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PHOTO DEGRADATION RATE OF CIPROFLOXACIN IN SOLID AND LIQUID FORMS AND WITH SOME PHARMACEUTICAL EXCIPIENTS SYSTEMS

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ABSTRACT

Objectives: this study was aimed to assessment the reaction kinetics of the photo-degradation of ciprofloxacin on experimentally under the effect of sun-light for solid, liquid forms and induced some pharmaceutical excipients in ciprofloxacin.
Methods: Ciprofloxacin in solid and liquid forms will be expose directly to sun-light, and add some pharmaceutical excipient to determine the photo-degradation rate of ciprofloxacin by means of HPLC.
Results: Photolysis of ciprofloxacin in aqueous state and solid form under the effect of sunlight following first order interactions kinetics.

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INTRODUCTION

Ciprofloxacin is an antibiotic used to treat a number of bacterial infections, including infections of bones and joints, endocarditis, gastroenteritis, malignant otitis externa, respiratory tract infections, cellulitis, urinary tract infections, prostatitis, anthrax, and cancroids (The American Society of Health-System Pharmacists, 2015). Ciprofloxacin interacts with certain foods and several other drugs leading to undesirable increases or decreases in the serum levels or distribution of one or both drugs. Ciprofloxacin should not be taken with antacids containing magnesium or aluminum, highly buffered drugs (sevelamer, lanthanum carbonate, sucralfate, didanosine), or with supplements containing calcium, iron, or zinc. It should be taken two hours before or six hours after these products(Sean C Sweetman, 2009). Magnesium or aluminum antacids turn ciprofloxacin into insoluble salts that are not readily absorbed by the intestinal tract, reducing peak serum concentrations by 90% or more, leading to therapeutic failure. Additionally, it should not be taken with dairy products or calcium-fortified juices alone, as peak serum concentration and the area under the serum concentration-time curve can be reduced up to 40%. However, ciprofloxacin may be taken with dairy products or calcium-fortified juices as part of a meal(Medicine and Healthcare products Regulatory Agency, 2010). Ciprofloxacin 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 molecular weight is 331.4 g/mol. It is a faintly yellowish to light yellow crystalline substance[5]. Drug stability plays a very important role in pharmaceutical research and development for a newly developed drug product, stability analysis not only provides useful information regarding the degradation of the drug product, but also determines an expiration dating period of the drug product(Sean C Sweetman, 2009). For the purpose of safety and quality assurance, most regulatory agencies such as FDA require that an expiration dating period be indicated on the immediate container label for every drug product on the market(Amin MI and Bryan JT, 1973). Stability testing is the primary tool used to assess expiration dating and storage conditions for pharmaceutical products. Many protocols have been used for stability testing, but most in the industry are now standardizing on the recommendations of the International Conference on Harmonization. These guidelines were developed as a

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cooperative effort between regulatory agencies and industry officials from Europe, Japan, and the United States (International Conference on Harmonization (ICH), 2003). Degradation reaction in pharmaceutical formulations take place at definite rates and are chemical in nature. They depend on such conditions as concentration of reactants, temperature, pH, radiation, and catalysts(Khan and Akhtar, 2015). The common stress conditions include acidic pH, basic pH, neutral pH, different temperature and humidity conditions, oxidation, reduction and photo-degradation(Harmonization, 2003). These studies help to determine the significant related substances to be used in method development, and to determine the degraded product formed under stress conditions(Harmonization, 2003).

MATERIALS AND METHODS

Chemicals and Regents

All chemicals and reagents used were of a HPLC grade. Triethylamine solution was obtained from AppliChem, Germany. Acetonitrile HPLC grade was obtained from BDH Labs, England. Orthophospharic acid 85 % were obtained from BDH laboratory, ENGLAND.

Ciprofloxacin was kindly supplied from Dr. Reddys laboratories Ltd. India.

Excipients: Methyl Parben (BP, USP), Magnesium Stearate (BP, USP), and Propyl Parben (BP, USP) from Gamphray Laboratories-India. Sodium benzoate (BP, USP) - Gerestar-Germany.

Methods, instrumentation and chromatographic conditions

Analysis of ciprofloxacin photodegraded compounds was carried on a Waters HPLC system 1525, consisting of LC binary pump series 1525, UV/Visible detector 2489, and auto sampler series 2707.The column used was a C18; Waters Spherisorb®5.0µm ODS2 4.6 mm x 250mm. (USA). The mobile was a mixture of 87 volumes of 0.025M phosphoric acid (adjusted with trimethylamine to a pH 3.0 ± 0.1) and 13 volumes of acetonitrile(The American Society of Health-System Pharmacists, 2015). The Chromatographic Conditions used was Flow rate of 1.5 ml/min, Injection volume 50 µl, Column oven temperature was ambient, and detection wave length was 278 nm(Meyer. V.R, 1994).

Preparation of standard stock solutions: Stock standard solution having concentration of 0.1 mg/ml was prepared by dissolving pure drug of ciprofloxacin in mobile phase.

Experimental design and Degradation conditions

Preparation of decomposed ciprofloxacin solid by sun-light

Few grams of solid ciprofloxacin were placed between two glass plates (20 x 20 cm), sealed with gum tape and directly exposed to sunlight for six months (March to August). Samples were taken every month and tested for degradation by HPLC. From the chromatograms obtained, the reaction rate (k) of photo degradation ciprofloxacin were calculated and plotted against interval time, Table 1, Figure.1.

Preparation of serial concentrations of decomposed ciprofloxacin by sun-light

Different solutions of ciprofloxacin were prepared with a concentration of 25, 50, 75, 100 and 125 µg/ml.

These solutions were separately transferred to conical flasks and directly exposed to sunlight. Samples were taken at 0, 30, 60, 90, 120 and 150 minutes and analysis by HPLC method. From the chromatograms obtained, the reaction rate (k) of photo degradation ciprofloxacin were calculated and plotted against a concentration (Table 2), (Figure. 2)

Table 1. Reaction rate (K) of decomposed ciprofloxacin by sun-light versus time

Interval time / month	Reaction rate (k)- month^{-1}
1	0.3802
2	0.4855
3	0.5955
4	0.6853
5	0.7268
6	0.9212

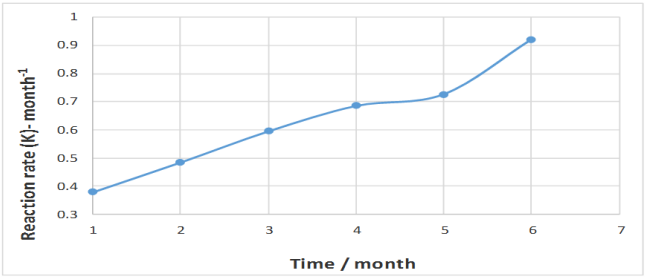

Figure 1. Effect of time on the reaction rate (k) of decomposed ciprofloxacin by sun light

Table 2. Reaction rate (k) of different concentration of decomposed ciprofloxacin liquid by sun light versus concentration

Concentration µg/ml	Reaction rate (k) –min $^{-1}$
25	0.1171
50	0.0989
75	0.0665
100	0.0361
125	0.0135

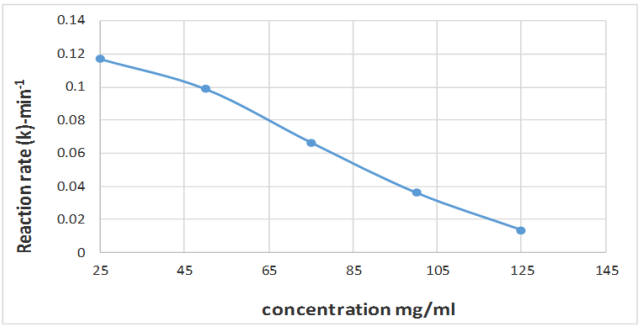

Figure 2. Effect of concentration on the reaction rate (k) of decomposed ciprofloxacin by sun light

Preparation of decomposed of ciprofloxacin with pharmaceutical excipients by sun –light

The required pharmaceutical excipient (Table 3) was weighed, transferred to a 250 ml volumetric flask and dissolved in small volume of distilled water. Twenty-five ml of ciprofloxacin e (25 mg / 100 ml-50 % methanol) were added to the flask containing pharmaceutical excipient; the volume was completed to the mark with distilled water. The flask was exposed directly to sunlight. Samples were taken at 15, 30, 45, 60, 75, 90, 105 and 120 minutes and tested by HPLC, and calculated the reaction rate of decomposed ciprofloxacin which plotted versus excipients (Table 3), (Figure. 3).

Table 3. Reaction rate (K) of decomposed ciprofloxacin by sun light versus some pharmaceutical excipients

Excipients name	Concentration %	pH-value	Reaction rate (K)-min^{-1}
Methyl paraben	0.10%	(4.60)	0.3139
Propyl paraben	0.10%	(5.28)	0.4276
Sodium benzoate	0.05%	(7.17)	0.6246
Magnesium stearate	0.10%	(7.44)	0.6295
Control (without excipients)	-	(7.14)	0.6225

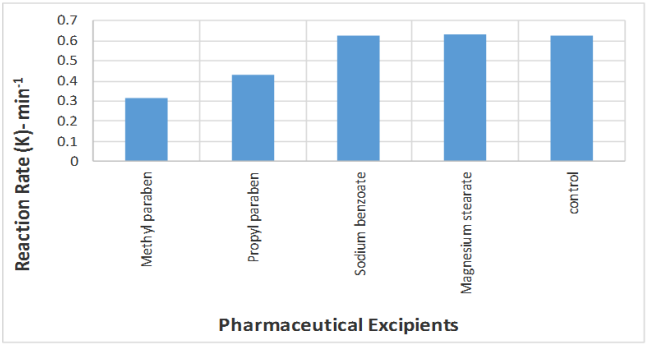

Figure 3. Effect of pharmaceutical Excipients on the reaction rate (k) of decomposed ciprofloxacin by sun light

RESULTS AND DISCUSSION

The companies that manufacture pharmaceutical products known to ensure that these products are suitable for their intended use and that does not put patients at risk due to inadequate safety و quality and/or efficiency of the product. Under the experimental degradation conditions, it is expected that sunlight effect contribute significantly to decomposition of ciprofloxacin.

Effect of time on the reaction kinetics of ciprofloxacin solid under sun-light

Figure 1 shows the reaction kinetic evaluation of ciprofloxacin solid under simulated sun light, were observed significant changes on the timescale of experiment. Table 1 combine the reaction kinetic rate calculated from the photo degradation of ciprofloxacin solid under sunlight. The experimental results reveals to first – order kinetics(Amin MI and Bryan JT, 1973). Ciprofloxacin was readily degraded by sunlight dependent on the time exposure to sunlight.

Effect of concentration on the reaction kinetic of ciprofloxacin solid under sun-light

Figure 2 illustrate the reaction rate assessment of ciprofloxacin under sunlight in water with different concentrations. The reaction rate decreased with increase concentration of ciprofloxacin. Table 2 compiles the reaction rate from the phot- degradation of ciprofloxacin with different concentration under sun-light. The experimental data fitted to first – order kinetics. The degradation decreased by increase concentration of ciprofloxacin. With higher concentration of the investigated compounds, the outermost molecules absorb the energy, and hence protect the inner molecules from the absorption of sun-light and therefore from degradation. Moreover, it is clear visible that from data obtained ciprofloxacin in solvent was photo-degraded at a faster rate in purified water compared to their degraded in solid forms.

Effect of Some pharmaceutical excipients on the reaction rate of ciprofloxacin liquid under sun-light

Figure 3 shows the reaction rate results obtained due to the influence of some pharmaceutical excipients on the reaction kinetics rate of ciprofloxacin under effect of sunlight, were note there is a disparate impact of each excipient. Table 3 illustrates reaction kinetics of decomposed ciprofloxacin with excipients under sunlight. Some pharmaceutical compounds used in this work reduces the rate of decomposition kinetics of ciprofloxacin by sun-light as methyl paraben and propyl paraben respectively and other were found to increase the reaction rate such as sodium benzoate and magnesium stearate compared to the control. Without the presence of pharmaceutical excipients, the reaction rate of ciprofloxacin increased.

Conclusion

In this article research we focus to determine which factor affected to stability of ciprofloxacin, we can conclude from the present study we found that ciprofloxacin unstable under sunlight in the solid and liquid state. The reaction kinetic of photo- decomposition of ciprofloxacin reveal first order reaction. Some pharmaceutical additives used in this research increases the stability property and therefore we recommend that additives to be use in the formulation of this product.

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