Development and Evaluation of Floating matrix Tablets of Gabapentin for the treatment of Epilepsy

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*Abstract:*The current study sought to lengthen Gabapentin's gastrointestinal retention time (GBPT). Gabapentin floating matrix tablets were prepared by direct compression method with free flowing powder using selected drug and excipients authenticated by Fourier-transform infrared spectroscopy (FTIR) of HPMC K4, Potassium bicarbonate, magnesium stearate, and talc in variable concentration for different formulation (T-1 to T-9) Drug content and in vitro drug release studies were performed on floating matrix tablets. Among the various formulations, the optimized formulation (T6) demonstrated a better in-vitro release pattern of 99.99 percent in 12 hours.The findings suggested that direct compression is a suitable method for producing floating matrix tablets of gabapentin, and that it can outperform conventional immediate release dosage forms in terms of therapeutic efficacy. The current study found that a combined mix matrix system containing hydrophobic and hydrophilic polymers reduced burst drug release from tablets.

Index terms: Gabapentin, matrix systems, floating tablet, sustained release systems.

INTRODUCTION

The goal of any drug delivery system is to provide a therapeutic amount of drug to the appropriate site of action in the body in order to achieve and then maintain the desired drug concentration. The use of controlled release (modified release) dosage forms is becoming more popular. These more sophisticated systems can be used to change the pharmacokinetic behaviour of drugs in order to provide twice or once-daily dosage. The oral route of drug administration is the most common and convenient method of drug administration. Typically, once-daily or twice-daily preparations deliver the drug through the GIT[1-6].

According to recent research and patent literature, there is a growing interest in novel dosage forms that are retained in the stomach for an extended and predictable period of time.

Gabapentin (Neurontin) is an anticonvulsant and analgesic medication. It was initially developed to treat epilepsy, but it is now also used to treat neuropathic pain. It is recommended as a first-line treatment for neuropathic pain caused by diabetic neuropathy, post-herpetic neuralgia, and central neuropathic pain.Gabapentin binds to Auxillary subunits of voltage-sensitive calcium channels in cortical neurons. Gabapentin raises GABA synaptic concentrations, improves GABA responses at non-synaptic sites in neuronal tissues, and lowers monoamine neurotransmitter release [7-10].

MATERIALS AND METHOD

Gabapentin was received as a gift sample from Alembic Pharma , Vadodra. Ethyl cellulose, HPMC K4, Potassium bicarbonate, Talc, Magnesium Stearate , Aerosil and Avicel was procured by Mapromax, Life sciences Pvt. Ltd., Dehradun.

Preparation of Gabapentin Floating Matrix Tablets

Gabapentin floating matrix tablets were created using direct compression.[11-12]. Before use in formulation, all polymers, drugs, and excipients were filtered through sieve no. 40.The polymers chosen for tablets are: - HPMC K15 and HPMC K4.For the study, excipients such as talc, citric acid, potassium bicarbonate, and magnesium stearate were chosen.

Table. 1 Various formulations of Gabapentin floating matrix Tablets

Excipients(mg)	**T1**	**T2**	**T3**	**T4**	**T5**	**T6**	**T7**	**T8**	**T9**
Gabapentin	100	100	100	100	100	100	100	100	100
HPMC K 4	160	180	200	-	-	-	80	90	100
HPMC K 15	-	-	-	150	170	200	80	90	100
Lactose	45	25	05	50	35	05	45	25	05
Potassium bicarbonate (KH CO3)	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: Wet granulation was used to create the matrix tablets. Separately, gabapentin, polymer, and other excipients were filtered through a 40 mesh sieve. 100mg of Gabapentin polymer and excipients were accurately weighed and thoroughly mixed for at least 15 minutes. The mixing product was filtered through a sieve with a mesh size of 20. For 30 minutes, the granules were dried in an oven at 400°C[13-17.]The granules that resulted were also sieved through an 18 mesh sieve. Before final compression, these dried granules were lubricated with a specific amount of talc and magnesium stearate. A ten-station lab press compression machine was used to compress the tablets.

Table 2.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)**

T1	0.311±0.02	14.35±0.06	1.03±0.05	26.42±0.04	0.337±0.02
T2	0.325±0.04	15.61±0.07	1.23±0.04	27.17±0.01	0.359±0.04
T3	0.339±0.06	14.64±0.04	1.14±0.02	29.01±0.03	0.361±0.07
T4	0.307±0.04	13.46±0.01	1.13±0.06	27.57±0.07	0.317±0.06
T5	0.287±0.03	12.29±0.05	1.25±0.03	26.77±0.09	0.321±0.05
T6	0.271±0.01	16.35±0.03	1.15±0.01	25.61±0.06 0	0.345±0.01
T7	0.297±0.04	14.46±0.07	1.20±0.03	26.16±0.03	0.357±0.03
T8	0.307±0.05	15.61±0.04	1.19±0.05	29.11±0.09	0.366±0.02
T9	0.320±0.06	13.85±0.09	1.21±0.00	28.05±0.02	0.359±0.04

***(n=3)**

Post-compressionParameter : All prepared samples were tested for thickness, hardness, and weight variation, friability, and drug content, with the results shown in table 2. The average weight derivation was found to be within the [18-21]official limits.

Table 3. 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)
T1	3.79 ±0.03	6.13 ± 0.21	952±0.29	0.5216± 0.04	98.53±0.48
T2	3.70 ±0.05	6.70 ± 0.30	951±0.67	0.6325 ±0.04	99.23±0.57
T3	3.88 ±0.03	6.51 ± 0.50	949±0.45	0.5215 ±0.08	99.77±0.67
T4	3.91 ±0.06	5.81 ± 0.50	951±0.71	0.6532 ±0.10	99.27±0.23
T5	3.89 ±0.03	6.81 ± 0.51	948±0.15	0.6485 ±0.04	98.42±0.61
T6	3.91 ±0.05	5.88 ± 0.51	953±0.31	0.5499 ±0.08	99.47±0.34
T7	3.87 ±0.04	6.80 ± 0.47	949±0.04	0.5325 ±0.10	99.87±0.56
T8	3.85± 0.04	9.83 ± 0.49	948±0.71	0.5369 ±0.15	97.37±0.60
T9	3.84± 0.04	9.73 ± 0.29	951±0.52	0.5425 ±0.15	98.50±0.61

***(n=3)**

Dissolution rate studies

The sample (T1, T2, T3, T5, and T6 and T7) was tested for drug release in vitro using a USP-type II dissolution apparatus (T1, T2, T3, T5, and T6 and T7) (Paddle type). The dissolution medium, 900 ml 0.1N HCl, was placed in the dissolution flask at a temperature of 370.50C and a speed of 75 rpm. In each basket of the dissolution apparatus, one Gabapentin Floating Matrix tablet was placed. [22-25]The apparatus was left running for 12 hours. After 30 minutes, 1.0 hour, 1.30 hour, 2.0 hour, 4.0 hour, 6.0 hour, 8.0 hour, 10.0 hour, and 12 hour, 5 ml samples were withdrawn. Every time, the fresh dissolution medium was replaced with the same amount of sample.

Table 4 ***In vitro* drug release study of Floating Matrix tablet**

Time	% Cumulative Drug Release						
(hr)	T1	T2	T3	T4	T5	T6	T7
0.5	8.23	7.34	7.23	7.24	7.23	7.55	8.32
1	12.32	10.23	10.34	11.45	10.45	11.22	12.23
1.5	26.23	22.42	23.56	24.23	31.23	38.21	32.13
2	42.45	40.32	46.32	45.23	47.23	47.33	47.14
3	76.54	65.11	60.23	67.21	50.56	78.02	71.13
4	82.23	76.33	73.35	75.11	55	89.13	96.23
6	82.55	97.13	89.37	87.13	56	99.17	99.34
8	83	97.1	90.23	94.23	57.25	99.77	94.14
12	84.21	97.23	95.23	99.26	57.85	99.89	94.56

Fig.1 *In vitro* drug release study of floating matrix tablets

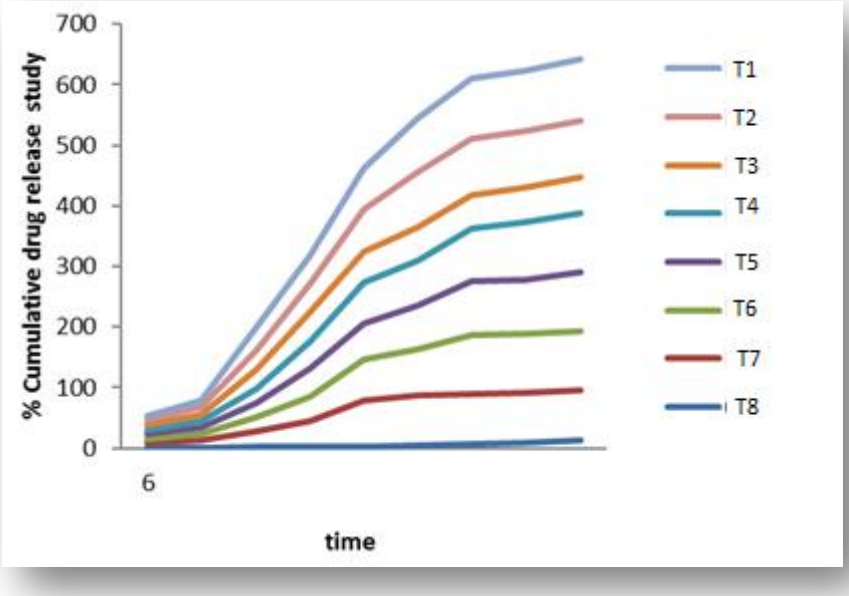

Table 5: Swelling index of Gabapentin Tablets in 0.1N HCl

Time (hr)	T1	T2	T3	T4	T5	T6	T7
1	75.3±0.30	53.3±0.30	83.5±0.20	62.2±0.20	67.3±0.20	101.3±0.20	80.5±0.30
2	83.2±0.30	56.3±0.20	87.6±0.20	66.3±0.20	45±0.20	113.3±0.30	78.6±0.2
4	96.1±0.20	67.2±0.30	84.4±0.20	87.4±0.20	42±0.20	122.4±0.20	89.6±0.3

6	91.3±0.30	75.4±0.30	78.3±0.20	101.0±0.20	56±0.20	126.7±0.10	84.4±0.1
8	101.2±0.30	80.1±0.30	72.2±0.20	97.2±0.20	67±0.20	131.2±0.15	84.2±0.3
10	103.1±0.30	78.3±0.20	62.7±0.20	96.3±0.20	86±0.20	127.2±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	123.4±0.10	87.3±0.4

RESULT AND DISCUSSION

Among all formulations, (T6) exhibits the desired release pattern, i.e. 99.99 percent in 12 hours, which could be attributed to optimal polymer concentration and uniform dispersibility of Gabapentin with compatible excipients.The swollen index of swelling index studies were performed on all prepared formulations, and the results are shown in Table 5.

All pre and post compression parameters were studied, and the results were 0.215g/cc, 0.286g/cc, 28.16 percent, 1.31 & 30^{o} for Bulk density, Tapped density, Carr's index, Hausners ratio, and Angle of repose. Evaluations for like weight variation, hardness, thickness, friability, and drug content show that all formulations' values were within the allowable range. The hardness of T8 and T9 formulations was found to be higher (5.81±0.50), (9.83±0.49), and (9.73±0.29) than that of other formulations[26].

In vitro drug release studies were performed on T1, T2, T3, T5, T6, and T7 formulations, with the result for instant release T6 formulation showing the best drug release (99.99 percent) when compared to other formulations.

CONCLUSION

The purpose of this study could have been to develop a floating matrix drug delivery system for gabapentin, which could be useful for reducing multidosing therapy in patients who have difficulty taking multiple doses of drug. Matrix tablets made with both HPMC and PEO quickly hydrate on the tablet's outer surface, forming a gelatinous layer. All formulation's pre and post compression parameters, such as bulk density, tapped density, and angle of repose. Carr's Index, solubility, and drug content are all factors to consider. The results demonstrated that the developed formulation would increase Gabapentin activity while improving patient compliance.The results showed that the developed formulation would increase Gabapentin activity while improving patient compliance by lowering the dosing frequency of conventional formulations. The floating matrix tablet formulation may be a better option for controlled and effective delivery.

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