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News Item

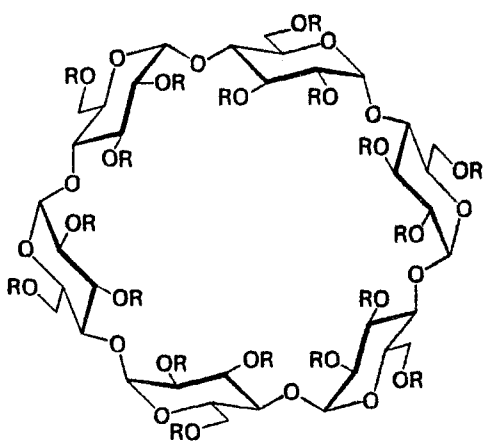
Unblocking the Ephedrine Detector

There is a major obstacle to developing a practical sensor for measuring the enantiomeric purity of drugs or their metabolites in physiological samples. Sodium, potassium and calcium ions, which are present in, for example, serum samples, swamp the sensor making it very difficult to detect a particular enantiomer of a drug at low concentration.

Dr David Parker's group at Durham University believe that they have found a way round the problem. They have taken the innovative step of basing their enantioselective sensor on a modified cyclodextrin. They say that their novel sensor can measure the concentration of the active (−)-isomer of ephedrine, the sympathomimetic decongestant and bronchodilator, down to a limit of $10^{-5.3}$ mol dm^{-3} in the presence of common serum ions (*J. Chem. Soc. Chem. Commun*, 1992, 153).

Parker says that his sensor succeeds where others have failed in that it works under conditions resembling those found in physiological samples. Work carried out during the 1970s and 1980s aimed to use chiral crown ethers as sensors. According to Parker these compounds are such strong ionophores that they were 'highly ineffective' at detecting arylammonium ions, such as ephedrinium, in the presence of metal ions.

The preparation of the cyclodextrin-based sensor was carried out by Parker's colleague Paul Bates using commercially available α-cyclodextrin (α-CD). He dioctylated α-CD at room temperature using bromooctane in the presence of NaOH, with dimethyl sulphoxide as solvent. Treatment at 60°C with NaH in



R = C_8H_{17}

peroctylated α-cyclodextrin

tetrahydrofuran then produced peroctylated α-CD. Ritu Kataky, who is sponsored by the SERC under its Molecular Sensors program, then incorporated this compound into the membrane of a potentiometric ion-selective electrode.

The researchers found that (+)-ephedrinium hydrochloride, (+)- and (−)-pseudoephedrine gave nernstian responses at 37°C. The results were affected very little by serum concentrations of Na^+, K^+, Ca^{2+} (150, 4.3 and 1.26 mmol dm^{-3}, respectively), which the authors added to simulate a clinical background of cations. By calibrating the electrode with solutions of predetermined enantiomeric purity Parker and his colleagues could then measure directly the enantiomeric purity of the fourth diastereoisomer, the biologically active (−)-ephedrinium salt. The modified cyclodextrin distinguishes between (−)-ephedrine and the other three diastereoisomers so it is possible selectively to discern varying amounts of this isomer. The electrode was found to be usable for at least three months.

Parker adds that, "Changing the size of the cyclodextrin's hydrophobic binding pocket allows us to detect dopamine down to 10^{-6} mol dm^{-3}". This limit is within the concentration range of the metabolite found in the cerebrospinal fluid of Parkinson's disease patients on L-dopa therapy. Parker emphasises that, "These results are preliminary and further work relies on securing funding".

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