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DISSOLUTION DEVELOPMENT OF CIPROFLOXACIN AND TINIDAZOLE IN COMBINED TABLET DOSAGE FORM

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ABSTRACT

Ciprofloxacin hydrochloride is a broad spectrum anti-microbial drug, listed in class 4 of biopharmaceutics classification of drugs. Tinidazole is a prodrug and antiprotozoal agent, listed in class 2 of biopharmaceutics classification of drugs. In the present study a new dissolution medium was developed, as there is no official dissolution medium available in the literature for combined dosage form containing ciprofloxacin and tinidazole. The composition of the dissolution medium was selected on the basis of solubility data .Solubility data revealed that 0.01 N HCl may be suitable as dissolution medium. The selected dissolution medium was used for the evaluation of combined dosage form containing ciprofloxacin and tinidazole. A reverse phase high performance liquid chromatography method was developed for estimation of ciprofloxacin and tinidazole in combined dosage form. The separation was achieved by Inertsil C18 (250X4.6mm) column, 5 µm and Buffer: Acetonitrile (82:18) as eluent, at a flow rate of 1.0 ml /min. Detection was carried out at 316 nm. The retention time of ciprofloxacin & tinidazole was found to be 5.6 and 9.7 minutes respectively. Linearity was in the range of 27.5 - 82.5µg/ml for ciprofloxacin, and 33µg/ml - 66µg/ml for tinidazole. The developed method was found to be accurate, precise and selective for the development of ciprofloxacin and tinidazole in combined tablet dosage form.

Key Words:- Ciprofloxacin Hydrochloride, Anti- microbial, Tinidazole, Anti-protozoal.

INTRODUCTION

Ciprofloxacin is a broad-spectrum anti-microbial agent of the Quinolones class (Brunton LL, 2011). Ciprofloxacin hydrochloride is soluble in water but low permeability drug (Indian Pharmacopoeia, 2007). The bactericidal action of Ciprofloxacin results from inhibition of the enzymes topoisomerase II (DNA gyrase) and topoisomerase IV, which are required for bacterial DNA replication, transcription, repair, strand supercoiling repair, and recombination. It exhibit many of pharmacological action for the treatment of infections caused by susceptible organisms: urinary tract infections, acute uncomplicated cystitis, chronic bacterial prostatitis, lower respiratory tract infections, acute sinusitis, skin and skin structure infections, bone and joint infections, complicated intra-abdominal infections, infectious diarrhoea, typhoid fever (enteric fever), uncomplicated cervical and urethral gonorrhea, and inhalational anthrax (Tripathi KD, 2008). Tinidazole is a prodrug and antiprotozoal agent (Sweetman SC and Martindale, 2003; Indian Pharmacopoeia, 2007). It has low solubility and high permeability. Sparingly soluble in water, slightly soluble in ethanol, in chloroform and in ether (Tripathi KD, 2008). The nitro group of Tinidazole is reduced in *Trichomonas* by a ferredoxin-mediated electron transport system. The free nitro radical generated as a result of this reduction is believed to be responsible for the

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antiprotozoal activity. The toxic free radicals covalently bind to DNA, causing DNA damage and leading to cell death. It is used to treat trichomoniasis caused by *T. vaginalis*, giardiasis caused by *G. duodenalis*, Intestinal amoebiasis and amoebic liver abscess caused by *E. histolytica* (Sani A. Ali *et al*., 2011; Horatio B. Fung and Thien-ly Doan, 2005).

Combination of ciprofloxacin and tinidazole is not official in any pharmacopoeia. Drug X containing 500 mg of ciprofloxacin and 600 mg of tinidazole is available in market. A survey of literature revealed that few chromatographic and spectrophotometric methods are reported for determination of ciprofloxacin (Pavani Padma Priya B, 2013) and tinidazole in individual (Jansari Sneha K *et al*., 2012) and combined dosage form (Sowjanya Gummadi *et al*., 2012; Sirisha T *et al*., 2014; Tagalpallewar VR *et al*., 2014; Dhavani Kanikanti and Karunapriya Chitra, 2012; Ravi Varma A *et al*., 2013). However there is no HPLC method reported for dissolution development of ciprofloxacin and tinidazole in combined dosage form. The present work describes a simple, precise and accurate HPLC method for the development of ciprofloxacin and tinidazole in combined tablet dosage form.

MATERIALS AND METHODS

The drug samples, ciprofloxacin hydrochloride and tinidazole were obtained as gift samples from the Gracure pharmaceuticals Pvt. Ltd., Bhiwadi. HPLC grade acetonitrile, methanol, water, orthophosphoric acid AR were purchased from Merck Co. Mumbai. And S.D. fine chemicals, Mumbai, respectively.

Dissolution experiments were performed using USP standard dissolution apparatus II (Electro lab TDT - 08L) at 37±0.5°c at a paddle speed of 50 rpm. The dissolution medium was 0.01 N HCl, 900ml selected as on the basis of Ciprofloxacin tablets mention in USP. A high performance liquid chromatography (Waters e2695), variable wavelength programmable PDA detector, with empower software was used. The chromatography column used was reverse phase Inertsil C18 column (250mmX4.6) mm, particle size 5 µm. Samples were withdrawn at 30 minutes. The dissolution medium was analyzed for ciprofloxacin and tinidazole by using HPLC. Results presented are the average of three experiments.

0.01N HCl was prepared as dissolution medium. A mixture of buffer (1.7 ml of orthophosphoric acid in 1000ml of water) and acetonitrile in the ratio 82:18 was used as mobile phase and was filtered through 0.45µ Millipore membrane filter. The flow rate of mobile phase was maintained at 1.0 ml /min. Detection was carried out at 316 nm at 25°c.

Standard solution is prepared in dissolution medium. A quantity of powder equivalent to about 55mg of USP ciprofloxacin hydrochloride and 66mg of tinidazole was weighed and transferred to 100ml volumetric flask containing 60 ml of diss olution medium and the mixture was sonicated .The volume was made up to 100 ml with dissolution medium. The contents were filter through whatmann filter paper No.1. Further dilutions were made to get a concentration of 55µg/ml of Ciprofloxacin and 66µg/ml of Tinidazole. Twenty microliters of the test and standard solutions were injected separately and chromatograms were recorded upto to 15 minutes.

The present work aimed at developing a simple, precise and accurate HPLC method for estimation of ciprofloxacin and tinidazole in combined tablet dosage form using the widely used Inertsil C18 (250X4.6)mm. The mobile phase was optimized with 1.7 ml of orthophosphoric acid and acetonitrile in the proportion 82:18 v/v. With the above mentioned composition of mobile phase a good resolution was achieved .Wavelength detection was carried at 316 nm as both the drug show good absorbance at this wavelength.

The testing of pharmaceutical dosage form for in vitro drug release and dissolution characteristics is very important for ensuring batch to batch quality control and to optimize formulations during drug development.

A batch of 20 tablets of combined dosage form was procured for comparative studies of innovator and sample. The dissolution experiments for commercial formulations of combined dosage form were performed using above *in vitro* dissolution conditions by selecting 0.01N HCl as dissolution medium.

RESULTS AND DISCUSSION

The comparative study of the dissolution rate of innovator and both of the pure drugs in 0.01N HCl was carried out.

The results indicated that the method develop for formulation containing ciprofloxacin and tinidazole in combined dosage form have dissolution rate slightly more as that of innovator. That difference is considered to be negligible and maximum dissolution was found in 0.01N HCl.

CONCLUSION

The performance of the selected dissolution medium (900) ml was confirmed by conducting dissolution experiments of commercial formulations, and the results were shown in Fig. 1&2. The release rate of combined dosage form was determined and compared with its innovator. It was found that more than 90 % 0f

combined dosage form was released in 30 minute. The result of the Present study clearly indicate that 0.01N HCl is suitable medium for in vitro dissolution testing of conventional combined dosage form.

Fig 1. The release of ciprofloxacin performed at different time interval. Dissolution studies of ciprofloxacin (500mg) were performed in 0.01N HCl.

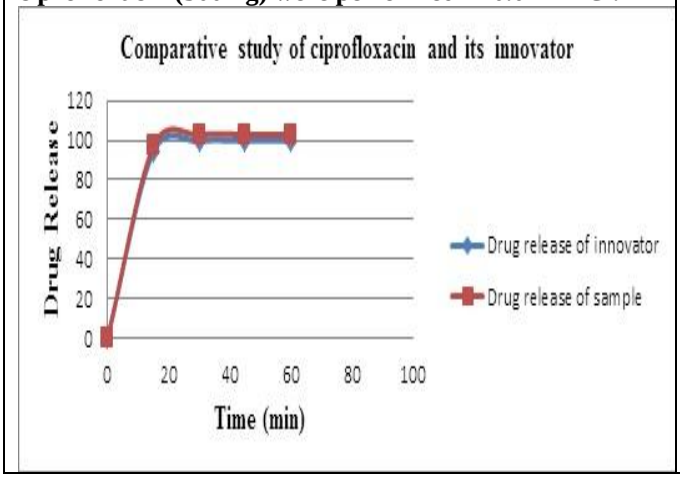
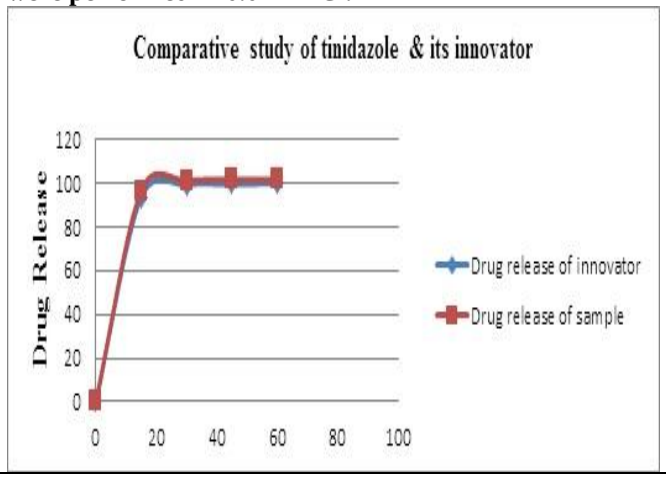


Fig 2. The release of tinidazole performed at different time interval. Dissolution studies of tinidazole (600mg) were performed in 0.01N HCl.



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