International Journal of Pharmaceutics, 52 (1989) 179–181
Elsevier

IJP 01761

Decomposition profile of ultraviolet-irradiated chloroquine

J. Ayoola Owoyale *

Department of Chemistry, Usmanu Danfodio University, Sokoto (Nigeria)

(Received 7 November 1988)
(Accepted 21 November 1988)

Key words: Chloroquine; Decomposition; Ultraviolet; Irradiation

Owoyale and Elmarakby (1982) reported that when chloroquine phosphate in phosphate buffer solution at pH 7.4 and 8 was irradiated with an ultraviolet (UV) lamp (254 nm) for 8 h, there was no destruction of the characteristic peaks at 254, 328 and 342 nm. However, they found that there was a gradual shift to longer wavelengths of the 254 nm peak and a new peak appeared at 272 nm at pH 8 which could not be explained. In order to explain this new peak, it was decided to further irradiate chloroquine phosphate buffer at pH 8 to monitor the fate of the 254 nm peak and the new 272 nm peak. This paper reports the findings and their implications.

Chloroquine diphosphate was obtained from the Pharmaceutical and Quality Control Unit of the Ahmadu Bello University, Zaria, Nigeria. Camag UV lamp type 2900 (Ger No. 850459) with fixed wavelengths of 254 nm and 366 nm was used for irradiating the sample solutions. The UV spectra were run on a Pye Unicam SP-8200 UV/VIS spectrophotometer. Thin-layer chromatography (TLC) was performed on Camlab pre-coated plastic sheets Polygram SIL.G/UV254. The chromatograms were developed in strong ammonia–methanol (1 : 20 v/v) and were examined under UV lamp (254 nm and 366 nm).

Initially, chloroquine phosphate solution (1 mg/ml) was added to 0.1 M phosphate buffer solution (pH 8) to a dilution of 10 μg/ml and irradiated for up to 90 h. The UV spectra of the irradiated samples were run at various time intervals.

The UV spectra at 20, 30, 40 and 90 h and of the non-irradiated cloroquine phosphate (control) are shown in Fig. 1. The peak at 272 nm had been reported to have started forming by 1 h up to 8 h and fluorescence was observed (Owoyale and Elmarakby, 1982). The 254 nm peak had shifted to 260 nm at 20 h. At 30 h there was reduction in absorbance of the 254 nm peak and was of equivalent height with the 272 nm peak (almost forming a plateau). The absorbance of the 328 nm and 342 nm peaks continued to decrease through the 30 h of irradiation and the fluorescence persisted. However, at 40 h these two peaks (328 nm and 342 nm) had flattened out and the 254 nm peak has disappeared giving way to an ill-defined peak at 272 nm. This situation remained virtually so up to 90 h. In addition, fluorescence which was observed up to 30 h had almost disappeared at 40 h.

The above findings show that ultraviolet irradiation of chloroquine phosphate at pH 8 using a 254 nm lamp could also cause the "spectral shift" phenomenon but at a slower rate than with the

* On sabbatical leave from: Department of Chemistry, University of Ilorin, Ilorin, Nigeria.
Correspondence: J.A. Owoyale, Department of Chemistry, University of Ilorin, Ilorin, Nigeria.

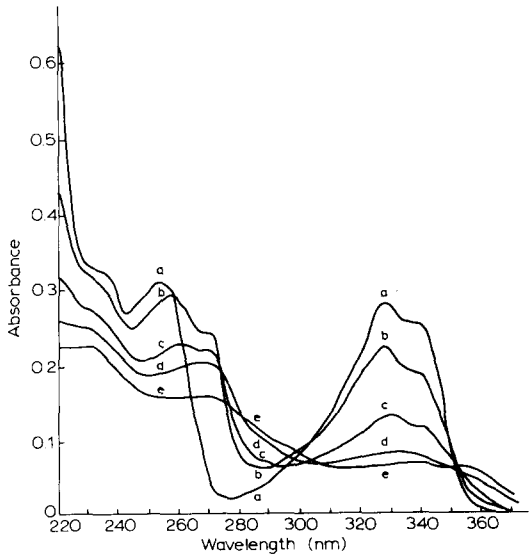

Fig. 1. UV spectra of irradiated chloroquine with a 254 nm UV lamp. Key: a = control (0 h); b = 20 h; c = 30 h; d = 40 h; e = 90 h.

366 nm lamp. Also the quenching of fluorescence followed the destruction of the characteristic peaks of chloroquine at 254, 328 and 342 nm.

As a result of the above observation, it was decided to find out whether a 272 nm peak also appeared when chloroquine phosphate in phosphate buffer solution (pH 8) was irradiated with a 366 nm UV lamp since Owoyale and Elmarakby (1982) had reported the appearance of fluorescence before the destruction of the characteristic peaks of chloroquine under these conditions.

Accordingly a 10 μg/ml chloroquine phosphate buffer solution (pH 8) was irradiated (366 nm lamp) for 3 h and a UV spectrum of the irradiated solution was run at half-hourly intervals.

The result of this irradiation is shown in Fig. 2. There was a drift of the 254 nm peak to higher wavelength accompanied by the appearance of the 272 nm peak already at 0.5 h of irradiation. The absorbance at 328 nm and 342 nm continued to decrease. At 2.5 h, the 254 nm and the new 272 nm peaks had formed a plateau. From 3 h, the 254 nm peak had disappeared and the 328 nm and 342 nm peaks had been destroyed (similar to Fig. 1e). These results are consistent with those obtained earlier using a 254 nm UV lamp. It was also noticed that a pink colouration developed in the irradiated solution of chloroquine phosphate.

It therefore appeared that upon irradiation with UV light, chloroquine phosphate in phosphate buffer solution is excited to form a fluorescent compound which is then broken down. To investigate this, chloroquine phosphate in phosphate buffer solution (pH 8) was irradiated at 366 nm over a period of 8 h. At various time intervals 8 ml of the irradiated solution was withdrawn, basified with ammonia and extracted into chloroform and the TLC of the extract was run.

As early as 0.5 h, a bluish white fluorescent compound at R_f 0.31 (UV = 366 nm) had appeared in addition to the unchanged chloroquine at R_f 0.54 (UV = 254 nm). By 1.5 h a pink fluorescent compound at R_f 0.40 (UV = 366 nm) and another compound at the origin (visible) had appeared. A fifth compound could be seen at 3 h at R_f 0.22 (pink fluorescence, UV = 366 nm). Altogether at least 4 decomposition products of chloroquine could be detected. By 6 h, the chloroquine and the first fluorescent compound (R_f 0.31) had disappeared. Findings in this laboratory and those of Sams and Carroll (1966) showed that this "spectral shift" phenomenon occurred too

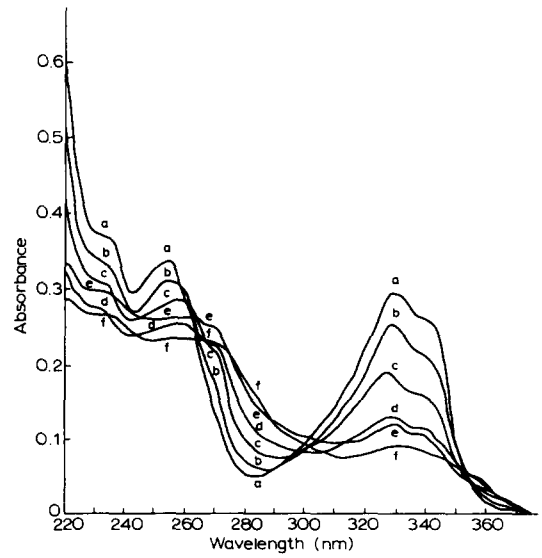

Fig. 2. UV spectra of irradiated chloroquine with a 366 nm UV lamp. Key: a = control (0 h); b = 0.5 h; c = 1 h; d = 1.5 h; e = 2 h; f = 2.5 h.

slowly at concentrations above 50 μg/ml. Therefore the isolation and characterization of the decomposition products could not be performed under the local prevailing working conditions.

On the basis of the present study, it would appear that the decomposition profile of UV-irradiated chloroquine in phosphate buffer solution can be said to involve the excitation of chloroquine to form fluorescent compounds (leading to the "spectral shift" phenomenon) which are further decomposed with resultant development of pink colouration and quenching of fluorescence. This compares well with the fluorescence, "spectral shift" phenomenon and colouration exhibited by a number of photoalleagic and/or photosensitive drugs when irradiated with a UV lamp, e.g. some sulphonamides (blue), chlorpromazine (yellow-brownish red), promazine (yellowish-brown) and promethazine (violet-red) (Storck, 1965). Also, the decomposition of chloroquine in phosphate buffer is faster when irradiated with a 366 nm UV lamp (2.5 h, Fig. 2) than with a 254 nm UV lamp (40 h, Fig. 1).

References

Owoyale, J.A. and Elmarakby, Z., On the ultraviolet 'spectral shift' phenomenon of chloroquine. *Int. J. Pharm.*, 12 (1982) 265–269.

Sams, W.M. and Carroll, N.V. The 'spectral shift' phenomenon of chloroquine. *Arch. Dermatol.*, 93 (1966) 123–128.

Storck, H., Photoallergy and photosensitivity. *Arch. Dermatol.*, 91 (1965) 469–482.