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Photo-degradation of Carbamazepine and Ciprofloxacin Hydrochloride in Water by Sunlight

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Abstract
Photo-degradation of two drugs, Carbamazepine and Ciprofloxacin Hydrochloride was investigated in dark and sunlight. Following the degradation of Carbamazepine spectrophotometrically in sunlight, shows a regular decrease with time. The two peaks appeared in its HPLC chromatograms were identified by GC-MS to give compounds of molecular weights 196 and 256 respectively, having a half-life 693 h., while in the dark, there is an up and down decrease in absorbance, indicating a rapid cleavage of the compound. Ciprofloxacin hydrochloride in sunlight shows a sharp decrease in absorbance but the degraded compound shown in its HPLC chromatogram was not identified, and the degraded compound has a half-life of 31.5 h. For ciprofloxacin hydrochloride, no degradation was noticed in the dark. This proves that carbamazepine is more stable than ciprofloxacin hydrochloride.

Keywords: Photo-chemical, photo-transformation, hydrolysis, photo-stability

1. Introduction

Since years, it is known that pharmaceuticals and their active metabolites occur in the environment. Pharmaceuticals occur in rivers, coastal waters, and sewage, not only from human and animal excretion but also through discarding of unused drugs and the release from production sites. They end up in surface water mainly through discharge of sewage treatment plant (STP) Effluent. Furthermore, there is great concern about the transformation and degradation by light (photo-degradation) and microorganisms (biodegradation) of these pharmaceuticals in the environment. Since bio-degradation and photo-degradation are the main removal pathways of pharmaceuticals in the natural aquatic environment, and their degradation pathways are essential for predicting the fate and the environmental impacts of these contaminants in natural waters.

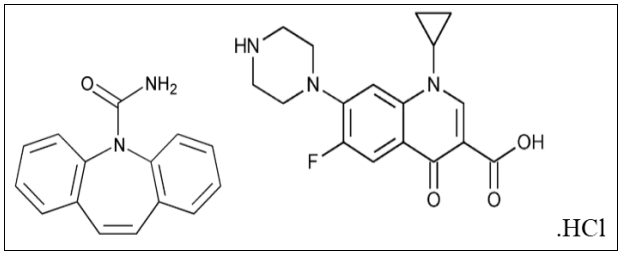


Fig 1: Chemical structure of Carbamazepine and Ciprofloxacin hydrochloride.

Carbamazepine is a first generation anticonvulsant used in the treatment of epilepsy and trigeminal neuralgia. [1] Ciprofloxacinis an antibiotic that can treat a number of bacterial infections. It is a second-generation fluoroquinolones [2]. Photo-degradation study of Carbamazepine and ciprofloxacin hydrochloridein aqueous mediumcan be followed by two different mechanisms, direct and indirect photolysis. In direct photolysis, the pharmaceutical molecules absorb solar radiation, which leads to a break-up of the molecules, while indirect photolysis involves naturally occurring molecules (photosensitizers) [3]. Photo-catalytic experiments on the pharmaceutical carbamazepine were conducted using sol-gel nitrogen-doped TiO_2-coated glass slides under a solar simulator. Carbamazepine was stable to photo-degradation under direct solar radiation [4]. Photo-degradation of four pharmaceuticals (i.e. carbamazepine, ibuprofen, ketoprofen and 17α-ethinylestradiol) in aqueousmedia was studied using a solar light simulator (Xe lamp irradiation) and sunlight experiments. These experiments were carried out in river and seawater and compared to distilled water; the latter was used to evaluate the direct photo-degradation pathways. Irradiation time was up to 400 min and 24 days for the solar light simulator and sunlight assays, respectively. Pharmaceutical photo-degradation followed first-order kinetics, and their half-lives calculated in every aqueous matrix. Carbamazepine had the lowest photo-degradation rate ($t_{½}$ =8–39 h) attributable to indirect photo-degradation. Indeed, its elimination was strongly dependent on the dissolved organic carbon (DOC) concentration present in solution [5]. To compare its attenuation efficiency, ciprofloxacin solutions were mixed with TiO_2 nanoparticles irradiated with two different light sources, a UV lamp and ordinary electric bulb. Insignificant degradation was witnessed when irradiations were made in absence of TiO_2. In contrast, prominent ciprofloxacin degradation was detected in the presence of 0.01mg/cm^3 of TiO_2. Close to 90 and 70 % of its original concentration was eliminated in 120 mints when the irradiation basis used, was a UV lamp and Ordinary electric bulb respectively. Without the use of TiO_2 nanoparticles, irradiation by UV lamp sources was also significant. The anti-bactacterial activity of chosen microorganisms was radically

inhibited when exposed to ciprofloxacin solution treated with photo-catalyst for short period of irradiation [6]. The concentrations ranging from 50-500 ppm of the ciprofloxacin was exposed to the sunlight and UV radiation. The duration of the exposure for the degradation, was 1 to 7 h. The UV rays, (15W and 30W) lamps were used for the study. The degradation was determined by the by zone of inhibition. The maximum degradation was demonstrated by the exposure of UV after 6 h duration. The photo-degradation was also at its maximum after 6 h of exposure. The UV and the photo-degradation proved to be the significant mode to control the pollution in the environment caused by ciprofloxacin residue [7]. Also the kineticstudyof the drugs is of a first order.

2. Materials and Methods

2.1 Materials

Chemicals & Apparatus

Carbamazepine (Assay 99.52%), Bajaj Healthcare Ltd, India. Ciprofloxacin hydrochloride (Assay 99.5 %), Aarti Drugs Limited, India, Phosphoric Acid, Daejung chemicals and Metals CO., LTD, Korea. Sodium Lauryl Sulfate, Wako Pure Chemical Industries, Korea. Methanol (HPLC) J.T.Baker, USA. Acetonitrile (HPLC), J.T. Baker, USA. Ethyl acetate, Oriental Chemical Industry, Korea. Tri-ethylamine, Daejung Chemical and Metal Co. Ltd, Korea. Distilled water, to pass analysis by USP.

Volumetric flasks (500, 1000 cm^3) Pyrexglass. Separation funnels Pyrex glass. Tubs glass, Membrane filter 45µm.

2.2 Instruments

Balance, Mettler A E 240, Switzerland UV-VIS. Spectrophotometer, S110.30-0103006P, Scino CO, Ltd, Korea. PH Meter 3510, 37560, Jenway, UK. Power sonic 405,100-220, Hwashin, Korea. HPLC, 05240, VARIAN, USA. GC-MS, QP2010 plus, Shimadzu.

2.3 Methods

Photo-degradation experiments

Carbamazepine

- Preparation of Calibration Curve:

For quantitative calculation of carbamazepine a standard calibration curve was prepared. The calibration curve was constructed read absorption by UV-VIS spectrophotometer in wavelength 285 nm of series dilutions (standard drug) of Carbamazepine 0.005, 0.010, 0.015, 0.020 and 0.025 mg/ cm^3 in sodium lauryl sulfate solution 1%.

- In sunlight:

A sample of carbamazepine 0.008g was dissolved in dm^3sodium lauryl sulfate solution 1% (con 0.008 mg/cm^3) exposed directly to sunlightin the period 26 May 2014 -22 September 2014 in Khartoum recorded absorption every six hours for period 312 hours.

- In Dark:

Another sample of carbamazepine 0.008g was dissolved in dm^3sodium lauryl sulfate solution 1% (con 0.008 mg/cm^3)and kept in dark condition in room temperature (NMT 30 ^{0}C) in the period 26 May 2014 -22 September 2014 in Khartoum recorded absorption every six hours for period 312 hours.

- HPLC method:

Mobile phase: water, methanol and acetonitrile (550:350:100) The flow rate of elution was 0.6 cm^3/ min. UV detector at 230 nm, column C18 (4.6mm-150 mm), inject 10µl.

Sample solution: filtered the sample in sunlight and sample in dark with 0.45 µm membranes and then injected in HPLC directly.

Standard solution: dissolve 0.008g of carbamazepine in dm^3sodium lauryl sulfate solution 1% (con 0.008 mg/cm^3)

- GC-MS Method:

Sample preparation:

50 cm^3 of sample in sunlight was prepared by liquid –liquid extraction after end in 20 cm^3 from ethyl acetate 5 cm^3 of the organic phase filtered with 0.45µm nylon membranes and read by GC-MS.

Working condition of GC- MS:

(i) GC-2010

- Column fused silica capillary column (30m X 0.25 mm i.d., 0.25µm.
- Liquid phase: methyl silicone or 5%phenlmethyl silicone.
- Column oven temperature:80.0˚C
- Injection temperature:280.00˚C
- Injection mode: split
- flow control mode:Pressure
- Pressure:90.0 kpa
- total flow: 70.3 cm^3/min
- column flow:1.32cm^3/min
- linear velocity: 42.3cm/sec
- purge flow: 3.0 cm^3/min
- spit ration: 50.0
- high pressure injection:0ff
- carrier gas saver: off
- splitter hold: off
- Oven temp. program

Rate	Temperature (˚C)	Hold time (min)
-	80.0˚C	1.00
25.00	225.0˚C	1.00
1.00	231.0˚C	0.00
10.00	280.0	5.00
45.00	320.0	3.00

(ii) GCMS-QP 2010 plus

- ion source temp:200.00˚C
- Interface temp:230.00 ˚C
- solvent cut time: 3.00min
- detector gain mode: relative
- detector gain:0.00kv
- Threshold:1000

(iii) MS:

- Start time:3.50 min
- End time:27.50 min
- ACQ mode: scan
- Event time: 0.50sec
- Scan speed:1666
- Start m/z:40.00
- End m/z:800.0

3. Ciprofloxacin Hydrochloride

- Preparation of Calibration Curve:

For quantitative Calculation of ciprofloxacin hydrochloride a standard calibration curve was prepared. The calibration curve was constructed to read absorption by UV-VIS spectrophotometer in wavelength 276 nm of series dilutions (standard drug) of ciprofloxacin hydrochloride 0.001, 0.003, 0.005, 0.007and 0.009 mg/cm^3 in distilled water.

- In sunlight:

A sample of ciprofloxacin hydrochloride 0.0029g equal (0.0025g ciprofloxacin) was dissolved in 500cm^3 distilled water (con 0.005mg/cm^3) exposed directly to sunlight in the period 17 June 2014 -29 June 2014 in Khartoum recorded absorption every six hours for period 54 hours.

- In Dark:

Another sample of ciprofloxacin hydrochloride 0.0029g equal (0.0025g ciprofloxacin) was dissolved in 500 cm^3 distilled water (con 0.005 mg/cm^3) and kept in dark condition in room temperature (NMT 30^{0}C) in the period 17 June 2014 -29 June 2014 recorded absorption every six hours for period 54 hours.

- HPLC method:

Mobile phase: 0.025M phosphoric acid adjusted with tri-ethylamine pH 3.0±0.1 and acetonitrile (87:13)

The flow rate of elution was 1.0 cm^3/min UV detector at 278 nm column C18 (4.6-250mm) inject 10µl.

Sample solution: filtered the sample in sunlight and sample in dark with 0.45 µm membranes and then injected in HPLC directly.

Standard solution: dissolve 0.0029g of ciprofloxacin hydrochloride in 500cm^3 distilled water (con 0.005 mg/cm^3).

4. Results and Discussion

Results

- For the calibration curve of Carbamazepine the linear R^2 = 0.999.

- For the calibration curve of Ciprofloxacin the linear R^2= 0.999.

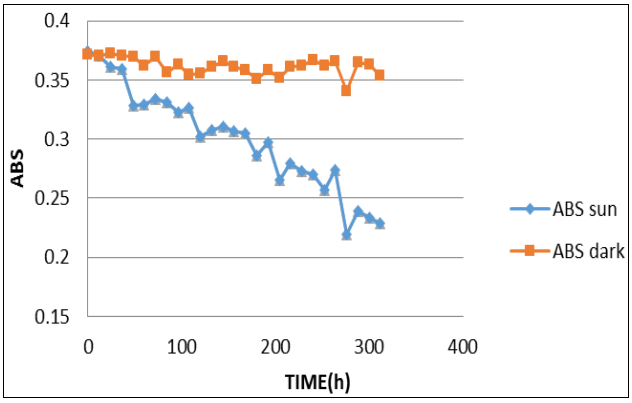


Fig 2: The Curve of absorption of carbamazepine in sunlight and dark.

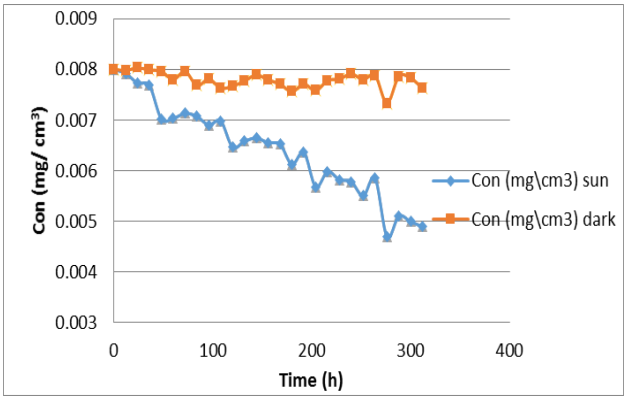


Fig 3: The Curve of concentration of carbamazepine in sunlight and dark.

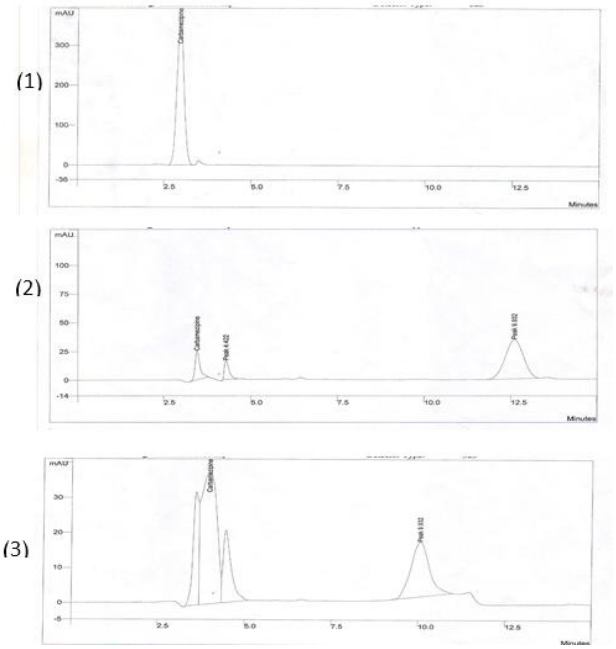
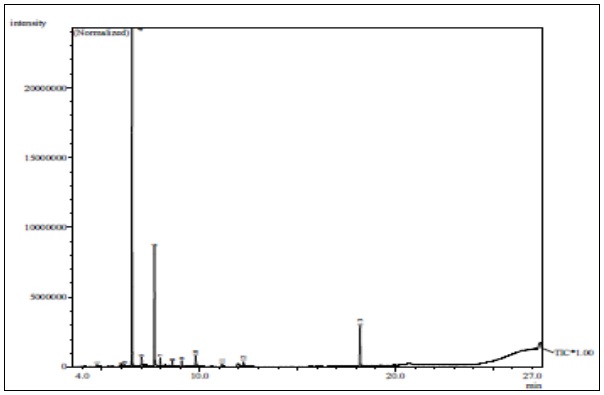


Fig 4: HPLC chromatograms of carbamazepine standard (1) and sample in sunlight (2) and sample in dark (3)



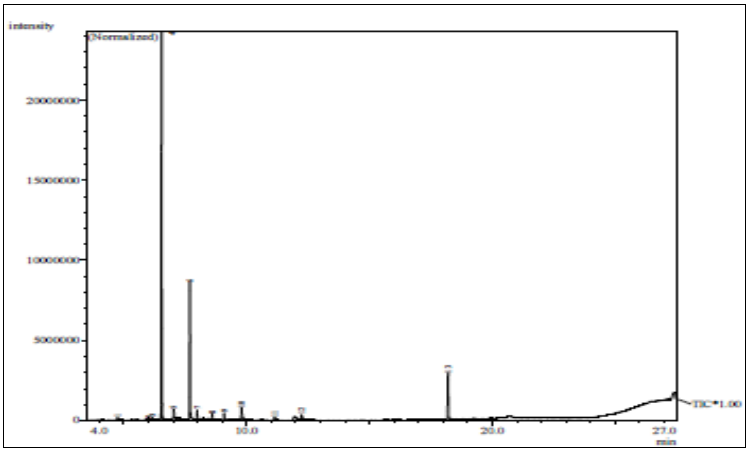


Fig 5: GC-MS Chromatograms of carbamazepine sample in sunlight.

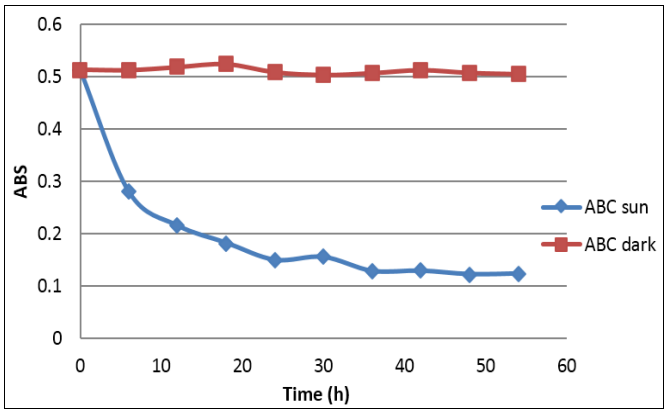


Fig 6: Curve of absorption of ciprofloxacin hydrochloride in sunlight and dark.

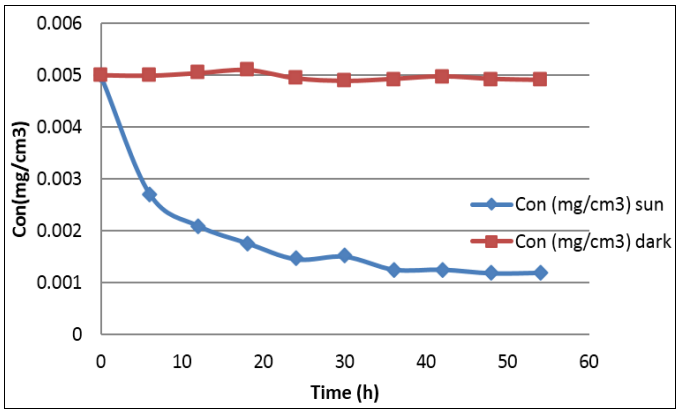


Fig 7: Curve of concentration of ciprofloxacin hydrochloride in sunlight and dark.

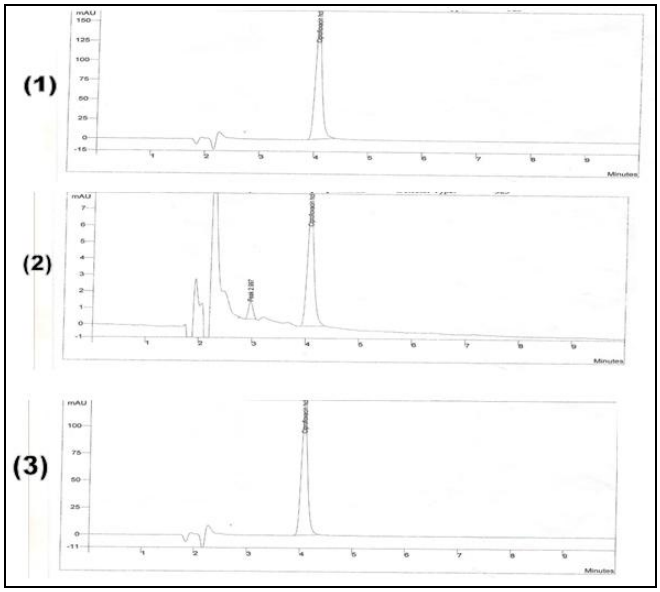


Fig 8: HPLC chromatograms of ciprofloxacin hydrochloride standard (1), sample in sunlight (2) and sample in dark (3).

-Kinetics:
*Half-life of Carbamazepine
Rate constant (K) = 0.001
$t_{½}$ = In2/K = 0.693/K = 693 h
*Half-life of Ciprofloxacin hydrochloride
Rate constant (K) = 0.022
$t_{½}$ = In2/K = 0.693/K = 31.5 h

5. Discussion

After exposing the two drug samples to the experimental conditions mentioned above, the flowing findings were noted.
The carbamazepine by UV-VIS. spectrophotometer, exposing the sample to sunlight, the absorbance of the sample decreased with time from 0 to 252 h and increased at 264 h, then followed by decrease until 276 h. We conclude that

concentration of carbamazepine sample in sunlight decreased with time. On comparing the chromatograms the standard of carbamazepine with the sample by HPLC two peaks appeared at retention time 4.289 min. and 12.606 min. The photoproducts wear identified by GC-MS to find the firstone, at 7.983 min of molecular weight 196, due to direct photo-degradation and hydrolysis of the original compound (I). The second peak appeared at 9.083 min, and its molecular weight 256 due to successive cleavages of the original compound ending with a compound of the structure (II) [8]. According to the first order equation, the half -life of carbamazepine was found to be 693 h. when flowing carbamazepine in dark by UV-VIS spectrophotometer, a noticeable up and down pattern of decrease and increase, indicating a rapid cleavage of the compound.HPLC run of the separated compound showed one peak of a retention time 10.057 min.

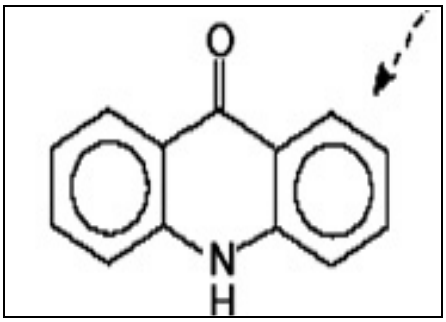


Fig 9

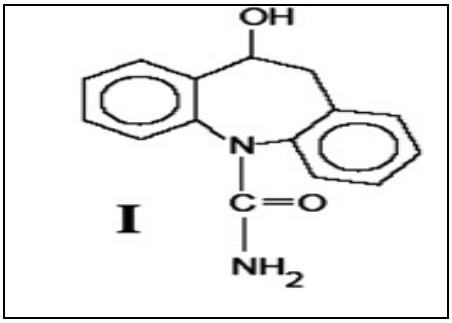


Fig 10

For the ciprofloxacin hydrochloride exposing the sample to sunlight and followed by UV-VIS. Spectrophotometer a sharp decrease in the absorbance was noticed, followed by a regular decrease. This was farther confirmed by HPLC, but the degraded compound was not detectable. According to the first order equation the half-life of ciprofloxacin hydrochloride was found to be 31.5 h. On testing the sample of ciprofloxacin hydrochloride in dark, no apparent change in concentration was noticed. Comparing the standard of ciprofloxacin hydrochloride with sample, by HPLC, identical chromatograms of the standard appeared, indicating reasonable stability.

6. Conclusion

The experimental results for carbamazepine and ciprofloxacin hydrochloride, in both sunlight and dark conditions, indicate the carbamazepine is more stable than ciprofloxacin hydrochloride.

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