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EFFECTS OF EXPOSURE OF CHLOROQUINE PICRATE TO THE SUN: A DIFFERENTIAL SCANNING CALORIMETRIC STUDY

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In a continuing study of the effect of exposure of chloroquine and its salt derivatives to the sun, the picrate was investigated. The picrate gives a sharp endothermic effect of melting at 209.2 °C, before it decomposes, to give an exothermic peak at 255.6 °C. The endothermic peak of melting at 209.2 °C was found suitable for the quantitative determination of chloroquine picrate in sun-exposed samples.

We earlier reported the effects of exposure of chloroquine phosphate to the sun, based on differential scanning calorimetry of the pure sample and the exposed samples [1]. In a continuing study of the sensitivity of chloroquine base and its derivatives to exposure to the sun, we now present findings on chloroquine picrate. The picrate crystallizes from an acetone-methanol mixture to give bright-yellow crystals melting at 206–207°.

The melting endotherm at 209.2° was used for quantitative determination of chloroquine picrate in samples exposed to the sun. The melting enthalpy $\Delta H = 75.83$ J/g determined for the pure sample was used as reference.

Experimental

Chloroquine picrate was prepared by reacting chloroquine phosphate with picric acid in aqueous solution. The resulting yellow precipitate was washed with water until free of picric acid, and then dried in an oven at 100° to remove traces of water. The absence of water and free picric acid was established by differential scanning calorimetry through the absence of the endothermic peaks accompanying

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volatilization of water at 100° and melting of picric acid at 142°. The melting point observed for the picrate (206–207°) was in agreement with the literature value [2].

The apparatus and method of investigation were the same as described previously for chloroquine phosphate [1]. The exposure was carried out on a 300 mg sample in a 5 ml beaker covered with cellophane film and exposed to the sun on a roof top. The exposure was made during the dry hot season in Sokoto, with an average daily temperature of 46°. In addition, separate portions (300 mg each) of chloroquine picrate were exposed to heat (100°) in an oven, and to UV light at 254 nm, in order to determine how the heat and UV components of sunlight affect the decomposition of chloroquine picrate.

Results and discussion

When freshly prepared and air-dried chloroquine picrate has a melting enthalpy of 75.83 J/g. The melting enthalpy increased to 81.98 J/g after the sample has been heated at 100° in the oven for 19 days. The decomposition of chloroquine picrate during exposure to the sun is shown in Table 1. For comparison, the decomposition of chloroquine phosphate during increasing exposure time is also shown (Table 2). As shown in Tables 3 and 4, chloroquine picrate is quite stable to heat, like the phosphate derivative. When kept in the oven at 100°, the picrate did not show any significant decomposition in 61 days. Accordingly, heat is not as significant a cause of decomposition as the UV component of sunlight. An analogous observation was made for chloroquine phosphate and sulphate [1, 3].

An observation which appears peculiar to chloroquine picrate (Table 3) is the initial steady increase in the enthalpy of melting during the first 19 days of exposure

Table 1 Differential scanning calorimetric data for chloroquine picrate exposed to sunlight

Exposure time days	Colour	Peak temperature, °C	ΔH, J/g
0	bright yellow	209.2	75.838
7	yellow	209.0	77.264
14	yellow	209.2	77.203
21	yellow	208.9	75.211
25	yellow	208.5	68.918
35	yellow	207.5	66.999
43	yellow	208.3	66.074
50	yellow	208.1	66.998
57	yellow	208.1	66.059
77	yellow	208.1	65.802

Table 2 Differential scanning calorimetric data for chloroquine phosphate exposed to sunlight

Exposure time, days	Colour	Peak temperature, °C	ΔH, J/g
0	white	196.5	60.103
3	cream	196.3	53.616
15	cream	195.0	40.780
23	pale yellow	194.4	41.651
30	pale yellow	193.4	40.315
37	pale yellow	193.8	36.387
52	pale yellow	193.1	35.866
59	pale yellow	193.0	35.498
73	pale yellow	191.2	33.155

Table 3 Differential scanning calorimetric data for chloroquine picrate exposed to heat at 100 °C

Exposure time, days	Colour	Peak temperature, °C	ΔH, J/g
0	bright yellow	209.2	75.838
7	bright yellow	209.3	66.567
14	yellow	209.3	80.220
19	yellow	209.2	81.981
39	yellow	208.1	79.419
47	yellow	208.7	69.378
51	yellow	209.2	70.824
61	yellow	208.1	68.897

Table 4 Differential scanning calorimetric data for chloroquine phosphate exposed to heat at 100 °C

Exposure time, days	Colour	Peak temperature, °C	ΔH, J/g
0	white	196.5	60.103
12	cream	196.4	53.050
19	pale yellow	196.4	51.909
26	pale yellow	196.5	49.639
39	pale yellow	196.8	55.863
56	pale yellow	195.6	48.685

to heat, followed by a decrease in ΔH. Apparently because of the large size of the picrate anion, freshly recrystallized chloroquine picrate is in a state of disorder. On heating in the oven, ordering may take place, leading to increased stability. Thus, the ordered crystalline sample would require a higher heat of melting. Unlike chloroquine phosphate and sulphate, chloroquine picrate shows an exothermic

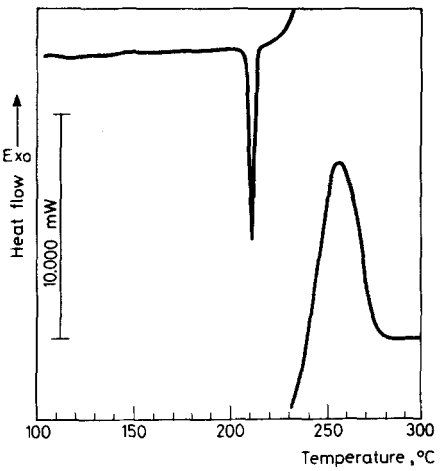

Fig. 1 Differential scanning calorimetric trace for freshly prepared chloroquine picrate

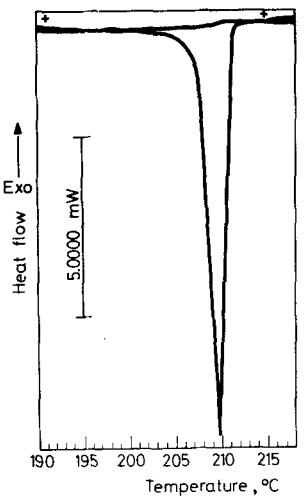

Fig. 2 Differential scanning calorimetric integration for endothermic peak of chloroquine picrate exposed to UV at 254 nm for 19 days

effect following the endothermic peak of melting (Fig. 1). This exothermic peak at 255.6° is accounted for by the intramolecular oxidation of the picrate, in which the nitro groups supply the required oxygen. This property makes organic compounds with a high proportion of nitro groups excellent explosives [4].

The exposure to UV light (λ = 254 nm) was more effective than heat and sun exposure. The endothermic peak increased with UV exposure for the first 19 days (ΔH = 78.32 J/g at 209.1°) before decreasing. The integrated peak is shown in Fig.

2; and is similar to the integrated endothermic peaks for sun and heat exposures. Integration of the endothermic peaks revealed maximum values for exposure to the sun after 7 days (ΔH = 77.26 J/g at 209.0 °C) and to heat after 19 days (ΔH = 81.98 J/g at 209.2°).

Apparently, UV light with a wavelength of 254 nm was energetically suitable for decoupling the bonding electrons in the C—N bonds of chloroquine picrate. While this UV component was available in the sun rays, the intensity was not as high. The decomposition of chloroquine picrate during exposure to UV radiation is shown in Table 5. For comparison, the decomposition of chloroquine phosphate with increasing exposure time is shown in Table 6.

Table 5 Differential scanning calorimetric data for chloroquine picrate exposed to UV at 254 nm

Exposure time, days	Colour	Peak temperature, °C	ΔH, J/g
0	bright yellow	209.2	75.838
7	bright yellow	209.0	75.789
14	bright yellow	209.0	76.279
19	yellow	209.1	78.322
39	yellow	207.5	66.835
47	yellow	208.1	69.408
54	yellow	208.1	68.339
61	yellow	207.8	64.857

Table 6 Differential scanning calorimetric data for chloroquine phosphate exposed to UV at 254 nm

Exposure time, days	Colour	Peak temperature, °C	ΔH, J/g
0	white	196.5	60.103
21	cream	196.1	52.089

As compared to the melting enthalpy of freshly prepared chloroquine picrate, the exposure of samples to sunlight for 77 days, to heat at 100° for 61 days, and to UV light at 254 nm for 61 days caused only 13%, 9% and 15% decomposition, respectively. Therefore, chloroquine picrate has a better stability than the phosphate and sulphate. However, the picrate may not be suitable for oral or parenteral administration, due to its possible hydrolysis into picric acid, which is very toxic [5].

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Zusammenfassung — In Fortführung einer Untersuchung über Veränderungen von Chloroquin und dessen Derivaten, wenn diese der Sonne ausgesetzt werden, wurden die Pikrate untersucht. Bei den Pikraten werden ein scharfer, dem Schmelzvorgang zuzuschreibender Effekt bei 209.2 °C und ein mit der Zersetzung einhergehender exothermer Peak bei 255.6 °C beobachtet. Der endotherme Peak bei 209.2 °C erwies sich als geeignet zur quantitativen Bestimmung von Chloroquinpikrat in der Sonne ausgesetzten Proben.

Резюме — В продолжении исследований влияния солнечного света на хлорокин и его соли, изучена его пикратная соль. Пикрат хлорокина показывает резкий эндотермический пик плавления при 209,2 °C с последующим экзотермическим пиком при 255,6 °C перед окончательным разложением. Установлено, что эндотермический пик плавления при 209,2 °C приемлем для количественного определения хлорокин пикрата в образцах, выдержанных на солнечном свету.