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Research Article

Formulation and Evaluation of Ciprofloxacin HCL Tablet

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Abstract

Ciprofloxacin HCL is a tablet made by wet granulation method. Ciprofloxacin is a broad spectrum fluoroquinolone antibiotic. It is mainly used for various bacterial infections including anthrax, biliary tract infection, bone and joint infection, gastrointestinal including traveller's diarrhea and campylobacter enteritis, shigella, meningococcal meningitis prophylaxis, surgical infection prophylaxis, tuberculosis, leprosy and topically in the treatment of eye infections.

The prepared Ciprofloxacin hydrochloride 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 the optimized batch is good to satisfactory, and having a good free-flowing property. The hardness, weight variation, and friability values are within the pharmacopeia limit. The *in vitro* dissolution studies show the maximum percentage of release of drug (86%) within 30 min.

Keywords: Introduction of Ciprofloxacin HCL tablet, mechanism of action, properties, formulation and evaluation

Introduction

Ciprofloxacin is an antibiotic used to treat a number of bacterial infections, including bone and joint infections, intra-abdominal infections, certain types of infectious diarrhea, respiratory tract infections, skin infections, typhoid fever, and urinary tract infections, among others. For some infections, it is used in addition to other antibiotics. It can be taken by mouth, in eye drops, or intravenously.[1,2]

Common side effects include nausea, vomiting, diarrhea, and rashes. Ciprofloxacin increases the risk of tendon rupture and worsening muscle weakness in people with neurological disorder myasthenia gravis. Rates of side effects appear to be higher than some groups of antibiotics such as cephalosporins, but lower than others such as clindamycin.[3]

Studies in other animals raise concerns regarding use in pregnancy. No problems were identified, however, in the children of a small number of women who took the medication. It appears to be safe during breastfeeding.[4]

It is a second-generation fluoroquinolone with a broad spectrum of activity that usually results in the death of the bacteria.[5,6]

Ciprofloxacin was introduced in 1987. It is on the World Health Organization's List of Essential Medicines, the most effective and safe medicines needed in a health system. It is available as a generic medication and is not very expensive. The wholesale cost in the developing world is between 0.03 and 0.13 USD a dose. In the United States, it is sold for about 0.40 USD per dose.[7-10]

Medical Uses

Ciprofloxacin is used to treat a wide variety of infections, including infections of bones and joints, endocarditis, gastroenteritis, malignant otitis externa, respiratory tract

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infections, cellulitis, urinary tract infections, prostatitis, anthrax, and chancroid.[1]

Ciprofloxacin only treats bacterial infections; it does not treat viral infections such as the common cold. For certain uses including acute sinusitis, lower respiratory tract infections and uncomplicated gonorrhea, Ciprofloxacin is not considered a first-line agent.[11]

It also features prominently in treatment guidelines for acute pyelonephritis, complicated or hospital-acquired urinary tract infection, acute or chronic prostatitis, certain types of endocarditis, certain skin infections, and prosthetic joint infections.[12-14]

In other cases, treatment guidelines are more restrictive, recommending in most cases that older, narrower-spectrum drugs be used as first-line therapy for less severe infections to minimize fluoroquinolone-resistance development. For example, the Infectious Diseases Society of America recommends the use of Ciprofloxacin and other fluoroquinolones in urinary tract infections be reserved to cases of proven or expected resistance to narrower-spectrum drugs such as nitrofurantoin ortrimethoprim/sulfamethoxazole.[15]

The European Association of Urology recommends Ciprofloxacin as an alternative regimen for the treatment of uncomplicated urinary tract infections, but cautions that the potential for "adverse events have to be considered".[13]

Although approved by regulatory authorities for the treatment of respiratory infections, Ciprofloxacin is not recommended for respiratory infections by most treatment guidelines due in part to its modest activity against the common respiratory pathogen *Streptococcus pneumonia*.[16-18]

"Respiratory quinolones" such as levofloxacin, having greater activity against this pathogen, are recommended as first-line agents for the treatment of community-acquired pneumonia in patients with important comorbidities and in patients requiring hospitalization (Infectious Diseases Society of America 2007). Similarly, Ciprofloxacin is not recommended as a first-line treatment for acute sinusitis.[19,20]

Ciprofloxacin is approved for the treatment of gonorrhea in many countries, but this recommendation is widely regarded as obsolete due to resistance development.[21,22]

Mechanism of Action

Ciprofloxacin is a broad-spectrum antibiotic of the fluoroquinolone class. It is active against both Gram-positive and Gram-negative bacteria. It functions by inhibiting DNA gyrase, and a type-II topoisomerase, topoisomerase IV, necessary to separate bacterial DNA, thereby inhibiting cell division.[23,24]

Uses

Ciprofloxacin is an antibiotic used to treat a number of bacterial infections. This includes bone and joins infections, intra-abdominal infections, certain types of infectious diarrhea, respiratory tract infections, skin infections, typhoid fever, and urinary tract infections.[1]

Properties

Chemical Properties

Ciprofloxacin is 1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-3-quinolinecarboxylic acid. Its empirical formula is C 17H 18FN3O3 and its molecular weight is 331.4 g/mol. It is a faintly yellowish to light yellow crystalline substance.

Ciprofloxacin hydrochloride (USP) is the monohydrochloride monohydrate salt of Ciprofloxacin. It is a faintly yellowish to light yellow crystalline substance with a molecular weight of 385.8 g/mol. Its empirical formula is $C_{17}H_{18}FN_3O_3HCl•H_2O$.[25]

Physical Properties

Colour: Faint to light yellow crystalline powder

Molecular Weight: 331.347 g/mol

Melting point: 255–257°C

Boiling Point: 581.8±50.0°C at 760 mmHg

Solubility: Soluble in dilute (0.1N) hydrochloric acid; practically insoluble in ethanol

PH: pH range for the 1.0% aqueous concentrates in vials is 3.3 to 3.9; the pH range for the 0.2% ready-for-use infusion solutions is 3.5 to 4.6.[26-29]

Formulation of Ciprofloxacin Tablet

Materials and Methods

Materials: Ciprofloxacin and all formulation excipient (talc, Mg stearate, avicil, saccharine, lactose, mannitol, aerosol, and banana flavour)

Table 1.Formulation Ingredients of Ciprofloxacin HCl

S. No.	Ingredients (mg/tablet)	F1	F2	Fop
1	Talc	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	Lactose	22	27	25
7	Mannitol	18	28	24
8	Aerosol	38	46	42
9	Banana flavor (mg)	28	32	30
Total	Wt. one tablet (mg)	621	621	621

Method: The parameters of authentication and pre-formulation 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 pre-formulation properties at which the temperature 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 determined by using two types of methods, one is conventional method and the other is digital.

Log P Value: Log p value is determined by using Partition Coefficient Phenomenon, in which 1 gm of drug is added in a separating funnel, containing equal portion of 25 mL of octanol and 25 mL of water. The separating funnel is shaken for 20–25 min which stabilizes the mixture. After stabilizing the mixture to remove water phase from separating funnel and filter it, take the absorbance of filtrate and calculate the log p value.

Table 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

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 form saturated solution.

Procedure

- To prepare different solutions in water, PH 1.2 acidic buffer, PH 6.8 phosphate buffer, and PH 7.4 phosphate buffer.
- The drug material is added into the above solutions till a supersaturated solution is formed. The mixture is placed in an orbital shaker for 24 hrs. After 24 hrs, mixture is filtered and given absorbance.
- To detect the concentration of drug that is soluble in different solutions.

Method of Formulation

Formulation of Ciprofloxacin HCL

The 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. The mixtures of two dishes containing mixture are mixed together in a mortal pastel and a blended solution [Guar (1 gm) and PVP (1 gm) in Iso Propyl alcohol up to 10 mL] is added until dough mass is formed. The prepared dough mass is passed into mesh 14 sieve, granules are prepared and prepared granules are dried in an oven for 10–15 min. After drying the granules, MCC and lubricating agent such as talc, Mg stearate and other flavouring agents such as banana flavour are added and mixed and passed through a mesh 16 sieve; fine granules are prepared. The compression is done by using the 8 station signal rotatory tablet punching machine having hardness of 4–5 kg/cm^2. All formulation ingredients are reported in Table 1.

Table 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
Results	Class of drug	BCS class

Evaluation Parameters[30,37]

Bulk Density

The 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 bulk density calculated according to the formula, bulk density=mass/volume.

Tapped Density

The ratio of bulk mass and tapped volume is known as tapped density. Tapped density is an important evaluation parameter that 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 the 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 ≤10 indicates free flowing properties and Carr's Index ≥10 indicates poor flowing properties.

Angle of Repose

The pile surface of powder is known as the 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 is used for determining the angle of repose:

θ-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 ≤40° indicates free flowing properties. The angle of repose ≥40° indicates poor flow of material.

Hardness or Crushing Strength

Hardness of the tablet is determined by using conventional hardness tester and digital hardness tester. The standard range of the hardness of Ciprofloxacin 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, the tablets were re-weighed and friability percentage was calculated. To give an initial weight of 20 tablet minimized these weight 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 tablet contained 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

Disintegration Test

In order to evaluate the disintegration capability of tablets, the test was performed as per the procedure described in the experimental section. The results are shown in Table 4. From the table, it can be seen that the average disintegration time for each formulation is less than 8 min. Standard deviation of the disintegration time from the average value is very low 0.639 to 0.834 suggesting the disintegration time of the drug is very close among the tablets. All the values comply with the USP specification indicating the good quality (oral absorption) of tablets in terms of disintegration time.

Dissolution Test

Tablet dissolution is a standardized method for measuring the rate of drug release from a dosage form. From the results as shown in Table 4, it is obvious that all brands of Ciprofloxacin HCl tablets show more than 80% release in the specific medium within 30 min, thus complying with USP specification. The result indicates good dissolution of the drug and suggests the proper absorption of the drug from GIT.

Table 4.Evaluation of Ciprofloxacin HCL Tablet

S. No.	Parameters	Fop	Conclusion
1	Bulk density (gm/cm^3)	0.58	Pass
2	Tapped density(gm/cm^3)	0.61	Pass
3	Angle of repose($^\theta$)	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	Dissolution test in minutes	80% (in 30 min)	Pass
10	Disintegration test in minutes	8 (min)	Pass

Conclusion

formulation studies of Ciprofloxacin HCl were performed, the super disintegrants and excipients used were compatible with Ciprofloxacin hydrochloride which can be prepared by wet granulation method using super disintegrants, namely, talc, Mg stearate, avicil, saccharine, lactos, mannitol, aerosol, and banana flavour. Ciprofloxacin HCL is prepared by the wet granulation process which is better than direct compression method because of the uniformed and good distribution of active ingredients. The hardness, weight variation, and friability values are within the pharmacopeia limit.

Conflict of Interest: None

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