LETTER TO THE EDITOR

Bactericidal Activity and Soap Solution Structure

SIR,—A recent paper by Berry, Cook and Wills,[1] shows variation in the bactericidal activity with concentration of potassium laurate, in the range 0 to 100 millimoles/l. This took place in the presence of certain added phenols, and took the form of peaks or breaks in the bactericidal activity-concentration curve. Soap concentrations of the following limiting activity were reported:

(*a*) a first limit of about 30 millimoles/l., identified with the Critical Micelle Concentration. At this point maximal bactericidal activity was observed,

(*b*) a second limit of about 45 millimoles/l., at which point minimal bactericidal activity was observed, and

(*c*) a third limit above 80 millimoles/l., which corresponded to a point above which the concentration-bactericidal activity curve was "normal" and extinction time decreased with increased concentration.

The authors offered a number of suggestions to explain this anomalous variation. There is, however, a possible alternative explanation. Abrupt changes in the physical property-concentration curves of a number of colloidal electrolytes have been pointed out by Ekwall[2,3]. Measurements of equivalent conductance, solubilisation properties, hydroxyl-ion activity and partial molal volume when plotted against concentration of potassium laurate, gave curves which showed distinct breaks at 6, 20, 28 and 50 millimoles/l. Similar curves for other association colloids showed similar breaks at various concentrations, which Ekwall termed concentration limits. In corroboration of these results, Brudney and Saunders[4] found distinct breaks in the diffusion coefficient-concentration curve of potassium laurate at 28 and 50 millimoles/l. Breaks in the diffusion coefficient-concentration curves for sodium dodecyl sulphate,[5] and other association colloids[6] have also been reported and were in most cases in accord with Ekwall's findings.

With potassium laurate, there is an interesting similarity between the physical properties-concentration curves and the bactericidal activity curves of Berry and others.[1] Slight variations in the actual figures for concentration limits are inevitable with variations in temperature, conditions of purity, additive concentrations, or applied forces. Further, all the limits cannot necessarily be shown by any particular method. Thus, using the Gouy Diffusiometer, the limits at 6 and 20 millimoles/l. could not be shown, since these concentrations were outside the range of the apparatus. Similarly, these limits have not been shown by the bactericidal measurements. However, the fundamental pattern is the same, that is, anomalies occur in the property-concentration curves for potassium laurate between 0 and 100 millimoles/l., and these anomalies occur as distinct peaks or troughs in these curves.

Presumably these abrupt changes in physical and bactericidal properties could have a common explanation in terms of solution structure. Hartley's soap solution structure theory seems to provide a basis for the explanation of anomalous diffusion coefficient-concentration curves,[7] in the terms of a change in effect on the micelles, of the gegenions.

The obvious similarity of the physical property-concentration curves and bactericidal activity-concentration curves leads one to believe that bactericidal

activity is a function of solution structure. I suggest that on these lines an explanation of the mode of antibacterial action, with a stronger theoretical background, could be developed.

NORMAN BRUDNEY.

Wellcome Chemical Works,
Dartford, Kent.

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REFERENCES

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(ABSTRACTS *continued from p. 998.*)

5 days. In 6 cases with uncomplicated pneumococcal pneumonia the clinical outcome was satisfactory; in a seventh patient the condition deteriorated on novobiocin and he was changed to penicillin therapy after 24 hours. Fourteen patients were treated for infections of the genito-urinary tract; cultures of urine prior to treatment all revealed *P. vulgaris*. Five of the patients were improved by novobiocin, though in 3 of these the cultures remained positive for *P. vulgaris*. Three patients derived no benefit, and in 6 the outcome was indeterminate. Proteus could be cultured from the urine of 8 of the 14 patients at the termination of therapy. The only side effects observed in this series of patients were mild skin eruptions which occurred in 2 cases; in one of these a second course of novobiocin did not cause a recurrence of the eruption. S. L. W.

Nystatin in Mycotic Infections. G. T. Stewart. (*Brit. med. J.*, 1956, **1**, 658.) Nystatin (Mycostatin) is an antibiotic prepared from *Streptomyces noursei*. It is an amphoteric crystalline polyene with the probable empirical formula $C_{46}H_{77}NO_{19}$, insoluble in water, but soluble in various alcohols and ethers. It is available as a pale-yellow lyophilised powder which is rapidly inactivated by heat, light and oxygen; tablets containing 500,000 units of the substance are prepared for clinical use. *In vitro* experiments show that nystatin inhibits cell-division and mycelial growth of candida and saccharomyces, including pathogenic strains isolated from a variety of human lesions. This effect is fairly complete against *C. albicans* at concentrations of 5–20 units/ml. Its mode of action is complex but highly specific. The presence of a chain of CH_2 groups, as in the alcohols, favours activity, while CHOH and CHO groups, as in various sugars, are antagonistic. Glycols, with combination of both, show intermediate properties. A series of 12 bronchitic patients with fungal hyphae demonstrable in direct examination of films made from sputum, and cultures positive for *C. albicans*, were treated with three to four daily oral doses of 500,000 units for 7 days. The moniliasis in these patients had developed as a sequel to antibiotic therapy. As a result of the treatment with nystatin 9 out of the 12 patients were rapidly and completely cleared of the mycotic infection. A similar result was obtained in 7 out of 8 cases of stomatitis. Apart from transient nausea no toxic effects were observed. Nystatin and antibacterial agents showed no mutual interference *in vitro* but when given prophylactically nystatin was not wholly successful in preventing mycotic superinfection in patients receiving antibacterial therapy. Resistance was not found to develop in strains after passage *in vitro* or on re-isolation during and after treatment. S. L. W.