previous studies of the angular dependence of the interaction between nucleophiles and certain electrophiles which possess intrinsic steric requirements (27, 28), as well as electrophiles in general (20, 29–32).

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NOTES

Determination of the Average Molecular Weight of Nonionic Emulsifiers by Vapor-Phase Osmometry

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Received October 5, 1982, from the *Faculty of Pharmacy, University of Montreal, Montreal, Quebec, H3C 3J7, Canada.* Accepted for publication January 10, 1983.

Abstract □ Standard nonionic emulsifiers are heterogenous by nature. Their reported molecular weight is unreliable, especially when several lots of the product are used in a study. The number-average molecular weights of two nonionic emulsifiers, poloxamer 188 and polyoxyethylene(23) lauryl ether were determined by vapor-phase osmometry. This determination is essential when the concentration should be given in molarity rather than in weight per volume. A discrepancy was noted between the number-average molecular weights of two lots of poloxamer 188. That difference is taken into account prior to the establishment of any comparison of the behavior of the emulsifiers.

Keyphrases □ Poloxamer 188—number-average molecular weight, vapor-phase osmometry □ Polyoxyethylene(23) lauryl ether—number-average molecular weight, vapor-phase osmometry □ Vapor-phase osmometry—determination of number-average molecular weights, poloxamer 188, polyoxyethylene(23) lauryl ether

Standard nonionic emulsifiers are chemically impure, with a composite nature that confers specific properties which render them suitable for numerous applications such as emulsification, wetting, foaming, *etc.* Because of this particular feature, determination of the molecular weight of nonionic emulsifiers is complicated and the analytical

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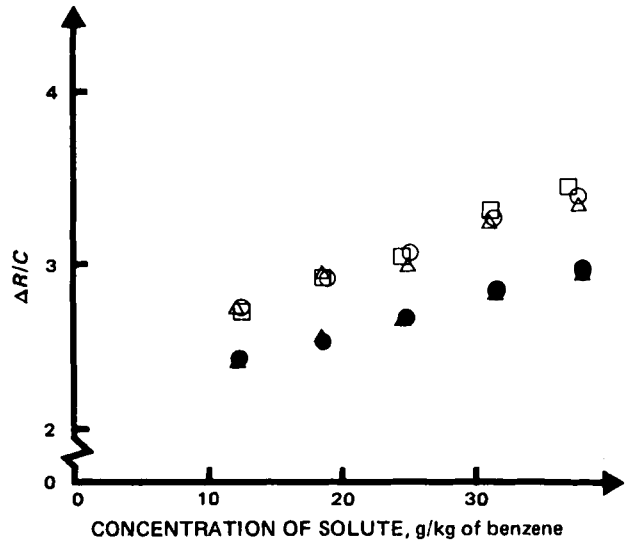

Figure 1—*Sample calculation curves of two lots of poloxamer 188. Key: (□, ○, △) three sets of data for lot WPTY 175B; (▲, ●) two sets of data for lot WXPG 112.*

method chosen must overcome the heterogeneity of the product, which renders impossible the consideration of the reported molecular weight. Methods involving the measurement of colligative properties are extensively used for estimating number-average molecular weights <20,000 (1–3). A prime interest in this area is directed toward vapor-phase osmometry as a rapid and reliable technique (4).

The number-average molecular weights of poloxamer 188 (I) and polyoxyethylene(23) lauryl ether (II) were determined by vapor-phase osmometry. Even if an estimation of the number-average molecular weights can be done from their formulas, a more systematic procedure should be employed to confirm the uniformity of the product, which can vary from lot to lot. These determinations were undertaken on both substances prior to their use in a study dealing with emulsifier behavior at the air–water and soybean oil–water interfaces.

EXPERIMENTAL

Two lots of I (WPTY 175B and WXPG 112)[1] and one lot of II (667)[2] were studied. The emulsifiers were dissolved in benzene (ACS grade) previously dried over calcium sulfate and filtered through a 0.45-μm cellulose membrane. Benzil (practical grade, mol. wt. 210.23) was used as the standard for calibration.

The measurements were performed on a molecular weight apparatus[3]. Since the accurate measurement of vapor pressure is difficult, the determination of the number-average molecular weights is based on the temperature difference between a solution and its solvent at the same vapor pressure. The apparatus consists of a thermostated chamber containing two thermistors where a pool of pure solvent is maintained at equilibrium with the environment. When a drop of solvent is placed on each thermistor, the rates of evaporation and condensation are equal in all parts of the system and the temperature is constant. When a drop of solution is placed on one thermistor, this equilibrium is upset and a change of temperature for one thermistor is reflected by a change in the resistance (ΔR) of the system. The calibration and calculation curves were obtained under the following experimental conditions: main oven temperature, 40.1 ± 0.1°C; sub-oven temperature, 35.3 ● 0.15°C; room temperature, 22°C; and equilibration time, 10 min.

[1] Pluronic-F_{68} (BASF-Wyandotte), a block copolymer containing 80% of polyoxyethylene units and 20% of polyoxypropylene units.
[2] Brij-35, Atlas Chemicals Div., ICI America, Inc.
[3] Hitachi/Perkin-Elmer Molecular Weight Apparatus, model 115.

Table I—Comparison of Reported and Experimentally Determined Number-Average Molecular Weights

	Number-Average Molecular Weight	
	Literature Value	Estimated by Vapor-Phase Osmometry
Poloxamer 188		
Lot WPTY 175B	8350[a]	7448.1 ± 95.8
Lot WXPG 112		8246.9 ± 4.8
Polyoxyethylene (23) lauryl ether (lot 667)	1200[b]	1264.4 ± 33.5

[a] Taken from Ref. 5. [b] Taken from Ref. 6.

RESULTS AND DISCUSSION

Determination of the Instrument Constant (K)—This constant is the same as the slope of the calibration curve showing the change in the ΔR values for the standard substance (benzil) in benzene at different concentrations (C). The range of concentration was chosen to generate ΔR values from 50 to 150. K was calculated using four sets of data. No significant difference has been noted between the slopes obtained from each set of data based on the Student's t test. Since the origin is included within the confidence limits (1%) of each intercept, the equation of the calibration curve can be represented as follows:

$$\Delta R = KC + b \qquad \text{(Eq. 1)}$$

where $b = 0$. The slope is calculated as the sum of ΔR values divided by the sum of the concentrations obtained for the four sets of data. Accordingly, the instrument constant (K) is equal to 18,000.150.

Determination of the Number-Average Molecular Weights—Sample calculation curves were obtained by plotting $\Delta R/C$ as a function of C for different concentrations of a sample dissolved in benzene (g of sample/kg of benzene). Figures 1 and 2 show the curves obtained for the two lots of I and for II. The number-average molecular weight is calculated using the following equation[4]:

$$\text{Number-average mol. wt.} = \frac{\text{Instrument constant } (K)}{\text{Intercept of the sample calculation curve}} \qquad \text{(Eq. 2)}$$

Table I shows the number-average molecular weights determined for each sample; these results are close enough to those reported, except for one lot of I. This difference may have a twofold significance. This particular lot was stored in our laboratory for over 3 years at room temperature in an air-tight container. One can suppose that the two lots of I were

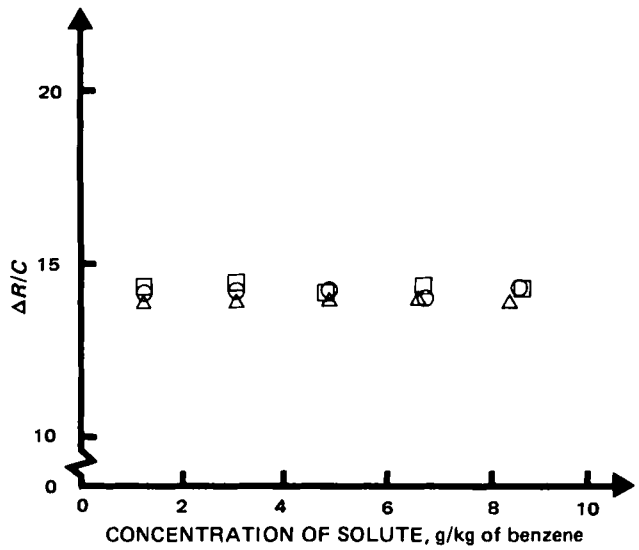

Figure 2—*Sample calculation curves of polyoxyethylene 23 lauryl ether. Key: (□, ○, △) three sets of data for lot 667.*

[4] Since the sample calculation curves were made in duplicate or triplicate, the mean intercept was used in each case for the calculation.

composed of different fractions or that "degradation" occurred during the storage period of lot WPTY 175B. No matter which hypothesis is retained, the product has not lost its activity as far as emulsifying or surface-active properties are concerned.

Nevertheless, the average molecular weight of an emulsifier ought to be known in order to determine its surface excess and to produce the curve of the surface pressure *versus* "molecular" cross-sectional area of the emulsifier (7). Relying on the reported molecular weight can generate misleading values for the aforementioned parameters, especially if the data are obtained from different batches of the same emulsifier. No comparison can be made between the behavior of different lots of one product unless a correction is made for the difference in their molecular weights.

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Alloxan Analogues as Potential Pancreatic-Imaging Radiopharmaceuticals

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Received August 19, 1982, from the **Center for Health Sciences, Lehigh University, Bethlehem, PA 18015* and the ‡*Biochemistry Department, McNeil Laboratories, Spring House, PA 19477.* Accepted for publication January 10, 1983.

Abstract □ Three families of alloxan derivatives, 5-arylthiobarbituric, 5-aryliminobarbituric, and 5-aryldialuric acids, were prepared as prospective radioiodine-transporting radiopharmaceuticals for the delineation of pancreatic insulinomas. Members of each class were screened for effects on blood sugar levels in a rat glucose tolerance assay. Transient hyperglycemia was observed with 5-(2,4-dichlorophenyl)iminobarbituric acid. No agent evaluated induced permanent diabetes at the doses tested.

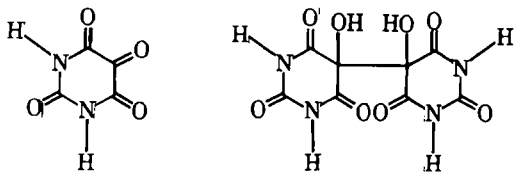
Keyphrases □ Alloxan—analogues, potential tumor-imaging agents, pancreatic insulinomas, effect on blood glucose levels, rats □ Tumor-imaging agents—alloxan analogues, pancreatic insulinomas, effect on blood glucose levels, rats

Alloxan and several of its derivatives are diabetogenic (1–3). While no definitive structure–activity studies have been reported, it appears that alloxan, alloxan monohydrate (II), alloxantin (I), and dialuric acid (III), without bulky substituents on nitrogen, are all able to induce frank diabetes (1–3). Some evidence supports a direct effect on the pancreas, for degranulation of β-cells is observed; [^{14}C]alloxan was shown to concentrate in the islet cells by autoradiography (4–7).

Development of radiopharmaceuticals for the scintigraphic imaging of occult pancreatic malignancies has been a goal of these laboratories for several years (8–11). In at least one previous study, it has been shown that substances with direct effects on serum glucose levels can, if radioisotopically labeled, preferentially delineate insulinomas (12, 13). Alloxan analogues would appear worthy of investigation in this regard.

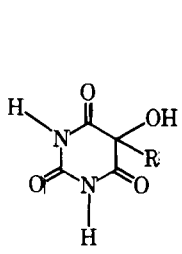
Three classes of alloxan derivatives have been prepared which differ from the parent molecule by possessing an aryl moiety at C-5. This pendant aromatic ring would provide a suitable locus for the attachment of radioiodine in the chemical agent actually selected for the tumor-imaging study. As an initial screen to select analogues for isotopic labeling, a glucose tolerance test was performed to assay diabetogenic potential. This procedure has been described previously (14). Candidates were selected from the three classes synthesized: 5-arylthiobarbituric acids (IV), 5-aryliminobarbituric acids (V), and 5-aryldialuric acids (VI).

A new and more facile synthesis of 5-arylthiobarbituric acids (IVa–c) was developed from triphenylphosphine–alloxan adducts (VII), whose synthesis was described in an earlier publication (15), and aromatic thiols (Scheme

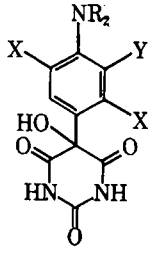


alloxan

I



II: R = OH
III: R = H



VIa: R = X = Y = H
VIb: R = Me, X = Y = H
VIc: R = Y = H, X = OMe
VId: R = Y = H, X = OEt

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