

## INFLUENCE OF PENTACARINAT ON THE IN-VITRO ACTIVITY OF THE NEUTROPHIL NADPH-OXIDASE SYSTEM

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Pentacarinat is used for prophylaxis and treatment of *Pneumocystis carinii* pneumonitis (Hay 1988). At concentrations within the therapeutic range after parenteral administration of a standard dose (4mg salt/kg), pentacarinat decreases the ability of stimulated neutrophilic granulocytes (NGs) to reduce nitroblue tetrazolium (Arnott & Hay 1989a). The drug also induces a dose-dependent reduction in superoxide production by NGs (Arnott & Hay 1989b). Superoxide is produced in stimulated NGs from oxygen consumed during the respiratory burst; this is achieved through action of a membrane-associated system known as NADPH oxidase. NADPH oxidase was isolated by differential centrifugation from a homogenate of stimulated NGs (Markert et al 1984). Superoxide generated by the enzyme complex was assayed as superoxide-dismutase inhibitable cytochrome c reduction using NADPH as electron donor (Babior & Cohen 1981). Protein was assayed using the method described by Lowry et al (1951).

Table 1 Effect of Pentacarinat on activity of the NADPH dependent oxidase of stimulated NGs.

Drug ( $\mu\text{g mL}^{-1}$ )	NADPH dependent oxidase activity (nmol/min/mg protein)		P <sup>1</sup>
	Mean	SD	
0.3	21.00	2.20	NS
0.7	16.57	2.08	<0.001
1.1	12.60	1.61	<0.001
1.5	8.41	1.69	<0.001
Control	20.72	1.79	

<sup>1</sup>Probability calculated relative to control.

Pentacarinat induced a dose-dependent decrease in NADPH-oxidase activity; the greater the concentration of drug, the lower the activity of the oxidase (Table). An HPLC assay for Pentacarinat based on that of Lin et al (1986) revealed that the drug was associated with the isolated NADPH oxidase.

The results may explain the Pentacarinat-induced depression in candidacidal capacity of NGs (Arnott & Hay 1989a); the NADPH oxidase system is responsible for the respiratory burst of stimulated NGs.

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Arnott, M. A., Hay, J. 1989a J. Antimicrob. Chemo. 23: 557-564

Arnott, M. A., Hay, J. 1989b J. Antimicrob. Chemo. 24: 339-345

Babior, B.M., Cohen, H.J. 1981. In Leukocyte Function, (Cline M.J., Ed) Churchill Livingstone, New York.

Hay, J. 1988 Pharm. J. 241: 600-603

Lin, J M-H. et al 1986 J. Liq. Chromatogr. 9: 2035-2046

Lowry, O.H. et al 1951 J. Biol. Chem. 193: 265-275

Markert, M. et al 1984 Methods in Enzymology 105: 358-365