COLLOIDAL OSMOSIS - ONCOTIC PRESSURE

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Definition of Osmosis and Related Terms

• Osmosis is the net water flow between two compartments separated by a semi-permeable membrane. Such a membrane allows the passage of water (solvent) but none of the other substances (solutes) that are dissolved in water such as salt, etc. (solutes).

• Osmotic flow occurs in the absence of hydrostatic pressure differences. Osmotic pressure is the hydrostatic pressure difference between the compartments that will stop the osmotic flow of water by creating an opposite hydraulic flow of the same magnitude.

• Osmolality (or osmolarity) is a measure of the osmotic pressure in concentration related terms. 1 mOsm/kg (milli-osmole per kilogram) is equivalent to 18.6 mmHg osmotic pressure at room temperature in dilute crystalloid solutions according to the van’t Hoff law.

REMARK: Osmolality is one of the colligative properties of solutions which depend on only the number of dissolved particles (molecules, ions) in a unit volume of the solution (or unit weight of the solvent) but is not affected by the chemical nature of the solutes.

Oncotic Pressure

Oncotic pressure results from the presence of large particles (colloids) in solution. Usually the number of particles per volume, due to their size, is much smaller, thus the colloidal osmotic effect is much smaller.

• The colloidal osmotic (oncotic) pressure is known to play a major role in the maintenance of water balance of bodily tissues as first quantitated by E.H. Starling in 1896. Again, oncotic pressure means the magnitude of hydrostatic pressure needed to stop the colloidal osmotic flow. A relevant example is concerned with preventing water loss from capillary vessels due to blood pressure which tends to force water through the vessel walls into the tissue. The oncotic pressure of proteins in the blood, however, tends to induce water flow into the vessel. When the blood pressure exceeds the oncotic pressure of the plasma, tissue edema occurs in the surrounding tissue.

• Oncotic pressure can induce fluid flow even when no semi-permeable membrane is present, or when the membrane had been damaged and has become leaky.

• Macromolecules, including proteins, are often electrically charged at neutral pHs. In such cases, the Gibbs-Donnan potential (due to uneven distribution of ions) may contribute significantly to the oncotic pressure.

Cornea and Imbibition Pressure

• The cornea mainly consists of a connective tissue, the stroma; its exterior surface is protected by the epithelium and its interior surface by a single endothelial cell layer.

• The stroma is partially dehydrated which keeps the tissue transparent. The imbibition pressure (~40 mmHg) is the oncotic pressure of collagen fibrils and ground substance in the stroma.
• The five cell layer thick epithelium provides the semi-permeable membrane. The endothelial layer keeps the tissue partially dehydrated.

• The cornea is also under tension due to the intraocular pressure (15 – 20 mmHg). This tension favors the transport of water out of the cornea.

**Corneal Epithelium - Is it semi-permeable?**

• An intact corneal epithelium is an imperfect semi-permeable membrane. This provides for the efficacy of hypertonic (5%) salt solutions instilled in the eye to remove water.

• In a dry eye, the epithelial layer is often damaged, mostly due to impaired hydrodynamic lubrication or prior refractive surgery. This causes a loss of semi-permeability in the epithelium.

• The use of hypertonic salt solution is ill advised in such an eye as it can no longer remove water as salt enters the cornea. Increased tonicity may then even destroy keratocytes of the stroma.

• Topically applied aqueous solutions with an oncotic pressure of 65 mmHg will remove excess water from the stroma even in the absence of an epithelium.

**WHY 65 mmHg?**

• We have seen that the imbibition pressure of the stroma is -40 mmHg. Negative sign indicates that it is attempting to move water from the tears, so it has to be overcome by the oncotic pressure of the eye drop.

• The intraocular pressure of the eye is contained by the sclera and the cornea, most of the tension change occurs in the stroma. This partially supports the hydraulic flow to the tears by about 15 mmHg.

• Excess water is present in the loose and often damaged epithelium in the form of microcystic edema.

• Excess water can also accumulate along the basement membrane forming a weak boundary layer leading to diminished adhesion and to recurrent erosion.

• Oncotic pressure between 60 to 70 mmHg has to be achieved by careful selection of polymers with a certain molecular size and concentration without enhancing the viscosity of the formulation above a level harmful to the lid - globe interfaces.

**Osmosis in Life Processes**

• When the osmolality of body fluids is measured, the total osmolality = crystalloid + colloid. Total osmolality is mostly crystalloid as the colloid component is much smaller, less than 0.5 % of the total.

• Ironically, osmotic flow almost anywhere in the body is colloidal osmosis, i.e. the water balance (homeostasis) is governed by the oncotic pressure of bodily fluids.

• Biological membranes are permeable to small molecules and ions. Thus only large molecules are able to create an osmotic effect in the body.

• This renders osmolality measurements irrelevant unless oncotic pressure is directly measured across a membrane with porosity similar to biological membranes.
OSMOLALITY OF AQUEOUS TEARS

The total osmolality of the aqueous tears determined by the freezing point depression (300 mOsm/kg) has received much attention in the past thirty years. Since the oncotic pressure of tears (2 mmHg) is less than 0.1% of the total osmotic pressure of tears (5,450 mmHg), the colloidal osmolality of the tears has received practically no attention. Some other numbers:

- Colloidal osmolality of the tears is twenty-fold less than that of the corneal stroma
- Colloidal osmolality of the stroma is less than 1% of the total osmolality of isotonic saline

The high theoretical values of the crystalloid osmotic pressure are misleading as the osmotic process does not exist in the absence of semi-permeable membranes.

So, despite its small relative magnitude, the oncotic pressure plays a major role in the homeostasis of water in the body.

Corneal Epithelium

- The corneal epithelium is non-keratinized and thus transparent. When intact, this tissue is able to act as an imperfect semi-permeable membrane as the mobility of small molecules and ions across the tissue is considerably lower than that of water.
- This is why hypertonic salt solutions (5%) topically applied are able to withdraw water from the stroma as long as the epithelium is intact.
- With dry eye, the epithelium is usually water-logged and loses its semi-permeability. The use of hypertonic salt solutions is contraindicated in such eyes as they are dysfunctional and excess salt in the stroma is harmful to the keratocytes.
- For this reason, only isotonic solutions with high oncotic pressure are able to provide for the removal of excess water.

Clinical Advantage of Excess Water Removal

- Excess water in the corneal epithelium weakens tissue integrity (microcystic edema) and may accumulate along the basement membrane forming a weak boundary layer. This latter occurrence is thought to be the primary reason for spontaneously and repeatedly occurring epithelial erosion.
- Damage to the epithelium may occur if the hydrodynamic lubrication of the lid is impaired due to tear layer instability under the lids. Refractive surgery can be harmful to epithelial integrity which can be further exacerbated by interfering with the normal hydrodynamic lubrication mechanism of the lid by the use of ophthalmic ointments.
- Loosened epithelium also has less than complete wetability by tears leading to tear film instability, a major factor in the pathogenesis of the dry eye syndrome in more than 2/3rd of dry eye patients.

Thus, when epitheliopathy of the corneal surface is present, the prescription of an ophthalmic lubricant with high oncotic pressure is clearly indicated, while hypertonic formulations should be avoided.

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