DIFFERENTIAL PULSE POLAROGRAPHY (DPP) IN THE ASSESSMENT OF CLAY ADSORBENT - DRUG INTERACTIONS

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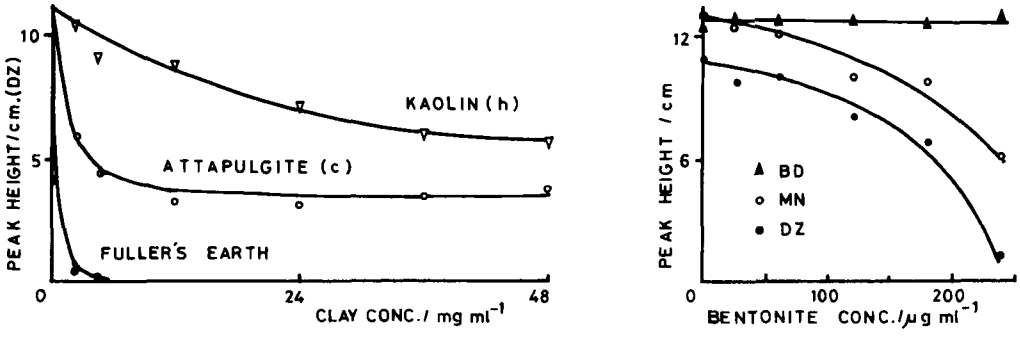
The presence of formulation excipients as well as the drug to be analysed in polarography can have varying and sometimes unpredictable effects on the assay results: Chatten et al (1977) found negligible effects for many tabletting excipients on the analysis of some progestogens but Lannigan (1984) reported calibration slope and reduction peak potential changes by some polyethylene glycols (PEG) in analyses of bendrofluazide (BD), diazepam (DZ), and hydrocortisone. To assist interference prediction and thus assay sample pretreatment in DPP we have examined the effect of five pharmaceutical clays on DPP analyses of DZ, BD, and metronidazole (MN), and assessed the effect of one, bentonite, on assays of a further nine electroreducible drugs.

The experiments were performed with a PAR 174A polarograph and a PAR 303 dropping mercury electrode (dme), and interference was assessed by mixing together appropriate volumes of a stock suspension of clay in supporting electrolyte and of drug in the same medium, shaking, and analysing without pretreatment after $\not<$ 30 minutes settling. Either drug or clay concentrations were varied but in the former experiments only one clay, bentonite, was studied. Drug concentrations of 30μg ml^{-1} or a range of 0-30μg ml^{-1}, and clay concentrations of 120μg ml^{-1} or a range of 0-48mg ml^{-1} were used as appropriate.

Analytical reduction peaks at -0.80, -0.15, and -1.82 V (vs. Ag/AgCl reference) for DZ, MN, and BD respectively showed no voltage shifts on clay addition in contrast with the 40-50 mV shifts for DZ and MN polarographed with PEG 4000. However peak heights for DZ and MN were reduced and sometimes eliminated (example below) by all clays whilst those for BD were influenced only by bentonite and Fuller's earth with all effects being clay concentration dependent.



Molecules adsorbed on the negatively charged bentonite surface would thus seem to be unavailable for reduction at the dme. Calibration graphs for analyses (n=5) could be drawn with altered characteristics for DZ and MN in the presence of bentonite, but the drug concentration range was not wide enough for this to be seen for BD. These data illustrate the indifference of the clays to the dme surface and lack of electrode process interference in contrast with PEG and PVP [Lannigan et al, (1981)] and it would appear that free electroactive drug concentrations could be determined by DPP without sample pretreatment in adsorption experiments or in pharmaceuticals containing such adsorbents or complexing agents which have no affinity for the dme surface.

Chatten, L.G. et al (1977) Analyst 102: 323-329.
Lannigan, N.A. (1984) Ph.D. Thesis, University of Strathclyde.
Lannigan, N.A. et al (1981) J. Pharm. Pharmac., Suppl. 33: 9P.