Original Research Article

Ciprofloxacin hydrochloride mediated enhanced solubilization and stability by UV-spectroscopy

Abstract

In the case of solubility limited absorption, creating supersaturation in the GI fluid is very critical assupersaturation may provide great improvement of oral absorption. The techniques to create the so-called supersaturation in the GI fluid include microemulsions, emulsions, liposomes, complexations, polymeric micelles, and conventional micelles. Ciprofloxacin was chosen because it is practically insoluble in water; hence its salt form is used commercially, which is soluble in water. The objective of the present investigation was to enhance the solubility of ciprofloxacin by formulating solid dispersions techniques in water soluble carriers have attracted considerable interests as a mean of improving the dissolution rate & hence possibly bioavailability range of hydrophobic drugs. The poor solubility of ciprofloxacin leads to poor dissolution & hence variation in bioavailability. The purpose of present investigation was formulation & evaluation of controlled release floating capsule of ciprofloxacin with improved solubility & dissolution rate. In the present study solid dispersions using various carriers like mannitol & lactose in different ratios were prepared by solvent evaporation method. The prepared solid dispersions were characterized for drug content, solubility & dissolution rate. The dissolution rate substantially improved for ciprofloxacin from its solid dispersions compared with the pure drug. Dissolution rate increased with increasing carrier content.

Keywords: Ciprofloxacin, Spectroscopy, Solubilization, dissolution

Introduction

The poor solubility and low dissolution rate of poorly water soluble drugs in the aqueous gastro-intestinal fluids often cause insufficient bioavailability ratherthan the limited permeation through the epithelia and the formulation of poorly soluble drugs for oral delivery now presents one of the major challenges tom formulation scientists. Hence, novel technologies for drug solubilization are required which can increase drug solubilization and overcome the issues of traditional excipients(1). Ciprofloxacin is an antibiotic used to treat a number of bacterial infections. This includes bone and joint infections, intra abdominal infections, certain type of infectious diarrhea, respiratory tract infections, skin infections, typhoid fever, and urinary tract infections, among others. Product development scientists often encountersignificant difficulties in solving the problem of poorwater solubility of drug candidates in the development ofpharmaceutical dosage forms(2). As a matter of fact, morethan one-third of the drugs listed in the U.S.Pharmacopeia fall into the poorly water-soluble or water-insoluble categories. It was reported a couple of decadesago that more than 41% of the failures in new drugdevelopmentbiopharmaceuticalshavebeenpropertiesattributedtopoorwatersolubility, while it was still indicated recently thatabout 50% failure of drug candidates was due to poor“drug-like” properties. It is commonly recognized in thepharmaceutical industry that on an average more than40% of newly discovered drug candidates are poorlywater soluble. Poor “drug like” properties of leadcompounds led to ineffective absorption from the site ofadministration, which has been designated as animportant part of the high clinical failure due to poorpharmacokinetics(3-5).Ciprofloxacin is a synthetic broad-spectrum antimicrobial agent for intravenous (I.V.) administration. Ciprofloxacin, a fluoroquinolone, is 1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-3-quinolinecarboxylic acid. Its empirical formula is $C_{17}H_{18}FN_3O_3$ and its chemical structure is in Figure 1:

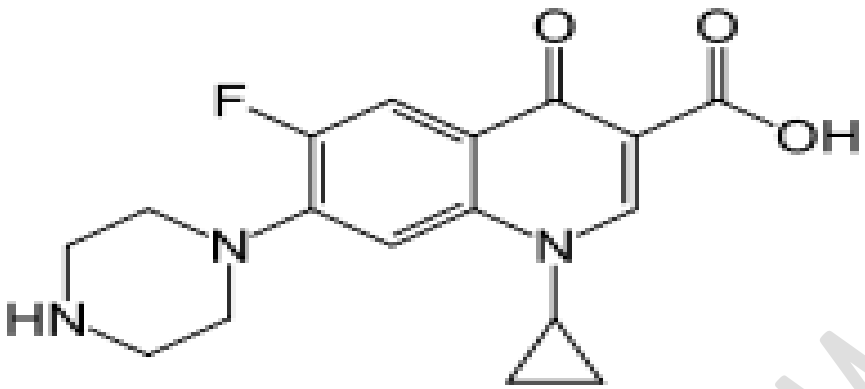

Fig. 1: Structure of ciprofloxacin

Surfactant micelles are found to facilitate drug absorption along with shielding the active drug molecules from adverse environmental conditions. The study of molecular-level interactions between the drug and micelles can be used to predict several pharmacokinetic and pharmacological properties of drugs, viz., transport, biodistribution, accumulations, and therefore their efficacy. When a sufficient amount of a surfactant is dissolved in water, the surfactant molecules form colloidal clusters (micelles) of various shapes in which the polar head groups point outward and the hydrophobic ends point toward the coreof the micelle. The threshold concentration at which the formation of micelle begins is known as critical micelle concentration (cmc). Micellar core is capable of incorporating hydrophobic substances present in the system. In past, various ionic surfactants such as cetyltrimethyl ammonium bromide (CTAB), dodecyl trimethyl ammonium bromide (DTAB), tetradecyltrimethyl ammonium bromide, sodium dodecyl sulfate (SDS), sodium lauryl sulfate, alpha olefin sulfonate, alkylbenzene sulfonate, both alone and their mixtures have been studied in association with various poorly water-soluble drugs, viz., ibuprofen,(1,2)naringenin,(3)danazol,(4)gliclazide,(5) and so forth. Nonionic surfactants, viz., Brij 351 and Tween 80,5 have also been studied in association with poorly soluble drugs for enhancing their solubility(6-7).

Material and Method

Ciprofloxacin (Pellets Pharma Ltd), Croscarmellose Sodium (Diocon Pharma Ltd), Distilled Water, Methanol, Dichloro methane, Potassium Di-hydrogen Phosphate, Sodium Hydroxide.

Identification of the Drug

Melting Point Determination

The Thiel's tube method of melting point determination in liquid paraffin was used in the present study.

UV Spectrum

UV Scanning was done for pure drug between 200 and 400 nm using 0.1N HCl as dilution medium the λmax was found at 277 nm(8).

Preparation of Standar curve:

Standard stock solution containing ciprofloxacin hydrochloride was prepared by dissolving 10mg in 100ml of methanol and then diluted with 1N NaOH and 1N HCL separately to get series of dilution ranging from 2-10 µg/ml and then absorbance recorded at 272 nm and 278 nm respectively against reagent blank. Calibration curve was prepared by plotting concentration versus difference in absorbance and found to be linear in the concentration range of 2-10 µg/ml Shown in Figure 2.

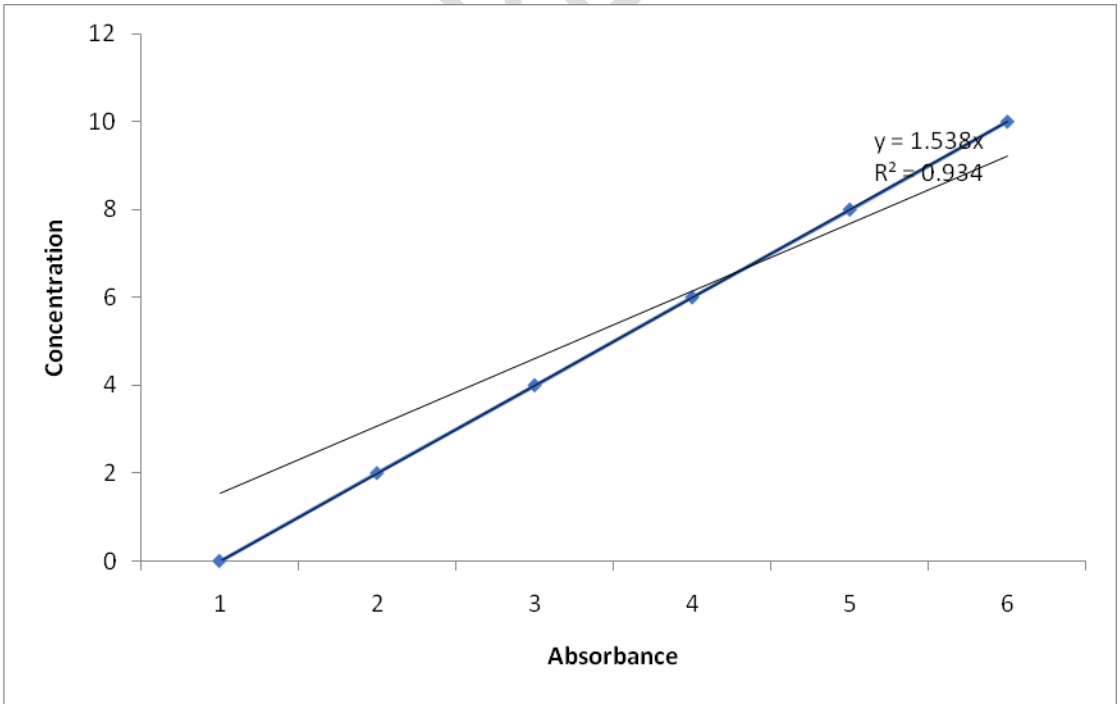

Figure 2: Standard curve of ciprofloxacin in 277 nm

Selection of surfactant and cosurfactant

We studied different formulations in which Km ratio surfactant with different HLB values were screened such as tween 20, tween 80 cosurfactant such as polyethylene glycol400 and glycerol and oil such as castor oil (9).

Estimation of Ciprofloxacin

The standard solutions of Ciprofloxacin were subsequently diluted with pH 7.2 phosphate buffer to obtain series of dilutions containing 5,10,15,20, and 30 µg of ciprofloxacin solution (9). The absorbances of the above dilutions were measured in a Spectro 2080 plus Analytical Technologies limited UV Spectrophotometer at 288 nm using distilled water as blank the figure 3 showen the wavelength (10).

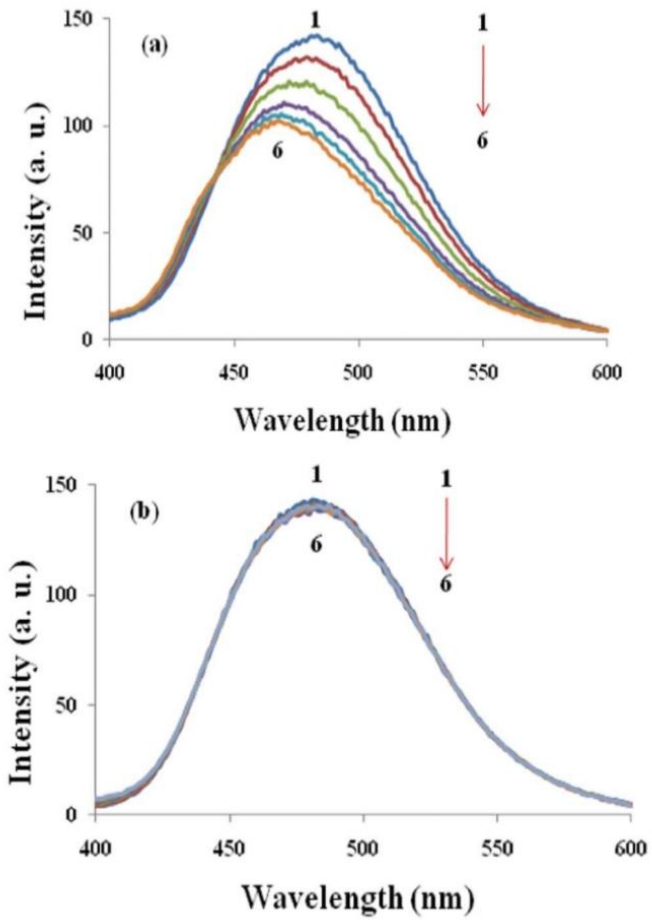

Figure3. UV Spectra of ciprofloxacin

Drug solubility

The amounts of drug present in the formulations were determined with the help of UV spectrophotometric method. For each batch, 100 mg of sample was placed in to the volumetric flask and added methanol and the mixer were diluted with the pH 7.2 phosphate buffer(11).

Table 1: kinetic profile of ciprofloxacin f-3 (cogrinding) solid dispersion

Amount of drug dissolved				**Log% Drug remained**		
S.NO	**Time**	**OD**		**%Drug dissolved**		**%Drug remained**
1	0	0	0	0	100	2
2	5	0.213	88.7	74.89	25.11	1.4
3	10	0.232	92.38	82.63	8.28	1.2
4	15	0.23	94.04	89.52	6.37	0.91
5	20	0.35	96.12	93.41	5.47	0.62
6	25	0.44	99.04	100	0	-

Physical characterization of formulations

***In-vitro* drug release studies**

Optimal formulation for each ciprofloxacin and drug were dialysed against water to harness their drug release profile. Briefly, 2 mL of formulation was pipette inside a visking tube (12-14 kDa) (Medicell, UK) and dialysed against distilled water (200 mL) at room temperature(12-13) release profile showen in figure 4.

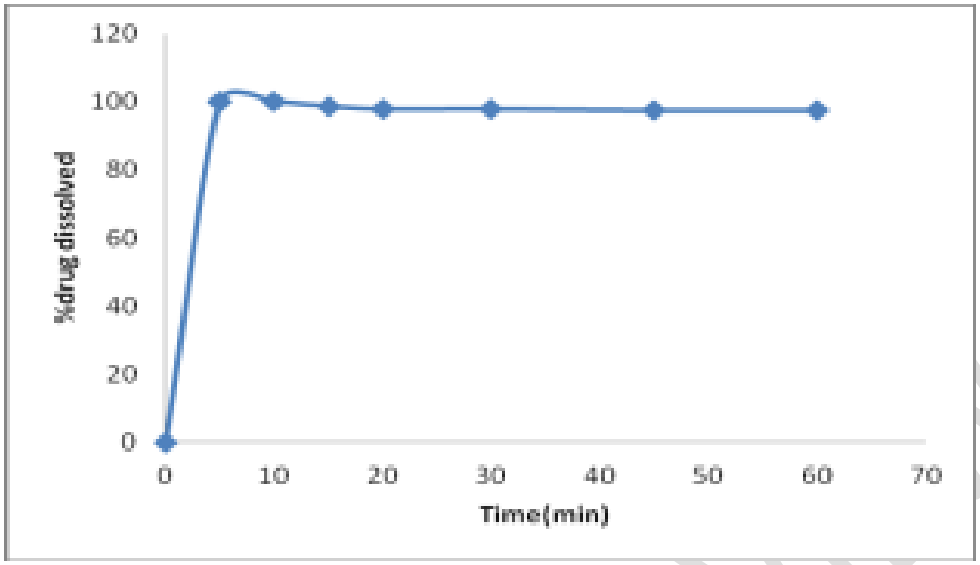

Fig 4: zero order kinetic profile of ciprofloxacin

Results and Discussion

As the pure drug has shown poor dissolution property, in order to enhance the dissolution rate we used different methods for preparing solid dispersions

Melting point

The melting point of ciprofloxacin was found at 255^{o}Cwhich matched with reported data.

UV Spectrum

The UV spectra of ciprofloxacin in 0.1 N HCl was scanned between 200 and 400 nm at medium scanningspeed using 10 µg/mLsolution in 1 cm quartz cell. Λmax of 277 nm was found as earlier reported (Rajia et al., 2011). This was utilized for preparation of standard curve.

Solubility studies

Solubility of the drug in microemulsion formulation and the individual ingredients of the microemulsion is shown in Figure 5. The solubility of ciprofloxacin in theoptimized formulation is 81.18 mg/mLwhereas in Tween80, PEG 400, Castor oil is 38.318, 41.486, 45.94 mg/mL respectively.

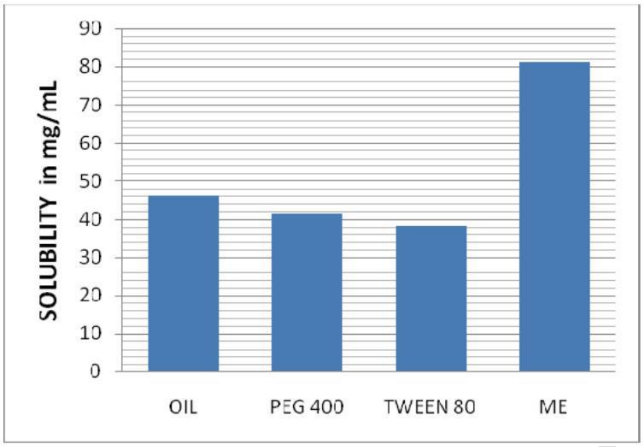

Fig.5. Solubility study

Conclusion

This study was undertaken with an aim to formulate an antibiotic drug in the form solid dispersion to overcome the poor solubility drawback of the drug. The selected antibiotic agent was ciprofloxacin. The drug ciprofloxacin has poor solubility in the water, under class 2 of BCS of classification of drug its solubility,and increased solubility was attempted by formulating as a solid dispersion with polymer by using various techniques. Solid dispersions were prepared by using the Crosscarmelose sodium as a disintegrated in 1:1 ratio of different techniques.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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