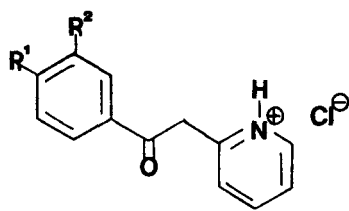


THE ACTIVITY OF 2-(2-PYRIDYL)ACETOPHENONES AGAINST
CANDIDA ALBICANS

B.Cox, R.D.Waigh, Department of Pharmacy, University of Manchester,
Manchester M13 9PL, UK.

The antibacterial activity of 2-(2-pyridyl)acetophenones has been known for thirty years (Beckett *et al* 1955). The activity may in some cases be linked to chelation of metal ions: electron withdrawing groups on the benzene ring favour the enol form (Branch 1956, 1957) which forms chelates with, for example, iron (II) and copper (II) ions. Electron donating substituents tend to favour the keto form, but this is not necessarily associated with lower antibacterial activity.

A series of derivatives (Fig.1) has now been examined for activity against the pseudomycelial form of *Candida albicans*, cultured in Eagles minimum essential medium supplemented with non-essential amino acids and 10% v/v foetal calf serum (Borgers *et al* 1979).



- a) $R^1 = R^2 = H$
- b) $R^1 = CH_3, R^2 = H$
- c) $R^1 = Cl, R^2 = H$
- d) $R^1 = CH_3O, R^2 = H$
- e) $R^1 = NO_2, R^2 = H$
- f) $R^1 = Br, R^2 = H$
- g) $R^1 = H, R^2 = CH_3$
- h) $R^1 = H, R^2 = Cl$
- i) $R^1 = H, R^2 = CH_3O$
- j) $R^1 = H, R^2 = NO_2$
- k) $R^1 = Cl, R^2 = Cl$

Fig. 1.

A plot of $\log_{10}(1/MIC)$ against Hammett's substituent constant σ shows a very reasonable correlation ($r=0.926$) (Fig.2), demonstrating that a trend in the structure-action relationship applies with the fungus which was not clear with the bacteria studied earlier. It is not yet certain, however, whether chelation of metal ions results in increased transport into the cell causing toxic effects, or whether the effect is to deny the cell the traces of heavy metals which it requires.

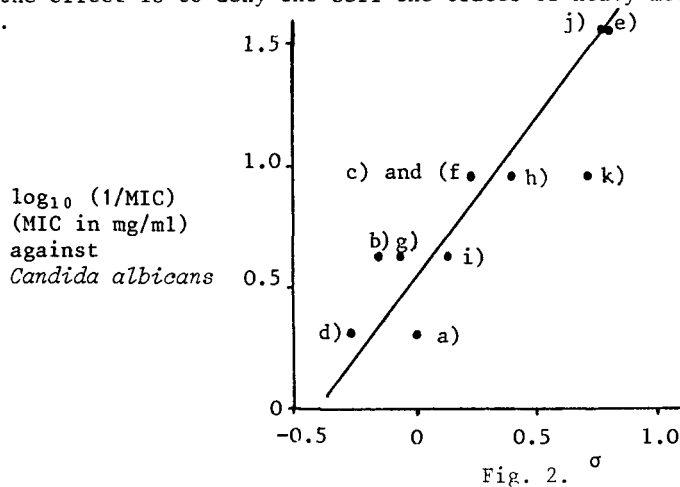


Fig. 2.

- Beckett, A.H. *et al* (1955) J. Pharm. Pharmacol. 7: 717-730
 Branch, R.F. (1956) Nature 177: 671-672
 Branch, R.F. (1957) Nature 179: 42-44
 Borgers, M. *et al* (1979) Postgrad. Med. J. 55: 687-691