References

Cassidy, M. M., Tidball, C. S. (1967) Cellular mechanism of intestinal permeability alterations produced by chelation depletion. J. Cell Biol. 32: 685–698

Francis, M. D., Centner, R. L. (1978) The development of diphosphonates as significant health care products. J. Chem. Educ. 55: 760–766

Harinck, H. I. J., Papapoulos, S. E., Blanksma, H. J., Moolenaar, A. J., Vermeij, P., Bijvoet, O. L. M. (1987) Paget's disease of bone: early and late responses to three different modes of treatment with aminohydroxypropylidene bisphosphonate (APD). Brit. Med. J. 295: 1301–1305

Irani, R. R., Moedritzer, K. (1962) Metal complexing by phosphorus compounds. VI. Acidity constants and calcium and magnesium complexing by mono- and polymethylene diphosphonates. J. Phys. Chem. 66: 1349–1353

Ishizawa, T., Hayashi, M., Awazu, S. (1987) Enhancement of jejunal and colonic absorption of fosfomycin by promoters in the rat. J. Pharm. Pharmacol. 39: 892–895

Mautalen, C. A., Casco, C. A., Gonzalez, D., Ghiringhelli, G. R., Massironi, C., Fromm, G. A., Plantalech, L. (1984) Side effects of disodium aminohydroxypropylidenediphosphonate (APD) during treatment of bone diseases. Brit. Med. J. 288: 828–829

Nadai, T., Kondo, R., Tatematsu, A., Sezaki, H. (1972) Drug-induced histological changes and its consequences on the permeability of the small intestinal mucosa. I. EDTA, tetracycline and sodium laurylsulfate. Chem. Pharm. Bull. 20: 1139–1144

Nakanishi, K., Masada, M., Nadai, T. (1983) Effect of pharmaceutical adjuvants on the rectal permeability of drugs. III. Effect of repeated administration and recovery of the permeability. Ibid. 31: 4161–4166

Nishihata, T., Tomida, H., Frederick, G., Rytting, J. H., Higuchi, T. (1985) Comparison of the effects of sodium salicylate, disodium ethylenediaminetetraacetic acid and polyoxyethylene-23-lauryl ether as adjuvants for the rectal absorption of sodium cefoxitin. J. Pharm. Pharmacol. 37: 159–163

Reitsma, P. H., Bijvoet, O. L. M., Potokar, M., van der Wee-Pals, L. J. A., van Wijk-van Lennep, M. M. L. (1983) Apposition and resorption of bone during oral treatment with (3-amino-1-hydroxypropylidene)-1,1-bisphosphonate (APD). Calcif. Tissue Int. 35: 357–361

Suzuka, T., Furuya, A., Kamada, A., Nishihata, T. (1987) Effect of phenothiazines, disodium ethylenediaminetetraacetic acid and diethyl maleate on *in vitro* rat colonic transport of cefmetazole and inulin. J. Pharmacobiodyn. 10: 63–71

Tidball, C. S., Lipman, R. I. (1962) Enhancement of jejunal absorption of heparinoid by sodium ethylenediaminetetraacetate in the dog. Proc. Soc. Exp. Biol. Med. 111: 713–715

Van Holten-Verzantvoort, A. Th., Bijvoet, O. L. M., Hermans, J., Harinck, H. I. J., Elte, J. W. F., Beex, L. V. A. M., Cleton, F. J., Kroon, H. M., Vermeij, P., Neijt, J. P., Blijham, G. (1987) Reduced morbidity from skeletal metastases in breast cancer patients during long-term bisphosphonate (APD) treatment. Lancet ii: 983–985

Van Hoogdalem, E. J., Stijnen, A. M., de Boer, A. G., Breimer, D. D. (1988a) Rate-controlled absorption enhancement of rectally administered cefazolin in rats by a glyceride mixture (MGK). J. Pharm. Pharmacol. 40: 329–332

Van Hoogdalem, E. J., van Kan, H. J. M., de Boer, A. G., Breimer, D. D. (1988b) Rate-controlled absorption enhancement of rectally administered cefoxitin in rats by salicylate. J. Controlled Release 7: 53–60

J. Pharm. Pharmacol: 1989, 41: 341–342
Communicated February 29, 1988

Continuous shear rheometry of o/w emulsions; control of evaporation in cone/plate geometry

LARA O. ORAFIDIYA, *Dept. of Pharmaceutics, Obafemi Awolowo University, Ile-Ife, Oyo State, Nigeria*

Abstract—Volatile solvents may evaporate during cone/plate viscometry so that false rheograms develop. This surface evaporation was prevented in a cod-liver oil-in-water emulsion stabilized with zanthoxylum gum by layering a film of cod-liver oil on the exposed surface of the emulsion test sample. The oil layer effectively prevented evaporation and did not alter significantly the rheological behaviour of the test material.

A disadvantage of a cone and plate viscometer is the evaporation of solvent from the exposed surface of the material under test. Such evaporation can increase because of the heat generated at high shearing speeds (Mckennell 1956) or because of long sweep-times (Davis et al 1968; Barry 1974). As a result, for materials such as those which contain gums, the apparent viscosity increases and a clockwise hysteresis loop forms under cyclic testing even for time independent materials (Davis et al 1968).

Zanthoxylum gum is the gummy exudate from the tree, *Zanthoxylum tessmannii* (Engl.) Waterm., family Rutaceae. In the course of studying the emulsifying properties of the gum, cod-liver oil-in-water emulsions were prepared. A Ferranti-Shirley cone and plate viscometer was used to determine the viscosity of the emulsions. The emulsions exhibited apparent shear thickening with hysteresis as indicated by a clockwise loop. The area of the loop and the apparent viscosity at maximum shear rate, however, increased significantly when the sample was left for some time on the viscometer and when the anti-evaporation hood was not used. It was then suspected that the clockwise hysteresis loop probably arose from evaporation of water from the exposed surface of the sample under test, which increased the apparent viscosity of the sample with time.

Method

A 50% w/w emulsion of cod-liver oil-in-water, stabilized with 4·17% w/w zanthoxylum gum was prepared in a stainless steel cup using the Silverson mixer. Mixing was for 5 min and the temperature of the emulsion was not allowed to exceed 25°C during mixing by circulating water at 12°C around the stainless steel cup. The emulsion was passed 5 times through the "Q.P." hand homogenizer; packed in glass bottles and stored at 25°C for 2 days. A Ferranti-Shirley viscometer fitted with a cone of radius 3·5 cm and a cone angle of 0·005852 radians was used to study the flow properties of the emulsions. Water at $25 \pm 0{\cdot}1$°C was circulated through the plate. A maximum speed of 100 rev min^{-1} was used. About 1 mL of the emulsion was used for each test. With a sweep time of 600 s, the cone and plate assembly was employed, respectively, without the anti-evaporation hood, with the anti-evaporation hood, and with cod-liver oil carefully layered on the exposed surface of the extruded emulsion between the cone and plate, using a 2 mL syringe with a needle (Fig. 1).

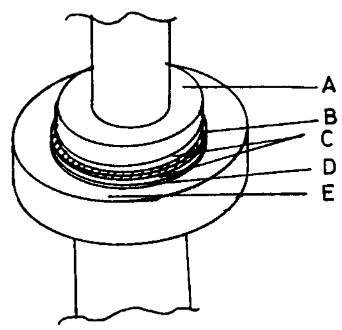

FIG. 1. Schematic illustration of the oil film on the extruded emulsion in a cone/plate geometry. A = Cone housing. B = extruded emulsion. C = film of oil. D = plate. E = platform on which plate is mounted.

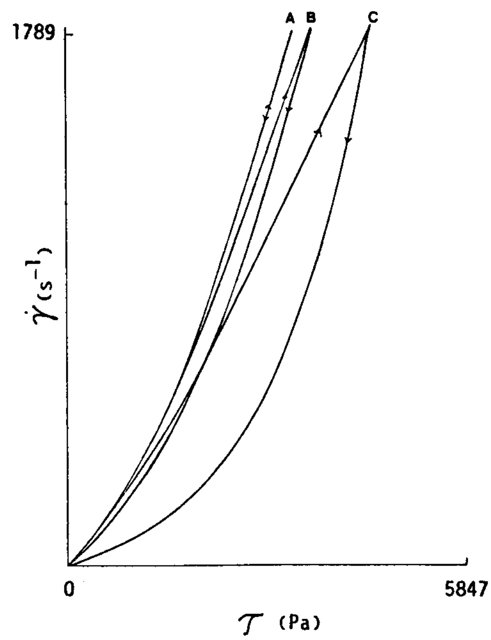

FIG. 2. Effect of evaporation on the rheograms of 50% w/w cod-liver oil emulsion stabilized with 4·17% w/w zanthoxylum gum. A = with cod-liver oil layer. B = with anti-evaporation hood. C = without anti-evaporation hood.

The cod-liver oil layer was not allowed to drop below the raised edge of the plate onto the supporting platform as this led to gradual drainage of the oil. Sweep times of 120 s, 240 s and 480 s were also used with those samples tested when the anti-evaporation hood only was used.

Results and discussion

The rheograms in Fig. 2 illustrate the effect of evaporation during viscosity measurements of the emulsion on the Ferranti-Shirley viscometer. While the sample with a cod-liver oil layer was pseudoplastic with no hysteresis loop, those tested with and without the anti-evaporation hood had clockwise hysteresis loops with the downward curves lying close to the torque axis. The area of the loops and the apparent viscosity at maximum shear rate were greater when the anti-evaporation hood was not used. The rheograms obtained at sweeptimes of 120 s and 240 s, with the anti-evaporation hood employed, did not have a hysteresis loop. Clockwise hysteresis loops were observed with sweep times of 480 s and 600 s (Fig. 3). The area of the loop and

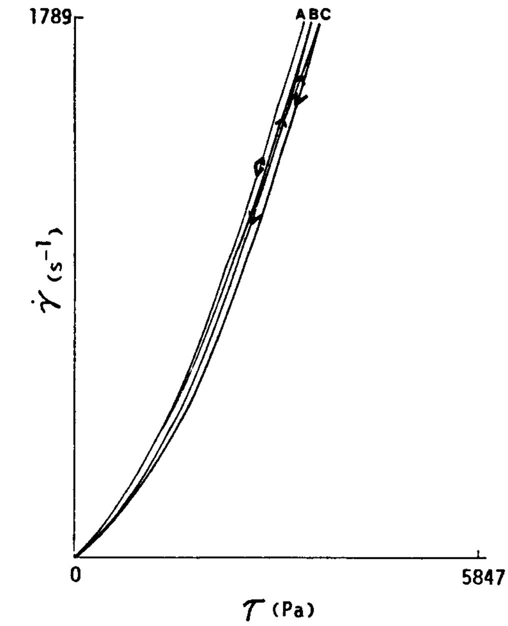

FIG. 3. Rheograms of 50% w/w emulsion of cod-liver oil, stabilized with 4·17% w/w zanthoxylum gum, at different sweep times (with anti-evaporation hood). A = 120 s, 240 s. B = 480 s. C = 600 s.

the apparent viscosity at maximum shear rate were greater at the sweep time of 600 s.

These observations clearly show that the increase in viscosity and the development of the hysteresis loops, which imply shear-thickening, are caused by evaporation of water from the exposed surface of the emulsion under test. The effect is greater when the test period is increased by using longer sweep times. The cod-liver oil prevented water from evaporating, hence, the up and the down curves coincided. The cod-liver oil also did not contribute to the viscosity of the emulsion as the rheogram of the test emulsion with the cod-liver oil layer is similar to those obtained at shorter sweep time (120 and 240 s) using the anti-evaporation hood. The anti-evaporation hood had not effectively prevented the evaporation of water. Shorter sweep times minimized the effect of evaporation on the rheogram of the emulsion. However, short sweep times are usually not recommended when large cones are used because of the "fly-wheel" effect (Cheng 1967). It could therefore, be suggested that a layer of oil on the exposed surface of an o/w emulsion under cyclic testing on the Ferranti-Shirley viscometer would prevent evaporation better than the anti-evaporation hood.

The author is appreciative of the contribution of Prof. B. W. Barry of the School of Pharmacy, University of Bradford, England, to this study.

References

Barry, B. W. (1974) in Bean, H. S., Beckett, A. H. & Carless, J. E. (Eds) Advances In Pharmaceutical Sciences, Vol. 4, Academic Press, London, pp. 1–72

Cheng, D. C-H. (1967) Hysteresis loop experiments and the determination of thixotropic properties. Nature (London) 216: 1099–1100

Davis, S. S., Shotton, E., Warburton, B. (1968) Some limitations of continuous shear methods for the study of pharmaceutical semi-solids. J. Pharm. Pharmacol. Suppl. 20: 157S–167S

Mckennell, R. (1956) Cone-plate viscometer. Comparison with coaxial-cylinder viscometer. Anal. Chem. 28: 1710–1714