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**Short Communications**

# On the ultraviolet 'spectral shift' phenomenon of chloroquine

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Sams and Carroll (1966) described the effect of sunlight and ultraviolet (UV) irradiation of chloroquine diphosphate in phosphate buffer. They noted that at pH 7.4 there was a marked depression in the absorption peaks of chloroquine (328 and 342 nm) and an increase in the 267–300 nm region. This phenomenon, they suggested, was due to radiation between 290 and 310 nm. A number of other drugs are also known to enter into photochemical reactions when irradiated with UV light. Some of these include quinacrine, hydroxychloroquine and riboflavin (Sams and Carroll, 1966) and sulfonamides, phenothiazines and tetracyclines (Storck, 1965). In studying the stability of antimalarials, we decided to investigate, among other factors, the effect of sunlight and UV irradiation on buffered solutions of various antimalarials. Accordingly it was decided to re-examine the effect of sunlight and UV irradiation on chloroquine. However, in the present study two fixed wavelengths were used for irradiation, both wavelengths falling outside the 290–310 nm range suggested by Sams and Carroll (1966). In addition a study was carried out on the effect of sunlight on chloroquine diphosphate in different pHs and not only at pH 7.4 as Sams and Carroll (1966) did. The additional information thus obtained is reported in this paper.

Chloroquine diphosphate was obtained from the Pharmaceutical and Quality Control Unit of the Ahmadu Bello University, Zaria, Nigeria. The source of UV light was a Camag UV lamp Type 2900 (Ger No. 850459) with fixed wavelengths of 254 and 366 nm. The UV spectra were run on a Pye Unicam SP8-100 spectrophotometer in the range 360–220 nm.

Sams and Carroll (1966) showed that there was no 'spectral shift' when chloroquine diphosphate was heated in phosphate buffer at pH 7.4 even at 52°C. In addition they showed that when chloroquine diphosphate in the phosphate buffer was exposed to sunlight through window glass (which absorbs radiation below 320 nm) the 'spectral shift' phenomenon was almost completely blocked, whereas sunlight irradiation through Corning 0-54 filter (which absorbs radiation below 300 nm) only

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partially blocked this phenomenon. The above findings suggest that light and not heat is responsible for the 'spectral shift' phenomenon of chloroquine diphosphate in phosphate buffer. Accordingly all the solutions used as control in this study were kept at room temperature and not the temperatures recorded for the experimental samples (< 37°C).

Separate aqueous solutions of chloroquine diphosphate were each added to different 0.1 M phosphate buffer solutions (pH 5.8, 6.4, 7.4 and 8.0) to a final dilution of 10 μg/ml. Four ml of the resulting solutions was placed in quartz cells and irradiated with UV light at either 254 or 366 nm for 8 h. The UV spectra of chloroquine diphosphate in the different buffers irradiated with UV light at 254 and 366 nm and the corresponding non-irradiated samples (controls) were run at 1, 3 and 8 h. Another similar set of 4 ml samples of chloroquine diphosphate in the appropriate buffers as above was placed in quartz cells and was exposed to June sunlight in Samaru (approximately 32°C) for 8 h. The UV spectra of these samples in the different buffers at the end of 8 h and the corresponding controls were also run.

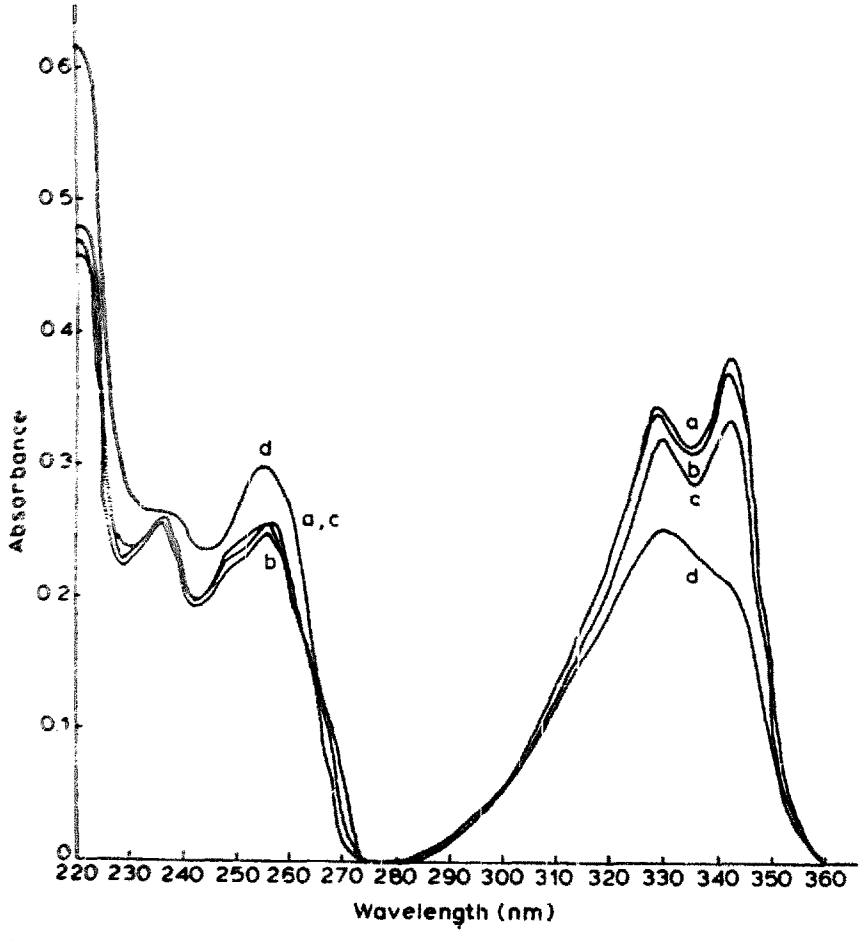


Fig. 1. Chloroquine diphosphate in buffer solutions (control). Key: (a)=pH 5.8; (b)=pH 6.4; (c)=pH 7.4; (d)=pH 8.0.

The UV spectra of the non-irradiated chloroquine diphosphate were similar at pH 5.8, 6.4 and 7.4 (Fig. 1) and accordingly the UV spectrum for pH 7.4 was chosen to represent the control in both the UV irradiation and sunlight experiments (Figs. 2 and 3). However, at pH 8, peaks at 328 and 324 nm were slightly flattened and depressed (Fig. 1). When irradiated with a 366 nm UV lamp, there was, during the first 3 h, a decrease in absorption in the range 310 nm to 350 nm. an increase in the range 260 nm to 310 nm and slight increases in the range 230–260 nm for all the solutions at pH 5.8, 6.4, 7.4 and 8.0. This pattern generally remained for 8 h with samples in the pH 5.8 and 6.4 buffers (Fig. 2). However, for pH 7.4 and 8.0, there was not only a sharp decrease in absorption in the ranges 310–350 nm and 230–260 nm at 8 h but also destruction of the peaks in these two regions (Fig. 2). In addition fluorescence was observed for the first two hours at pH 7.4 and 8 and the intensity of the fluorescence was determined on a Perkin-Elmer MPF-44A fluorescence spectrophotometer (approximately 2 times stronger for pH 8).

With irradiation using a 254 nm UV lamp, there was virtually no effect on chloroquine diphosphate at pH 5.8, 6.4 and 7.4. At pH 7.4 and 8.0, fluorescence was

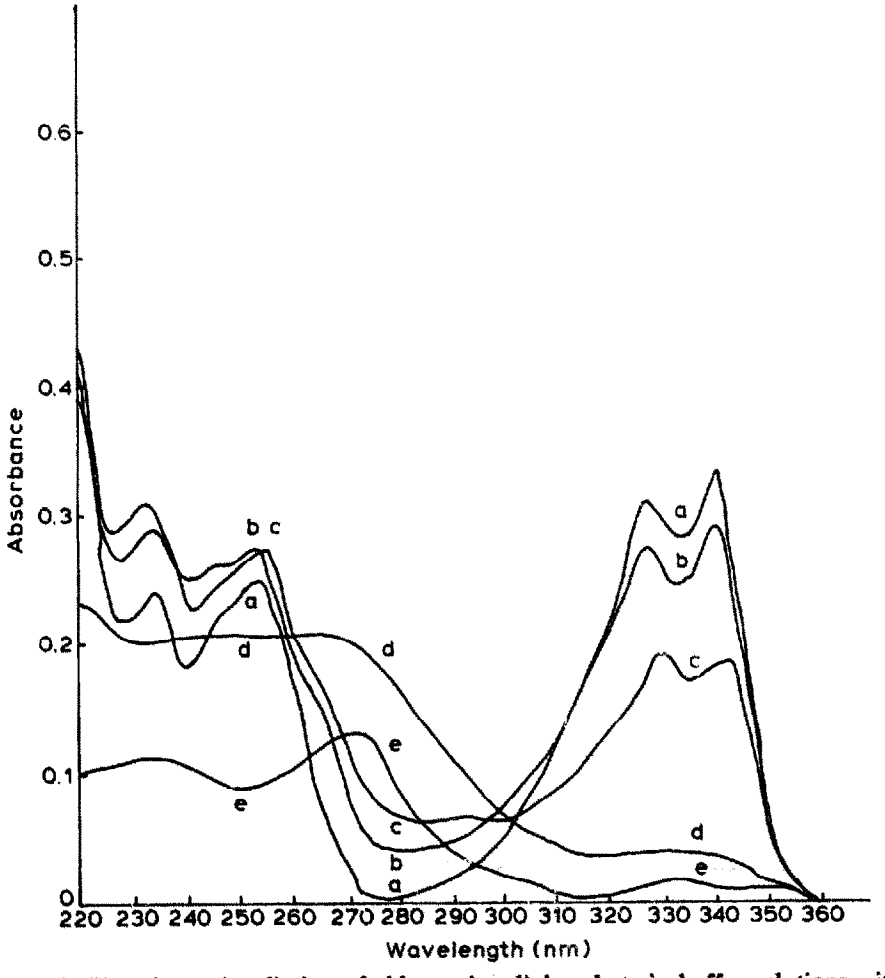


Fig. 2. Eight hours irradiation of chloroquine diphosphate in buffer solutions with a 366 nm UV lamp. Key: (a)= control (pH 7.4); (b)=pH 5.8; (c)=pH 6.4; (d)=pH 7.4; (e)=pH 8.0.

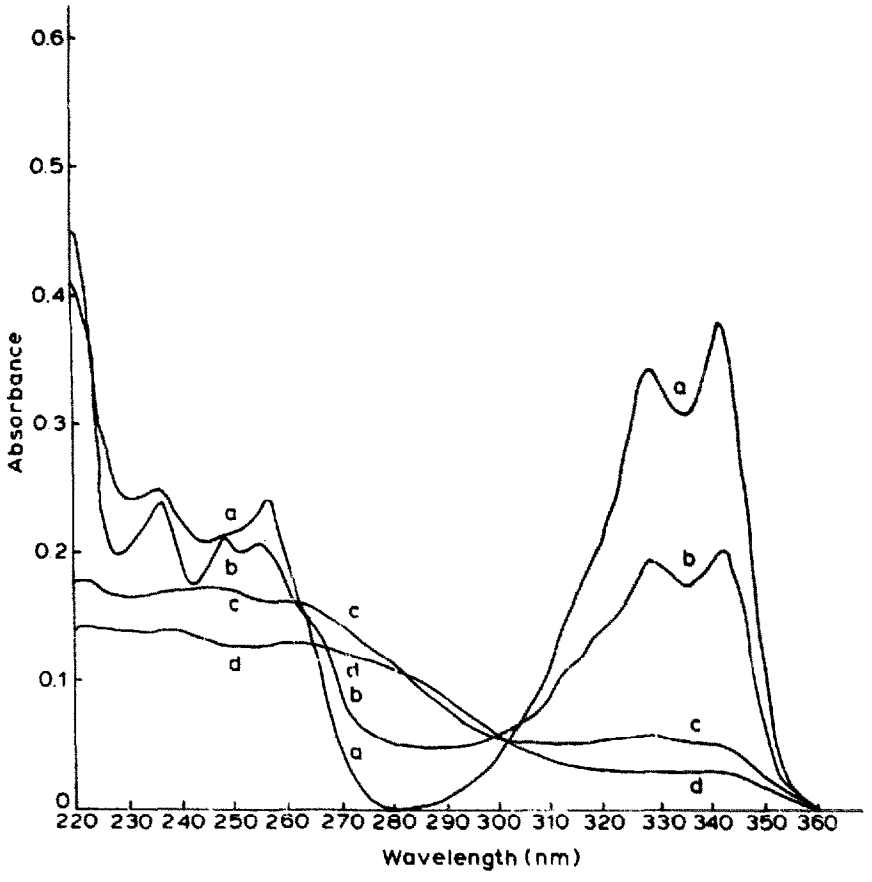


Fig. 3. Chloroquine diphosphate in buffer solutions exposed to sunlight for 8 h. Key: (a)=control (pH 7.4); (b)=pH 5.8; (c)=pH 6.4; (d)=pH 7.4.

also observed throughout the 8 h of the experiment, with fluorescence at pH 8 being approximately 1.5 times stronger. At pH 8, an inflection represented the usual peak at 342 nm and in addition there was a depression of the peaks in the 310–350 nm range and a gradual shift to longer wavelengths of the 254 nm peak with increasing time of radiation (Fig. 4). Also at pH 8 a new peak started to appear at 272 nm after 1 h and this peak increased progressively during the 8 h of the experiment (Fig. 4).

The effect of sunlight on the various chloroquine diphosphate-buffered solutions followed a similar pattern to that described under irradiation with the 366 nm UV lamp. The depression and flattening of peaks at 328 and 342 nm were already observed at 8 h at pH 6.4 with these being more marked at pH 7.4 (Fig. 3). The spectrum of chloroquine diphosphate at pH 8 (which was, however, exposed to September sunlight) was identical to that at pH 7.4 (Fig. 3).

The destruction of the characteristic peaks of chloroquine diphosphate at pH 7.4 and at higher pH when irradiated with a 366 nm UV lamp tends to suggest that radiation above 310 nm could also produce the 'spectral shift' phenomenon. Though there was no appreciable shift on irradiating chloroquine diphosphate with a 254 nm

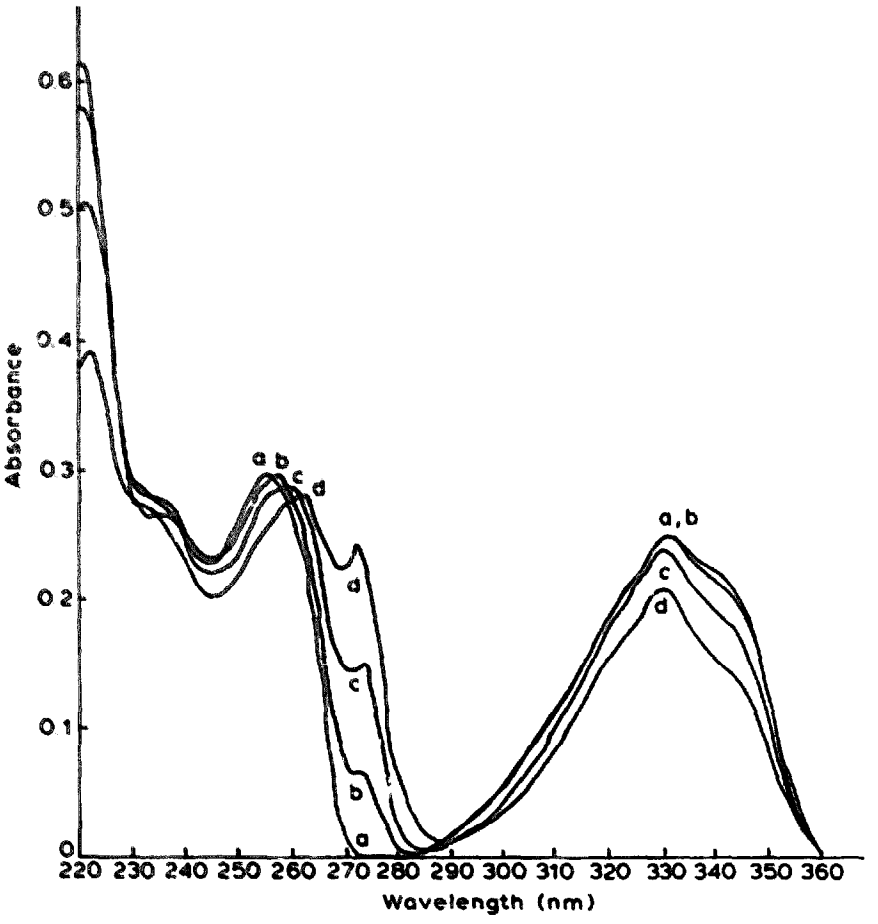


Fig. 4. Irradiation of chloroquine diphosphate in phosphate buffer (pH 8) with a 254 nm UV lamp. Key: (a) = control (pH 8); (b) = after 1 h; (c) = after 3 h; (d) = after 8 h.

UV lamp, it was interesting to note the appearance of a new peak at 272 nm at pH 8. It is not yet known what may be responsible for this.

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