Research Article

# Formulation and Evaluation of Sustained Release Tablets of Bupropion HCl

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**ABSTRACT**

Bupropion is a drug primarily used as an antidepressant and smoking cessation aid. Bupropion is presumed to be a dopamine-norepinephrine reuptake inhibitor and is an effective antidepressant. It is available as three oral formulations: (i) Bupropion immediate release (IR) [Wellbutrin®] administered three times daily; (ii) bupropion sustained release (SR) [Wellbutrin SR®]. Administered twice daily; and (iii) bupropion extended/modified release (XR) [Wellbutrin XL®/Wellbutrin XR®] administered once daily. All three formulations are bioequivalent in terms of systemic exposure to bupropion. The objective of the present investigation is to design and evaluate sustained release dosage form of bupropion hydrochloride and compare with innovator product (Wellbutrin sustained release tablets). Sustained release tablets were prepared by dry granulation method using HPMC and Microcrystalline Cellulose as matrixing agents. The Prepared Granules were evaluated for Angle of repose, bulk density, tapped density, compressibility index, Hausner's ratio. The granules shown satisfactory flow properties and compressibility. Tablets were tested for weight variation, thickness, hardness, friability and in vitro drug release as per official procedure. Formulation of sustained release tablet of bupropion hydrochloride as formulation batches F-1 to F-8 with a variation in the quantities.

**Keywords:** Sustained release Tablets, bupropion hydrochloride, Hydroxy propyl methyl cellulose, Microcrystalline Cellulose, dissolution.

## INTRODUCTION

Bupropion serves as an atypical antidepressant fundamentally different from most commonly prescribed antidepressants such as selective serotonin reuptake inhibitors (SSRIs). It is an effective antidepressant on its own, but is also popular as an add-on medication in cases of incomplete response to first-line SSRI antidepressants.

The oral route for drug delivery is the most popular, desirable, and most preferred method for administering therapeutically agents for systemic effects because it is a natural, convenient, and cost effective to manufacturing process.

One of the most common approach used for prolonging and controlling the rate of drug release is incorporating the drug in a hydrophilic colloidal such as Hydroxypropyl methyl cellulose, Hydroxypropyl cellulose, carbopols, chitosan, alginates and gelatin etc.

The mechanism and kinetics of release of drugs incorporated in these polymer matrices depends on the type and amount of polymer as well as on the physico-chemical properties of drug substance. Generally the drug release from these matrices includes penetration of fluid, followed by dissolution of drug particles and diffusion through fluid filled pores. The diffusion of drug through a rate limiting step.

The main objective of the bupropion HCl is to formulate Bupropion hydrochloride tablets tamper resistant and any adulterant of the tablet after its manufacture is almost certain to be observed. The developed tablets were evaluated for various compressional characteristics like, weight variation, friability, hardness, diameter and thickness etc.

## MATERIALS AND METHODS

### Materials

Bupropion HCl was obtained as a gift sample from Lara labs pvt.Ltd Hyderabad. Microcrystalline cellulose, Eudragit, Carbopol, HPMC and Magnesium stearate from Sisco research laboratories Pvt. Ltd Mumbai.

### Methods

Bupropion HCl were prepared by direct compression method. All the ingredients were weighed accurately. The drug was mixed with the release rate enhancing disintegrants and other excipients, except magnesium stearate, in ascending order of their weight.

The powder mix was blended for 20 min to have uniform distribution of drug in the formulation. Then, magnesium stearate was added and mixed for not more than 1 min (to ensure good lubrication).

About 500 mg of the powder mix was weighed accurately and fed into the die of single punch machinery and compressed using 8 mm flat-surface punches.

### Preformulation Parameters

#### *Bulk density (gm/ml)*

Bulk density of a compound varies substantially with the method of crystallization, milling or formulation.

Bulk density is determined by pouring pre sieved blend into a graduated cylinder via a large funnel and the volume and weight are measured.

$$\text{Bulk density} = \frac{\text{weight of blend}}{\text{Bulk volume of blend}}$$

### *Tapped density*

Tapped density is determined by placing a graduated cylinder containing a known mass of blend and mechanical tapper apparatus, which is operated for a fixed number of taps until the powder bed volume has reached a minimum volume. Using the weight of the drug in the cylinder and this minimum volume, the tapped density may be computed:

$$\text{Tapped density} = \frac{\text{weight of blend}}{\text{Tapped volume of blend}}$$

### *Carr's Compressibility Index (CI)*

Carr's index is measured using the values of bulk density and tapped density. The following equation is used to find the Carr's index:

$$\text{Carr's Index} = \frac{(\text{Tapped Density} - \text{Bulk Density})}{\text{Tapped Density}} \times 100$$

### *Hausner's Ratio*

It indicates the flow properties of the powder and ratio of Tapped density to the Bulk density of the powder or blend.

$$\text{Hausner's Ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}}$$

### *Angle of Repose*

The manner in which stresses are transmitted through a bead and the beads response to applied stress are reflected in the various angles of friction and response. The method used to find the angle of repose is to pour the powder on a conical heap on a level, flat surface and measure the included angle with the horizontal.

$$\text{Tan}\theta = \frac{h}{r}$$

Where, h= height of the heap, r= Radius of the heap

## Post Compression Parameters

### *Hardness Test*

This is the force required to break a tablet in a diametric compression. Hardness of the tablet is determined by Stock's Monsanto hardness tester which consists of a barrel with a compressible spring. The pointer moves along the gauze in the barrel fracture.

### *Tablet Size and Thickness*

Control of physical dimensions of the tablets such as size and thickness is essential for consumer acceptance and tablet-tablet uniformity. The diameter size and punch size of tablets depends on the die and punches selected for making the tablets. The thickness of tablet is measured by Vernier Callipers scale. The thickness of the tablet related to the tablet hardness and can be used as initial control parameter. Tablet thickness should be controlled within a ± 5%. In addition thickness must be controlled to facilitate packaging.

### *Friability*

This test is performed to evaluate the ability of tablets to withstand abrasion in packing, handling and transporting. Initial weight of 20 tablets is taken and these are placed in the friabilator, rotating at 25 rpm for 4 min. The difference in the weight is noted and expressed as percentage. It should be preferably between 0.5 to 1.0%.

$$\%\text{Friability} = \frac{(W_1 - W_2)}{W_1} \times 100$$

Where, $W_1$= weight of tablets before test, $W_2$ = weight of tablets after test

### *Weight Variation of Tablets*

It is desirable that all the tablets of a particular batch should be uniform in weight. If any weight variation is there, that should fall within the prescribed limits.

Twenty tablets were taken randomly and weighed accurately. The average weight was calculated by:

$$\text{Average weight} = \frac{\text{weight of 20 tablets}}{20}$$

### *Dissolution Method*

Dissolution media was taken as water, 900ml placed in the vessel and the USP apparatus – II (paddle) was assembled. The medium was allowed to equilibrate to temp of 37 ± 0.5 °C. Tablet was placed in the basket and placed in the vessel; the apparatus was operated for at 50 rpm. At definite time intervals, 5 ml of the fluid was withdrawn; filtered and again 5 ml of the fluid was replaced. The samples were analyzed using UV.

## RESULTS AND DISCUSSION

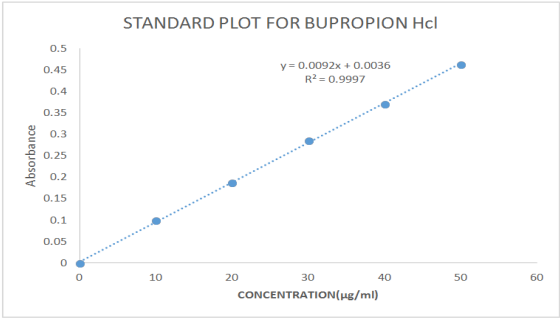


**Figure 1:** Calibration curve of Bupropion HCl at $\lambda_{Max}$ = 298 nm

Eight formulations of sustained release tablets were developed employing different proportions form F1-F8. In the preformulation studies the Micromeritic flow properties of the Blend were assessed by determining angle of repose, compressibility index, and Hausner's ratio**.** All the finished products were evaluated for thickness, hardness, friability, weight variation and dissolution rate. Dissolution rate study was performed in 900ml using USP-II (paddle) apparatus.

### *Angle of repose*

The values obtained for Angle of repose for all formulation are tabulated in table, the values were found in the range from $25.75^0$ – $29.19^0$ indicate good flow property of the power blend Shown in Table 2.

### *Carr's index & Hausner's ratio*

Carr's index and Hausner's ratio values range between 13.8889 – 18.9189% and 1.562 – 1.2333 respectively indicating that the powder blends have the required flow property for direct compression shown in Table 2.

### *Bulk density & Tapped density*

Bulk density and Tapped density values were within the limits indicating that the powder blends have the required flow for direct compression shown in Table 2.

### *Weight Variation*

All tablets passed weight variation tests as the % variation was within the pharmacopeia limits and weight of all tablets was found to be uniform with low standard deviation. Drug content of all batches were within the acceptable range which shows the proper mixing of drug with the excipients shown in Table 3.

### *Hardness*

Hardness was found to be within the range of 7.9-8.5, indicates that these tablets have good mechanical strength with sufficient hardness shown in Table 3.

### *Friability*

Friability values were found to be less than 1% in cases and considered to be satisfactory shown in Table 3.

### *Dissolution Studies*

The dissolution studies for the optimized formulation and the marketed formulation is compared. Results showed that % cumulative releases of optimized (f3) were high compared to the marketed drug product shown in Table 4.

In the comparative analysis of dissolution profile of market product, the F3 formulation showed similar result with market product shown in Fig 3.

**Table 1:** Formulation of Bupropion HCl Tablets

| Ingredients (mg) | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 |
|---|---|---|---|---|---|---|---|---|
| Bupropion HCl | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 |
| Microcrystalline cellulose | 195 | 170 | 145 | 220 | 195 | 145 | 195 | 145 |
| Hydroxypropyl Methycellulose | 100 | 125 | 150 | 75 | -- | -- | -- | -- |
| Carbopol | -- | -- | -- | -- | 100 | 150 | -- | -- |
| Eudragit | -- | -- | -- | -- | -- | -- | 100 | 150 |
| Magnesium stearate | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Total weight | 500 mg | 500 mg | 500 mg | 500 mg | 500 mg | 500 mg | 500 mg | 500 mg |

**Table 2:** Pre-compression parameter of sustained release tablets of Bupropion HCl prepared by Direct Compression Method

| S. No | Formulations | Bulk Density (gm/ml) | Tapped Density (gm/ml) | Angle of Repose | C. Index | Hausner's Ratio |
|---|---|---|---|---|---|---|
| 1 | F1 | 0.4051 | 0.4997 | 25.74 | 18.9189 | 1.2333 |
| 2 | F2 | 0.4411 | 0.5172 | 26.28 | 14.7059 | 1.1720 |
| 3 | F3 | 0.4084 | 0.5037 | 26.06 | 18.9189 | 1.2333 |
| 4 | F4 | 0.4313 | 0.5206 | 27.4 | 17.1428 | 1.2069 |
| 5 | F5 | 0.41579 | 0.4828 | 28.72 | 13.8889 | 1.1613 |
| 6 | F6 | 0.4057 | 0.4691 | 28.65 | 13.5135 | 1.1562 |
| 7 | F7 | 0.4582 | 0.54000 | 29.19 | 15.1512 | 1.1785 |
| 8 | F8 | 0.4571 | 0.5387 | 28.72 | 15.1515 | 1.1785 |

**Table 3:** Post Compression Parameters of Sustained Release Tablets of Bupropion HCl Prepared by Direct compression method

| S. No | Formulations | Weight Variation (mg) | Hardness (kg/cm$^2$) | Drug Content Uniformity (%) | Friability (%) |
|---|---|---|---|---|---|
| 1 | F1 | 499.6 | 8.5 | 97.92 | 0.28 |
| 2 | F2 | 500.5 | 8.1 | 98.3 | 0.59 |
| 3 | F3 | 500.2 | 7.9 | 99.01 | 0.61 |
| 4 | F4 | 500.7 | 8.3 | 100.5 | 0.64 |
| 5 | F5 | 499.8 | 8.2 | 98.9 | 0.54 |
| 6 | F6 | 500.5 | 8.1 | 101.02 | 0.70 |
| 7 | F7 | 500.3 | 8.4 | 99.6 | 0.76 |
| 8 | F8 | 500.4 | 8.3 | 100.01 | 0.87 |

**Table 4:** Drug Release Profile of sustained release Tablets of Bupropion HCl.

| Time in hrs | % Cumulative Drug Release (% CDR) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | Marketed formulation |
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2 | 27 | 28 | 32 | 30 | 29 | 28 | 23 | 26 | 33.7 |
| 4 | 35 | 32 | 42 | 41 | 32 | 39 | 32 | 34 | 50 |
| 8 | 43 | 46 | 63 | 50 | 42 | 63 | 35 | 55 | 61.3 |
| 12 | 63 | 61 | 72 | 61 | 61 | 68 | 61 | 70 | 71.7 |
| 16 | 71 | 70 | 76 | 71 | 75 | 75 | 71 | 77 | 87 |
| 20 | 80 | 82 | 95 | 84 | 87 | 78 | 82 | 86 | 97.7 |

**Table 5:** Kinetic values obtained from different plots of formulation F3

| Formulation | Zero order ($R^2$) | First order ($R^2$) | Higuchi ($R^2$) | Peppas ($R^2$) | Hixon crowell ($R^2$) |
|---|---|---|---|---|---|
| F3 | 0.8906 | 0.8883 | 0.9753 | 0.9853 | 0.9448 |

## CONCLUSION

The present study is to develop and evaluate Anti-Depressant Drug of Bupropion HCl sustained release oral tablets. Based on Literature survey and Compatibility

Tests excipients like Microcrystalline Cellulose, HPMC, carbopol, Eudragit, Magnesium Stearate were used. In this present study, the tablets were prepared by using direct compression technique. In order to optimize the product, different formulations were developed. All the formulations were evaluated for physical characteristics, *in-vitro* Dissolution studies. The blends were analyzed for the parameters such as Bulk density, Tapped density, Compressibility index, Hausner's ratio, Angle of repose and results were found to be within the limits. Based on the results of dissolution studies and marketed with innovators. F3 was found to be the best among trails.

Finally we have found that all formulations (F1 to F8), only one formulation (F3) released the drug 95% within 20hrs.

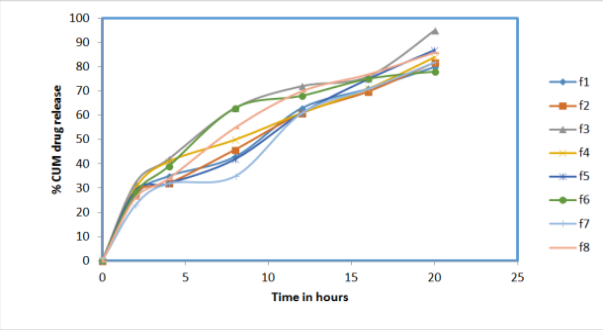


**Figure 2:** Drug Release Profile of sustained release Tablets of Bupropion HCl (F1-F8)

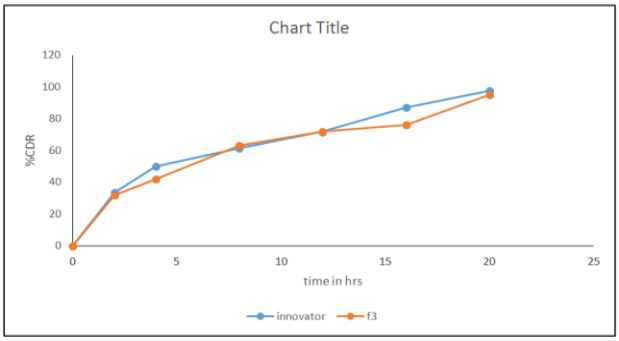


**Figure 3:** *In vitro* drug release of for marketed formulation and optimized F3 formulations

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