05	05	05	05	05	05
Magnesium stearate	05	05	05	05	05	05	05	05	05
Total Weight (mg)	330	330	330	330	330	330	330	330	330

Method of preparation: The matrix tablets were prepared by wet granulation method. Gabapentin, polymer and other excipients were passed through 40 mesh sieve separately. 100mg quantity of Gabapentin polymer and excipients were weighed properly and mixed thoroughly for at least 15 min. The mixing product was passed through the 20 mesh size sieve. The granules were dried at 40^0C in an oven for 30 min. The granules thus formed were also passed through 18 mesh size sieve. These dried granules were lubricated with given quantity of talc and magnesium stearate before final compression. Tablets were compressed on a 10 station lab press compression machine.

RESULTS AND DISCUSSION

Table No. 5: Results of Pre-Compression Properties of Gabapentin Floating Matrix Tablets

Formulation code (Blend)	Bulk Density (gm/ml±SD)	Carr's index (%± SD)	Hausner ratio (%± SD)	Angle of repose (degree± SD)	Tapped Density (gm/ml±SD)
F1	0.311±0.02	14.35±0.06	1.03±0.05	26.42±0.04	0.337±0.02
F2	0.325±0.04	15.61±0.07	1.23±0.04	27.17±0.01	0.359±0.04
F3	0.339±0.06	14.64±0.04	1.14±0.02	29.01±0.03	0.361±0.07
F4	0.307±0.04	13.46±0.01	1.13±0.06	27.57±0.07	0.317±0.06
F5	0.287±0.03	12.29±0.05	1.25±0.03	26.77±0.09	0.321±0.05
F6	0.271±0.01	16.35±0.03	1.15±0.01	25.61±0.06 0	0.345±0.01
F7	0.297±0.04	14.46±0.07	1.20±0.03	26.16±0.03	0.357±0.03
F8	0.307±0.05	15.61±0.04	1.19±0.05	29.11±0.09	0.366±0.02
F9	0.320±0.06	13.85±0.09	1.21±0.00	28.05±0.02	0.359±0.04

***(n=3)**

Post-compression Parameter:

All prepared were subjected to thickness, hardness, and weight variation, friability and drug content and results given in table 6. The derivation from the average weight was found to be in the prescribed official limits.

Table No. 6: Results of Post Compression Properties of Gabapentin Floating Matrix Tablets

Formulation code	Thickness (mm) (±SD)	Hardness (kg/cm^3) (±SD)	Weight variation (%) (±SD)	Friability (%) (±SD)	Drug content (%) (±SD)
F1	3.89 ±0.03	6.13 ± 0.21	952±0.29	0.5216± 0.04	98.53±0.48
F2	3.90 ±0.05	6.70 ± 0.30	951±0.67	0.6325 ±0.04	99.23±0.57
F3	3.89 ±0.03	6.51 ± 0.50	949±0.45	0.5215 ±0.08	99.77±0.67
F4	3.91 ±0.06	5.81 ± 0.50	951±0.71	0.6532 ±0.10	99.27±0.23
F5	3.89 ±0.03	6.81 ± 0.51	948±0.15	0.6485 ±0.04	98.42±0.61
F6	3.90 ±0.05	5.78 ± 0.51	952±0.31	0.5489 ±0.08	99.57±0.34
F7	3.87 ±0.04	6.80 ± 0.47	949±0.04	0.5325 ±0.10	99.87±0.56
F8	3.86± 0.04	9.83 ± 0.49	948±0.71	0.5369 ±0.15	97.37±0.60
F9	3.89± 0.04	9.73 ± 0.29	951±0.52	0.5425 ±0.15	98.50±0.61

***(n=3)**

Dissolution rate studies

In vitro drug release of the sample (F1, F2, F3, F5, and F6and F7) was carried out using USP-type II dissolution apparatus (Paddle type). The dissolution medium, 900 ml 0.1N HCl was placed into the dissolution flask maintaining the temperature of 37±0.5^{0}C at 75 rpm. One Gabapentin Floating Matrix tablet was placed in each basket of dissolution apparatus. The apparatus was allowed to run for 12 hours. Sample measuring 5 ml were withdrawn after 30 min., 1.0 hr, 1.30 hr, 2.0 hr, 4.0 hr, 6.0 hr, 8.0, 10.0 hr & 12 hr. The fresh dissolution medium was replaced every time with the same quantity of the sample.

Table No. 7: *In vitro* drug release study of Floating Matrix tablet

Time	% Cumulative Drug Release						
(hr)	F1	F2	F3	F4	F5	F6	F7
0.5	8.23	7.14	7.23	7.24	7.23	**7.45**	8.32
1	12.32	10.23	10.34	11.45	10.45	**11.23**	12.23
1.5	26.23	22.42	23.56	24.23	31.23	**38.23**	32.13
2	42.45	40.32	46.32	45.23	48.23	**46.32**	47.14
3	76.34	66.11	60.23	67.21	50.56	**67.02**	71.13
4	82.23	77.33	71.35	75.11	55	**88.13**	91.23
6	82.55	97.13	89.37	87.13	56	**99.13**	92.34
8	83	97.1	90.23	94.23	57.25	**99.87**	93.14
12	84.21	97.23	96.23	99.26	57.85	**99.99**	94.56

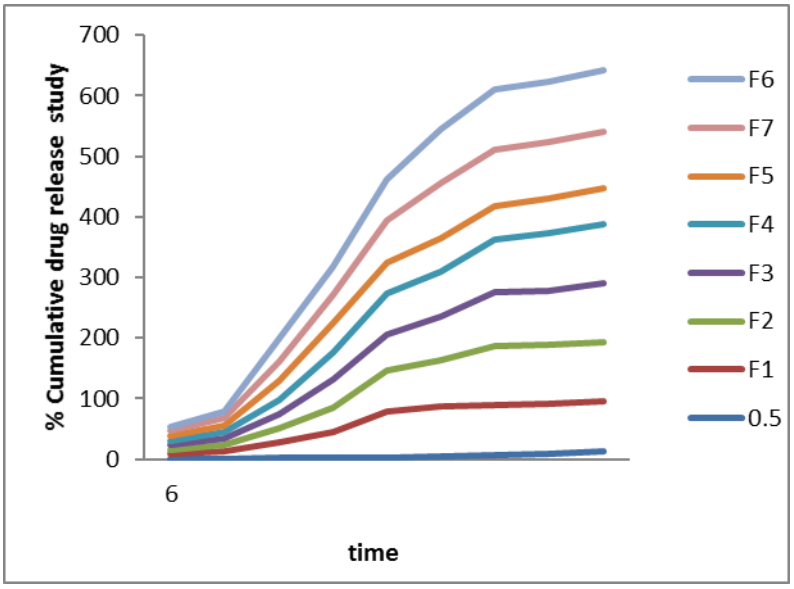

Figure No. 4: In vitro drug release study of floating matrix tablets

RESULTS: Among the entire formulations (F6) shows better release pattern as desired i.e. 99.99% in 12 hrs, might be due to optimal polymer concentration and uniform dispersibility of Gabapentin with compatible excipients.

Swelling index: All prepared formulations were subjected for swelling index study and results are given in Table 08.

Table No. 08: Swelling index of Gabapentin Tablets in 0.1N HCl

Time (hr)	F1	F2	F3	F4	F5	F6	F7
1	76.3±0.30	53.3±0.30	83.5±0.20	62.2±0.20	67.3±0.20	101.4±0.20	80.5±0.30
2	83.2±0.30	56.3±0.20	83.6±0.20	66.3±0.20	45±0.20	112.3±0.30	78.6±0.2
4	97.1±0.20	66.2±0.30	85.4±0.20	87.4±0.20	42±0.20	121.4±0.20	80.6±0.3
6	91.3±0.30	75.4±0.30	78.3±0.20	101.0±0.20	56±0.20	127.7±0.10	85.4±0.1
8	101.2±0.30	80.1±0.30	71.2±0.20	97.2±0.20	67±0.20	130.2±0.15	88.2±0.3
10	102.1±0.30	79.3±0.20	63.7±0.20	96.3±0.20	86±0.20	126.2±0.05	84.4±0.5
12	101.2±0.30	78.2±0.20	52.4±0.20	95.5±0.20	45±0.20	122.4±0.10	87.3±0.4

The results are as follows:

❖ All pre and post compression parameters were studied like Bulk density, Tapped density, Carr's index, Hausner's ratio, Angle of repose were found respectively 0.215g/cc, 0.286g/cc, 28.16%, 1.31 and 30º.

❖ Evaluations for like weight variation, hardness, thickness, friability, drug content indicate that value were within permissible limit for all formulations. The hardness of F8 and F9 formulation was observed more (5.81±0.50), (9.83±0.49) and (9.73±0.29) than compare to other formulations.

❖ *In vitro* drug release study of F1, F2, F3, F5, F6 & F7 formulation was carried out and based on the result for instant release F6 formulation showing best drug release (99.99%) as compare to other formulation F1, F2, F3, and F5 respectively 84.21%, 97.23%, 99.26% and 57.85%.

SUMMARY AND CONCLUSION

The might be purpose of this research was to develop floating matrix drug delivery system of Gabapentin which might be helpful for reducing multi dosing therapy of patients who

experience difficulty in taking multidose of drug. Matrix tablets prepared using both HPMC and PEO quickly hydrate on the outer tablet surface to form a gelatinous layer. All pre and post compression parameters of all formulation like bulk density, tapped density, angle of repose. Carr's Index, solubility, melting point, partition -coefficient, determination of λ max, FT-IR and drug content. The results demonstrated that the developed formulation would increase the activity of Gabapentin and improve patient compliance by reducing the dosing frequency of conventional formulations. The floating matrix tablet formulation might represent a better alternative for controlled and efficacious delivery.

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