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The molecular weight of liquid paraffin by cryoscopy

A. Pearson, N. Shankland and E.G. Salole

Department of Pharmacy, University of Strathclyde, Glasgow (U.K.)

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Summary

The number-average molecular weight for spectroscopy-grade liquid paraffin was determined by cryoscopy in benzene to be 348. Attention is drawn to the importance of empirically obtaining the cryoscopic apparatus constant, minimising the error in temperature measurement by ensuring the constancy of ambient conditions and keeping the total freezing-point depression within 0.5°C.

In the course of examinations of the solid-state properties of drugs in semi-solid topical formulations (Pearson et al., 1985; Shankland et al., 1985), the solubilities of model compounds in liquid paraffin, a common component of cream bases, were required. The dependence of equilibrium drug saturation solubility on temperature can be described by the van't Hoff equation:

$$\ln x_2 = -\frac{\Delta H}{R}\left(\frac{1}{T_2} - \frac{1}{T_1}\right) \tag{1}$$

To calculate x_2, the mole fractional solubility of drug, the molecular weight of solvent is required — but, unexpectedly, a value for liquid paraffin was unavailable. Therefore the number-average molecular weight of the liquid paraffin being used was determined experimentally by cryoscopy.

The theoretical basis and practical aspects of cryoscopic measurement have been thoroughly discussed by Bonnar et al. (1958). Essentially, the complex rigorous equation for calculating molecular weight can be reduced to the traditional form:

$$M = 1000K \cdot W/w \cdot \theta \tag{2}$$

where M is the molecular weight of solute, K the first cryoscopic apparatus constant, W (g) the total weight of solute added, w (g) the weight of solvent and θ (deg.) the observed freezing-point depression. Since $\theta = T - T_0$, where T and T_0 are the freezing-points of solution and pure solvent, respectively (as read on the differential thermometer scale), the molecular weight equation can be rearranged to:

$$T = 1000K \cdot W/M \cdot w + T_0 \tag{3}$$

Having determined K for a particular apparatus and solvent using a standard solute, the value of M for an unknown sample may be calculated from the slope of a graph of T against W.

The cryoscopic apparatus was of traditional design (Findlay, 1954): consisting of a 2.5 cm diameter cryoscope tube, fitted with a Beckmann differential thermometer (0.001 deg. sensitivity;

Correspondence: A. Pearson, Department of Pharmacy, University of Strathclyde, Glasgow G1 1XW, U.K.

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E-Mil, Corning, U.K.), within a 4.5 cm diameter air-jacket and ice-bath. 20.00 g benzene ($\nless$ 99.9% purity, $\ngtr$ 0.01% water; HPLC grade, Aldrich Chemical Co., U.K.) in the cryoscope tube were gently stirred by a magnetic follower at slow speed, and crystallization of supercooled solutions induced by the resulting agitation of a few glass beads (100 mesh, BDH, U.K.) in situ.

The experimental procedure described by Bonnar et al. (1958) was followed, with measurement of 'steady-state' freezing-points (i.e. the maximum temperatures achieved on crystallization). Naphthalene ('molecular weight determination grade', Fisons, U.K.) was used to determine the cryoscopic apparatus constant. The method was validated with 1,3-dinitrobenzene (> 99% purity, Fluka, U.K.) and the molecular weights of the proprietary liquid paraffin Nujol (batch DD057, Perkin-Elmer, U.S.A.) and spectroscopy-grade liquid paraffin (batch 17, Fisons) determined.

Cryoscopic data and the molecular weights derived from them are listed in Table 1. The result for dinitrobenzene indicated that the precision and accuracy of the method were well within the limits to be expected of cryoscopy. Nujol was found to have a number-average molecular weight of 338, and the mean value for liquid paraffin was 348.

TABLE 1

CRYOSCOPIC DATA AND DERIVED NUMBER-AVERAGE MOLECULAR WEIGHTS FOR DINITROBENZENE AND LIQUID PARAFFINS

10^3 W (g)	T (°C)	*r*	M
Dinitrobenzene (mol. wt. = 168.11)			
0.00	3.241		
35.96	3.304		
65.28	3.361		
94.50	3.410		
		0.9996	169.77
Nujol			
0.00	3.247		
45.88	3.296		
93.03	3.336		
		0.9981	338
Liquid paraffin			
0.00	3.210		
46.88	3.258		
93.80	3.304		
161.34	3.363		
		0.9992	344.6
0.00	3.202		
186.41	3.346		
253.59	3.406		
		0.9994	352.2

W = total solute added; T = average (2–3 cycles) Beckmann thermometer scale reading; *r* = correlation coeff. of regression T on W; M = calculated number-average molecular weight.

The cryoscopic apparatus constant used to calculate the molecular weights was determined empirically, and checked between experiments. It is important to do this because the value of K depends on the particular apparatus and procedure used, and particularly the presence of impurities in the solvent (notably water in the case of benzene). The use of the 'standard' constants often quoted in the reference literature, e.g. 5.12 for benzene (Riddick and Bunger, 1970; Kaye and Laby, 1973), is to be deprecated because these values are derived from calorimetric data, whereas in cryoscopic practice the value of K varies widely, e.g. for benzene from 4.86 (Bonnar et al., 1958) to 6.247 (this work). It should also be noted that Eqn. 2 is valid only in the limit when Raoult's Law applies, i.e. W and θ approach zero; in practice this means that θ should not exceed 0.5 deg. in total. Finally, in our experience it is essential that the relatively large stem of the Beckmann thermometer be maintained in a constant environment (i.e. protected from direct sunlight and draughts) in order to avoid errors in temperature measurement due to convection currents within the stem casing; siting the apparatus in a fume-cupboard may be adequate, but there is a risk of solvent loss by evaporation.

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