and Gellene, 1969; Godwin-Austen, Tomlinson & others, 1969; Yahr, Duvoisin & others, 1969).

Department of Pharmacology,   M. HENNING
University of Göteborg,   A. RUBENSON
S-40033, Göteborg, Sweden.

December 15, 1969

REFERENCES

BARTOLINI, G. & PLETSCHER, A. (1969). *J. Pharm. Pharmac.*, **21**, 323–324.
BLASCHKO, H. & CHRUSCIEL, T. L. (1960). *J. Physiol., Lond.*, **151**, 272–284.
BUTCHER, L. L. & ENGEL, J. (1969a). *J. Pharm. Pharmac.*, **21**, 615–616.
BUTCHER, L. L. & ENGEL, J. (1969b). *Brain Res.*, **15**, 233–242.
CALNE, D. B., STERN, G. M., LAURANCE, D. R., SHARKEY, J. & ARMITAGE, P. (1969). *Lancet*, **1**, 744–747.
CARLSSON, A. (1964). *Acta neuroveg.*, **26**, 484–493.
CARLSSON, A. (1969). Paper read at the Laurentian Conference on L-dopa, Val David, Que. Canada, November 9–11, 1969.
CARLSSON, A., LINDQVIST, M. & MAGNUSSON, T. (1957). *Nature, Lond.*, **180**, 1200.
COTZIAS, G. C., PAPAVASILION, P. S. & GELLENE, R. (1969). *New Engl. J. Med.*, **280**, 337–345.
GAILLARD, J. M., SCHAEPPI, R. & TISSOT, R. (1969). *Archs int. Pharmacodyn. Thér.*, **180**, 423–437.
GODWIN-AUSTEN, R. B., TOMLINSON, E. B., FREARS, C. C. & KOK, H. W. L. (1969). *Lancet*, **2**, 165–168.
HENNING, M. (1969a). *Acta pharmac. tox.*, **27**, 135–148.
HENNING, M. (1969b). *Acta physiol. scand.*, Suppl. 322.
HOLTZ, P. & PALM, D. (1966). *Ergebn. physiol.*, **58**, 1–580.
PORTER, C. C., WATSON, L. S., TITUS, D. C., TOTARO, J. A. & BYER, S. S. (1962). *Biochem. Pharmac.*, **11**, 1067–1077.
SVENSSON, T. H. & WALDECK, B. (1969). *Europ. J. Pharmac.*, **7**, 278–282.
YAHR, M. D., DUVOISIN, R. C., SCHEAR, M. J., BARRET, R. E. & HOEHN, M. M. (1969). *Arch. Neurol.*, **21**, 343–354.

Multiple-drop formation in emulsions

The term "multiple emulsion" has been used to describe the phenomenon in which drops of the disperse phase themselves contain smaller droplets which are normally considered to have the same composition as the continuous phase (Clayton, 1943). Multiple-drops appear to form most readily where an emulsion is inverting from oil-in-water to the water-in-oil type or vice-versa—conditions under which no one form of the emulsion is favoured (Seifriz, 1925). Various theories have been suggested to explain their formation (Bancroft, 1912; Parke, 1934; Pavlushenko & Yanishevski, 1959).

We have recently been making a phase rule investigation of a model four-component emulsion, and wish to report a case of multiple-drop formation arising from the presence of three liquid phases under certain conditions.

The present case of multiple-drop formation, which is restricted to the three-phase region, indicates the possibility that some of the former reports may arise from a similar cause, since three-phase formation in systems containing surfactants may be

a common occurrence (Mulley & Metcalf, 1964). The system concerned contains a non-ionic surfactant of the polyoxyalkanol type, $C_8H_{17}.[OCH.CH_2]_6.OH$ (abbreviated to C_8E_6) (Mulley, 1967), water and two "oils", dodecane, and n-octanol. Three of these components form two pairs of partially miscible liquids, water-dodecane and water-octanol, other component pairs are miscible in all proportions. The four components form a single pair of partially miscible liquids at low surfactant concentrations, but a third liquid phase at certain higher concentrations above about 1%. This third phase contains a larger proportion of surfactant than either of the two other liquid phases.

Consideration of the possible physical forms which dispersions containing three liquid phases can take, leads to the following conclusions. Where no multiple-drops occur, three forms of a three-liquid phase dispersion are possible. These are systems in which one of the phases is continuous, the two others being dispersed as individual droplets within it. Where multiple-drops are formed, providing no phase exists in both a continuous and dispersed state, a further six dispersion types are possible. In these there is a continuous phase containing drops of a second phase with internal drops of the third. Should a continuous phase also be present as a dispersed phase within droplets of one of the other liquids, then more complex systems may be formed.

According to the phase rule, when three liquid phases occur within a four-component system at a fixed temperature the system is univariant. If the composition is fixed the system automatically becomes invariant. The three liquid phases may be represented, in a regular tetrahedron used to describe the system (Ricci, 1951), by a triangular plane. The apices of the triangle are at points on the surface of the three-phase region, and represent the composition of the individual phases. Any overall composition lying in the same triangular plane forms phases of the same composition, but the relative proportion of each may vary.

Multiple-drop formation was investigated in the three-phase region at 25°. Most of the work was conducted at an overall composition of 5·3% C_8E_6, 42·9% water, 45·6% dodecane and 6·2% octanol. Separation of the equilibrated phases, followed by analysis, gave their compositions as:—phase one: 2, 0·57, 88·7 and 8·73; phase two: 13·1, 24·5, 49·58, and 12·82; phase three: 0·5, 99·31, 0·12 and 0·07% respectively. Dispersions of various phase-volume ratios were prepared by a gentle hand-shaking technique. The emulsions so formed were finely dispersed, but relatively unstable. Their physical characteristics were examined microscopically. When one phase was present in high proportion (approximately 95%) emulsions belonging to the first three types described above were observed. When the phases were more equal in volume, not only individual droplets of the two disperse phases were present, but also multiple-drops belonging to one or more of the other six possibilities. Multiple-drops where the continuous phase was also present as droplets internal to one of the other phases were likewise observed in the same dispersions. In these complex situations it seems that the number of drops observed belonging to each type is a function of their relative rates of formation and stability.

Multiple-drop formation could be important in emulsion products or in processes involving emulsion formation where components are mainly present in internal droplets and therefore relatively inaccessible; conversely the internal droplets may provide a locus of high concentration of a particular component from which diffusion is restricted. Ordinary emulsions have these properties to some degree, and examples where such effects have been noted include systems containing preservatives (Bean, Konning & Malcolm, 1969) or biologically active compounds (Ghanem, Higuchi & Simonelli, 1969) and in emulsion polymerization (Harkins, 1947). Three-liquid systems may also be of use in solvent extraction and other processes in which partition is important (Christensen, 1962).

Postgraduate School of Studies in Pharmacy,   B. A. MULLEY
University of Bradford,   J. S. MARLAND
Bradford 7, U.K.
December 11, 1969

REFERENCES

BANCROFT, W. C. (1912).   *J. phys. Chem.*, **16**, 739–758.
BEAN, H. S., KONNING, G. H. & MALCOLM, S. A. (1969). *J. Pharm. Pharmac.*, **21**, 173S–181S and references cited therein.
CHRISTENSEN, J. A. (1962).   *Acta. chem. scand.*, **16**, 2363–2367.
CLAYTON, W. (1943).   *The Theory of Emulsions and their Technical Treatment*, 4th edn, p. 252, London: J. & A. Churchill.
GHANEM, ABDEL-HALIM, HIGUCHI, W. I. & SIMONELLI, A. P. (1969).   *J. pharm. Sci.*, **58**, 165–174.
HARKINS, W. D. (1947).   *J. Am. chem. Soc.*, **69**, 1428–1444.
MULLEY, B. A. (1967).   *Non-ionic Surfactants.* Editor: Schick, M. J., p. 422, New York: Marcel Dekker.
MULLEY, B. A. & METCALF, A. D. (1964).   *J. Colloid Sci.*, **19**, 501–515.
PARKE, J. B. (1934).   *J. chem. Soc.*, 1112–1115.
PAVLUSHENKO, I. S. & YANISHEVSKI, A. V. (1959).   *Zh. prikl. Khim.*, **32**, 1495–1502.   *Chem. Abstr.*, **53**, 19479g.
RICCI, J. E. (1951).   *The Phase Rule and Heterogeneous Equilibrium*, p. 390. New York: D. Van Nostrand.
SEIFRIZ, W. (1925).   *J. phys. Chem.*, **29**, 738–749.

The use of a compression modulus to describe compaction behaviour

Several authors, including Carless & Leigh (1969) have used a compression modulus of the form log (P)/(D) (where P is a function of axial pressure, and D is a function of density of the compact) to describe the compaction behaviour of particulate materials.   The following results may indicate a need for caution in certain instances when using a parameter of this type.

In a discussion of the effect of moisture on the compaction of sodium chloride at a series of pressures, Huffine (1953) quoted mean values of the "pressing modulus", $d \log P_a/dV_r$ proposed by Bal'shin (1938), although the relation between the logarithm of applied pressure P_a, and the relative volume V_r was not linear over the entire range of applied pressure.   The "pressing modulus" was shown to increase when the particulate material was previously exposed to conditions of elevated humidity. Huffine considered that this implied an increase in the resistance to consolidation of the compressed material.   However, inspection of Huffine's data (Table 1) shows that at each applied pressure, the relative volume was greatest for the dry material.

Table 1. *Effect of moisture on the relative volume of compacts prepared from 24–28 mesh sodium chloride (Huffine, 1953)*

Applied pressure (p.s.i.)	Relative humidity of storage for 24 h			
	0%	36·4%	54·2%	74·9%
1880	1·374	1·355	1·329	1·278
9410	1·150	1·126	1·146	1·101
33940	1·020	1·001	1·005	1·014
61200	1·001	0·987	0·993	1·001
$d \log P_a/dV_r$	3·17	3·32	3·58	3·67