Original Research Article

Ciprofloxacin hydrochloride mediated enhanced solubilization and stability by UV-spectroscopy

Abstract

In the case of solubility limited absorption, creating super saturation in the GI fluid is very critical as -super saturation may provide great improvement of oral absorption. The techniques to create the so-called super saturation 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 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 increase ining carrier content.

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Keywords: Ciprofloxacin, Spectroscopy, Solubilization, dissolution

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Introduction

The poor solubility and low dissolution rate of poorly water soluble drugs in the aqueous gastro-intestinal fluids often cause in–sufficient bioavailability rather than 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 solubilizsation are required which can increase drug solubilizsation 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 encounter significant difficulties in solving the problem of poor water solubility of drug candidates in the development of pharmaceutical dosage forms(2). As a matter of fact, more than 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 decades ago that more than 41% of the failures in new drug development biopharmaceuticals have been properties attributed includingto poor water insolubility, while it was still indicated recently that about 50% failure of drug candidates was due to poor "drug-like" properties. It is commonly recognized in the pharmaceutical industry that on an average more than 40% of newly discovered drug candidates are poorly water soluble. Poor "drug like" properties of lead compounds led to ineffective absorption from the site of administration, which has been designated as an important part of the high clinical failure due to poor pharmacokinetics(3-5). (ciprofloxacinCiprofloxacin) 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 Figure 1:

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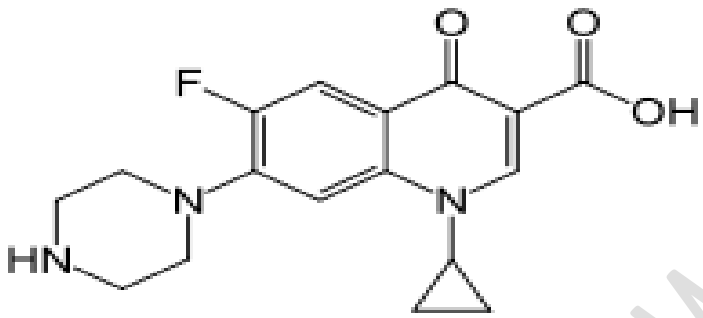

Fig. 1: Structure of ciprofloxacin

Surfactant micelles are found to facilitate drug absorption along with shielding ~~of~~ the active drug molecules from adverse environmental conditions. The study o~~f~~n 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 core of 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 cetyl trimethyl ammonium bromide (CTAB), dodecyl trimethyl ammonium bromide (DTAB), tetradecyl trimethyl 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, Di~~c~~ ~~C~~hloro methane, Potassium Di-hydrogen Phosphate, Sodium Hydroxide.

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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~~l~~ as dilution medium the λ max was found at 277 nm(8).

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 p~~P~~hosphate buffer to obtain series of dilutions containing 5,10,15,20, and 30 µg of c~~C~~iprofloxacin solution (9). The absorbance~~e~~es of the above dilutions were measured in a Spectro 2080 plus Analytical ~~technologies~~ Technologies limited U-V Spectrophotometer at 288 nm using distilled water as blank (10).

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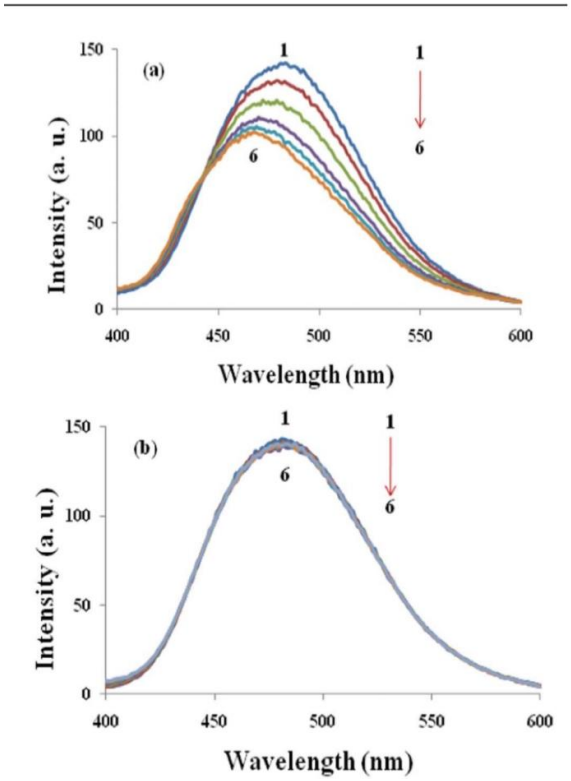

Figure2. UV Spectra of ciprofloxacin

Drug solubility

The amounts of drug present in the ~~taken oven~~ formulations were determined with the help of U-V s~~S~~pectrophotometric method. For each batch, 100 mg of sample was ~~taken~~ placed in to the volumetric flask and added methanol and the mixer ~~was~~ 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	97.38	91.72	8.28	0.918
4	15	0.23	99.04	100	0	-

Physical characterization of formulations

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

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

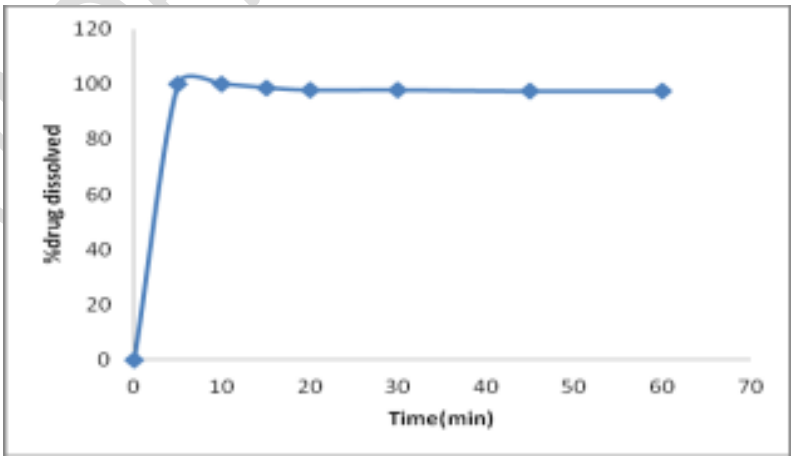

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Fig 3: zero order kinetic profile of ciprofloxacin

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 mMelting point of ciprofloxacin was found at 255^{0}-255^{o} C which 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 scanning speed using 10 µg/ml mL solution in 1 cm quartz cell. Λ max 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 Fig. 3. The solubility of cCiprofloxacin in the optimized formulation is 81.18 mg/ml mL whereas in Tween80, PEG 400, Castor oil is 38.318, 41.486, 45.94 mg/mL respectively.

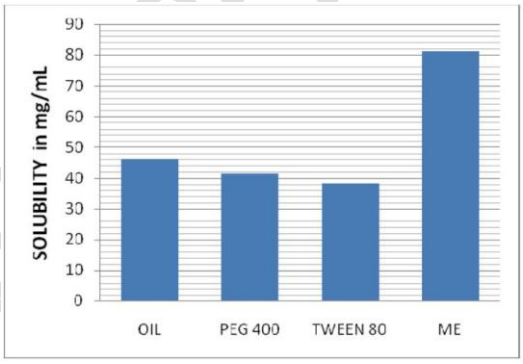

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Fig.4. Solubility study

Conclusion

This study was undertaken with an aim to formulate an aAntib Biotic drug in the form solid dispersion to overcome the poor solubility drawback of the drug. The selected aAntibiotic agent was cCiprofloxacin. The drug cCiprofloxacin is havinghas poor solubility in the water, under class 2 of BCS of classification of drug its solubility. was tried to increaseand increased solubility was attempted by formulating in the form ofas 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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