

Conversion Between Osmolality and Osmolarity of Infusion Solutions

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Abstract

In order to be applied into the body, intravenous fluids should be formulated to have an osmotic pressure similar to that of biological fluids. Physiologic acceptability of large-volume parenteral formulations in clinical practice is largely determined due to the osmotic effect of the dissolved solutes. Therefore, it is generally recommended that the labelling should list osmolarity. However, the declared osmolarity is not consistent with the principle of osmometry which measures osmolality. Then, the conversion of the measured osmolality to declared osmolarity is necessary. The conversion factor, defined as the ratio of molarity and molality of the solution, necessitates the measurement of the solution density and the expression of water content in solution. In this work, the relationship between molarity and molality of the aqueous solutions of nine parenteral solutes is studied. The equations for the interconversion between molarity and molality, employing the experimentally obtained mean molal volume of the dissolved solute, are proposed. The original equation allowing the estimation of the molal volume of the solute in aqueous solution from its true powder density is introduced and recommended for nonelectrolytes as well as the hydrates of electrolytes.

Keywords

Parenteral solutions • Osmolarity • Osmolality • Molal volume

Introduction

Large-volume parenteral preparations should ideally be free of any undesired adverse effects on body tissue and, therefore, the concentration of solutes must be considered in osmotic relationships. To express the concentration of osmotically active particles in the solution, two concepts are generally used: the osmolar concentration (osmolarity, c_{osm}) in osmol per litre of solution and/or the osmolal concentration (osmolality, m_{osm}) in osmol per kilogram of water. The confusion often exists between these terms. The label of infusions is required to state the osmolarity which is simpler and more practical in the delivery of liquid dosage form. In contrast, osmotic pressure of the solution is determined by the total number of particles, regardless of molecular nature, per kilogram of solvent. Thus, osmolality is a practical way of giving an overall measure of the contribution of the various solutes present in a solution to the osmotic pressure of solution. As the biological solutions are mainly water, generally, the difference between osmolarity and osmolality is considered to be acceptably small [1]. However, the clinical importance of careful distinction between these terms should be emphasized.

In general terms, the weight of an osmol is the gram molecular weight of a substance which, when dissolved in one kilogram of water, is osmotically equivalent to one mole of an ideally behaving non-electrolyte dissolved in one kilogram of water [2]. Each osmol of the solute added to 1 kg of water contributes to the osmotic pressure of solution decreasing the freezing point approximately by 1.86° . This physical change is measurable and it permits accurate estimation of osmolality:

$$\text{Eq. 1.} \quad m_{osm} = \frac{\Delta T}{1.86}$$

where T (K) is the absolute temperature, ΔT is the actual freezing point depression of the aqueous solution, and $1.86 \text{ K}\cdot\text{kg}/\text{mol}$ is the freezing point constant of aqueous solution.

It is commonly assumed that the numerical values of osmolarity do not differ significantly from those of osmolality. This assumption may be reasonable in ideal solutions which infer very diluted solutions ($< 0.1 \text{ mol}/\text{kg}$) or infinite dilution. If the concentration increases ($> 0.1 \text{ mol}/\text{kg}$) the conversion of measured osmolality to osmolarity becomes unavoidable. To obtain numerical values of osmolarity, the conversion factor f defined as the ratio of osmolarity and osmolality has been published previously [2–4]. This conversion factor has also been shown to be the difference between the solution density h (kg/l) and the mass of solute M_0 (kg) dissolved in the solution:

$$\text{Eq. 2.} \quad f = \frac{c_{osm}}{m_{osm}} = h - M_0$$

Thus, the conversion factor could also be considered equal to the “concentration of water” in solution or, in another way, to the water content.

Due to mathematical manipulation of the Eq. 2, the osmolarity can be then estimated from the measured osmolality as follows:

$$\text{Eq. 3.} \quad c_{osm} = m_{osm} \cdot f$$

The conversion factor f has also been expressed in terms of the partial molal volume V_{mol} (l/mol) of the dissolved solute at infinite dilution [5, 6]:

$$\text{Eq. 4.} \quad f = h_v (1 - V_{mol})$$

where h_v is the density of water at 25°C (i.e. 0.99707 kg/l). For example, the partial molal volume 0.01663 l/mol has been estimated for sodium chloride and 0.02674 l/mol for potassium chloride. The method employing the partial molal volume is relatively rigorous but it was not recommended for the parenteral mixtures [4]. As the partial molal volume expresses the volume of one mol of solute at infinite dilution, it is not influenced by solution concentration. However, the values of the partial molal volume are difficult to obtain. On the other hand, the molal volume of the dissolved solute at the actual solution concentration V_m (l/mol) can be estimated experimentally by measurement the change in the solution volume when one additional mole of the solute is added as referred for monosaccharides [7].

In this work, the aqueous solutions of nine parenteral solutes were studied. The relationship between molarity c (mol/l) and molality m (mol/kg) in the range of 0.1 to 1.0 mol/l and/or mol/kg, respectively, was investigated in order to convert osmolality to osmolarity. The conversion factor necessitates the measurement of the solution density. Here, the conversion factor in terms of the experimentally obtained mean molal volume of the dissolved solute was investigated instead. In addition, the estimation of the mean molal volume of the solute in aqueous solution from its true powder density was studied in this work.

Results and Discussion

Conversion factor

Generally, the large-volume parenteral formulations should be labelled with the osmolarity (osmol/l). Indeed, osmolarity cannot be measured. Based on theory of colligative properties, osmometer will read osmolality (osmol/kg) which is directly proportional to the total solute concentration expressed in molality (mol/kg). However, labels and leaflets for parenteral fluids state the concentration of dissolved solutes in molarity way (mol/l). The mutual conversion between molality and molarity and/or osmolality and osmolarity, therefore, becomes necessary. In order to investigate the relationship between these concentrations, here, aqueous solutions of nine parenteral solutes were prepared in the concentration range of 0.1–1.0 mol/l (molarity) and/or 0.1–1.0 mol/kg (molality), respectively.

The conversion factor f is required to convert osmolality to osmolarity. Solving this, the relationship observed between molality m and osmolality m_{osm} is shared similarly between molarity c and osmolarity c_{osm} :

$$\text{Eq. 5.} \quad \frac{m}{m_{osm}} = \frac{c}{c_{osm}}$$

Due to the mathematical manipulation, then, the osmolarity can be calculated as follows:

$$\text{Eq. 6.} \quad c_{osm} = m_{osm} \cdot \frac{c}{m}$$

According to the Eq. 3, the ratio c/m constitutes the conversion factor f .

Tab. 1. Data for mutual conversion between molarity and molality of the mannitol solutions

Concentration (mol/l resp. mol/kg)	h_c (kg/l)	f	h_m (kg/l)	V (l)	V_m (l/mol)
0.1	1.0062	0.9880	1.0060	1.0121	0.1210
0.2	1.0124	0.9760	1.0120	1.0241	0.1205
0.3	1.0185	0.9638	1.0178	1.0363	0.1210
0.4	1.0247	0.9518	1.0235	1.0483	0.1208
0.5	1.0309	0.9398	1.0290	1.0603	0.1206
0.6	1.0371	0.9278	1.0345	1.0723	0.1205
0.7	1.0432	0.9157	1.0398	1.0843	0.1204
0.8	1.0494	0.9037	1.0450	1.0964	0.1205
0.9	1.0556	0.8916	1.0501	1.1085	0.1206
1.0	1.0618	0.8796	1.0551	1.1205	0.1205

Preparing solutions in molarity way, the conversion factor was determined using the Eq. 2 as the difference between the measured density of the solution h_c (kg/l) and the dissolved solute mass M_0 (kg) [4]. The ratio of the solution molarity c (mol/l) and the factor of conversion (c/f) gives the solution molality m (mol/kg). For the mannitol solutions, the experimental data for the molality estimation are illustrated in the left part of Table 1. The relationship between the conversion factor and molarity of the mannitol solutions was described by the linear regression with the coefficient of correlation $r = -0.9999$:

$$\text{Eq. 7.} \quad f = 1 - 0.1204 \cdot c$$

The slope of the linear regression (Eq. 7) allowed the mean molal volume of mannitol $V_m = 0.1204$ l/mol could be estimated. At the actual concentration, the molal volume of the solute dissolved in the solution could be calculated from the solution molarity and molality [7]:

$$\text{Eq. 8.} \quad V_m = \frac{m - c}{m \cdot c}$$

In solutions prepared in molality way, the total mass of solution M (kg) is the sum of the dissolved solute mass and the water mass which in our experiments always constituted one kilogram. To convert molality to molarity, the volume of the solution V (l) is essential. This can be calculated as the ratio of the solution mass and the solution density h_m (kg/l). Afterwards, molarity of the solution can be estimated as the ratio of the solution molality and its volume (m/V). For the mannitol solutions again, the right part of Table 1 illustrates the experimental data for the molarity estimation.

In survey, the conversion of molarity to molality necessitates the conversion factor while the solution volume is wanted for the conversion of molality to molarity; both conversions require the measurement of the solution density.

Molal volume

As noted above, the experimental measurements are essential to obtain the solution density since the routine label of large-volume parenteral preparations does not state it. The method employing the partial molal volume of the solute was also recommended in solving of the interconversion between osmolarity and osmolality [5, 6]. As defined at infinite dilution, where concentration tends to zero, the partial molal volume is not influenced by the concentration of solution. In a wide range of concentration, however, the dependence of the partial molal volume on the partial molal fraction of the solution is not linear. Nevertheless, this non-linear relationship is generally considered to be approximately linear in a narrow concentration range. In this work, the relationship between the molal volume of the dissolved solute and the concentration of the aqueous solution (molarity and/or molality) was studied in the concentration range of 0.1–1.0 mol/l and/or mol/kg, respectively.

Generally, the total volume of solution constitutes of water volume and the volume of the dissolved solute. Each particle dissolved in water decreases the water particles by a given amount; the more solute particles, the lower water content will be. The water content, thus, reflects the molal volume of dissolved solute [5]. Because the water content in solution was shown to be equal to the conversion factor f [4], on the other hand, using the conversion factor, the molal volume of the solute could be estimated.

Assuming one litre of the solution of given molarity c , thus, the conversion factor f can be expressed in terms of the solute molal volume V_m due to the mathematical manipulation of Eq. 4 as follows:

$$\text{Eq. 9.} \quad f = \frac{c}{m} = 1 - (c \cdot V_m)$$

If the solution volume remains constant the molal volume of the solute expresses the decrease in the water content in the solution of given molarity.

In solution of the given molality m , constituted of one kilogram of water, similarly, the molal volume V_m of the solute dissolved influences the solution volume V according to:

$$\text{Eq. 10.} \quad V = 1 + (m \cdot V_m)$$

If the water content remains constant the increase in the volume of the solution of given molality corresponds to the molal volume of the solute. As the example, Table 1 is completed with the values of the molal volume of mannitol, V_m (l/mol), determined at the actual solution molality as follows:

$$\text{Eq. 11. } V_m = \frac{V-1}{m}$$

where V is the volume of solution in litre and m is the solution molality in mol/kg. From the experimentally obtained data, the mean molal volume 0.1206 l/mol was detected for mannitol. Comparing this value with that of 0.1204 l/mol, obtained as the numerical slope of the linear regression (Eq. 7), no significant differences were observed. This indicated that the mean molal volume of the solute can be estimated either from the solution molarity and/or molality, respectively, with comparable results. From a practical aspect, however, the preparation of solution on molal rather than molar concept is more precise as weight-to-weight relationship is not influenced by temperature changes during dissolution of the solute.

Tab. 2. Estimation of molal volume V_m of investigated solutes from true density H

Solute	Mol (kg)	H (kg/l)	Estimated V_m (l/mol)	Measured V_m (l/mol)
Glucose (G)	0.18016	1.54	0.117	0.112
Fructose (F)	0.18016	1.67	0.108	0.112
Sorbitol (S)	0.18217	1.49	0.122	0.120
Mannitol (M)	0.18217	1.52	0.120	0.121
Sodium chloride (SC)	0.05844	2.17	(0.027)	0.019
Potassium chloride (PC)	0.07455	1.98	(0.038)	0.029
Calcium chloride (CC)	0.21908	1.68	0.130	0.132
Magnesium chloride (MC)	0.20331	1.56	0.130	0.128
Sodium acetate (SA)	0.13608	1.45	0.094	0.095

The approximately linear relationships between the experimentally obtained values of molal volume and concentration of solution of all investigated parenteral solutes were observed. In conclusion, therefore, they were characterized with their experimentally obtained mean molal volumes in Table 2. The relationship between the measured V_m and the molecular weights (mol, in kg) of the solutes was described by the non-linear regression (Eq. 12) and it is shown in Figure 1.

$$\text{Eq. 12. } V_m = 0.0902 \cdot \ln(\text{mol}) + 0.2707$$

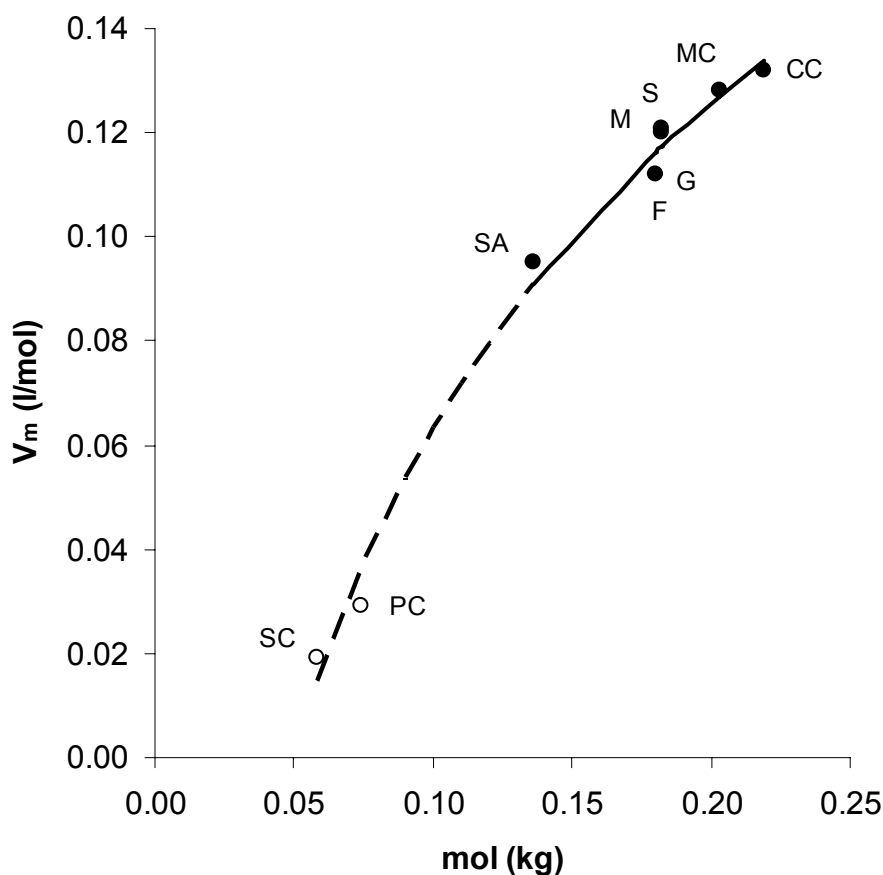


Fig. 1. Relationship between mean molal volume (V_m) and mol of solute (sodium chloride SC, potassium chloride PC, magnesium chloride MC, calcium chloride CC, sodium acetate SA, Sorbitol S, mannitol M, glucose G, fructose F)

The full curve shows data for saccharides and the hydrates of electrolytes in the upper part of the Figure 1. The downwards dashed curve continues out of the coordinate origin describing the relationship for the strong electrolytes sodium chloride (SC) and potassium chloride (PC) plotted with empty dots. It can be seen that the mean molal volumes of sodium chloride and potassium chloride are lower than they might be. This assertion can be verified due to the linear extrapolation of the full upper part of the curve in Figure 1 to the coordinate origin and plotting, for example, urea, which with its mol = 0.060 kg and the mean molal volume $V_m = 0.044$ l/mol, will be located on that extrapolated line.

In survey, considering that the volume of solution is a simple sum of both the water and the solute volumes, the experimentally obtained mean molal volume could be employed in the interconversion between molality and molarity by using two proposed equations:

$$\text{Eq. 13.} \quad m = \frac{c}{1 - (c \cdot V_m)}$$

$$\text{Eq. 14.} \quad c = \frac{m}{1 + (m \cdot V_m)}$$

which allow the Eq. 8, previously referred for monosaccharides [7], can be derived. This presumption cannot be accepted for strong electrolytes when the volume of the solution decreases during dissolution.

To use the proposed equations 13 and 14, however, the mean molal volume of dissolved solute necessitates the measurement of the molal volume at given solution concentration as these values are difficult to obtain. A method, in which the mean molal volume V_m of solutes in aqueous solutions was estimated from their true powder density H , was investigated in this work:

Eq. 15.
$$V_m \approx \frac{\text{mol}}{H}$$

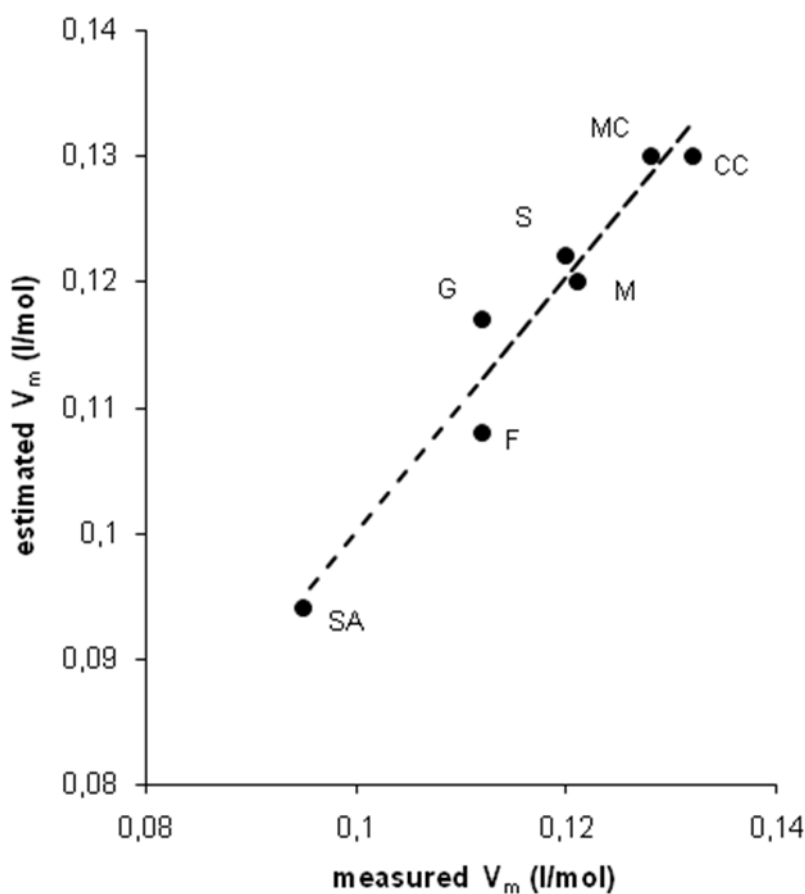


Fig. 2. Comparison of measured and estimated molal volumes (V_m) of solutes (magnesium chloride MC, calcium chloride CC, sodium acetate SA, sorbitol S, mannitol M, glucose G, fructose F)

In Table 2, true densities H (kg/l) of used solutes are listed. The right part of Table 2 compares the experimentally obtained V_m -values (Eq. 11) with those estimated using Eq. 15. Results are illustrated in Figure 2. For monosaccharides and, surprisingly, also for the hydrates of electrolytes (sodium acetate trihydrate, calcium chloride hexahydrate, and magnesium chloride hexahydrate), data have shown good correlation. The average V_m -

value estimated (0.1173 l/mol) did not differ from that experimentally obtained (0.1171 l/mol). In case of the strong electrolytes sodium chloride and potassium chloride, the measured V_m were much lower than those estimated using Eq. 15. In the middle part of Table 2, thus, they are shown in brackets.

Conclusions

As observed experimentally, the influence of the solution concentration within the range of 0.1 to 1.0 mol/l and/or mol/kg, respectively, on the molal volume of studied nine parenteral solutes was not significant. Therefore, the changes of the solution volume resulting from the solute dissolution could be characterized in terms of the mean molal volume.

In order to convert the measured osmolality to the declared osmolarity, the conversion factor, defined as the ratio of solution molarity and its molality, is essential. The conversion necessitates the measurement of solution density. In this work was shown that, instead, the mean molal volume of solute could also be used wherever density of the solution is not available.

A method, in which the mean molal volume of solutes in aqueous solutions was estimated from their true powder density H , was proposed in this work. As the values of the mean molal volume estimated was close to those experimentally obtained, the method could be recommended in case of non-electrolytes (glucose, fructose, sorbitol, and mannitol) and/or hydrates of electrolytes (calcium chloride, magnesium chloride, sodium acetate). However, that estimation could not be applied to the strong electrolytes sodium chloride and potassium chloride where the lower measured values than those estimated are preferable.

Experimental

Materials

Monosaccharides (glucose, fructose, mannitol, and sorbitol) and/or electrolytes (sodium chloride, potassium chloride, calcium chloride hexahydrate, magnesium chloride hexahydrate, and sodium acetate trihydrate) of pharmaceutical quality were used.

Preparation of solutions

In concentration range of 0.1–1.0 mol/l and/or mol/kg, respectively, aqueous solutions of nine solutes were prepared at $20 \pm 0.5^\circ\text{C}$. In molarity way, the solutions were prepared 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. In molality way, the solutions were prepared by dissolving of the corresponding gram molecular weight of solute (with precision of 0.1 mg) in 1.0 kg of water. The purified water was used throughout the study.

Measurement of density

Density in kg per litre of all prepared aqueous solutions of the investigated solutes was measured with 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 is presented in Table 1 either as h_c when preparing solutions in molarity way or h_m when preparing solutions in molality way, respectively.

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Authors' Statement

Competing Interests

The authors declare no conflict of interest.

References

- [1] Campbell I.
Osmolarity and partitioning of fluids.
Surgery. 2004; 22: 48c–48e.
doi:10.1383/surg.22.2.48.27923
- [2] Reich I, Poon CY, Sugita ET.
Toncity, osmoticity, osmolality and osmolarity.
In: Limmer D (ed.): Remington: The science and practice of pharmacy. 20th ed.
Philadelphia: Lippincott Williams & Wilkins, 2000: 248–249.
- [3] Murty BSR, Kapoor JN, De Luca PP.
Compliance with USP osmolarity labeling requirements.
Am J Hosp Pharm. 1976; 33: 546–551.
PMid:1274973
- [4] Gatlin L, Kulkarni P, Hussain A, DeLuca PP.
Determining osmolarities. A practical approach for multicomponent intravenous and parenteral nutrient solutions.
Am J Health Syst Pharm. 1979; 36: 1357–1361.
PMid:116545
- [5] Streng WH, Huber HE, Carstensen JT.
Relationship between osmolality and osmolarity.
J Pharm Sci. 1978; 67: 384–386.
doi:10.1002/jps.2600670330
- [6] Huber HE, Streng WH, Tan HGH.
Osmolality of parenteral solutions.
J Pharm Sci. 1979; 68: 1028–1032.
doi:10.1002/jps.2600680829
- [7] Zatloukal Z.
[Estimation of osmotic pressure of infusion solutions of monosaccharides].
Ceska Slov Farm. 1994; 43: 125–127.