substitution. Such behaviour must be taken as a warning against the use of calculated partition coefficients in structure-activity studies.

REFERENCES

DRABER, W. (1973). Paper presented at First Internfitional Structure-Activity Conference, Prague, June 27–29.
LEO, A., HANSCH, C. & ELKINS, D. (1971). *Chem. Rev.*, **71**, 525–616.
SAHA, N. C, BHATTACHARJEE, A., BASAK, N. G. & LAHIRI, A. (1963). *J. Chem. Eng. Data*, **8**, 405–408.

Hydrophobic substituent constants from thin-layer chromatography on polyamide plates

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The use of reversed-phase chromatography for the determination of hydrophobic substituent constants is quicker and more convenient than is the determination of partition coefficients (Dearden & Tomlinson, 1972). However, difficulties are sometimes experienced during saturation of the plates with the stationary phase, and this procedure is also time-consuming. Draber, Buchel & Dickore (1972) showed that, within a given series of substituted triazinones, the use of polyamide plates gave R_M values that correlated well with log P (octanol–water). The polyamide itself acts as the lipophilic phase, and the plates can thus be used as received.

We have investigated whether the relation reported by Draber & others (1972) was general or not, by determining octanol–water partition coefficients and R_M values of seventeen alkyl derivatives of paracetamol, and R_M values of twelve *p*-substituted acetanilides; partition coefficients of the latter compounds were taken from Dearden & Tomlinson (1971). The solvent used in the chromatographic work was water–acetone–dioxan, 2:1:1 by volume. Plates were Merck Polyamid 11 F254, 20 cm $\times$ 20 cm. Triazinone data were taken from Draber (1973). ΔR_M and π-values for all three series of compounds were plotted on the same axes, and with the exception of three compounds, which gave points slightly below the line, a good rectilinear correlation was obtained. The regression equation is:

$$\Delta R_M = 0{\cdot}027 + 0{\cdot}456\pi; \ n = 42, \ r = 0{\cdot}991, \ s = 0{\cdot}075,$$

where r is the correlation coefficient and s is the standard deviation. Thus the general validity of the relation is established for widely differing classes of compounds.

The points lying below the line represent *N*-methylacetanilide, 3,5-diisopropyl-4-hydroxy-acetanilide and 3,5-di-t-butyl-4-hydroxy-acetanilide. The hydrogen bonding ability of all of these compounds is low, due to either blocking or shielding of hydrogen bonding groups. This has a more marked effect on ΔR_M than on π because of the rigidity of the polyamide molecules, which cannot approach hindered groups on the solute molecules so closely as can octanol.

Polyamide may also be considered as a model protein, and in fact a better correlation is found between log K (binding constant to bovine serum albumin, Dearden & Tomlinson, 1970) and ΔR_M than between log K and π, for the *p*-substituted acetanilides:

$$\log K = 4{\cdot}381 + 0{\cdot}483\pi; \ n = 12, \ r = 0{\cdot}925, \ s = 0{\cdot}146$$

$$\log K = 4{\cdot}359 + 0{\cdot}939\Delta R_M; \ n = 12, \ r = 0{\cdot}981, \ s = 0{\cdot}076.$$

Thus the method may also be useful as a convenient way of determining a protein-binding parameter.

REFERENCES

DEARDEN, J. C. & TOMLINSON, E. (1970). *J. Pharm. Pharmac.*, **22**, *Suppl.*, 53S–59S.
DEARDEN, J. C. & TOMLINSON, E. (1971). *Ibid.*, **23**, *Suppl.*, 73S–76S.
DEARDEN, J. C. & TOMLINSON, E. (1972). *Ibid.*, **24**, *Suppl.*, 115P–118P.
DRABER, W., BUCHEL, K. H. & DICKORE, K. (1972). *Proc. 2nd Int. Congr. Pestic. Chem.*, **5**, 153–175.
DRABER, W. (1973). Paper presented at First International Structure-Activity Conference, Prague, June 27–29.

Intragranular solute migration in a test granulation dried by fluidization and vacuum tumbler drying

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Intragranular solute migration has been studied in large masses of about 1 cm in diameter (Ridgway & Rubenstein, 1971) but little work has been done using granules of a size used in practice.

Test granulations were prepared by wet massing heavy kaolin B.P. (200 g) with 50 ml of sodium chloride solution (10%w/w) equivalent to 26·0 mg of salt per g dry weight. Wet granules from a sieve mesh 2800 μm were dried in a laboratory fluid bed dryer or in an evacuated vessel rocked back and forth in a water bath at 50° to simulate vacuum tumbling drying (Goodhart, Draper & Ninger, 1970).

The dry granules and dust from the bag filter were separated into fractions on sieves ranging from 2057 to 45 μm in aperture and the intragranular migration in the two larger sizes examined by prolonged sieving on a 250 μm mesh sieve and determining the salt content of the abraded powder at intervals (Fig. 1A and 1B).
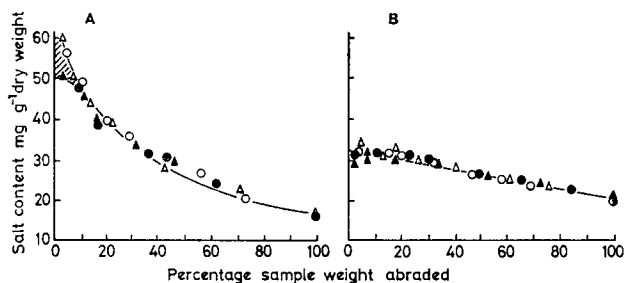

FIG. 1. Percentage sample weight abraded at different salt contents. A, granules dried by fluidization; △2057 μm and ○ 1680 μm mesh, both after 30 min drying; ▲, ● same fractions after 8 h drying. B, granules dried by tumbler drying (30 min), same sized fractions as in A, two separate batches ○●, △▲.

The mean solute content of the granule fractions was found from a crushed sample of each. The granules dried by fluidization lost about 4% of their calculated salt content. This loss appeared as an enrichment of the finer dust in the bag filter and that passing through 53 and 45 μm mesh assayed 35·5 and 44·1 mg of salt per g dry weight respectively. The vacuum dried granules yielded similar quantities of fine dust but the same fractions contained only 27·3 and 27·9 mg per g dry weight and the granules were close to the calculated salt content.

Prolonged fluidization caused little further change in the solute profile of the two largest sizes and the solute loss after 8 h (equivalent to the cross hatched area of Fig. 1A) was about 3% of the content after 30 min drying.

It is therefore concluded that the main loss occurs by abrasion of the solute rich outer layers in the early stages before the granules develop their full dry strength.

REFERENCES

GOODHART, J. W., DRAPER, J. R. & NINGER, F. C. (1970). *J. pharm. Sci.*, **59**, 540–547.
RIDGWAY, K. R. & RUBENSTEIN, M. H. (1971). *J. Pharm. Pharmac.*, **23**, *Suppl.* 11S–17S.