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## Temperature dependence of the molality of some pharmaceutical solutions

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The chemical structure of solutions as well as the number of molecules and ions in solution are changing with the temperature especially in preparations containing several components [1, 2]. This effect has significance particularly for isotonic water eye drops, injections and infusion solutions. Colligative properties of solutions occurring as consequence of intermolecular effects can be studied by means of a suitable electro-thermoosmometer [3, 4]. In solutions of some pharmaceutical molecules, association/dissociation processes take place. In this cases at temperature change the molality of solution is changed. The molality of a preparation at the freezing point can be different from that measured at 37 °C due to the temperature dependence of the association/dissociation processes.

In the present study the temperature dependence of the molality of some commercially available infusion solutions, eye drops and infusion preparations containing dextrans of various average molecular weights have been investigated. For determining molecular concentrations, a calibration curve has been plotted by means of 5–6 sodium chloride standard aqueous solutions with a molality between 0.01 and 1.00 Osm/l. The molality of an unknown solution was taken from the calibration curve on the basis of the scale.

**Table: Molality of some pharmaceutical solutions measured with a cryoscope (at 0 °C) and with a thermoosmometer (at 37 °C)**

Preparations		Molality (mOsm/l)	
		0 °C	37 °C
Infusions:	Sodium lactate	258.0	122.6
	Sodium lactate/lactic acid	206.9	90.7
Eye drops:	Normastigmin <sup>®</sup> with pilocarpine	472.0	282.3
	Atropine	258.0	198.5
	Neomycin	311.2	125.0
	Rifampicin	302.9	75.0

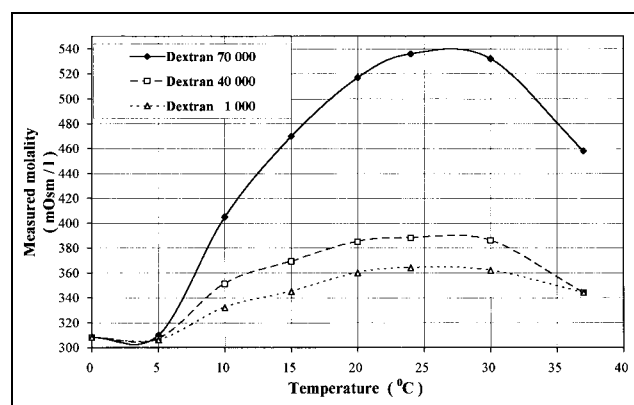


Fig.: Temperature dependence of the molality of infusion solutions containing dextran

Molality values measured with the cryoscope (0 °C) and the thermoosmometer (37 °C) are given in the Table. Differences between the values can be well seen. When investigating infusion solutions containing dextrans of various average molecular weights it was found that the molality of the solutions increased with increasing temperature but decreased at temperatures >25 °C (Fig.). The increase was more stressed in the case of solutions containing dextran of higher average molecular weight. This can be explained with the fact that large molecules disintegrate to smaller ones. A decreasing range indicates association as the contrary process.

Consequently it can be stated that molality of certain pharmaceutical preparations can change during storage or in the place of application.

## Experimental

### 1. Materials

Infusions containing sodium lactate/lactic acid, dextran 1000, dextran 40000 or dextran 70000. Eye drops containing Normastigmin<sup>®</sup> with pilocarpine, atropine, neomycin or rifampicin and sodium chloride solution series for calibration.

### 2. Methods

#### 2.1. Freezing point decrease

The osmomolality of a solution related to a given temperature can be calculated from the freezing point decrease determined experimentally by a Cryoscope Apparatus (SOTE, Budapest) [5] on a diluted solution of known concentration of a material of known molecular weight.

Freeze-point decrease is proportional to the molality:

$$\Delta T = \Delta T_M \cdot c \quad (1)$$

$$c(\text{Osm/l}) = \Delta T / 1.86 \quad (2)$$

where  $\Delta T$  = freezing point decrease of the solution (K or °C),  $\Delta T_M$  = molar freeze-point decrease and  $c$  = molality that is number of molecules dissolved in 1000 g of solvent.

#### 2.2. Thermoosmometry

One standard hanging drop and one sample hanging drop was applied onto the thermistors of Digital Thermoosmometer (KKI, Budapest) [4].

## References

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