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FORMULATION AND EVALUATION OF GASTRORETENTIVE CIPROFLOXACIN HCL EFFERVESCENT TABLET

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ABSTRACT

Ciprofloxacin HCL is an effervescent Tablet is made by Wet Granulation Method. Ciprofloxacin is a broad spectrum Fluroquinolon antibiotics. Is mainly used for various Bacterial Infections. In this tablet bitter taste was masked by saccharine as sweeting agent furthermore the effervescent effect of citric acid, tartaric acid and sodium bicarbonate lead to Effervescent activity by realising the CO_2 Molecule. Tablets are rapidly dissolved and rapidly absorbed and give maximum activity. The Prepared Effervescent Tablet is Evaluated In terms of bulk density, tapped density, angle of repose, Carr's Index and, hardness test, weight variation test, friability test and *in vitro* study. 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 (99.26) with in end of 5 min.

KEY WORDS

Effervescent Tablet, Wet Granulation, Ciprofloxacin HCL, Fluroquinolon antibiotics and Broad spectrum antibiotic.

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INTRODUCTION

The Effervescent tablets are the tablet are immediately dissolved or Solubilized when come into contact with aqueous media having basic reaction between acid and base by realising CO_2 Molecule. Effervescent tablet having rapidly dissolved and rapidly absorbed as compared to Conventional tablet dosage from and give maximum Bioavailability. In Ciprofloxacin HCL, Ciprofloxacin is a Broad Spectrum Fluroquinolon

Antibiotic. The Effervescent tablet of Ciprofloxacin HCL is having reaction between acid such as citric acid and Tartaric acid with base such as sodium bicarbonate under reaction CO_2 is released bulk of tablet is reduced, Tablet was rapidly disintegrated or dissolved by contact with GI Environment of the body. These are the Tablet having Short Half Life. This are the Tablet is mainly used for the of bacterial infections includes bone and joint infections, intra-abdominal infections, certain type of infectious diarrhoea, respiratory tract infections, skin infections, typhoid fever, and urinary tract infections, among others, for some infections it is used in addition to other antibiotics. This are the Tables are rapidly dissolved and rapidly absorbed and give immediate action and maximum bioavailability[1,2,3].

MATERIALS AND METHOD

MATERIALS

Ciprofloxacin HCL and all Formulation Excipient (Talc, Mg stearate, Avicil, Saccharine, Citric Acid, Tartaric Acid, NaHCO3, Banana Flavour) 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 Ciprofloxacin 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 Ciprofloxacin 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.

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 Ciprofloxacin HCL

Calibration Curve is determined by using UV Spectrophotometric 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 λmax 276 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 and 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 Weak, After One Weak the Drug Excipient Compatibility Study is Determine by using TLC (Thin Layer Chromatography), IR (Infrared Spectroscopy).

METHOD OF FORMULATION

The Formulation of Ciprofloxacin HCL Effervescent Tablet is prepared by the Wet Granulation Method. The Specific amount of Ciprofloxacin and Saccharine is weighed and divided into two petri plates in equal amount. One of the dish can added into Citric acid, Tartaric acid and one of the dish is added into sodium Bicarbonate. The mixtures of two dishes containing mixture are mixed together in mortal pastel and add blend solution [Guar (1gm) and PVP (1 gm) in Iso Propyl alcohol up to 10 ml] till dough mass is formed. The prepared dough mass is passed into mesh 14 sieve granules are prepared and prepared granules are dried in oven for 10 - 15 min.

After drying the granules add MCC and Lubricating agent such as Talc, Mg Stearate other Flavouring agent such as Banana Flavour are Mixed and passed into mesh 16 sieve, fine granules are prepared. The Compression is done by using the 8 station signal rotatory tablet punching machine having hardness is 4 - 5 kg/cm^2. The all formulation ingredients are reported in Table No.1.

EVALUATION PARAMETERS[4-11]

Bulk density

It is a ratio of Bulk 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.

Bulk density = Mass / Volume

Tapped Density

It is a Ratio of Bulk 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.

Carr's Index is less than or equal to **<10** indicates free flowing properties and Carr's Index is greater than **>10** indicates poor flowing Properties.

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.

$$\theta = \text{Tan}^{-1} (h/r)$$

Where,

θ - Angle of repose,

h - Height of the powder cone,

r -Radius of the powder cone.

The Angle of repose is **less than or equal to 40°** indicates free flowing properties. The angle of repose is **greater than 40°** indicates poor flow of material.

Hardness or Crushing strength

Hardness of Tablet is determined by using Conventional Hardness Tester and Digital Hardness Tester. The Standard range of the hardness of Effervescent tablet is 4 -5 kg/cm^2.

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 tablet 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,

Weight variation - [X*/ X] × 100

X - Actual weight of the tablet

X -* Average weight of the tablet

Effervescent Time

The One Tablet is added into the 100 ml PH 1.2 Acidic Buffer in beaker and calculate total Effervescent time of the tablet. In case Ciprofloxacin HCL tablet Total Effervescent time is 5 min.

***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 Effervescent 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 30 min. and tem. 37±0.5˚C having 5, 10, 15, 20, 25, 30 min. of interval. After every 5 min. 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 Ciprofloxacin HCL is determined by Conventional and Digital Method and Melting Point of Ciprofloxacin HCL is Reported in Table No.2.

Log P Value

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

Solubility Studies

The Solubility of Ciprofloxacin 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 Ciprofloxacin HCL in water

The Calibration Curve of Ciprofloxacin HCL is determined by using U.V. Spectroscopic Method. In which the Absorbance of Ciprofloxacin 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 Ciprofloxacin 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 Ciprofloxacin HCL is reported in Table No.6.

Tapped Density

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

Friability Test

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

Weight variation test

All 20 Effervescent tablet is passed the weight variation test as per pharmacopoeial limits. The weights of all 20 tablets are uniform and the weight variation of Ciprofloxacin HCL is reported in Table No.6.

***In vitro* drug release studies**

The *In vitro* drug release studies of Ciprofloxacin HCL Effervescent tablet is determined in PH 1.2 Buffer, in which 99.26 % drug is releases at the end of 30 min. And the *in vitro* drug released of Ciprofloxacin HCL is reported in Table No.6 and *in vitro* drug released of Ciprofloxacin HCL shown in Figure No.3.

Table No.1: Formulation Ingredients of Ciprofloxacin HCL

S.No	Ingredient (mg / tablet)	F_1	F_2	F_{OP}
1	Talc (mg)	18	22	20
2	Mg stearate (mg)	20	18	20
3	Avicil (mg)	62	60	60
4	Ciprofloxacin (mg)	250	250	250
5	Saccharine (mg)	150	150	150
6	Citric Acid (mg)	22	27	25
7	Tartaric Acid (mg)	18	28	24
8	NaHCO3 (mg)	38	46	42
9	Banana Flavour (mg)	28	32	30
Total wt. One Tablet (mg)		621	621	621

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

S.No	Parameters	Result	Std.
1	Melting Point (˚c)	311 - 318˚c	311 - 320˚c
2	Log p Value	0.35	0.36

Table No.3: Solubility of Ciprofloxacin HCL in different solvents

S.No	Medium	Concentration of drug Soluble (mg /ml)
1	Water	0.8
2	PH 1.2 Acidic Buffer	0.23
3	PH 6.8 Phosphate Buffer	1.28
4	PH 7.4 Phosphate Buffer	1.82
Result	**Class of drug**	**BCS Class IV**

Table No.4: Calibration of Ciprofloxacin HCL in Water

S.No	Concentration	Absorbance
1	0	0
2	2	0.204
3	4	0.408
4	6	0.626
5	8	0.835
6	10	0.998

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 Ciprofloxacin HCL	0.78	0.79
2	Ciprofloxacin HCL + Talc	0.75	0.78
3	Ciprofloxacin HCL + Mg stearate	0.80	0.84
4	Ciprofloxacin HCL + Avicil	0.76	0.74
5	Ciprofloxacin HCL + Ciprofloxacin	0.74	0.78
6	Ciprofloxacin HCL + Saccharine	0.72	0.74
7	Ciprofloxacin HCL + Citric Acid	0.82	0.78
8	Ciprofloxacin HCL + Tartaric Acid	0.81	0.80
9	Ciprofloxacin HCL + NaHCO3	0.75	0.79
10	Ciprofloxacin HCL + Banana Flavour	0.74	0.75

Table No.6: Evaluation of Ciprofloxacin HCL Tablet

S.No	Parameters	F_{OP}	Conclusion
1	Bulk Density (gm/cm3)	0.58	Pass
2	Tapped Density (gm/cm3)	0.61	Pass
3	Angle of Repose (θ)	22.14	Pass
4	Carr's Index (%)	4.91	Pass
5	Hardness Test (kg/cm^2)	4.9	Pass
6	Friability Test (%)	0.6	Pass
7	% of Weight variation test	99.86	Pass
8	*In Vitro* Drug release (%)	99.26	Pass

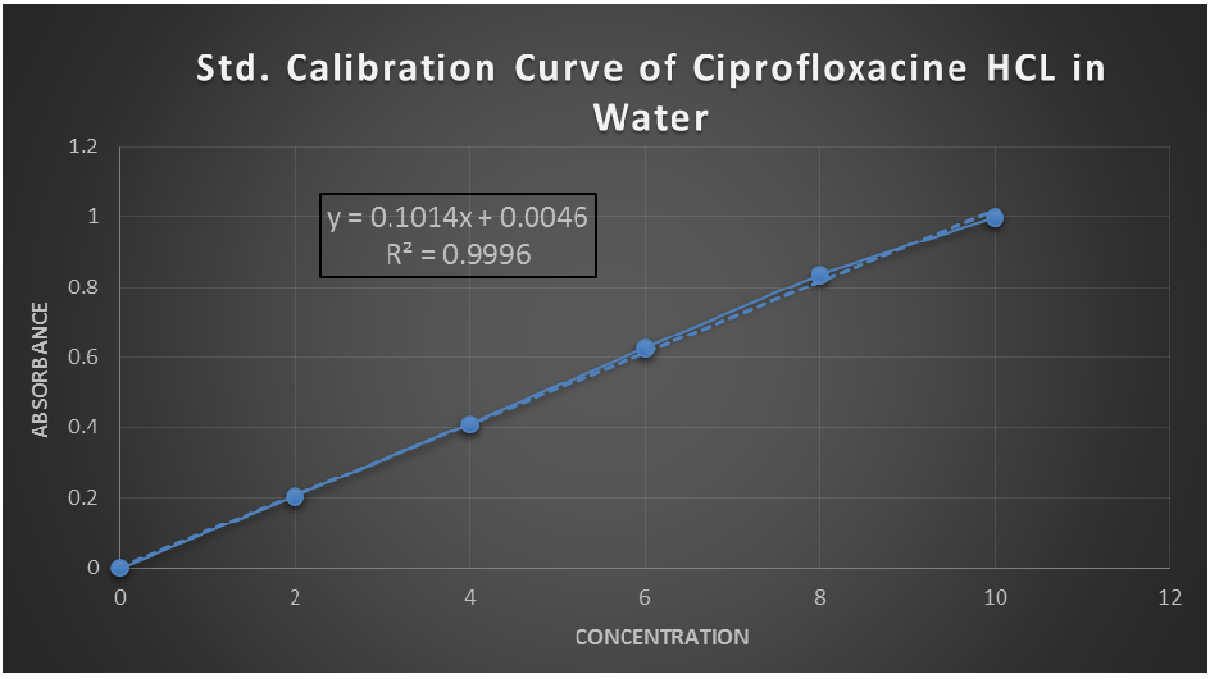

Figure No.1: Calibration curve of Ciprofloxacin HCL in Water

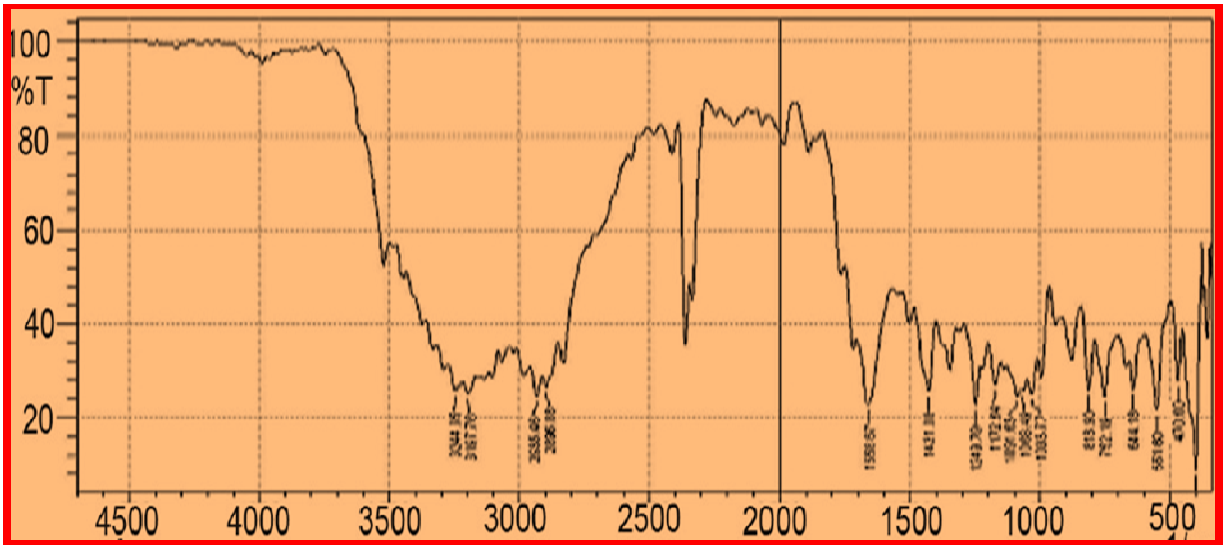

Figure No.2: IR of Pure drug Ciprofloxacin HCL

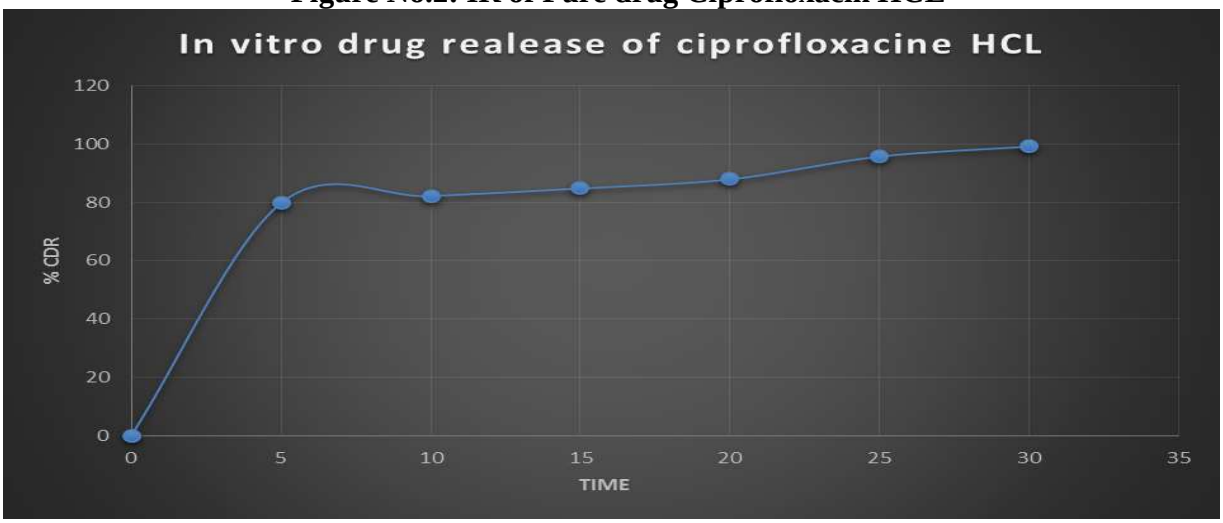

Figure No.3: *In vitro* drug release of Ciprofloxacin HCL in PH 1.2 Acidic buffer

CONCLUSION

The Effervescent Tablet of the Ciprofloxacin HCL is Prepared by the Wet Granulation Process is better than direct compression method because the Uniformed and good distribution of active ingredients. This tablet was rapidly disintegrated and dissolved while come into contact with water and GI media by realising the CO_2 Molecule under reaction between citric acid, Tartaric acid with Sodium Bicarbonate. 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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