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Paraquat: Estimation of Mutagenic Potential in the Salmonella typhimurium Mutagenicity Assay.

by Diana Anderson

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SUMMARY

Paraquat was assayed in the *Salmonella typhimurium* mutagenicity plate incorporation assay and it was not mutagenic.

On many occassions the compound was ~~assayed~~ tested using TA 1535 and TA 1538 strains with and without the presence of rat liver postmitochondrial supernatant (PMS) and cofactor (S-9 mix) from rats administered phenobarbital. It was also tested using the TA 1535, TA 1538, TA 98 and TA 100 strains with S-9 mix made from rats administered Aroclor, with PMS but without cofactor and also without S-9 mix. A concentration range was used between 0.16 - 5000 µg of paraquat dichloride per plate to maximize the chance of producing an effect. In all cases, there was no biologically significant increases above solvent control levels.

The lack of effect was not due to the insensitivity of the system used, since a positive response was clearly demonstrated with the positive control compounds.

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MATERIALS AND METHODS

Test material: paraquat dichloride (99% pure)

Positive controls used:
1. N-2 acetylaminofluorine (AAF)
2. 2-Nitrofluorene (2NF)
3. 2(1-Chloro-2-isopropylaminoethyl)naphthalene (CPE)
4. Mecloretharnine (nitrogen mustard)

They were dissolved in dimethylsulfoxide (DMS).

Mutant strains:
TA 1535, TA 1538, TA 98 and TA 100 — all require histidine for growth.

Microsomal activation system:
9000 g supernatant (PMS or S-9) was prepared from livers of rats (Sprague-Dawley; 200 g) which received ip 500 mg of Aroclor (PCB mixture)/kg bw or received 0.1% Na-phenobarbital in their drinking H_2O for 5 days — 5 days before the rats were sacrificed. PMS + cofactors were mixed in the ratio of 1:3 (S-9 mix)

Agar plates (Top Agar & Petri plates)
Top agar (0.6% agar + 0.5% NaCl; 100 ml) was mixed with 10 ml of a solution which was 0.5 mM in L-histidine HCl and 0.5 mM in biotin. This mix (2 ml) + paraquat + mutagen was poured into 9 cm Petri plates containing 30 ml of solidified agar (1.5% Bacto-Difco agar) & 2% glucose. Incubation time: 48-72 hrs at 37°C. Conc. of paraquat dichloride/plate: 0.16, 0.8, 4, 20, 100, 500, 2500 & 5000 µg.

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RESULTS

(were also presented separately for each series)

3 series of experiments were carried out and the results were averaged. Mutagenicity was measured by an increase in the number of mutant colonies in relation ~~as~~ to controls. For example, 2-fold increases in colony counts above solvent control values were considered mutagenic (BN Ames, J McCann & E Yamasaki, Mutation Res. 31:347; 1975).

Paraquat was not mutagenic as measured by the Salmonella typhimurium plate incorporation assay. The 3 highest levels were generally toxic (few colonies or none were present).

NOEL: 100 µg paraquat dichloride/plate.

LEL: Not determined. (500 µg and higher levels/plate were toxic: few or ~~none~~ no mutant colonies were present).

Core - Minimum

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