

ANTIMICROBIAL ACTIVITY IN LOCAL ANAESTHETICS; A POSSIBLE SCREEN FOR TISSUE TOXICITY?

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Some local anaesthetics (LAs) possess antimicrobial properties (Schmidt & Rosenkranz 1970). In particular, tetracaine (amethocaine) has been shown to have an anti-bacterial action and to induce turbidity increases in non-growing bacterial cultures at concentrations that are used during the induction of local anaesthesia (Salt & Traynor 1979).

Tetracaine and procaine are chemically related in that both may be considered as esters derived from p.aminobenzoic acid and a β -hydroxy tertiary amine; the tetracaine having increased lipophilic character due to butyl chain substitution in the p.amino group. Dibucaine and lidocaine, however, are LA's of the amide type, the former being of relatively increased lipophilic nature.

The ability of these compounds to induce turbidity increases in non-growing bacterial cultures has been assessed and values for their minimum inhibitory concentrations (MIC) determined by both the tube dilution method and by the method of direct assessment of growth inhibition in shaken cultures described by (Salt & Wiseman 1970). The medium used throughout consisted of (g.l⁻¹): NH₄Cl, 3.0; MgCl₂.6H₂O, 0.2; Na₂SO₄, 0.2; KH₂PO₄, 9.25; K₂HPO₄, 5.57; casamino acids (vitamin free), 0.2; thiamine, 0.001; nicotinic acid, 0.001; trace elements solution (Cruickshank 1970), 5 ml.l⁻¹; final pH 6.5; supplemented, when growth was required, with glucose (to 3 g.l⁻¹). Conditions of cultivation, the harvesting and preparation of cell suspensions, and the method of measuring induced turbidity changes were as described previously (Salt & Traynor 1979).

Values obtained for MIC's against *E. coli* (NCTC 9001) were (tube dilution/direct assessment, mg.ml⁻¹): tetracaine 0.9/1.25; procaine 28/37.5; dibucaine 0.8/0.5; lidocaine 18/22.5. Of the four compounds used, only tetracaine (an ester) and dibucaine (an amide) induced marked increases in culture turbidity at normal in-use concentrations (0.5 - 1.5%). The general pattern of these changes was essentially as described previously (Salt & Traynor 1979). These two LA's also have the lowest MIC's and are generally considered to be relatively more effective (as local anaesthetics) than the other two compounds used.

Perhaps the most obvious example of this similarity between relative anti-bacterial activity and LA effectiveness is the significant difference between tetracaine and procaine, which are essentially the higher and lower members, respectively, of an approximately homologous series. A similar argument may be applied to dibucaine and lidocaine, the more lipophilic dibucaine showing marked anti-bacterial properties. It must however be emphasised that all four compounds are effective anaesthetics. Taking them as a single group it seems probable that the MIC's listed above give a more realistic indication of relative LA effectiveness than the induced turbidity changes, which may well be reflecting the potential tissue toxicity of the compounds concerned.

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