COLLEGE OF PHARMACY

STERILE PRODUCTS
PHT 434

ADJUSTMENT OF TONICITY OF PARENTERAL SOLUTIONS BY FREEZING POINT DEPRESSION METHOD

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OBJECTIVE OF LABORATORY

- *Adjustment of tonicity of parenteral solutions / electrolytes using freezing point depression method (FPD method).*

Freezing point depression method

- Freezing point of blood / tears or other body tissue is approximately -0.52
- Freezing point of water is zero.
- Whenever any drug or electrolyte is added in water, the freezing point of water will decrease.
- Therefore, this method depends freezing point depression (Δ T) because of drug (**Table)**

Freezing point depression method

Solution, 1% w/v drug	ΔT_f, °C
Apomorphine hydrochloride	0.08
Boric acid	0.29
Calcium gluconate	0.09
Pilocarpine nitrate	0.14
Potassium chloride	0.45
Sodium chloride	0.58
Sodium sulphacetamide	0.14

Freezing point depression method

- FPD (Δ T) value as given in table means 1% of drug solution causes this much of depression in freezing point.
- As freezing point of blood or other isotonic solution is 0.52 so we can calculate % amount of drug which will cause FPD of 0.52 (means this solution will be isotonic)
- For example if 1% of drug cause FPD of 0.3 ((Δ T=0.3) then x % will cause a depression of 0.52
- X= (0.52/Δ T) 1% = 0.52/0.3= 1.73
- i.e 1.73 % of this drug will be isotonic.
- For dextrose Δ T=0.1, i.e. 1% dextrose causes FPD of 0.1
- % of dextrose which will be isotonic?
- X= (0.52/Δ T) 1% = 0.52/0.1= 5.2% dextrose.

Freezing point depression method

- Adjustment of tonicity by FPD method depends on freezing point depression because of drug /substances. (**Table)**
- This value is subtracted from 0.52 (isotonic)
- Remaining FPD is achieved by **addition of adjusting substance** to make the final solution isotonic with blood.

$$w\% = \frac{0.52 - a}{b}$$

Freezing point depression method

$$w\% = \frac{0.52 - a}{b}$$

$w\%$ = conc. gm/100 ml of adjusting substance.

a = FPD of 1% of unadjusted substance(table)
X percentage strength

b = FPD of 1% of adjusting substance (table)

Freezing point depression method

- Prepare and supply 0.5% isotonic solutions of Major body electrolytes (Na, K, Ca Mg, Cl, & phosphate) by using available solutes in the laboratory.
- Write procedure in brief.
- Solute used as electrolyte /drug
- Solute used as adjusting substance
- Calculation steps
- Final amount of both solutes used to prepare isotonic solution.

Freezing point depression method

ΔTf 1% Sucrose = 0.06 °C
ΔTf 1% Dextrose = 0.101 °C
ΔTf 1% Ascorbic acid = 0.105 °C
ΔTf 1% Citric acid = 0.11 °C
ΔTf 1% $ZnSO_4$= 0.15 °C
ΔTf 1% $MgSO_4$= 0.19 °C
ΔTf 1% Sodium citrate = 0.2 °C
ΔTf 1% $BaCl_2$ = 0.23 °C
ΔTf 1% Boric acid = 0.29 °C
ΔTf 1% Na_2SO_4= 0.32 °C
ΔTf 1% $(NH_{4)2}SO_4$= 0.33 °C
ΔTf 1% Na_3PO_4= 0.37 °C
ΔTf 1% $NaHCO_3$= 0.38 °C
ΔTf 1% $CaCl_2$= 0.44 °C
ΔTf 1% KCl= 0.46 °C
ΔTf 1% $MgCl_2$= 0.52 °C
ΔTf 1% NaCl = 0.58 °C

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ΔTf 1% Dextrose = 0.101 °C
ΔTf 1% KCl= 0.46 °C
ΔTf 1% $MgCl_2$= 0.52 °C
ΔTf 1% $MgSO_4$= 0.19 °C
ΔTf 1% Na_2SO_4= 0.32 °C
ΔTf 1% Na_3PO_4= 0.37 °C
ΔTf 1% NaCl = 0.58 °C
ΔTf 1% $NaHCO_3$= 0.38 °C
ΔTf 1% Sodium citrate = 0.2 °C
ΔTf 1% Sucrose = 0.06 °C
ΔTf 1% $ZnSO_4$= 0.15 °C

Freezing point depression method

- IF FPD (Δ T) value is not provided then it can be calculated.
- $\Delta T = i K_f m$
- i : van 't Hoff factor, unitless constant directly associated with the degree of dissociation of the solute in the solvent.
- Substances which do not ionize in solution, like DEXTROSE, GLUCOSE, have i = 1.
- Substances ionizing into two ions, like NaCl, have i = 2.
- Substances ionizing into three ions, like $MgCl_2$, have i = 3.
- **Note 1:** Ion pairing effect lowers the i values for example NaCl has an actual i = 1.8 because of ion pairing.
- **Note 2:** Substances that ionize ***partially*** in solution will have i values between 1 and 2 usually.

Freezing point depression method

- $\Delta T = i K_f m$
- Take a 1.0-molal solution of sugar and measure its FPD. Now examine a 1.0-molal solution of NaCl and $MgCl_2$,. FPD will be two times and three times that of sugar NaCl and $MgCl_2$ respectively as 2 ions and 3 ions in these solutes
- K_f is cryoscopic constant. The Greek prefix cryo- means "cold" or "freezing." In a more generic way, it is called the "**molal freezing point depression constant**."
- Unit of K_f is °C kg/mol
- m: molality of solution, i.e. number of moles of solute per kg solvent.
- **Note 2:** Substances that ionize ***partially*** in solution will have i values between 1 and 2 usually.

THANK YOU FOR ATTENTION

GOOD LUCK ..