

## The relationship between Osmolarity and Osmolality of Infusion Solutions of Monosaccharides

Z. Šklubalová\*, Z. Zatloukal

Charles University in Prague, Faculty of Pharmacy, Department of Pharmaceutical Technology, Heyrovského 1203, 500 05 Hradec Králové, Czech Republic

### Abstract:

Concentration of Osmotically active solutes plays a key role in an acceptance of parenteral infusions by patients. It is generally recommended that labels of infusions should list osmolarity (osmol/l). However, osmometer can only read osmolality (osmol/kg). The conversion of the experimental readings to the declared osmotic concentration wants to study the relationship between osmolality and osmolarity. The conversion factor defined as ratio of the solution molarity and its molality was introduced to convert osmolality to osmolarity. Unfortunately, the conversion factor changes with dilution. In this work, the total molal volume of the solute in aqueous solution, which is not influenced by the solution concentration, was used instead for aqueous solutions of monosaccharides. The method allowing estimation of the solute molal volume from its molal weight and true powder density was demonstrated. Finally, the original equation employing true density of the powder was recommended for conversion osmolality to osmolarity.

**Keywords:** *Infusions, Molal volume, Osmolality, Osmolarity, Parenterals*

### Introduction:

Concentration of parenterals is generally expressed in molarity way (mol/l), i.e. in number of moles (gram molecular weight) of solute in one litre of solution. However, concentration of the solutes in parenterals must be also considered in osmotic relationships. Apart from molarity, therefore, the knowledge of the osmotic concentration is essential for the medical staff and labelling of parenterals with osmolarity is generally recommended. The basic advantage of employing osmolarity ( $c_{os}$ ) is that the number of osmols is assigned to the volume of the solution (osmol/l) which is useful in an application of the liquid dosage form. However, osmometric measurement gives osmolality ( $m_{os}$ ) in which osmotic effect of the dissolved solutes relates to the number of osmotically active particles per kilogram of solvent (osmol/kg). This way, osmolality is directly proportional to the solution molality (mol/kg). Because the confusion often exists between these terms, the investigation of mutual relationship between these concentrations is wanted.

It is generally considered that the numerical values of osmolality do not differ significantly from those of osmolarity and the differences could be neglected [1]. This assumption is reasonable only in diluted solutions such

as the usual electrolyte infusions. If the concentration increases the conversion of osmolality to osmolarity becomes necessary.

In order to calculate osmolarity, the conversion factor  $f$  defined as the ratio of osmolarity and osmolality has been introduced [2]. This conversion factor has also been said to be the difference between solution density and the mass of solute dissolved in the solution; in another way, it could be considered equal to the water content in the solution. Although this concept is generally accepted for mutual conversion between osmolality and osmolarity [3], unfortunately, it is influenced by the actual solution concentration. Moreover, the knowledge of the solution density is required.

The method employing the partial molal volume of solute was also introduced [4]. Because defined at infinite dilution, the partial molal volume is useful for diluted parenteral solutions. However, the values of the partial molal volume are difficult to obtain. For the more concentrated infusions of monosaccharides, the total (integral) molal volume was recommended [5]. This can be estimated experimentally due to the measurement of changes in the solution volume during dissolving of the solute and can be expressed in terms of molarity  $c$  (mol/l) and molality  $m$  (mol/kg) of the solution as follows:

$$V_{\text{exp}} = \frac{m - c}{m \cdot c} \quad (1)$$

where  $V_{\text{exp}}$  (l/mol) is the total molal volume.

In this work, the relationship between molarity in the range of 0.1 to 1.0 mol/l and molality of aqueous solutions of the parenteral monosaccharides was investigated. The calculation of the total molal volume from the experimental data is illustrated for mannitol. The method allowing the estimation of the molal volume of the solute in aqueous solution from its true powder density was studied. For monosaccharides, the original equation employing true powder density is proposed for conversion of osmolality to osmolarity finally.

### Materials and Methods:

#### Materials

Four different anhydrous monosaccharides (glucose, fructose, mannitol, and sorbitol) of pharmaceutical quality were used. In Table 2, their mol in kg (kgmol) is shown. Water for injection was used throughout the study as the solvent.

#### Methods

All solutes were previously dried in an oven to constant mass according to recommendations of European Pharmacopoeia. Aqueous solutions with molarity in the range of 0.1 – 1.0 mol/l were prepared at  $20 \pm 0.5^\circ\text{C}$  by dissolving of the corresponding gram-molecular weight of solute (with precision of 0.1 mg) in an appropriate volume of water and filling up with water to the total 1.0 litre of solution.

Relative densities  $h$  (kg/l) were measured using a pycnometer at  $20 \pm 0.5^\circ\text{C}$ . The solution density was calculated as the ratio of the mass of solution and the mass of water at the same temperature of measurement. The mean value of five measurements was used. The densities of the mannitol solutions are summarized in Table 1 as the example.

### Results and Discussion:

Pharmaceutical labelling regulations recommend a statement of the osmolarity

(osmol/l). However, osmolarity cannot be measured. Osmometer gives osmolality (osmol/kg). The interconversion between molality and molarity and/or osmolality and osmolarity is, therefore, wanted. To study the relationship between these concentrations, here, aqueous solutions of four parenteral solutes were prepared in the concentration range of 0.1 – 1.0 mol/l. The mass of mannitol  $M$  (kg) required to obtain given molar concentration is illustrated in Table 1 as well as the solution densities  $h$  (kg/l) allowing the calculation of conversion factor  $f$  [2]:

$$f = h - M \quad (2)$$

Conversion factors in range of 0.8797 - 0.9881 were obtained in consequence to the solution concentration changes. To convert molarity to molality, the relationship between molality  $m$  and osmolality  $m_{\text{os}}$  can be shared similarly between molarity  $c$  and osmolarity  $c_{\text{os}}$ . Then, the conversion factor can also be expressed as ratio of solution molarity and its molality [6]:

$$c_{\text{os}} = m_{\text{os}} \cdot \frac{c}{m} \quad (3)$$

following the expression of molality (mol/kg) as ratio of molarity and the conversion factor:

$$m = \frac{c}{f} \quad (4)$$

Using Eq. 1, the experimental molal volume  $V_{\text{exp}}$  was calculated from molarity and molality. Data for the solutions of mannitol of graded molarity are presented in the last column of Table 1. The linear regression was detected between the solution molarity  $c$  (mol/l) and the conversion factor,

$$f = 1 - 0.120 \cdot c \quad (5)$$

as well as between the solution molality  $m$  (mol/kg) and the reciprocal value of conversion factor, respectively:

$$\frac{1}{f} = 1 + 0.120 \cdot m \quad (6)$$

The slopes of linear regressions (5) and (6) are equal to the value of the total molal volume of mannitol  $V_{\text{exp}} = 0.120$  l/mol.

**Table 1:** Estimation of molality by conversion factor for aqueous solutions of mannitol

c (mol/l)	M (kg)	h (kg/l)	f	m (mol/kg)	V <sub>exp</sub> (l/mol)
0.1	0.0182	1,0063	0,9881	0,1012	0.119
0.2	0.0364	1,0125	0,9761	0,2049	0.120
0.3	0.0547	1,0187	0,9640	0,3112	0.120
0.4	0.0729	1,0249	0,9520	0,4202	0.120
0.5	0.0911	1,0310	0,9399	0,5320	0.120
0.6	0.1093	1,0372	0,9279	0,6466	0.120
0.7	0.1275	1,0434	0,9159	0,7643	0.120
0.8	0.1457	1,0496	0,9039	0,8851	0.120
0.9	0.1640	1,0558	0,8918	1,0092	0.120
1.0	0.1822	1,0619	0,8797	1,1368	0.120

**Table 2:** Measured (V<sub>exp</sub>) and estimated (V<sub>m</sub>) molal volume of monosaccharides in aqueous solutions

Solute	Mol (kg)	H (kg/l)	Molal volume (l/mol)		Difference (%)
			V <sub>exp</sub>	V <sub>m</sub>	
Fructose	0.18016	1.580	0.112	0.114	1.8
Glucose	0.18016	1.544	0.112	0.117	4.5
Mannitol	0.18217	1.514	0.120	0.120	0
Sorbitol	0.18217	1.507	0.120	0.121	1.0

As shown in the last column of Table 1, V<sub>exp</sub> of mannitol converged fast to this value. Similarly, the experimental data were processed for the solutions of the other studied monosaccharides. The detected total molal volumes V<sub>exp</sub> are summarized in Table 2.

The experimentally obtained total molal volume could be employed in the interconversion between molality and molarity of the solution considering that the volume of solution is a simple sum of the water and the solute volumes. The additive behaviour in the aqueous solution was observed for all investigated monosaccharides. Thus, two proposed equations could be utilized to change

molarity to molality and conversely molality to molarity as shown below. If the solution molarity is known, then, molality can be calculated as follows:

$$m = \frac{c}{f} = \frac{c}{1 - c \cdot V_{exp}} \quad (7)$$

where number 1 means one litre of solution. Similarly, molarity of the solution can be expressed from its molality:

$$c = m \cdot f = \frac{m}{1 + m \cdot V_{exp}} \quad (8)$$

where number 1 means one kilogram of water.

In practice, the preparation of solution on molal rather than molar concept is much easier and precise as weight-to-weight

relationship is not influenced by temperature changes during dissolution of the solute.

However, determination of the total molal volume of the dissolved solute necessitates measurement at the different solution concentrations. To avoid this, a method, in which the molal volume  $V_m$  of solute in aqueous solution was estimated from its true powder density  $H$ , was also investigated in this work:

$$V_m \approx \frac{\text{kgmol}}{H} \quad (9)$$

In Table 2, true densities  $H$  (kg/l) of the used solutes are listed [7]. The right part of Table 2 compares the measured molal volume ( $V_{exp}$ ) with that calculated using Eq. 9 ( $V_m$ ). Data have shown good correlation. The difference of 4.5% detected for anhydrous glucose probably resulted from the loss on drying. Therefore, glucose monohydrate could be recommended instead. In addition, the molal volume of urea  $V_m = 0.045$  l/mol could also be mentioned here which could be useful in the interconversion between molarity and molality of its high concentration aqueous infusions.

Based on the experimentally obtained results, the original equation (10) employing true density of the powder solute could be recommended wherever the conversion of the experimental osmolality of monosaccharide infusions to the declared osmolarity is wanted:

$$c_{os} \approx \frac{m_{os}}{1 + m_{os} \cdot \frac{\text{kgmol}}{H}} \quad (10)$$

where  $c_{os}$  is osmolarity (osmol/l) and  $m_{os}$  is osmolality (osmol/kg) of the solution.

### Conclusions:

The conversion factor defined as ratio of the solution molarity and its molality is useful to convert osmolality to osmolarity. However, it changes with dilution of solution. In contrast, the total molal volume of dissolved solute was introduced here for monosaccharides, which is not influenced by the solution concentration. Unfortunately, both conversion factor and total molal volume need measurement of the solution density. Then, the estimation of the molal volume of solute from its true powder density was also investigated. As data showed good correlation with those experimentally obtained, finally, the original equation employing true density of the powder has been proposed for conversion osmolality to osmolarity.

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