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Design, Development And Evaluation of Matrix Tablet of Gabapentin with Natural Polymer

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A B S T R A C T :

The work's objective is to create and assess gabapentin matrix tablets utilising natural polymers in different ratios, including acacia, agar agar, guar gum, and xanthan gum. Nowadays, gabapentin, an anti-epileptic medication, is also used to treat neuropathic pain. It has a plasma half-life of around five to seven hours and is quickly absorbed from the GIT. Because of its brief biological half-life, gabapentin is challenging to maintain at steady state concentrations. Traditional dose forms only spend a brief amount of time in the stomach and intestine. Therefore, a dosage form that lengthens the duration of a drug's residency in the absorption site is required. FTIR analysis was performed on gabapentin, excipients, and the pure drug (gabapentin) in the preformulation. Formulations F1 through F12 with varying proportions of natural polymers such as acacia, agar-agar, guar gum, and xanthan gum underwent an in vitro drug release investigation.

Keywords: Matrix tablet, Controlled release tablet, Sustained release tablet, Gabapentin, Epilepsy

1. Introduction

Many of the earliest controlled-release systems were designed to provide a delivery profile that would result in a sustained high blood level of the medication. With conventional medication delivery methods, the blood level of the drug increases with each dosage and then falls until the subsequent dosage. The crucial aspect of conventional drug administration is that the agent's blood level must stay between a minimum value, below which the medicine loses its effectiveness, and a maximum value, which might indicate a dangerous level. These challenges have led scientists to develop a medicine delivery method that can stay in the stomach for an extended and consistent amount of time. A controlled drug delivery system that can release drugs at a predetermined, predictable, and regulated pace is being developed. The primary goal of an oral CDDS's de novo design should be to enhance and anticipate the medications' bioavailability2. The medication must be well absorbed throughout the GIT, ideally by passive diffusion, for oral CRDDS to be effective. A controlled release dosage form is one that delivers one or more medications either locally or systemically to a designated target organ over a predetermined amount of time in a predefined pattern. Because of the versatility in dosage form design, more focus is being placed on the development of oral controlled release drug delivery systems. Modifying GI transit time, minimising first-pass elimination, and delivering a medication to the intended location at a therapeutically appropriate rate are the three primary problems facing oral drug delivery systems. With fewer side effects and dose frequency, the control release dosage form offers better maintenance of an appropriate and effective medication level for an extended period of time.

1.1 The following categories apply to modified release oral medication delivery systems:

Restricted release
Long-term release
Extended-release
Delayed Release
Postponed release

1.1.1 Controlled release drug delivery system

The fundamental idea behind a controlled release drug delivery system is to maximize a drug's utility by minimizing side effects and curing or controlling a disease condition as quickly as possible with the least amount of the drug given via the most effective route. This is achieved by optimizing the drug's biopharmaceutics, pharmacokinetics, and pharmacodynamics properties. Certain aspects, such as site targeting, regulated release rate, and dosage management, are absent from the immediate-release drug delivery method. Over the course of a prescribed treatment time, the optimal drug delivery system should administer the medication at a pace determined by the body's needs.

1.1.1 Matrix Tablet

Matrix tablets are solid oral dosage forms in which the medicine is embedded within a polymer or other excipients' matrix to regulate its release. These systems are engineered to facilitate sustained or regulated drug release, which is especially advantageous for chronic illnesses necessitating long-term therapy.

2. .Material and Methods

Apparatus and chemicals: Gabapentin by torrent pharmaceutical ltd., Gujarat, Acacia, agar, Xanthium gum, by Ankit pulps chemicals pvt, Maharashtra, Lactose and magnesium stearate by Zytex biotech pvt limited, Gujarat.

Methods: Preparation of matrix tablet of gabapentin

After precisely weighing the active component (gabapentin) and each of the other ingredients, they were each passed through sieve number 60. The ingredients were then fully combined by triturating for up to fifteen minutes. For punching to tablets using the direct compression method, the combined powder was greased and then completely mixed one more. Table No. 5 provided the composition of several tablet batches

Table 1: Formulation for Matrix Tablet of Gabapentin formulation

Ingredient	F1 (mg)	F1 (mg)	F1 (mg)	F1 (mg)	F1 (mg)	F1 (mg)	F1 (mg)	F1 (mg)	F1 (mg)	F1 (mg)	F1 (mg)	F1 (mg)
Gabapentin	300	300	300	300	300	300	300	300	300	300	300	300
Acacia	125	150	175	-	-	-	-	-	-	-	-	-
Agar-agar				125	150	175	-	-	-	-	-	-
Guar gum	-	-	-	-	-	-	125	150	175	-	-	-
Xanthan gum	-	-	-	-	-	-	-	-	-	125	150	175
Magnesium stearate	25	20	15	25	20	15	25	20	15	25	20	15
Calcium carbonate	50	30	10	50	30	10	50	30	10	50	30	10
Total weight	500	500	500	500	500	500	500	500	500	500	500	500

3. Experimental work

Preformulation Studies

Preformulation is the study of a medicinal ingredient's physical and chemical qualities, both by itself and when mixed with other ingredients. The goal of preformulation research is to find the physicochemical features and excipients that might have an impact on the final product's manufacturing process, formulation design, and pharmacokinetic-biopharmaceutical aspects.

3.2 Determination of solubility

We examined solubility in several liquids, such as ethanol, methanol, absolute ethanol, acetone, chloroform, ether, water, 10% v/v HCl, and 10% w/v sodium hydroxide.

UV and FTIR Spectroscopy

We next scanned the solution with 10µg/ml at 270 nm to find the wavelength of maximum absorbance. There was a comparison between the reference standard FT-IR spectra of Gabapentin and the FT-IR spectrum of Gabapentin that was obtained.

4. Result and discussion

Preformulation Study

4.1.1 Description

Gabapentin is white crystalline powder with bitter taste

4.1.2 Result of Solubility

It was observed that gabapentin was insoluble in heptane, ethyl acetate, diethyl ether. And soluble in water and methanol.

4.2 Result of Melting Point

The melting point of the medicine was found to be close to the figure given, which confirmed that the drug samples that were received satisfied the requirements. The melting point of a certain drug component will change based on any contaminants that may be there. It is said that gabapentin melts around 165°C.

4.3 UV Spectroscopy

A peak with an absorbance was seen at 270 nm in a solution of 10µg/ml in methanol. The identity of the gabapentin molecule is confirmed by the absorbance maxima at 270 nm, which is one of its hallmarks.

4.3.1 FT-IR Spectroscopy

The drug's infrared spectra was similar to that of Gabapentin usual spectrum, which meant that the sample was clean. This confirms that the identification of gabapentin is correct.

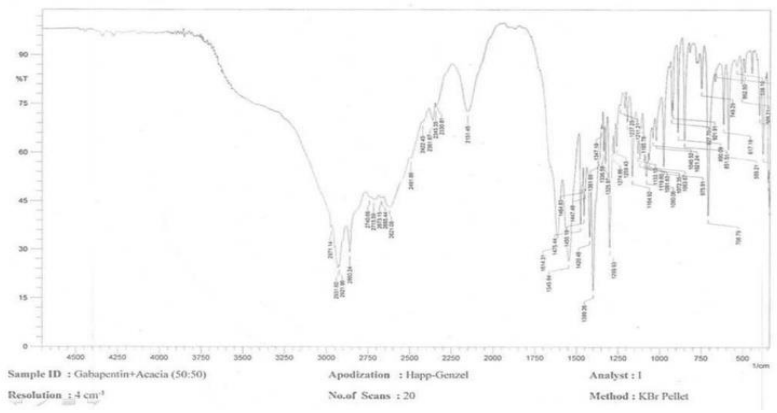

Fig 1. FT-IR of Gabapentin

4.4 Drug - Excipients Compatibility Study

FT-IR Spectroscopy

FTIR examination of the physical mixes of the drug and excipients showed that the drug and excipients were compatible.

When you look at the IR spectra of Gabapentin, excipients, and their combination, you can see that all of the unique bands in Gabapentin are still there.

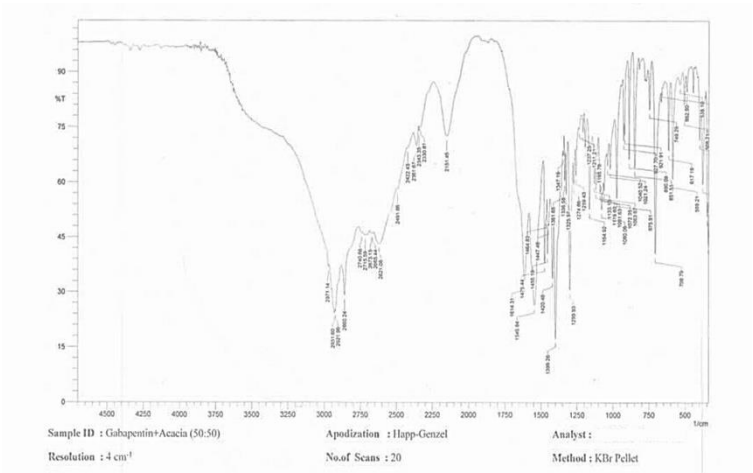

Figure 2 FT-IR Spectra of Gabapentin and Excipients Acacia

4.5 Evaluation of Matrix Tablet

4.5.1 Pre compression parameters

Table.No.:2. Evaluation parameters of powder blend.

Formulation	Angle of repose(θ)	Bulk density (g/ml) ± SD	Tapped density (g/ml) ± SD	Carr's index	Hausner's Ratio
F1	26.42±0.04	0.311±0.02	0.337±0.02	14.35±0.06	1.03±0.05
F2	27.17±0.01	0.325±0.04	0.359±0.04	15.61±0.07	1.23±0.04
F3	29.01±0.03	0.339±0.06	0.361±0.07	14.64±0.04	1.14±0.02
F4	27.57±0.07	0.307±0.04	0.317±0.06	13.46±0.01	1.13±0.06
F5	26.77±0.09	0.287±0.03	0.321±0.05	12.29±0.05	1.25±0.03
F6	25.61±0.06	0.271±0.01	0.345±0.01	16.35±0.03	1.15±0.01
F7	26.16±0.03	0.297±0.04	0.357±0.03	14.46±0.07	1.20±0.03
F8	29.11±0.09	0.307±0.05	0.366±0.02	13.61±0.04	1.19±0.05
F9	28.05±0.02	0.320±0.06	0.359±0.04	13.85±0.09	1.21±0.00
F10	25.61±0.03	0.271±0.02	0.345±0.01	16.35±0.02	1.15±0.01
F11	29.57±0.07	0.307±0.03	0.317±0.04	15.46±0.01	1.13±0.05
F12	27.17±0.02	0.325±0.04	0.359±0.04	15.61±0.06	1.23±0.04

Table.No.:3. Evaluation of post compression parameters of formulations

Formulation	Weight variation (n=20) (mg ± SD)	Hardness (kg/cm^2±SD)	Friability (%)	Drug content (%± SD)	Thickness (%± SD)
F1	502±0.29	6.6±0.1	0.69	99.13±0.04	5.2±0.007
F2	501±0.67	6.4±0.2	0.67	98.19±0.01	5.3±0.006
F3	498±0.45	7.0±0.3	0.74	99.09±0.12	5.2±0.011
F4	504±0.71	6.7±0.5	0.71	98.19±0.09	5.3±0.008
F5	499±0.15	7.2±0.2	0.65	99.17±0.07	5.2±0.009
F6	501±0.31	6.8±0.4	0.63	98.61±0.03	5.2±0.013
F7	496±0.04	6.5±0.3	0.76	99.13±0.17	5.3±0.004
F8	497±0.71	7.3±0.3	0.70	98.11±0.14	5.2±0.012
F9	503±0.52	7.4±0.5	0.68	98.21±0.05	5.3±0.05
F10	499±0.34	6.5±0.4	0.78	99.13±0.07	5.3±0.008
F11	501±0.71	6.7±0.5	0.73	99.19±0.11	5.3±0.006
F12	502±0.68	6.4±0.2	0.69	98.19±0.02	5.3±0.002

4.5.7 In-vitro release of study

The dissolution release profile of different formulations was examined in vitro. The formulations F1 through F12 were shown to dissolve in vitro based on the findings of controlled release tests. Formulation F8, which has a 12-hour release profile, was chosen to formulate the matrix tablet.

Time in hours	Cumulative drug release											
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**	**F11**	**F12**
0	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
1	22.18	20.44	15.32	21.26	20.01	14.36	8.48	7.46	6.82	7.02	6.32	5.32
2	40.32	38.62	33.28	39.98	38.56	33.46	16.42	15.38	14.02	14.96	12.42	11.76
3	60.66	58.16	50.24	59.86	58.28	50.68	30.26	29.2	26.32	28.46	27.64	25.2
4	79.68	77.24	63.48	78.28	77.22	62.94	42.38	39.86	35.8	38.58	38.48	34.84
5	90.14	89.18	78.64	90.26	88.16	78.42	58.24	56.28	52.48	56.62	54.5	50.88
6	99.38	92.46	85.92	99.42	92.48	86.02	69.76	64.46	58.26	64.82	59.28	57.42
7		99.22	92.32		99.84	92.64	75.22	70.52	63.74	70.92	64.72	62.68
8		-	99.04			99.62	88.12	81.72	71.78	82.84	72.94	70.12
9	-	-	-		-		95.42	88.84	79.92	89.1	82.46	78.42
10	-	-	-		-		99.24	94.38	85.82	95.22	89.24	84.86
11								99.48	95.1	99.74	96.32	94.98
12									98.26		99.88	97.86

Table.No.:5. In vitro Dissolution profile gabapentin Matrix Tablet release tablets

4.6 Release kinetics:

Table 28 : Kinetic studies of matrix Tablets

Time (hrs)	Log Time	√Time	Cumulative %drug release	Log cumulative % drug release	Cumulative % Drug remained	Log Cumulative %drug remained
0	0	0	0	0	100	2.000
1	0	1.000	6.32	.8007	93.68	1.971
2	0.3010	1.414	12.42	1.094	87.58	1.942
3	0.477	1.732	27.64	1.433	72.36	1.859
4	0.6020	2	38.48	1.585	61.52	1.789
5	0.698	2.236	54.5	1.736	45.5	1.658
6	0.7781	2.449	59.28	1.772	40.72	1.609
7	.8450	2.645	64.72	1.811	35.28	1.547
8	.9030	2.828	72.94	1.862	27.06	1.432
9	.954	3	82.46	1.916	17.54	1.244
10	1	3.162	89.24	1.950	10.76	1.031
11	1.041	3.316	96.32	1.983	3.68	.5658
12	1.079	3.464	99.88	1.999	.12	-0.920

4.7 Stability Studies of best Formulation

Table.No.:6. Stability studies of optimized formulation F8

Parameters	Initial	1st Month	2nd Month	3rd Month
Description	White colour, Caplet shape, Polymer coated tablet.	Complies	Complies	Complies
Average weight (mg)	501±0.71	501±0.55	501±0.22	501±0.12
Thickness (mm)	5.62	5.62	5.62	5.62
Hardness (kg/cm2)	6.7	6.7	6.7	6.7
Assay (%)	99.45	99.45	99.27	99.14
Dissolution	96.75	96.67	96.52	96.43

Conclusion

The primary goal of the current study was to use polymers such as acacia, agar-agar, guar gum, and xanthan gum to create controlled-release tablets with 300 mg of gabapentin for the treatment of epilepsy. The medicine's bioavailability and therapeutic efficacy are enhanced by the drug delivery system's regulated release.

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