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## FORMULATION AND EVALUATION OF GASTRORETENTIVE FLOATING SUSTAINED RELEASED METFORMIN HCL TABLET

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### ABSTRACT

The Metformin HCL Gastroretentative Floating Sustained released Tablet is formulated by the Wet Granulation technique. This Tablet is containing both Effervescent as well as Non Effervescent system. The HPMC K 100 Swellable polymer is responsible for the Floating. (Non-Effervescent system) and The Sodium Bicarbonate is responsible for the effervescent system. A combination of HPMC K 100 and Xanthum Gum shows better sustained release activity. The Prepared Gastroretentative Floating Sustained released Tablet is Evaluated In terms of bulk density, tapped density, angle of repose, Carr's Index and, weight variation test, friability test and *in vitro* study, Total Floating Time. The result associated in Optimized batch is good to Satisfactory and having a good free flowing property. The weight variation and friability these values are within the pharmacopeia limit. The *in vitro* Dissolution studies show Maximum percentage of release of drug (99.25) within end of 8 Hours.

### KEYWORDS

Gastroretentative, Floating, Sustained released, Effervescent and Non effervescent.

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### INTRODUCTION

The Oral Route of administration is one of the specific routes of administration having more patient acceptance or convenience. The Metformin HCL is oral Sustained Floating tablet is made by wet Granulation Method. This are the tablet is mainly float on the surface of liquid medium or float on the liquid medium. The floating tablet having density is less than 1 and the tablet containing Effervescent as well as Non effervescent system in which the swellable polymer such as HPMC K 100 and Xanthum gum is responsible for the floating of tablet (Non Effervescent system) and the tablet containing

Sodium Bicarbonate (act as base) come into contact with GI Fluid Effervescent is generated (Effervescent system) Bulk of the Drug is reduced, the Tablet is Floated. This are the Tablet is release in prolonged action in extended Period of Time. The Metformin HCL Tablet is Ant hyperglycemic agent to reduce the blood sugar level and it is mainly used for the Type II Diabetes Mellitus<sup>1-4</sup>.

## **MATERIAL AND METHOD**

### **Material**

Metformin HCL and all Formulation Excipient or Polymer (PVP K30, HPMC K100, Xanthum Gum, Sodium Bicarbonate, and Talc) was obtained from Pharmaceutics Laboratory of R. C. Patel Institute of Pharmaceutical Education and Research, Shirpur 425405, Maharashtra State, one of the NBA and NAAC accredited and AICTE approved institutes in India.

### **METHOD**

The parameters of Authentication and Preformulation are carried out by pure drug Metformin HCL for Maintaining their Quality, Purity and Standard.

## **AUTHENTICATION PARAMETERS**

### **Melting Point Method**

Melting Point determination is one of the preformulation property in which the temperature at which it changes state from solid to liquid at atmospheric pressure. At the melting process the solid and liquid can exist equilibrium. The Melting point of Metformin HCL pure drug is determine by using two types of method one is Conventional method and another is Digital method.

### **Log P Value**

Log p value is determined by using Partition Coefficient Phenomenon. In which The 1 gm of drug is added in separating funnel containing equal portion of 25 ml of Octanol and 25 ml of Water. The separating funnel is shaking 20 – 25 min. and stabilized the mixture. After stabilizing the mixture to remove water phase from separating funnel and filter it. Take Absorbance of Filtrate and calculate the log p value (concentration of drug soluble in

water phase divided by concentration of drug soluble in organic phase).

### **Solubility Studies**

The Term Solubility is defined as maximum amount of solute that can be dissolved in a given amount of solvent to form a homogenous system at specified temperature and Specific Pressure to from Saturated Solution.

### **Procedure**

To Prepare a different solutions Water, PH 1.2 Acidic Buffer, PH 6.8 Phosphate Buffer, PH 7.4 Phosphate Buffer.

The drug material is added in to above solutions till Supersaturated Solution is from.

The Mixture can Placed in Orbital Shaker for 24 hrs. After 24 hrs. Filter the mixture Take Filtrate and Give Absorbance.

To detect the Concentration of Drug is Soluble in Different Solutions.

### **Calibration Curve of Metformin HCL**

Calibration Curve is determined by using UV Spectrophotometry methods. In which 10 mg drug is added in 100 ml of water (100 µg/ml Solution). To Prepared different Dilutions (0, 2, 4, 6, 8, 10, 12) of above solution (100 µg/ml Solution). Take Absorbance in respective  $\lambda_{max}$  240 nm.

## **PREFORMULATION STUDIES**

### **Drug-Excipient Compatibility Studies**

Drug is an active part of dosages form and it is mainly responsible for therapeutic value and Excipient substances which are included along with drugs being formulated in a dosage form so as to impart specific qualities to them. It is important for determination of Stability of the dosage forms. It's also used for development of new drug delivery system as well as investigation of new drug Product.

### **Procedure**

The Equal portion of Drug and Excipient (1:1 ratio) is added in Ampules and the Ampules are placed in Stability Chamber for one Week, After One Week the Drug Excipient Compatibility Study is Determine by using TLC (Thin Layer Chromatography) (In TLC mobile phase is methanol: water: glacial acetic acid), IR (Infrared Spectroscopy) (In IR 1:9 ratio (drug : KBR)).

## METHOD OF FORMULATION

The Metformin HCL Floating Tablet is formulated by the Wet Granulation Method. The Metformin HCL, HPMC K100, Xanthum Gum, Sodium Bicarbonate, are weighed accurately and add in Mortar and Pastel for their proper mixing. To prepared binder solution of PVP K 30 in isopropyl alcohol (1 gm 10 ml I.P.A.) and add in mix. Till Dough mass is formed. The prepared dough mass is passing through the mesh 12 sieve granules are prepared and the prepared granules are dried in oven for 10 – 15 min. After drying the granules add Lubricating agent such as Talc and passed into mesh 40 sieve, fine granules are prepared. The Compression is done by using the 8 station signal or multi rotator tablet punching machine. The all formulation ingredients are reported in Table No.1.

## EVALUTION PARAMETERS<sup>5,12</sup>

### Bulk density

It is a ratio of weight mass and Bulk Volume is known as Bulk Density. Amount of Powder is Weighed Separately and transferred into 100 ml of measuring cylinder, initial volume of Powder Material is measured and calculated bulk density according to following formula.

$$\text{Bulk density} = \text{Mass} / \text{Volume}$$

### Tapped Density

It is a Ratio of weight Mass and Tapped Volume is known as Tapped Density. Tapped density is Important Evaluation Parameter is determined by placing a graduated cylinder containing a known mass of powder Undergoes Tapping in Manually (100 Tapes) as well As Using a Mechanical apparatus under powder bed volume has reached a minimum volume. The Tapped Density is calculated by following Formula.

Tapped density = Weight of Powder/ tapped volume of Powder

### Compressibility Index or Carr's Index

The Calculation of Compressibility index is based on the Tapped density and Bulk density. It is a ratio of Tapped density and Bulk Density i.e. Compressibility Index.

### Angle of Repose

It defines as the Pile surface of Powder is known as Angle of Repose. In this method of determination of angle of repose in which the angle of repose is to pour the powder a conical on a level, flat surface and measure the included angle. The Following Formula for determination of angle of repose.

$$\theta - \tan^{-1} (h/r)$$

Where,

$\theta$  - Angle of repose,

h - Height of the powder cone,

r -Radius of the powder cone.

### Friability Test

The friability of 20 tablets was determined Using Friability Tester. 20 tablets from each formulation were weighed and tested at a speed of 25 rpm for 4 min. After removing of tablets were re-weighed and friability percentage was calculated. To give an initial weight of 20 tablet Minimized these wt. by friability after the 20 tablet, divided by friability after 20 tablets multiply by 100, to get the appropriate friability of the 20 tablets.

### Weight variation test

Weight variation was carried out to ensure that, each of tablets contains the proper amount of drug. The test was carried out by weighing the 20 tablets individually using analytical balance, then calculating the average weight, and comparing the individual tablet weights to the average. The percentage of weight variation is calculated by using the following formula,

$$\text{Weight variation} - [X^*/ X] \times 100$$

X - Actual weight of the tablet

X\* - Average weight of the tablet

### In vitro drug release studies

It is a Process in which Solid Material Dissolved in Liquid Medium per Unit Time Period. It is mainly based on Sink Condition. Dissolution of Floating Tablet is determined by Paddle Type (USP II) of Dissolution Apparatus. The tablet was added into cylindrical vessel containing 900 ml PH 1.2 Acidic media having 75 rpm for 8 hours and tem.  $37 \pm 0.5^\circ\text{C}$  having 1, 2, 3, 4, 5, 6, 7, 8hour of interval. After every 1 hour. 5 ml sample was Withdrawn and appropriate quantity of sample take absorbance by

using U.V. spectroscopy technique and determine rate of dissolution of tablet.

## RESULTS AND DISCUSSION

### Authentication Parameters

#### Melting Point Method

The Melting Point of Metformin HCL is determined by Conventional and Digital Method and Melting Point of Metformin HCL is Reported in Table No.2.

#### Log P Value

Log P Value is determined by Partition Coefficient Phenomenon and Log P Value of Metformin HCL is reported in Table No.2.

#### Solubility Studies

The Solubility of Metformin HCL in Given Solution. (Water, PH 1.2 Acidic Buffer, PH 6.8 Phosphate Buffer, PH 7.4 Phosphate Buffer) is Reported in Table No.3.

#### Calibration Curve of Metformin HCL in water

The Calibration Curve of Metformin HCL is determined by using U.V. Spectroscopic Method. In which the Absorbance of Metformin HCL in Different Concentration (0, 2, 4, 6, 8, 10, and 12) is reported in Table No.4. And The Calibration Curve is shown in Figure No.1.

## PREFORMULATION STUDIES

The Drug and Excipient Compatibility studies determined by TLC (Thin Layer Chromatography) and IR (Infrared Spectroscopy) Method In which The TLC of Drug, Drug and Excipient before Stability Chamber and After Stability Chamber is reported in Table No.5. And the IR of Pure drug Metformin HCL is shown in Figure No.2.

## EVALUATION PARAMETERS

### Bulk density

It is important parameter for determination of Flow characteristic in which the Bulk Density of Metformin HCL is reported in Table No.6.

### Tapped Density

It is important parameter for determination of Flow characteristic in which the Tapped Density of Metformin HCL is reported in Table No.6.

### Compressibility Index or Carr's Index

The compressibility index is determined on the basis of Tapped density and bulk density and it is important for determination of flow characteristic in which the Compressibility Index or Carr's Index of Metformin HCL is reported in Table No.6.

### Angle of Repose

It is important flow property for determination of flow of material and the value associated in angle of repose is less than 40° is indicate good flow property in which angle of repose of Metformin HCL tablet is reported in Table No.6.

### Hardness or Crushing strength

The hardness is determined by using a conventional or digital hardness tester in which the hardness of Metformin HCL tablet is reported in Table No.6.

### Friability Test

The Friability of Tablet is always less than 1% and the Friability of Metformin HCL is reported in Table No.6.

### Weight variation test

All 20 Gastroretentative Floating Sustained released tablet is passed the weight variation test as per pharmacopoeial limits.

The weight of all 20 tablets is uniform and the weight variation of Metformin HCL is reported in Table No.6.

### In vitro drug release studies

The *In vitro* drug release studies of Metformin HCL Floating tablet is determined in PH 1.2 Buffer, in which 99.25 % drug is releases at the end of 8 hours. And the in vitro drug released of Metformin HCL is reported in Table No.6 and the in vitro drug released shown in Figure No.3.

### Total Floating Time

The One Tablet is added into the 100 ml PH 1.2 Acidic Buffer in beaker (The Tablet is float in PH 1.2 acidic buffer) and calculate total Floating time of the tablet. In case Metformin HCL tablet Total Floating Time is 10 min. The Total Floating Time of Tablet is reported in Table No.6.

**Table No.1: Formulation Ingredients of Metformin HCL**

S.No	Ingredient (mg / Tablet)	F <sub>1</sub>	F <sub>2</sub>	F <sub>OP</sub>
1	Metformin HCL (mg)	300	300	300
2	PVP K30 (mg)	3	4	5
3	HPMC K100 (mg)	50	130	150
4	Xanthum Gum (mg)	5	10	15
5	Sodium Bicarbonate (mg)	30	30	30
6	Talc (mg)	5	5	5
	Total wt. of One Tablet (mg)	393	479	505

**Table No.2: Melting Point and Log P Value of Metformin HCL**

S.No	Parameters	Result	Std.
1	Melting Point (°C)	223 - 225°c	223 - 226°C
2	Log p Value	0.4	0.5

**Table No.3: Solubility of Metformin HCL in different solvents**

S.No	Medium	Concentration of drug Soluble (mg /ml)
1	Water	16.99
2	PH 1.2 Acidic Buffer	8.23
3	PH 6.8 Phosphate Buffer	4.28
4	PH 7.4 Phosphate Buffer	3.82
Result	Class of drug	BCS Class III

**Table No.4: Calibration of Metformin HCL in Water**

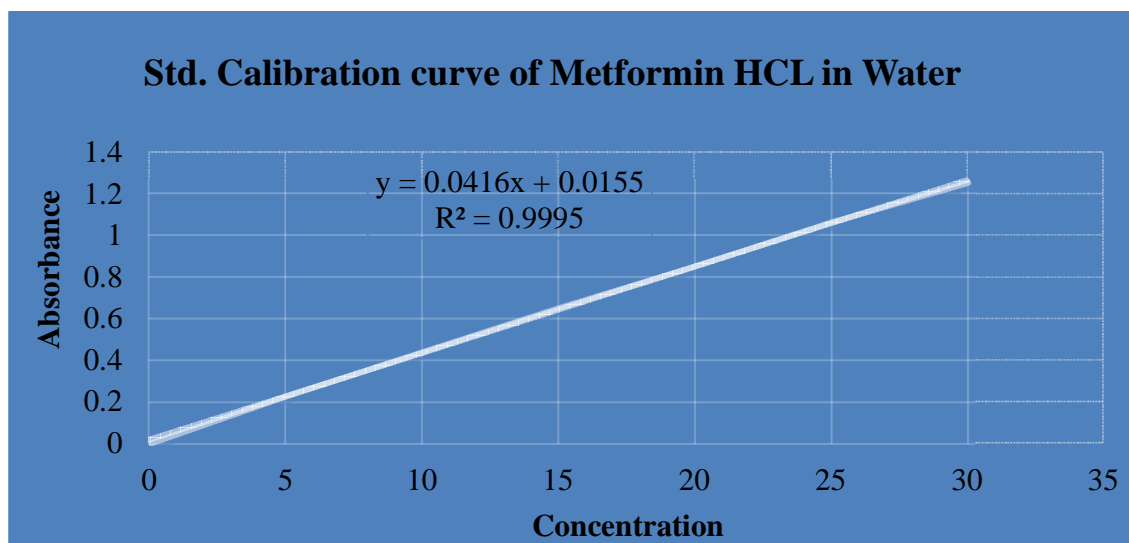
S.No	Concentration	Absorbance
1	0	0
2	2	0.228
3	4	0.439
4	6	0.651
5	8	0.85
6	10	1.061
7	12	1.25

**Table No.5: TLC of Drug and Drug and Excipient**

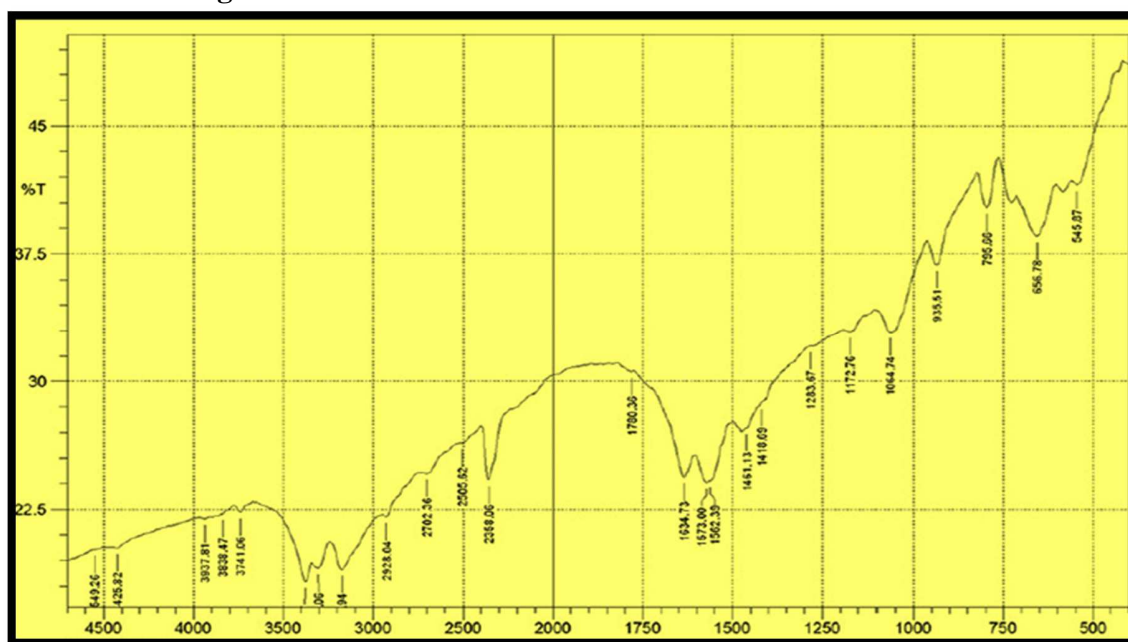
S.No	Samples (Pure From of Drug material) (Drug + Excipient Mixture)	Retention factor of drug Before the Stability Chamber	Retention factor of drug After the Stability Chamber
1	Pure Drug Metformin HCL	0.75	0.77
2	Metformin HCL + PVP K30	0.78	0.76
3	Metformin HCL + HPMC K100	0.79	0.83
4	Metformin HCL + Xanthum Gum	0.77	0.79
5	Metformin HCL + Sodium Bicarbonate	0.76	0.77
6	Metformin HCL + Talc	0.75	0.78

**Table No.6: Evaluation of Metformin HCL Tablet**

S.No	Parameters	F <sub>OP</sub>	Conclusion
1	Bulk Density (gm/cm <sup>3</sup> )	0.61	Pass
2	Tapped Density (gm/cm <sup>3</sup> )	0.78	Pass
3	Angle of Repose (θ)	21.13	Pass
4	Carr's Index (%)	4.91	Pass
5	Friability Test (%)	0.6	Pass
6	% of Weight variation test	99.85	Pass
7	<i>In Vitro</i> Drug release (%)	99.25	Pass
8	Total Floating Time (Min.)	8	10 (std.)



**Figure No.1: Calibration curve of Metformin HCL in Water**



**Figure No.2: IR of Pure drug Metformin HCL**

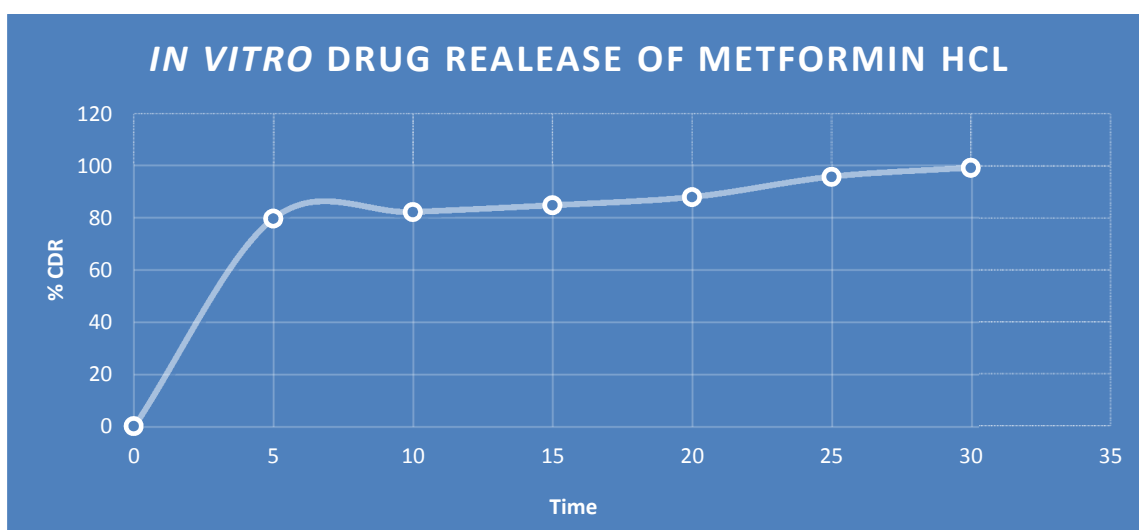


Figure No.3: *In vitro* drug release of Metformin HCL in PH 1.2 Acidic buffer

## CONCLUSION

The Metformin HCL Floating Tablet is formulated by the Wet Granulation Method, having density less than 1. The tablet is Gastroretentive floating sustained released tablet containing both Effervescent as well as Non Effervescent system. The HPMC K 100 Swellable polymer is responsible for the Floating. (Non-Effervescent system) and the Sodium Bicarbonate is responsible for the effervescent system. The result associated in Optimized batch is good to Satisfactory and having a good free flowing property. The hardness, weight variation, and friability these values are within the pharmacopeia limit. The *in vitro* Dissolution studies show Maximum percentage of release of drug.

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## CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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