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# Design and Release of Carbamazipine Extented Release Matrix Tablets

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## ABSTRACT

Epilepsy is a chronic condition of the central nervous system, number of situation consuming in public unusually working brain cell, advent of motor, sensory autonomic and psychic index. Carbamazepine reduces discomfort related thru trigeminal neuralgia after 24-48hrs.The immediate discharge tablet of CBZ essential to be managed 3-4 times a day. Prolonged discharge matrix preparation of CBZ (200mg) has great effect to manage it.

**Methodology:** Crystalline properties of CBZ in continue discharge hydrophilic matrix tablet founded on hydroxyl propyl methyl cellulose (HPMC).

Hydrophilic matrix system reduces the frequency of drug dosing.

Hydrophilic matrix tablet of CBZ utilse hydroxyl propyl methyl cellulose of low viscosity grade in the concentration of 27.85% was developed.

**Result:** Presence of sodium lauryl sulphate (SLS) in the preparation improve the solubility of the CBZ permitted extra than 98.1% of CBZ to discharge of the finish of 24hrs.

**Keywords:** CBZ (Carbamazepine); HPMC (hydroxyl propyl methyl cellulose).

## INTRODUCTION

Carbamazepine has anti consultant properties and relives a discomfort related thru the trigeminal neuralgia frequently 24-48hrs. Thus the goal of this learning stayed to progress a 24hrs prolonged discharge hydrophilic matrix preparation of CBZ (200mg) thru a drug discharge profile in the USP approved standard.

Our trial reduce compressibility index, great dose, little water solubility and to form different polymorphs under humid condition.

### Extended release dosage form

A dosage form which allows at least two folds reduction in dosage frequency as compared to that drug presented as an immediate release.

### Matrix system

The matrix system is most often used for a drug controlled release for a pharmaceutical dosage form. Matrix system must be considered the chemical nature of support (generally, the support are formed by polymeric net).
The physical state of drug (dispersed under molecular or particulate form or both).

### Classification of matrix system

1. Mineral Matrix (drug retained in support, absorbed on the support)
2. Lipid Matrix (delivery by diffusion, by surface erosion)
3. Hydrophilic Matrix (unlimited swelling, limited control delivery)
4. Inert Matrix (control delivery by diffusion)

## AIMS AND OBJECTS

### Aims

The aim of present study is to design and release characterization of carbamazepine extended release matrix tablet formulation developed to reduce dose frequency and to maintain constant plasma drug concentration and to reduce adverse effects.

### Objects

Carbamazepine has anti consultant properties and relives a discomfort related thru the trigeminal neuralgia frequently 24hrs-48hrs. Thus the objective of this study stayed to develop a 24hrs extended release hydrophilic matrix preparation of CBZ (200 mg) Table 1.

## MATERIALS AND METHODS

### Material used

**Table 1:** This table provides a list of resources which are used for preparation of Carbamazepine matrix tablet.

| S.No. | Preparation Ingredients | Use |
|---|---|---|
| 1 | Carbamazepine | API |
| 2 | Hydroxy Propyl Cellulose (Low Viscosity Grade) | ER Matrix former |
| 3 | Hydroxy Propyl Cellulose (High Viscosity Grade) | ER Matrix former |
| 4 | Hydroxy Propyl Methyl Cellulose | ER Matrix former |
| 5 | Microcrystalline Cellulose | Diluent |
| 6 | Lactose | Diluent and channalising agent |
| 7 | Sodium Carboxy Methyl Cellulose | Viscosity increasing agent |
| 8 | Sodium Lauryl sulphate | Solubilizer |
| 9 | Polyvinyl Pyrilidone K- 30 | Binder |
| 10 | Talc | Glidant |
| 11 | Colloidal Silicone Dioxide | Glidant |
| 12 | Magnesium stearate | Lubricant |
| 13 | Color Sunset yellow lake | Coloring agent |
| 14 | Iso Propyl Alcohol | Solvents |
| 15 | HPLC grades water | Mobile Phase |
| 16 | Methanol (HPLC grade) | Mobile Phase |
| 17 | Methylene chloride (AR grade) | Mobile Phase |
| 18 | Octadecyl silane | HPLC Column |

**Key:** ER stands for Extended Discharge.

### Equipment's used:

1. Metler Toledo AB 204-S Electronic Balance
2. Electromagnetic Sieve Shaker EMS-8
3. Electrolab ETD-1020 Tap density Tester (USP)
4. Dr. Sheleunizer Pharmatron Model 5-Y Tablet Hardness Tester
5. Electrolab Roche Friabalator (USP) EF.1W
6. Troical nortex dehumidifier
7. Trans-O- Sonic Sonicator
8. Hot air Oven
9. Planetary Mixer-Chef for granulation
10. Mitutoyo-Vernier Capillary
11. Sieves since Electro Pharma
12. Loss On drying tester HB-43, Halogen by Metler Toledo
13. Differential Scanning Calorimeter-822 by Metler Toledo
14. Perkin Elmer-Lambda 25 UV/Vis Spectrophotometer
15. Electrolab, TDT-80L Dissolution Tester USP
16. Cadmach 16 Station Compression Machine
17. Cone Blender.

### General methods for formulation of ER tablets

1. Wet granulation
2. Density and compressibility index of CBZ granules

3. Compressibility index
4. Hausner ratio
5. Loss on drying
6. Average weight of tablets
7. Diameter of tablets
8. Thickness of tablets
9. Hardness test
10. Friability test
11. Dissolution test
12. Tolerances
13. Test Aliquots
14. Assay by HPLC (HPLC Grade water , methanol, methylene chloride).

**Formulation trials chart**

Relative Preparation Elements for all 12 Preparations Table 2.
(Entirely amounts are specified in mg)

**Table 2:** Table viewing the relative preparation elements for entirely 12 preparation test sets.

| S.NO. | Ingredients | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 | F10 | F11 | F12 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Extended discharge polymer concentration (%) | 30 | 27 | 20 | 20 | 12 | 12 | 20 | 27.9 | 35 | 27.8 | 28 | 27.8 |
| 2 | Carbamazepine | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 |
| 3 | HPC(low viscosity grade) | 105 | nil | nil | nil | nil | nil | nil | nil | Nil | nil | nil | nil |
| 4 | HPC(high viscosity grade) | nil | 94.5 | 70 | 70 | 42 | 42 | nil | nil | Nil | nil | nil | nil |
| 5 | HPMC | nil | nil | nil | nil | nil | nil | 70 | 97.5 | 123 | 97.5 | 97 | 97.5 |
| 6 | Microcrystalline Cellulose | nil | 21 | 45.5 | 46 | 74 | 33.5 | nil | nil | Nil | nil | nil | 12.8 |
| 7 | Lactose | nil | nil | nil | nil | nil | 50 | 46 | 17 | Nil | nil | 22 | nil |
| 8 | Luctocel 1000 P | nil | nil | nil | nil | nil | nil | nil | nil | Nil | 17.5 | nil | nil |
| 9 | Sodium Lauryl sulphate | 10 | 5.25 | 5.25 | 5.3 | 5.3 | 5.25 | 5.3 | 5.25 | 5.25 | 5.25 | nil | 0.5 |
| 10 | Polyvinyl Pyrilidone K- 30 | nil | 10 | 10 | 10 | 10 | nil | 10 | 12 | 8 | 11.5 | 12 | 20 |
| 11 | Talc | 12.3 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 8 | 10 | 10 | 10 |
| 12 | Aerosil 200 | 14.5 | 4 | 4 | 4 | 4 | 4 | 4 | 3 | 2 | 3 | 3 | 4 |
| 13 | Magnesium stearate | 8.18 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 4 | 5 | 5 | 5 |
| 14 | Color Sunset yellow lake | nil | 0.25 | 0.25 | 0.3 | 0.3 | 0.25 | 0.3 | 0.25 | 0.25 | 0.25 | 0.5 | 0.25 |
| 15 | Iso propyl Alcohol(ml) | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S |
| 16 | Average weight of Tablet | 350 | 350 | 350 | 350 | 350 | 350 | 350 | 350 | 350 | 350 | 350 | 350 |

## RESULTS AND DISCUSSION

Hydrophilic matrix method contain of polymer, medicine then extra excipient spread thru matrix.

Prolonged discharge drug (CBZ) remained expressed thru damp granulation method.

Prolonged discharge polymer, solubilizing proxy, diluents stayed approved over filter no. 24 by support of mixer ingredient remained saved aimed at water less mingling on sluggish rapidly this pointer towards development aimed at even matrix method. Later lubrication complete by support of talc, Aerosol 200 then mg. Stearate, formerly pellets remain prepared aimed at solubility also solidity stay done by support of Cad Mach drug solidity apparatus thru utilizing a hit extend of 10.5mm regular concave 200 adornment on one side sideway with counted line on alternative cross Figures 1-5 and Table 3-8.

**Formulation trail no.12 (F12)**

**Table 3:** Table showing *In vitro* discharge kinetics parameter for formulation trial No.12.

| Time (hrs) | % Cumulative drug discharged | log % cumulative drug discharged | % Cumulative drug rechiefing(x) | Log % cumulative drug rechiefing | log T | √T | (x)⅓ |
|---|---|---|---|---|---|---|---|
| 3 | 33.2 | 1.521 | 66.8 | 1.824 | 0.477 | 1.73 | 4.05 |
| 6 | 49.4 | 1.693 | 50.6 | 1.704 | 0.778 | 2.449 | 3.699 |
| 12 | 77.4 | 1.888 | 22.6 | 1.35 | 1.07 | 3.464 | 2.827 |
| 24 | 98.1 | 1.991 | 1.9 | 0.278 | 1.38 | 4.898 | 1.239 |

**Table 4:** Showing Zero order drug discharge kinetic along with its graph

| Zero order drug discharge kinetic | |
|---|---|
| Time(hrs) | % Cum drug discharged |
| 3 | 33.2 |
| 6 | 49.4 |
| 12 | 77.4 |
| 24 | 98.1 |
| Slope = 2.997 | $R^2$ = 0.928 |

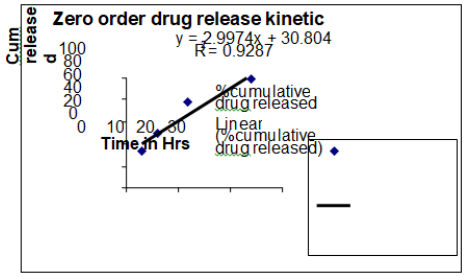


**Figure 1:** Showing Zero order drug discharge kinetic along with its graph.

**Table 5:** Showing first order drug discharge kinetic along with its graph.

| First order drug discharge kinetic | |
|---|---|
| Time(hrs) | log % Cum drug rechiefing |
| 3 | 1.8247 |
| 6 | 1.704 |
| 12 | 1.3541 |
| 24 | 0.278 |
| Slope = -0.0750 | $R^2$ = 0.9831 |

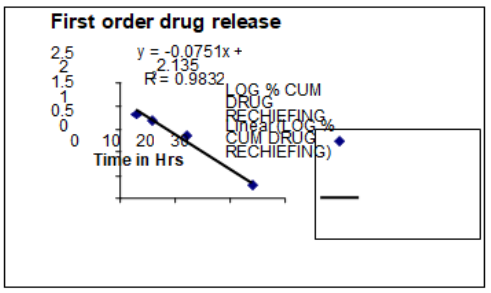


**Figure 2:** Showing first order drug discharge kinetic along with its graph.

**Table 6:** Showing Korsmeyer-Peppas drug discharge along with its graph.

| Korrsmeyer-peppas drug discharge kinetic | |
|---|---|
| log time | log % Cum drug discharged |
| 0.477 | 1.521 |
| 0.778 | 1.693 |
| 1.079 | 1.888 |
| 1.3802 | 1.991 |
| Slope = 0.533 | $R^2$ = 0.9857 |

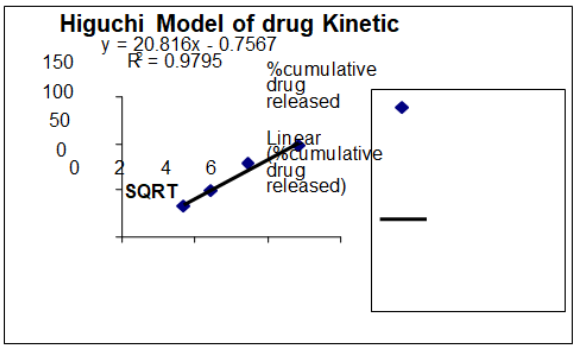


**Figure 3:** Showing Korsmeyer-Peppas drug discharge along with its graph.

**Table 7:** Showing Higuchi Model of drug discharge kinetic along with its graph.

| **Higuchi model of drug discharge kinetic** | |
|---|---|
| √T | %Cum drug discharged |
| 1.732 | 33.2 |
| 2.449 | 49.4 |
| 3.464 | 77.4 |
| 4.898 | 98.1 |
| Slope = 20.815 | $R^2$ = 0.9794 |

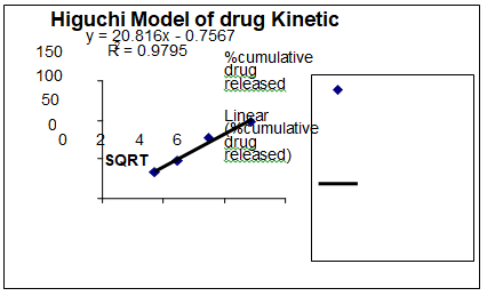


**Figure 4:** Showing Higuchi Model of drug discharge kinetic along with its graph.

**Comparative dissolution profile with commercial formulation**

**Table 8:** Showing comparative dissolution profile of commercial formulation along with f1 and f2 factor (dissimilar and similar factor respectively).

| **Time (min)** | **Rt** | **Tt** | **Rt-Tt** | **(Rt-Tt)^2** |
|---|---|---|---|---|
| 3 | 30.23 | 33.2 | 2.97 | 8.8209 |
| 6 | 58.322 | 49.4 | 8.922 | 79.60208 |
| 12 | 74.971 | 77.4 | 2.429 | 5.900041 |
| 24 | 92.1106 | 98.1 | 5.9894 | 35.87291 |
| ∑ | 255.6336 | 258.1 | 20.3104 | 130.1959 |
| Number of points | | 5 | | |
| f1 | 7.95 | | | |
| f2 | 64.2 | | | |

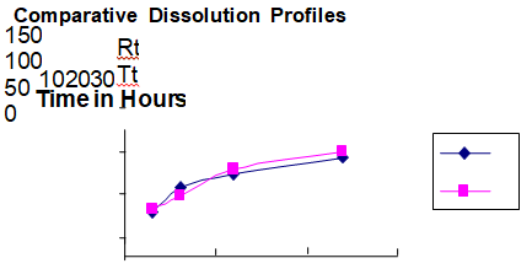


**Figure 5:** Showing comparative dissolution profile of commercial formulation along with f1 and f2 factor (dissimilar and similar factor respectively).

## DISCUSSION

**Formulation trial No.12**

***Extended Discharge Polymer used:*** Hydroxy Propyl Methyl Cellulose (Methocel K 100LV).

***Extended Discharge polymer concentration:*** 27.85%

***SLS Concentration:*** 0.5mg/tablet.

*In vitro* discharge data of Carbamazepine extended discharge(ER) tablet since the formulation trial No. 12 is displayed in table No.96.

The chief goalive of this trial is to slightly increase the % dissolution as compared to previous formulation trial. So need to add 0.5 mg/tab of Sodium Lauryl Sulphate (SLS).

In this formulation trial ER polymer *i.e*. hydroxy propyl Methyl cellulose (Methocel K 100LV) is used in the concentration of 27.85%.

Granulations are done with the help of Non Aqueous solvents such as Iso propyl Alcohol. Minor amount of IPA is used aimed at closing the binder *i.e.* polyvinyl pyrrolidone (PVP k-30).This solution used during the granulation for the formation of granules.

By observing *In-vitro* discharge data, it is experimental that, there is satisfactory retard the drug discharge and which is matches with the commercial formulation as under the USP limit.

On the basis of *in vitro* dissolution data, *In-vitro* discharge study stayed designed in several kinetics replicas such as zero order, first order, korsmeyer-peppas, Higuchi model and Hixson Crowell.

*In-vitro* discharge kinetics along with the figure stayed displayed in figure.

On the basis of comparison dissimilar and similar factor *i.e.* f1 and f2 factor with commercial formulation, it observed within the limit.

On the basis of correlation coefficient it follows first order and discharge mechanism behind the tablet is fickian diffusion.

To define the % of Carbamazepine current in ER tablet, five usual solutions stayed inserted in the HPLC arrangement and formerly two trial solutions was inserted in the similar HPLC Arrangement Figure 6-12 and Table 9.

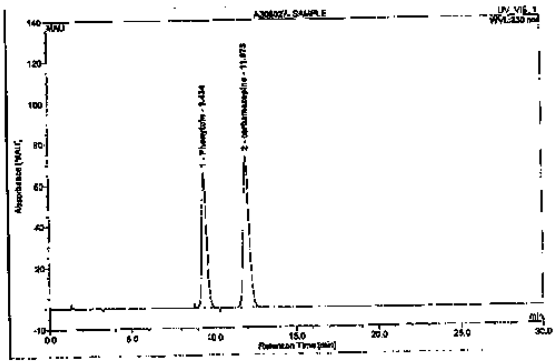

**Figure 6:** Graph showing for the sample 1.

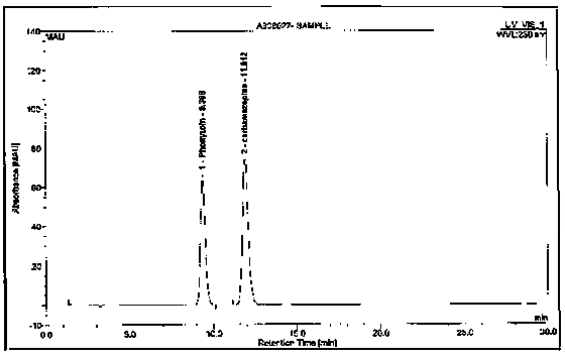

**Figure 7:** Graph showing for the sample 1.

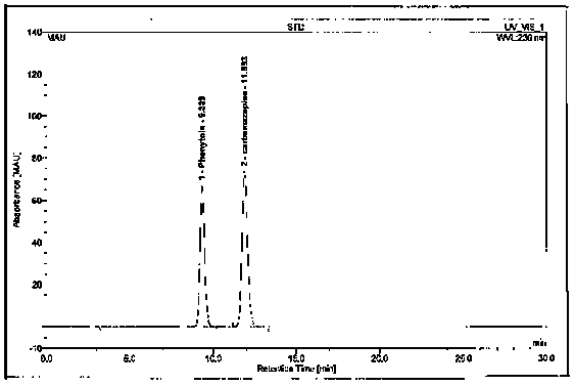

**Figure 8:** Graph showing for Stand 1.

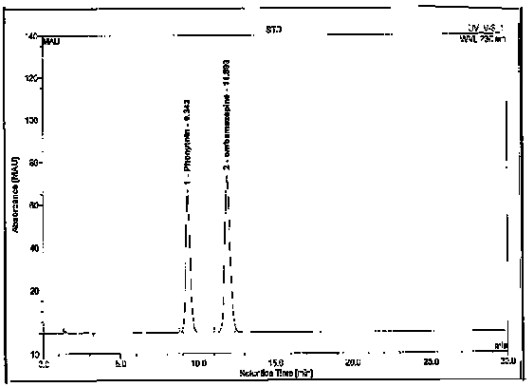

**Figure 9:** Graph showing for Stand 2.

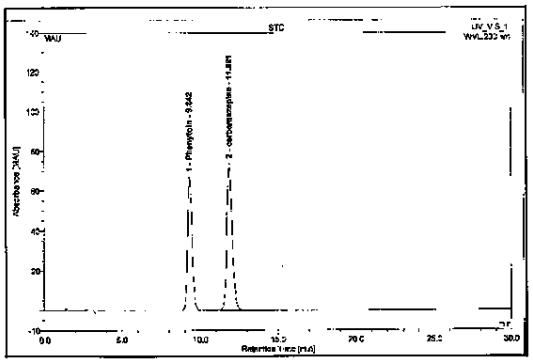

**Figure 10:** Graph showing for Stand 3.

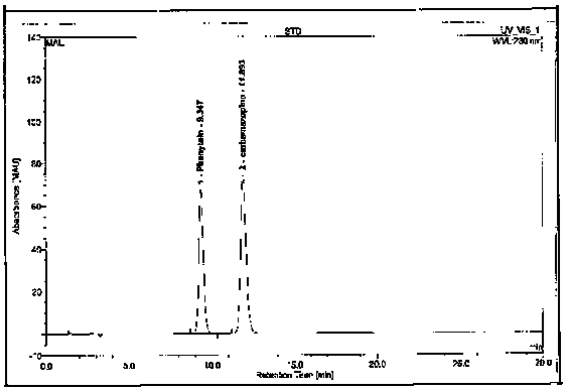

**Figure 11:** Graph showing for Stand 4.

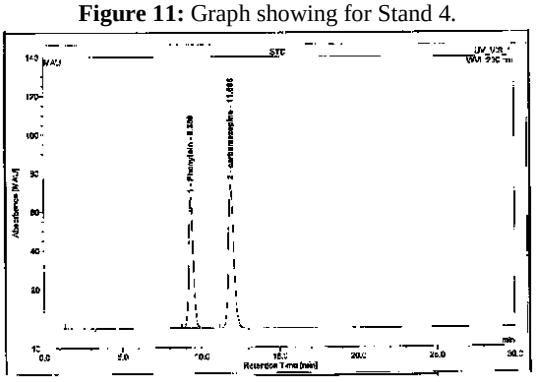

**Figure 12:** Graph showing for Stand 5.

**Table 9:** Showing the Peak Area of above HPLC graph.

| S.No. | Standard Area (SA) | Internal Standard (IS) | Ratio of SA to IS | Sample Area |
|---|---|---|---|---|
| 1 | 2936.06 | 2176.56 | 1.35 | 2965.46 |
| 2 | 2930.8 | 2171.19 | 1.35 | 2953.822 |
| 3 | 2937.53 | 2178.07 | 1.35 | - |
| 4 | 2941.76 | 2187.75 | 1.34 | - |
| 5 | 2939.14 | 2178.1 | 1.35 | - |
| Avg | 2937.058 | 2164.84 | 1.35 | 2959.64 |

Ratio of Avg.sample area to Internal stand area = 1.37.

By using formula which was mention in the material and method section

So,

% of Carbamazepine/tablet = 100.60%

FT-IR Spectrum of ER tablet of Formulation Trial No. 12

The FT-IR of extended discharge(ER) tablet of Carbamazepine was taken and is related thru the clean drug of Carbamazepine, and formerly it is detected that here is no change in functional group of pure drug after compression Figure 13-18 and Table 10.

The FT-IR spectrum is as follows,

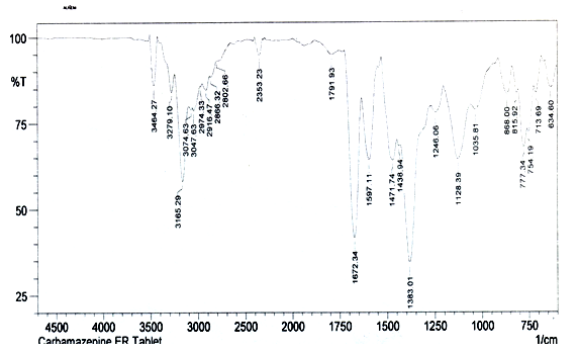


**Figure 13:** Comparative *In vitro* discharge data of Carbamazepine Extended Discharge(ER) tablets for all formulation trials.

**Table 10:** Showing the comparative *In-vitro* dissolution data after 3, 6, 12, and 24hr reading. Each reading is an average of 6 tablets.

| S.No. | Type of Formulation | Cumulative % discharge of carbamazepine | | | |
|---|---|---|---|---|---|
| | | 3hr | 6hr | 12hr | 24hr |
| 1 | Commercial | 30.23 | 58.322 | 74.97 | 92.11 |
| 2 | F1 | 37.3 | 69.7 | 90.6 | 92.5 |
| 3 | F2 | 19 | 38.2 | 66.1 | 82.5 |
| 4 | F3 | 12.4 | 26.1 | 51.4 | 78 |
| 5 | F4 | 16.6 | 40.5 | 73.3 | 86.5 |
| 6 | F5 | 27.6 | 46.9 | 71.7 | 81.1 |
| 7 | F6 | 28.6 | 58.1 | 73.5 | 83.3 |
| 8 | F7 | 42.3 | 65.8 | 73.6 | 82.2 |
| 9 | F8 | 35.8 | 67.7 | 83.2 | 94.5 |
| 10 | F9 | 33.7 | 66 | 90.8 | 93.4 |
| 11 | F10 | 40.5 | 75 | 92.3 | 96 |
| 12 | F11 | 25.43 | 50.43 | 72.06 | 92.5 |
| 13 | F12 | 33.2 | 49.4 | 77.4 | 98.1 |

Higuchi Model and Hixson-Crowell model of drug discharge.

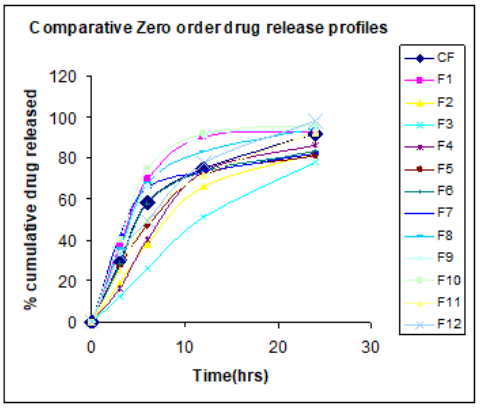


**Figure 14:** Graph showing the comparative zero order drug discharge profiles for all 12 formulation trials with commercial formulation.

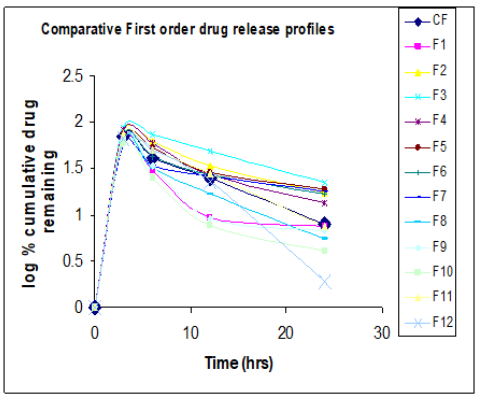

**Figure 15:** Graph showing the comparative First order drug discharge profiles for all 12 formulation trials with commercial formulation.

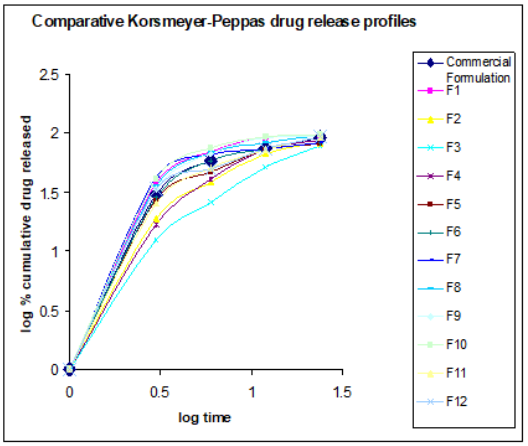


**Figure 16:** Graph showing the comparative Korsmeyer-Peppas drug discharge profiles for all 12 formulation trials with commercial formulation.

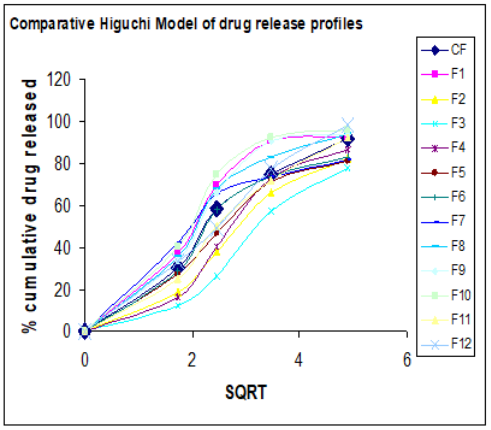


**Figure 17:** Graph showing the comparative Higuchi Model of drug discharge profiles for all 12 formulation trials with commercial formulation.

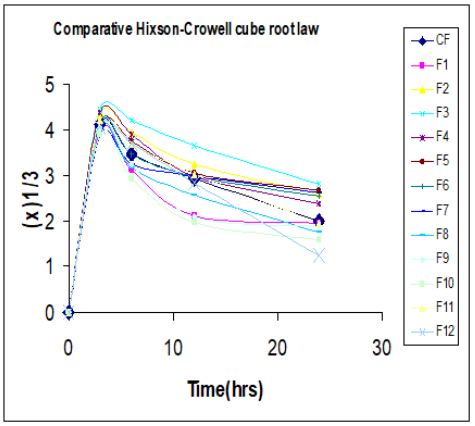


**Figure 18:** Graph showing the comparative Hixson Crowell cube root law for all 12 formulation trials with commercial formulation.

## CONCLUSION

Prolonged discharge hydrophilic matrix tablet of CBZ using HPMC of a little viscidness status in the concentration of 27.85% remained effectively established. SLS in the preparation improved solubility of the CBZ vis. 98.1% to discharge at the finish 24hrs.

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