Bulletin of Environment, Pharmacology and Life Sciences
Bull. Env. Pharmacol. Life Sci., Vol 12 [3] February 2023 : 87-93

Online ISSN 2277-1808
Journal's URL:http://www.bepls.com
CODEN: BEPLAD

ORIGINAL ARTICLE **OPEN ACCESS**

Formulation Development and Evaluation of Carbamazepine Chewable Tablets

Vaibhavkumar Jagtap[1]*, Kunal Ramesh Patil[1], Shakeeb Akhtar[2], Sufiyan Ahmad[3]
[1]Department of Pharmaceutics, A. R. A. College of Pharmacy, Nagaon, Dist. Dhule (M.S.), India.
[2]Department of Pharmaceutics, Royal College of Pharmaceutical Education and Research, Malegaon. Dist. Nashik (M.S.), India.
[3]Department of Pharmacognosy, Gangamai College of Pharmacy, Nagaon, Dist. Dhule (M.S.), India.
Correspondence Email: jagtapvaibhav77@gmail.com

ABSTRACT
Carbamazepine an anticonvulsant medication used primarily in the treatment of epilepsy and neuropathic pain. It is used in schizophrenia along with other medications and as a second-line agent in bipolar disorder. Aim of the present study was to develop, optimize and evaluate chewable tablet of carbamazepine. This study was specifically focused on formulation development which passes preformulation studies and optimization of the developed formulation. The formulations were evaluated on friability, hardness, weight variation, disintegration, in-vitro drug release and stability of optimized formulation. Nine formulations (F1 to F9) were prepared by using different concentration of different polymer. All the formulations were subjected for evaluation and optimized formulation (F8, Eudragit RS 30 D and Croscarmellose sodium) was found to be within the acceptable limits.F8 formulations shows the friability 0.5 %, Hardness 5.4 kg/cm, disintegrated in 3.5 minutes and in 60 minutes 98.73 % drug release were observed. Same formulation were subjected for stability study for 90 days. No any changes were observed after period of stability evaluation. It was concluded that carbamazepine chewable tablet can be developed and itis more efficient with Eudragit RS 30D and croscarmellose sodium as compared to othe disintegrating agent such as microcrystalline cellulose and lactose.
Keywords: *Chewable tablet, Carbamazepine, Eudragit, anticonvulsant*

Received 07.11.2022 Revised 21.01.2023 Accepted 25.01.2023

INTRODUCTION

Oral delivery is currently the gold standard in the pharmaceutical industry where it is regarded as the safest, most convenient and most economical method of drug delivery having the highest patient compliance. Methods to improve patient's compliance have always attracted scientists towards the development of fancy oral drug delivery systems. Among them, mouth dissolving drug delivery systems (MDDDS) have acquired an important position in the market by overcoming previously encountered administration problems and contributing to extension of patent life [1]. MDDDS have the unique property of rapidly disintegrating and/or dissolving and releasing the drug as soon as they come in contact with saliva, thus obviating the requirement of water during administration. Therefore, these dosage forms have lured the market for a certain section of the patient population which include dysphagic, bed ridden, psychic, and geriatric and paediatric patients. Research in developing orally disintegrating systems has been aimed at investigating excipients as well as technique to meet these challenges [2]. Technologies used for manufacturing of orally disintegrating tablets are either conventional technologies or patented technologies. In conventional freeze drying, tablet molding, sublimation, spray drying etc. and in patented Zydis technology, Orasolv technology, Durasolv technology, Wowtab technology, Flashdose technology are important. Important ingredients that are used in the formulation of ODTs should allow quick release of the drug, resulting in faster dissolution [3].

Chewable tablets

Chewable tablets are tablets that are required to be broken and chewed in between teeth before ingestion. These tablets are given to children who have difficult in swallowing and to the adults who dislike swallowing. Chewable tablets are chewed and broken into smaller pieces prior to swallowing and are not to be swallowed intact. In this way, the time required for disintegration is reduced and the rate of absorption of the medicament may increase. For the preparation of chewable tablets, mannitol is used as

the base. These tablets should have acceptable taste and flavour. They should disintegrate in a short time and produce cool sweet taste [4].

MATERIALS AND METHOD

Carbamazepine was purchased from Bajaj Healthcare, Boisar. Croscarmellose Sodium, microcrystalline cellulose, lactose and magnesium stearate was purchased from Loba chem Mumbai. Eudragit RS 30 D and HPMC K 15 was purchased from Yarrow chem products, Mumbai.

Formulation of Carbamazepine Chewable Tablet:

The processing of drug with excipients can be achieved without any need of granulation and related unit operations. By simply mixing in a blender, formulation ingredients can be processed and compressed into tablets without any of the ingredients having to be changed. This procedure is called direct compression and it is used in the manufacture of tablets when formulation ingredients can flow uniformly into a die cavity. The term direct compression was reserved for a small group of granular chemicals having all the physical characteristics that enable them to be directly compressed into tablets without an intermediate granulating step. As such, it was only used for chemicals, such aspotassium salts (chlorate, chloride, bromide, iodide, nitrate, and permanganate), ammonium chloride, and methenamine. The term direct compression (or direct compaction) is used to define the process by which tablets are compressed directly from powdered active drug substance and suitable excipients into a firm compact without employing the process of granulation. The successful application of direct compression technique in tablet manufacture especially for low and medium dosage range of drugs can be attributed to the availability of new excipients, modified form of old excipients, and the invention and utilization of new tablet machinery [5].

Formula of 150 mg Carbamazepine Chewable tablet:

Table No. 1: Formulation of Carbamazepine Chewable Tablet

Ingredient	F1	F2	F3	F4	F5	F6	F7	F8	F9
Drug	50	50	50	50	50	50	50	50	50
Croscarmellose Sodium	25	30	35	35	40	25	45	30	50
Lactose	30	30	30	30	30	30	20	30	20
microcrystalline cellulose	10	10	10	20	20	20	20	20	20
Eudragit RS30D	00	00	00	00	05	10	10	10	05
Magnesium stearate	15	15	15	05	05	10	15	10	05
HPMC-K15	20	15	10	10	00	00	00	00	00
Total weight	150	150	150	150	150	150	150	150	150

Pre-formulation Studies

It is the first step in the development of dosage forms of the drug substance. Preformulation testing is defined as the investigation of physical and chemical properties of a drug substance alone and when combined with excipients. The overall objective of preformulation testing is to generate information useful to the formulator in developing stable and bioavailable dosage forms that can be mass-produced.

Physical characterization

This includes are cording of colour, odour and taste of the new drug using descriptive terminology. Record of the colour of early batches is very usefulin establishing appropriate specifications for later production. Drugs generally have characteristic odors and tastes. Unpleasant ones are masked later during formulation [6]. The melting point of a drug can be measured by using technique Capillary Melting. Powder density may influence compressibility, sphericity, pellet porosity, dissolution and other properties [7].

Bulk density (BD)

Bulk density is the ratio of the mass of powder to the bulk volume of powder. Place the measuring cylinder on a plane surface. The fixed weight powder was filled in measuring cylinder. Make surface of powder in the cylinder at equal level and note the volume occupied by powder as bulk volume. The ratio of that fixed weight mass powder to its bulk volume considers as bulk density of the powder. The equationfor determining bulk density is given below:

$$\rho b = m / vb$$

Where,
ρb = Bulk density
m =Mass of powder
vb = Bulk Volume

Tapped density (TP)

The pre-weighed powder was filled in measuring cylinder. Then it was tapped in density tap tester. After 50 taps the volume was measured. It is a measure used to describe void space of powder.
The equation for determining tapped density is given below:

$$\rho t = m / vt$$

Where,
ρt = Tapped density
m = Mass of powder
vt = Tapped volume

Carr's Index (CI)

Compressibility is indirectly related to the relative flow rate, cohesiveness and particle size distribution of the powder. Tapped density (ρt) and bulk density (ρb) of powder material were used to measure compressibility of a powder material. It is a measure used to describe compression capability of the powder material. The equation for determining Carr's index is given below:

$$\text{Carr's index (\%)} = (\rho t - \rho b)/\rho t \times 100$$

Where,
ρb = Bulk density
ρt = Tapped density

Table No. 2: Relationship between % compressibility and flow ability

Sr. No.	Compressibility index	Flow
1.	5-45	Excellent
2.	12-16	Good
3.	18-21	Fair to possible
4.	23-35	Poor
5.	33-38	Very poor
6.	>40	Very poor

Hausner's Ratio (HR):

It is the ratio of bulk volume to tapped volume or tapped density to bulk density. It is a measure used to describe compressibility of powder. Tapped density (ρt) and bulk density (ρb) of powder material were used to measure Hausner's Ratio of a powder material. The equation for determining Hausner's Ratio is given below:

$$\text{Hausner's Ratio} = \rho t/\rho b$$

Where,
ρb = Bulk density
ρt = Tapped density [8]

Angle of Repose

The angle of repose is maximum angle possible between a pile of powder and horizontal plane. The angle of repose of powder blend was determined by using powder flow apparatus. The height of the funnel was adjusted in such a way the tip of the funnel just touched the apex of the powder blend (Almost 2cm was fixed from plane to tip of the funnel). The powder blend was allowed to flow through the funnel freely on to the surface. It is a measure used to describe flow ability of the powder material. The equation for determining Angle of Repose is given below:

$$\theta = \tan\text{-}1\ h/r$$

Where,
θ = Max. Angle between a pile of powder and horizontal plane
h = Height of pile of powder
r = Radius of the base of the conical pile

Solubility study:

The solubility was determined by weighing 10mg of the compound (API) to this 10 ml ofthe solvent were added, If not dissolved, further 10 ml of solvent was added successively and its effect was noted. Successive amounts of the solvents were gradually added until the API get completely dissolved when observed visually. The following table indicates the meanings of the terms used in statements of approximate solubility at 20°C-30°C [9].

Post compression evolution of chewable tablet of carbamazepine

The general appearance of the tablet was studied by the evaluation of the parameters like size, colour and odour. 10 tablets were visually observed [10].

Thickness

The thickness of the tablet was measured to determine the uniformity of size and shape. Procedure: The thickness of the tablet was measured using Vernier caliper [11].

Friability

Friability of the prepared formulations was determined by using Roche friabilator. Pre weighed sample of tablets was placed in the friability tester, which was then operated for 100 revolutions, tablets were deducted and reweighed. The friability of the tablets was calculated using the formula mentioned below.
A friabilator evaluates the ability to withstand mechanical stress during packaging, handling and shipping.

Hardness

The hardness test was performed to measure the tablet strength. Tablets should be hard enough to withstand packaging and shipping but not so hard as to create difficulty upon chewing. Procedure: Tablets were taken and its hardness were tested by using Dr. Schleuniger Pharmatron model 5Y tablet tester and the readings were noted.

Uniformity of weight

20 tablets were selected randomly and weighed individually and the average weight was calculated. Then the individual weight was compared to the average weight. Not more than two of the individual weights deviate from the average weight by the percentage deviation given below [11].

Disintegration Time:

This test is provided to determine whether tablets disintegrate within the prescribed time when placed in a liquid medium at the experimental conditions. Complete disintegration is defined as that state in which any residue of the unit except fragments of insoluble coating or capsule shell, remaining on the screen of the test apparatus or adhering to the lower surface of the disc, if used is a soft mass having no palpably firm core [12].

In Vitro Drug Release Studies

Aninvitro Drug Releases of Carbamazepine from its ODT was performed by using Dissolution Rate Test Apparatus with a paddle stirrer (USP type II) at 50 rpm. 900 ml of 0.1N HCl was used as dissolution medium which was maintained at 37±0.50C. Aliquots of dissolution medium (5ml) were withdrawn at different time intervals of 5, 10, 15, 20, 25, 30, 40, 50 and 60 minutes and filtered through Whatmann filter paper. The sample of dissolution fluid withdrawn at each time was replaced with fresh dissolution fluid. Filtered sample solution was suitably diluted with 0.1 N HCl and the amount of drug dissolved were determined by UV spectrophotometer, by measuring the absorbance of the sample at 284nm.

Stability Study

Stability study was carried out at 27±20C/ 40±5% RH and at room temperature for 90 days showed no significant change in colour, disintegration time but slightly change in cumulative % drug release due to absorbance of moisture shown by tablets so there is requirement of proper storage of tablets at optimum humidity for stability of optimized formulation (F8)[12].

RESULT AND DISCUSSION

Organoleptic Character and Melting Point

Table No.3: Organoleptic Characterization and Melting point determination of Drug

Sr. No.	Test	Observation
1.	Colour	White
2.	Odour	Odourless
3.	Melting Point	190.20 °C

Solubility Analysis

Table No. 4: Solubility Analyses

Sr. No.	Test	Observation
1	Water	Insoluble
2	Alcohol	Soluble
3	Acetone	Soluble

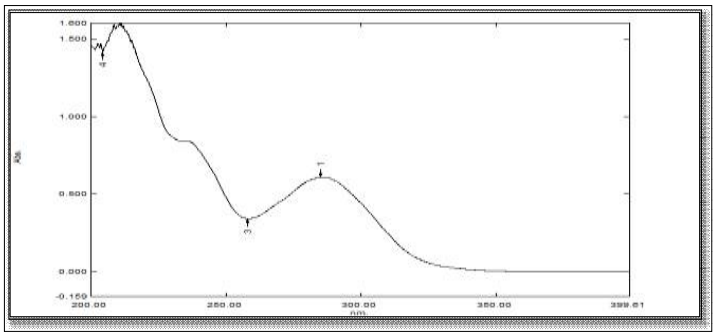


Fig. No. 1: UV – Spectra of carabamazepine

FTIR Spectra of Carbamazepine

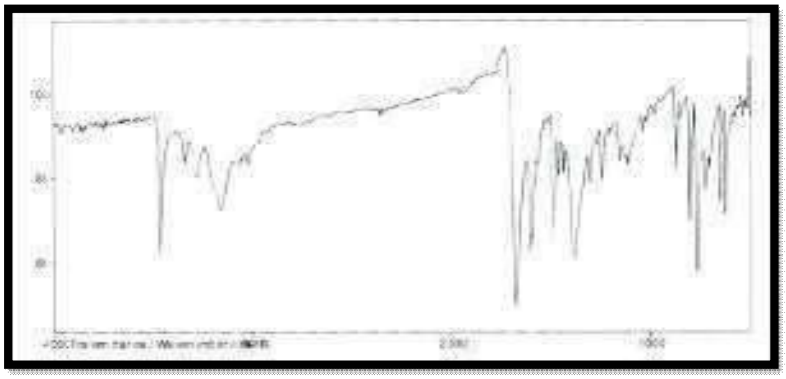
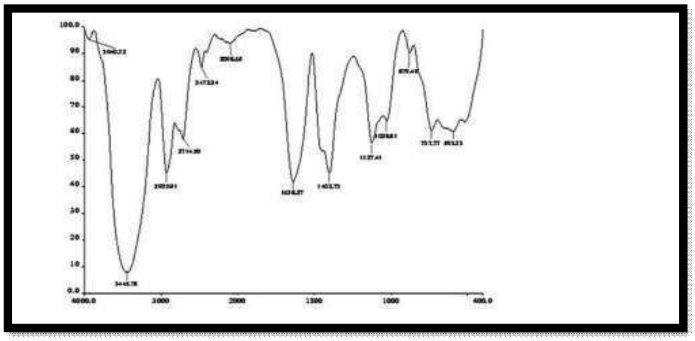


Fig. No.2: FTIR Spectra of Carbamazepine

FTIR Spectra of Eudragit RS30D

Fig. No. 3: FTIR Spectra of Eudragit RS30D



Pre Compressional Evolution of Blend

Table No. 5: Pre Compressional Evolution of Blend

Sr. No.	Angle of Repose	Bulk Density	Tapped density	Car's Index	Hausner's Ratio
F1	25.47±0.3	1.01±0.2	1.15±0.1	9.1±0.32	1.13±0.42
F2	27.45±0.4	0.96±0.3	1.13±0.3	10±0.28	1.17±0.45
F3	26.45±0.6	1.12±0.2	1.32±0.3	9±0.25	1.17±0.47
F4	28.45±0.7	1.04±0.4	1.11±0.4	7±0.45	1.06±0.41
F5	25.55±0.2	0.98±0.3	1.14±0.2	9±0.85	1.16±0.43
F6	26.15±0.2	0.96±0.2	1.05±0.4	7±0.56	1.09±0.45
F7	27.55±0.4	1.04±0.4	1.12±0.2	6±0.23	1.07±0.42
F8	29.01±0.4	0.98±0.4	1.13±0.2	8±0.15	1.15±0.45
F9	26.88±0.3	0.94±0.2	1.13±0.5	9±0.25	1.20±0.1

Post Compressional Evolution of Blend

Table No. 6: Post Compressional Evolution of Blend

Formulation	Thickness (mm)	Diameter (MM)	Hardness (kg/cm)	Friability (%)	Weight (mg)
F1	5.3±0.15	7.85±0.43	5.6±0.44	0.4±0.59	150.98±0.23
F2	5.32±0.34	6.54±0.37	5.2±0.26	0.5±0.36	150.21±0.41
F3	5.25±0.37	6.50±0.11	5.2±0.34	0.3±0.41	150.25±0.13
F4	5.32±0.28	5.58±0.64	5.8±0.49	0.2±0.74	150.88±0.42
F5	5.34±0.96	5.60±0.37	5.0±0.33	0.4±0.11	150.79±0.55
F6	5.30±0.73	5.54±0.25	5.0±0.24	0.3±0.24	150.22±0.97
F7	5.25±0.37	5.50±0.19	5.8±0.77	0.2±0.36	150.09±0.28
F8	5.27±0.16	8.52±0.73	5.4±0.29	0.5±0.47	150.69±0.63
F9	5.32±0.55	9.58±0.37	5.6±0.55	0.5±0.67	150.58±0.57

Disintegration Time

Table No. 7: Disintegration Time

Formulation	Disintegration Time (min)
F1	3.1
F2	4.2
F3	3.0
F4	2.4
F5	3.4
F6	3.9
F7	4.6
F8	3.5
F9	4.0

In Vitro Drug Release Studies

Table No.08: In Vitro Drug Release Studies

Time (min)	F1	F2	F3	F4	F5	F6	F7	F8	F9
10	25.82	31.98	33.45	23.67	12.12	32.13	37.77	30.12	32.35
20	36.83	37.13	47.98	34.43	25.56	39.27	44.32	41.56	48.48
30	53.54	54.11	61.55	59.88	35.19	45.50	52.89	58.23	72.35
40	72.43	76.98	78.12	79.91	41.37	68.20	78.98	80.45	81.12
50	90.44	88.17	91.78	86.55	65.94	89.10	92.98	90.23	91.78
60	92.02	92.12	93.23	95.76	87.94	90.25	99.11	98.78	96.67

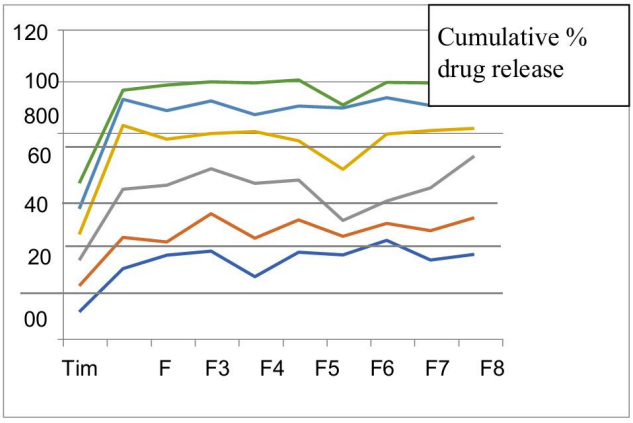


Fig. No. 4: Cumulative drug release

Stability Study

Table No. 9: Stability study

Time (days)	Appearance	Cumulative % drug release in 15 min	Drug content
Initial	White	100.17±0.22	99.30±1.24
45 days	White	99.13±0.12	95.24±1.64
90 days	White	97.89±0.21	90.12±1.15

The drug was subjected to study its organoleptic characters and melting point. The colour of the drug was found to be white and odour was odourless. The melting point was found to be 190-192°C. While the solubility studies were also being carried out and it was found that the drug is insoluble in water and soluble in alcohol and acetone. UV Visible spectra was also studied by using UV VIS Spectroscopy. FTIR Spectra determination was also carried out using FTIR Spectroscopy. The Functional groups present in Carbamazepine and excipients were studied and reported [10].

The blend was subjected for precompressional and post compressional evaluation which included determination of angle of repose, bulk density, tap density and Haussner's ratio along with F1 to F9 Formulations and their thickness, diameter, hardness, friability and weight variation was also studied. The disintegration time was found highest for F7 Formulation that is 4.6 minutes, which indicated that all the formulations got disintegrated within 5 minutes [11].

In vitro drug release study was done and readings were noted upto 60 minutes in interval of 10 minutes. Stability studies were also carried out using standard operating procedures for 3 months (90 Days) [12].

CONCLUSION

In this study, chewable tablet of carbamazepine succinate were successfully prepared by direct compression method using Suitable polymer. Fabricated tablets showed acceptable weight variation, hardness, and uniformity of drug content. The overall results explained that the tablets prepared by combination of Eudragit Rs 30 D& Orel disintegration agent Croscarmellose sodium, could be more efficient on floating and sustained release of magnesium stearate as compared to the tablets prepared using lactose, microcrystalline cellulose only. After performing 90 days stability studies no any changes were observed in drug release and drug continents. From the above study it was concluded that carbamazepine succinate chewable tablet with eudragit Rs 30 D and Croscarmellose sodium can be prepared.

REFERENCES

1. Gibson, M. (2001). Pharmaceutical preformulation and formulation. *Drugs and the pharmaceutical sciences*, *199*, 199.
2. Lachman, L., Lieberman, H. A., & Kanig, J. L. (1976). *The theory and practice of industrial pharmacy* (pp. 412-428). Philadelphia: Lea & Febiger.
3. Jain N.K. (2006). *Pharmaceutical product development*, CBS publishers & distributors, New Delhi. pp. 61-65.
4. Suzuki, H., Onishi, H., Takahashi, Y., Iwata, M., & Machida, Y. (2003). Development of oral acetaminophen chewable tablets with inhibited bitter taste. *International journal of pharmaceutics*, *251*(1-2), 123-132.
5. Patil, H., Prashar, B., Chandel, A., & Thakur, V. (2012). Formulation and evaluation of floating tablet of pantoprazole sodium sequihydrate. *Journal of Pharmacy Research*, *5*(9), 4659-4662.
6. Sing, R., Sharma P. K., Dhakad P.(2014), Preformulation Studies of Pantoprazole Sodium Susquihydratefor Sustained Release Mucoadhesive Microsphere. *Global Journal of Pharmacology*, 8(4),547-550
7. Lachman, L, Lieberman, A, Kinig, J. (2017). *The Theory and Practice of Industrial Pharmacy*, (pp430-457) 4th edition, Varghese Publishing House, Bombay.
8. Martin, A. (2001). Coarse dispersions. Physical Pharmacy. Baltimores, (423-454) M.D., Lippincott Williams and Wilkins.
9. Mark, G.(2009). Pharmaceutical preformulation and formulation, Drug and Pharmaceutical sciences, 2nd Edition, 190.
10. Pahwa, R., & Gupta, N. (2011). Superdisintegrants in the development of orally disintegrating tablets: a review. *International journal of pharmaceutical sciences and research*, *2*(11), 2767.
11. United States Pharmacopeia. (2009). 32-National Formulary 27.
12. Surver, C. et al. (2002) Bioavailabillity and Bioequivalence, Dermatological and Transdermal Formulation, Marcal Dekker, In: K. A. Walter (eds.), New York, 2002, 323-327.

CITATION OF THIS ARTICLE

Vaibhavkumar Jagtap, Kunal Ramesh Patil, Shakeeb Akhtar, Sufiyan Ahmad. Formulation Development and Evaluation of Carbamazepine Chewable Tablets. Bull. Env. Pharmacol. Life Sci., Vol 12[3] Feb 2023: 87-93.