# UNIT 8 MAINTENANCE OF BODY HOMEOSTASIS

**Structure**



## 8.1 INTRODUCTION

In this unit, we will study about body homeostasis and different types of body fluids. Homeostasis, as you would realize, is *a dynamic process that enables optimum conditions to be maintained for constituent cells*. It involves all the systems of the human body, such as endocrine, nervous, respiratory and renal systems. The most common example is the regulation of salt and water balance. In the previous unit we got to know how the kidneys play an important role in maintaining water content of the body.

The advantage of homeostasis is that the organism can adjust to changes without its component cells being adversely affected since their needs are met by the controlled internal environment. A possible disadvantage is that it requires the organism to invest effort into maintaining internal stability. For example, additional energy is required to maintain a warm body temperature in a cooler external environment. The concept of homeostasis is discussed in this unit.

Body fluids, on the other hand, are of different types and play a major role in maintaining homeostasis. In this unit we shall learn about the different body fluids and their role in homeostasis. Further, the methods used to measure and calculate these fluids will be discussed.

**Objectives**

After studying this unit, you will be able to:

- explain the concept of body homeostasis,
- enumerate the different body fluids essential to maintain body homeostasis,
- discuss various transport systems in the body, and
- describe body fluids and the methods of measuring and calculating these.

## 8.2 HOMEOSTASIS – AN INTRODUCTION

All the cells in our bodies are surrounded by a liquid called *tissue fluid* which has exactly the right conditions in which cells can work. Tissue fluid has the right temperature, the right amount of glucose and the right amounts of water and salt. How is this possible? *Homeostasis* is the important process that maintains these conditions at the right level.

Homeostasis is a term coined in 1959 to describe the physical and chemical parameters that an organism must maintain to allow proper functioning of its component cells, tissues, organs and organ systems. It is *the maintenance of equilibrium or constant conditions in a biological system by means of automatic mechanisms that counteract influences tending toward disequilibrium*. In simple terms, homeostasis is the state of sustained equilibrium in which all cells, and all life forms, exist.

An organism in homeostasis adapts to changed environmental conditions by adjusting its own internal state, for example, cold-blooded animals and warm-blooded animals that hibernate, adjust to colder temperatures by changing their own internal temperature, so that their entire system may remain in homeostasis. This ability to maintain a relatively constant internal environment is homeostasis.

With this basic understanding of homeostasis, let us learn about the body fluids next.

## 8.3 BODY FLUIDS

Earth, the motherly planet, has three-fourths of water. This makes the planet very special for every living organism to prosper and survive. Incidentally, one can observe that any organism, which is surviving on this planet, has 70% of water as an average content in its cell. This is applicable to both-unicellular and multi-cellular organisms.

The total amount of water in a 70 kg man is 42 litres, averaging 60% of his body weight. In a newborn infant, this may be as high as 75% of the body weight, but progressively decreases from birth to old age, with most of the decrease occurring in the first 10 years of life. Also, obesity decreases the percentage of water in the body, sometimes down to as low as 45%. This proportion is higher in young people and in adults. It is lower in elderly and obese people of all age groups. Of the total body water, it is interesting to note that about 20% is extracellular water and the remaining 40% is intracellular water.

The extracellular fluid consists of fluid in the blood and lymph vessels, cerebrospinal fluid and fluid in the interstitial spaces of the body. Interstitial fluids or tissue fluids bathes all cells of the body.

From our discussion above, we realize that there are certain fluid compartments in our body. These include the intracellular fluid and the extracellular fluid compartment. Let us get to understand each of these.

### 8.3.1 Intracellular Fluid Compartment

About 25 to 40 litres of fluid in the body are inside 100 trillion cells of the body and are collectively called *intracellular fluid*. Figure 8.1 presents the distribution of the intracellular fluid in the body. The fluid of each cell contains its own individual mixture of different constituents, but the concentrations of these constituents are reasonably similar from one cell to another.

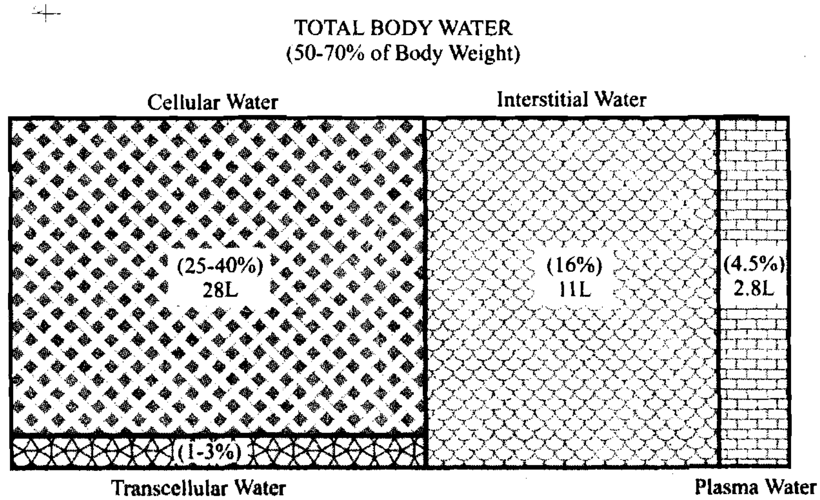


**Figure 8.1: Fluid compartments in the body**

## 8.3.2 Extracellular Fluid Compartment

All fluids outside the cells are called *extracellular fluids* and these fluids are constantly mixing. The total amount of fluid in the extracellular compartment averages 15 litres in a 70 kg adult.

The extracellular fluid can be divided into interstitial fluid, plasma, transcellular fluid which includes cerebrospinal fluid, fluids of the gastrointestinal tract and the potential spaces as highlighted in Figure 8.2. Let us learn about these, next.

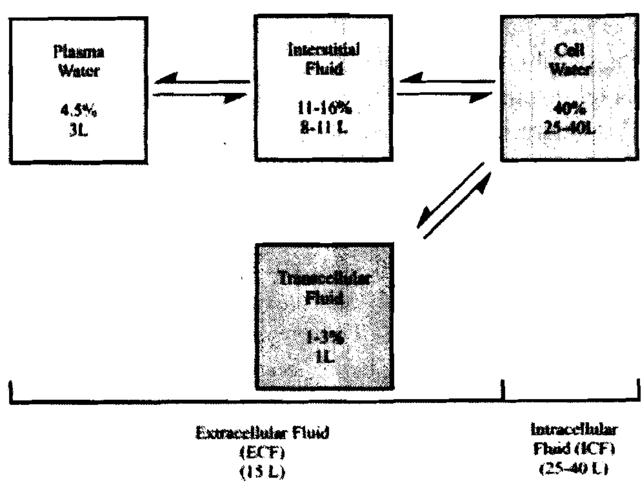


**Figure 8.2: Distribution of total body water**

a) *Interstitial fluid*

The interstitial fluid lies in the spaces between the cells. A small portion of it is free in the form of actual flowing fluid whereas the major portion is held tightly by hydrated substances in the interstitial spaces.

b) *Plasma*

The plasma, as you may already know, is the *non-cellular portion of blood.* Yes, it is an extracellular fluid. It communicates continuously with the interstitial fluid through pores in the capillaries. The plasma volume averages 3 litres in the normal adult.

c) *Fluid in other extracellular spaces*

*The cerebrospinal fluid* comprises all the fluid in the ventricles of the brain and in the subarachnoid spaces surrounding both – the brain and the spinal cord. *Intraocular* *fluid* is the fluid in the eyes and has properties similar to those of the cerebrospinal fluid and this fluid is a product of diffusion and secretions. All these fluids get classified as transcellular fluid as highlighted in Figure 8.2, which is a subdivision of the extracellular compartment. *Synovial fluid* in the joints, *glandular secretions* and *serous fluid* within the body cavities are all transcellular compartments.

Many spaces exist in the body that normally contain little fluid but under special conditions can become filled with large amounts. These are called *potential spaces*. An example of potential space is the space between visceral and parietal pleurae of the lungs. Normally, only 10 to 15 ml of fluid is present in the space, but under abnormal circumstances, the amount can become as great as several litres.

A moderate amount of extracellular fluid is normally in the *gastrointestinal tract.*

We have looked at the extracellular and intracellular fluid compartments in our body. You would realize that there is a tight control of the distribution of total body water between body compartments. Interestingly, these compartments remain in equilibrium with one another so that any changes in the osmolality of a compartment will result in the movement of water to maintain equal osmolality.

Blood, you would realize, contains both extracellular fluid (fluid of the plasma) and intracellular fluid (the fluid in the blood cells). The average blood volume of a normal adult is almost exactly 5 litres. On an average, approximately 3 litres of this is plasma and the remaining 2 litres is blood cells. However, these values vary greatly in different individuals and also depend on sex, weight and many other factors affecting the blood volume.

The percentage of red blood cell in the body is called the *haematocrit*. You may recall reading about this earlier in unit 2 as well. It is determined by centrifuging the blood in the 'haematocrit tubes' until the cells become packed tightly in the bottom of these tubes. The percentage of red blood cells in the blood can be determined roughly from the levels of the packed cells. Unfortunately, it is impossible for the red blood cells to be packed completely together, about 3 to 8% plasma remains entrapped among the cells. Therefore, the true cell percentage (H) averages about 96% of the measured haematocrit (Hct).

$$H = 0.96 \text{ Hct}$$

The normal hematocrit (H) is approximately 40 for a man and 36 for a woman. In severe anaemia, the haemaocrit may fall to as low as 10 but this small quantity of red blood cells is barely sufficient to sustain life. On the other hand, a few conditions like *polycythemia* (haematocrit rises to 65 and occasionally to 80) causes an increase in haematocrit due to excessive production of red blood cells. However, excessive haematocrit causes the blood to become so viscous that death results because of multiple plugging of the peripheral vascular tree.

With the discussion above, we hope you have a clear idea about the body fluid compartments. We read earlier that the total body water in adults of average built is about 60% of body weight. Do you know how the body water is measured or for that matter, how the body fluid is measured? The next section focuses on this aspect. Let us get to know about this.

## 8.4 MEASUREMENT OF BODY FLUID VOLUMES

In this section, we shall learn about the principles and techniques involved in measuring body fluid volumes. We shall get to know how the total body water is measured. How do we calculate the interstitial fluid volume and extracellular fluid volume? Further, the determinants of blood volume would also be highlighted.

Before we move on to the techniques involved in blood fluid measurements, let us first review the principle involved in measuring fluid volumes.

### 8.4.1 The Dilution Principle for Measuring Fluid Volumes

For measuring fluid volumes, a dilution principle is used. In this, the volume of any fluid compartment of the body can be measured by placing a substance in the compartment, allowing it to disperse evenly throughout the fluid and then measuring the extent to which the substance becomes diluted.

The procedure involves that a small quantity of dye or any other foreign substance is placed in a fluid chamber and the substance is allowed to disperse throughout the chamber until it becomes mixed in equal concentrations in all areas as shown in Figure 8.3. Then a sample of dispersed fluid is removed and the concentration of the substance is analyzed chemically, photoelectrically or by any other means. Volume of the chamber can then be determined by the following formula:

$$\text{Volume (ml)} = \frac{\text{Quantity of substance instilled}}{\text{Concentration per ml of dispersed fluid}}$$

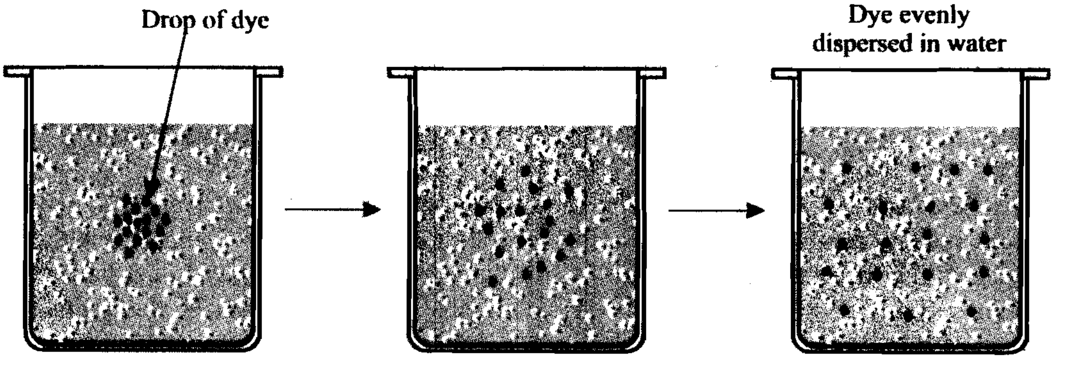


**Figure 8.3: The dilution principle**

Having studied the dilution principle for measuring body fluids, let us now get to know how the body fluids are measured. Let us start with the measurement of blood volume.

### 8.4.2 Determination of Blood Volume

The blood volume can be determined by use of certain substances. These substances are discussed in this section.

*What are the substances used in determining blood volume?*

A substance used for measuring blood volume must be capable of dispersing throughout the blood with ease and it must remain in the circulatory system for long enough for the measurements to be made.

The two major groups of substances that satisfy these conditions for measurement of blood volume are the substances that combine with red blood cells or substances that combine with plasma proteins as both red blood cells and plasma proteins remain reasonably well in the circulatory system and any foreign substance that combines with either of them likewise remains in the blood stream.

Substances that combine with red blood cells and that are used for determining blood volume are *radioactive iron, radioactive chromium* and *radioactive phosphate.* Substances that combine with plasma proteins are *vital dyes* and *radioactive iodine.* Let us get to know more about them.

a) *Radioactive Red Blood Cells*: In order to make red blood cells radioactive, tagging of red blood cells with radioactive chromium ( $^{51}Cr$) is done. A small quantity of $^{51}Cr$ is mixed with a few milliliters of blood removed from the person and this is incubated at 36°C for half an hour or more. After this time, most of the $^{51}Cr$ will have entered the red blood cells, but to remove the extra chromium from the mixture, the red blood cells are washed with saline.

The total content of $^{51}Cr$ is then determined with a Geiger or scintillation counter (apparatus for measuring the total number of radioactive disintegrations occurring in the sample per minute).

Then the radioactive cells are re-injected in the person. After mixing in the circulatory system for approximately 10 minutes, blood sample is taken from the circulatory system, and the radioactivity in this blood is determined, using dilution formula given above in dilution principle. Then actual volume is calculated i.e.

$$\text{Actual blood volume} = 1.1 \times \text{Measured blood volume}$$

b) *Dyes for Measurement of Plasma Volume*: A number of dyes, generally known as 'vital dyes', have the ability to combine with proteins. When such a dye is injected into the blood, it immediately forms a slowly dissociable union with the plasma proteins. Thereafter, the dye travels wherever the proteins travel.

The dye almost universally used for measuring plasma volume is T-1824, also called as *evans blue.*

In making determinations of plasma volume, a known quantity of the dye is injected and it immediately combines with the proteins and is dispersed throughout the circulatory system within approximately 10 minutes. A sample of the blood is then taken and the red blood cells are removed from the plasma by centrifugation. Then by spectrophotometric analysis of the plasma, one can determine the exact quantity of dye in the sample of the plasma. From the determined quantity of dye in each millilitre of plasma and the known quantity of dye injected, the plasma volume is calculated.

To be even more exact in measuring the plasma volume, the rate of loss of dye from the circulatory system during the interval of mixing must also be considered. On an average, 5% of the dye is lost per hour, part of it is carried into the interstitial spaces by the leakage of plasma proteins through the capillary walls whereas a part of it is excreted out into the urine.

No vital dye enters the red blood cells. Therefore, this method does not measure the total blood volume. The blood volume can be calculated from the plasma volume, provided the haematocrit is determined, by using the following formula:

$$\text{Blood Volume} = \text{Plasma Volume} \times \frac{100}{100 - 0.87\ \text{Haematocrit}}$$

c) *Radioactive Proteins*: If a sample of plasma is allowed to incubate with the radioactive iodine ( $^{131}I$ ) for 30 minutes or more, some of the protein combines with iodine and the iodinated protein can be separated from the remaining iodine by dialysis. The radioactive protein is then injected into the subject, and the plasma and blood volumes are determined in the same manner as that for vital dyes.

Next, we shall learn about the method involved in measuring extracellular fluid volume.

### 8.4.3 Measurement of Extracellular Fluid Volume

This method involves the use of dilution principle. A substance that can readily diffuse through the entire extracellular fluid chamber, which passes easily through the capillary membranes but as little as possible, passes through the cell membranes into the cells, is injected. After half an hour or more of mixing, a sample of extracellular fluid is obtained by removing blood and separating the plasma from the cells by centrifugation. Plasma, which is actually a part of extracellular fluid, is then analyzed for injected substance.

What are the substances used in this measurement? These are highlighted next.

*Substances used in measuring Extracellular Fluid Volume – The Concept of "Fluid Space"*

Substances that have been used for measuring extracellular fluid volume are:

- Radioactive sodium
- Radioactive chloride
- Radioactive bromide
- Thiosulphate ion
- Thiocyanate ion
- Inulin, and
- Sucrose

Some of these, especially sucrose and inulin, do not diffuse readily into all out-of-the way places of the extracellular fluid compartment. Therefore, the volume of extracellular fluid measured with these is likely to be lower than the actual volume of the compartment.

On the other hand, other substances such as radioactive chloride, radioactive bromide, radioactive sodium and thiocyanate ion are likely to penetrate into the cells to a slight extent and therefore, are likely to measure a space somewhat excess of the extracellular fluid volume.

Because no single substance can measure the exact extracellular fluid volume, one usually speaks of the 'sodium space', 'thiocyanate space', 'inulin space' etc.

Let us understand this concept better, with the help of an example presented herewith.

*Question*: 150 mg of sucrose is injected into a 70 kg man. The plasma sucrose level after mixing becomes 0.01 mg per ml. 10 mg has been excreted or metabolized during the mixing. What is the volume of distribution of sucrose?

$$\textit{Answer} = \frac{150\text{ mg} - 10\text{ mg}}{0.01\text{ mg/ml}}$$

$$= \frac{140 \times 100}{1} = 14{,}000\text{ ml.}$$

Hence, 14,000 ml is the space in which sucrose is distributed. Hence, it is known as 'sucrose space'.

While we are studying about the measurement of extracellular fluid, let us also look at the calculation of the interstitial fluid volume, which you learnt earlier is an extracellular fluid.

*How do we calculate the Interstitial Fluid Volume?*

Since any substance that passes into the interstitial fluid also passes into almost all other portions of the extracellular fluid, there is no direct method for measuring interstitial fluid volume separately from the entire extracellular fluid volume. However, if the extracellular fluid volume and plasma volume have both been measured, the interstitial fluid volume can be approximated by subtracting the plasma volume from the total extracellular fluid volume. In a 70 kg adult, the normal interstitial fluid volume is 12 litres.

Constituents of the interstitial fluid are responsible for the regulation of:

- Temperature
- pH
- Osmolarity
- Ionic concentration
- Oxygen-Carbon dioxide tension, and
- Several other vital features.

Finally let us get to know how total body water is measured.

## 8.4.4 Measurement of Total Body Water

Total body water is measured exactly the same way as extracellular fluid volume, except that a substance must be used that will diffuse into the cells, as well as, throughout the extracellular fluid compartment.

The substance that gives best result is *heavy water*, which can be analyzed quantitatively either by accurate specific gravity measurements of water samples or by infrared spectrophotometry. Heavy water is water containing *deuterium*, a heavy isotope of hydrogen ($D_2O$).

After administration of the heavy water, several hours are required for complete mixing with all the water of the body and appropriate corrections should be made for any fluid that is lost either into the urine or otherwise, during this period of mixing. The concentration of heavy water in the total body water can, at the end of the period of mixing is determined by simply measuring the heavy water concentration in plasma.

Another substance that has proved satisfactory for measuring the total body water is *antipyrine*, which diffuses almost uniformly into all cells of the body and which can be analyzed readily by chemical means. Antipyrine is a white powder formerly used to reduce fever and relieve pain.

**Check Your Progress Exercise 1**

1) What do you understand by the term homeostasis?

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2) What do you mean by 'intracellular fluid' and 'extracellular fluid'? Give examples.

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3) List the substances that are used to measure extracellular fluid.

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4) Explain how would you determine:

a) Haematocrit

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b) Total body water

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c) Interstitial fluid volume

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d) Blood Volume

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The discussion so far focussed on the body fluids. Next we shall learn about the body transport systems.

## 8.5 TRANSPORT ACROSS CELL MEMBRANES

In section 8.2, we got to know that the total body water in an average built adult is about 60% of body weight. About 20% is extracellular and the remainder 40% is intracellular. A large number of molecules must constantly transit between the inside and outside of the cell, most frequently one-at-a-time, but also in large packages. The plasma membrane acts as a selectively permeable barrier between the cell and the extracellular environment. Cell membranes help organisms maintain homeostasis by controlling what substances may enter or leave the cells.

Some molecules, which are large in size, cannot pass through semi permeable walls of the capillaries. These substances, which remain in the blood are plasma proteins, erythrocytes, thrombocytes and leukocytes – except those, which are amoeboid. On the other hand, electrolytes, enzymes, hormones, antibodies, nutritional materials, oxygen, carbon dioxide, water etc. are small molecules, which can pass through the capillary walls as highlighted in Figure 8.4. Transport across cell membranes may be governed only by physical processes.

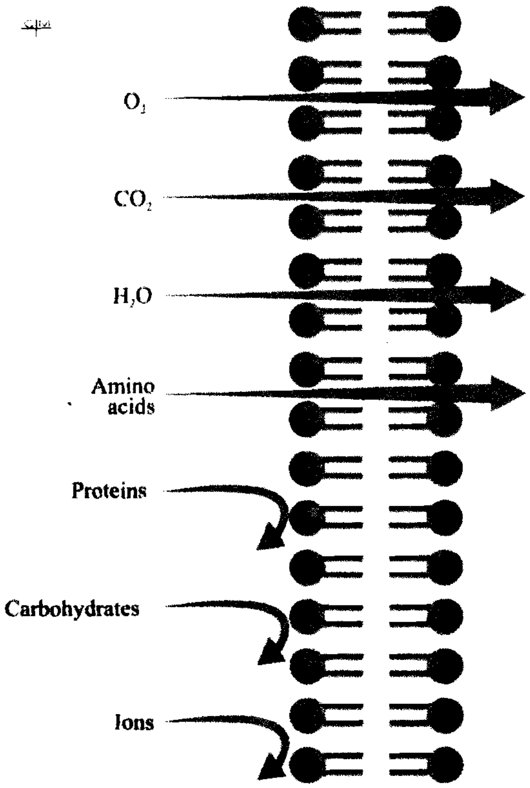


**Figure 8.4: Transport across cell membrane**

The molecules move from where the substance is more concentrated to where it is less concentrated. Here, the membrane acts like any other non-living semi-permeable structure. In such cases, the transport is called *passive transport.* Water crosses the cell membranes by diffusion and osmosis and some other substances cross by active transfer involving energy expenditure.

You would realize that all transport across cell membranes takes place primarily by two fundamental processes. These include:

- *Passive transport:* driven by the kinetic energy of the molecules being transported or by membrane transporters by facilitate crossing, and
- *Active transport:* depends upon the expenditure of cellular energy in the form of ATP hydrolysis.

For each of the two basic processes, several distinct types of transport – osmosis, simple diffusion, facilitated transport, couple transport, counter transport, dialysis etc. can be identified. In this section we shall learn about these mechanisms of transport across cell membranes. These transport systems help the cell to function properly. It helps to maintain homeostasis by transporting molecules.

Let us get to know about these important modes of transport. We shall start with the passive transport.

## 8.5.1 Passive Transport

Some substances such as water, oxygen and carbon dioxide, as illustrated in Figure 8.4, can cross the cell membrane without any input of energy by the cell. The movement of such substances across the membrane is known as *passive transport.*

A molecule or ion that crosses the membrane by moving down a concentration or electrochemical gradient and without expenditure of metabolic energy is said to be transported passively. Another name for this process is *diffusion.* All molecules and ions are in constant motion and it is the energy of motion – kinetic energy – that drives passive transport.

Transport of uncharged species across a membrane is dictated by differences in concentration of that species across the membrane – that is, by the prevailing concentration gradient. The difference in the concentration of molecules across a space is called a *concentration gradient.* If the molecules diffusing across the membrane from an area of high concentration to an area of low concentration were water molecules, the process would be called *osmosis.*

Glucose, sodium ions and choride ions are just a few examples of molecules and ions that must efficiently get across the plasma membrane but to which the lipid bilayer of the membrane is virtually impermeable. Their transport must therefore be "facilitated" by proteins that span the membrane and provide an alternative route or bypass. *Facilitated diffusion* is the name given to this process. It is similar to simple diffusion in the sense that it does not require expenditure of metabolic energy.

The three types of passive transport, we have discussed above are: diffusion, osmosis, and facilitated diffusion. Ultrafilteration is yet another passive transport system. Let us understand these processes in greater details now.

A) *Simple Diffusion*

Diffusion, we learnt is a simple *process of movement of individual molecules from one region to another.* Figure 8.5 illustrates passive transport where molecules move from an area of high concentration to an area of low concentration without the use or input of energy by the cell. This process we know is *diffusion.* Diffusion is driven entirely by the kinetic energy the molecules possess.

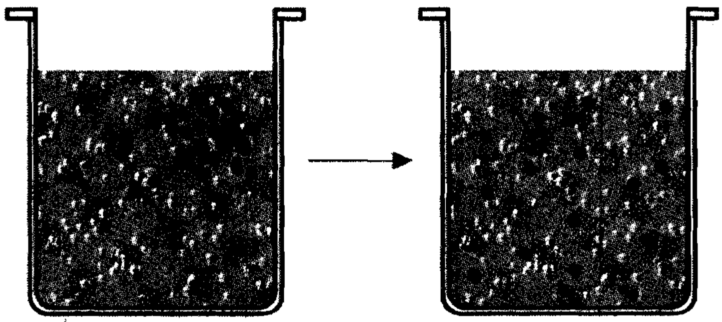

**Figure 8.5: Process of diffusion**

Let us look at this process in the context of our body. All the molecules and ions in the body fluids, including both – water molecules and dissolved substances – are in constant motion, each particle having its own separate way. The greater the motion, the higher is the temperature and the motion never ceases, except at absolute zero temperature. All the molecules and ions, as a result of random molecular motion, strike the cell membrane. The frequency of collision depends on the concentration of the dissolved substance.

If the substance is present on both sides of the membrane, the frequency of collisions is higher on the side on which the substance is present in a higher concentration. Higher the frequency of collisions, greater is the probability of particles striking a pore through which they can pass to the other side of the membrane.

The fluids on each side of the membrane are believed to penetrate the protein portion of the membrane with ease so that any dissolved substances can diffuse into this portion of the cell membrane.

The lipid portion of the membrane is entirely a different type of fluid medium, acting as a limiting membrane between the extracellular and intracellular fluids. There are basically two different methods by which the substances diffuse through the membranes:

- by becoming dissolved in lipid and diffusing through it, and
- by diffusing through minute pores that pass directly through the membrane at wide intervals over the surface.

If there is an electrical charge across the membrane, a charged particle will have a tendency to diffuse towards the oppositely charged side.

The influence of pressure gradient on the diffusion is somewhat non-specific. Pressure is the result of sum total of the collisions on a given side of the membrane. Pressure has a non-specific effect of driving the substances out. Hence, diffusion is increased from the side with the higher pressure to that with a lower pressure.

An example of application of diffusion process is dialysis. What is dialysis? Dialysis, you may recall reading in Unit 7, *is a procedure for cleansing the blood, in which the principles of diffusion are applied for the treatment of renal failure.* Kidney dialysis is used to substitute for the function of damaged/absent kidneys. In the patient's blood, nitrogenous waste products accumulate and electrolyte imbalance may occur due to renal failure. A solution is prepared in which the waste products are absent, electrolyte concentration is appropriately adjusted and nutrients are provided. The solution is separated from the patient's blood by a dialyzing membrane. The process of diffusion tends to normalize the composition in the patient's blood.

Having understood the diffusion process and its application, next, we move on to the other type of passive transport i.e. facilitated diffusion.

B) *Facilitated Diffusion*

As we discussed earlier, in facilitated diffusion, the transport is carried out by the carrier present in the cell membrane. The carrier helps to incorporate even a water-soluble substance in the membrane. Since the carrier merely facilitates diffusion, the process is called *facilitated diffusion*. Figure 8.6 illustrates the facilitated diffusion process.

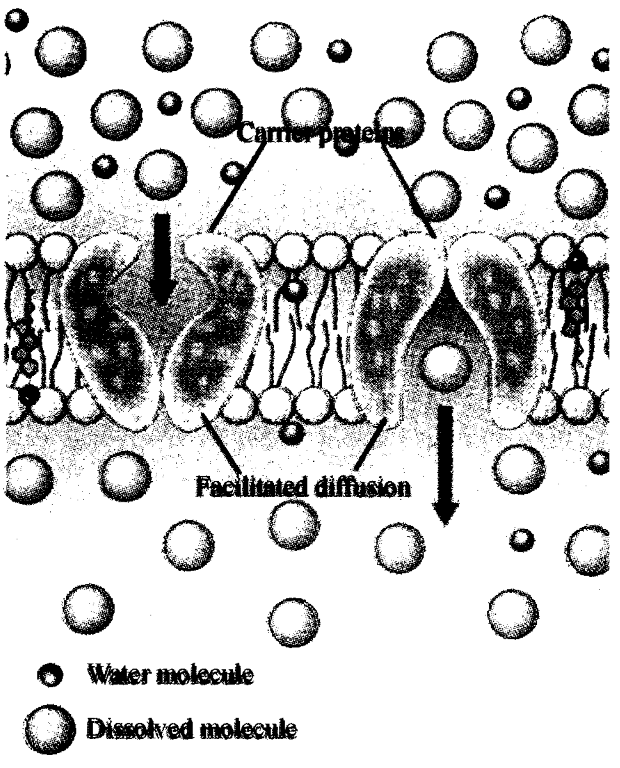


**Figure 8.6: Facilitated diffusion**

Facilitated diffusion is influenced by the following factors:

- Minor differences in the molecular structure may lead to a substantial difference in the rate of transport. Optimal transport depends on the precise fit between the molecule to be transported and the receptor site of the carrier.
- Substances with a similar molecular structure compete with one another for transport.
- Transport can be blocked by specific agents. If the blocking agent has a high affinity for the carrier, the blocking agent can also get transported and this block is known as *competitive block* (and can be overcome by high concentrations of substance whose transport has been blocked, hence is reversible). If the blocking agent binds to the carrier but does not get transported, it blocks the carrier irreversibly. Such a block is known as *non-competitive block.*

The relationship between the concentration of the substance and the rate at which it is transported is linear only up to a certain limit. After that, a further increase in the concentration does not increase the rate of transport. An example of facilitated diffusion is in small intestine where fructose is absorbed by facilitated transport.

Moving to the next process, i.e. osmosis.

C) *Osmosis*

Osmosis, quite simply, is the physical process, wherein there is transfer of a liquid solvent (water) through a semi-permeable membrane that does not allow the dissolved solids (solutes) to pass. Let us understand this process with the help of an example. Suppose a semi-permeable membrane separates two compartments. The membrane allows water to pass through but it does not allow the solute to pass through. On side A, there is water and on the other side B, there is solute dissolved in water. The membrane is permeable only to water, and the concentration of water is higher on side A. Hence, water diffuses from A to B, but in this type of solution, water is said to be transported by 'osmosis'.

Unlike simple diffusion, no matter how much water moves from A to B, the concentration of water will stay higher on side A because side B can have a more and more dilute solution of the solute. However, transport of water by osmosis does not occur indefinitely because osmosis of water increases the hydrostatic pressure of side B. Osmosis is said to stop when the excess hydrostatic pressure on side B equals the hydrostatic pressure exerted by the solute.

What do you mean by the term 'hydrostatic pressure'? Well to put in simple terms, *hydrostatic pressure is a pushing pressure*. Hence, the hydrostatic pressure on the side B tends to push the water from side B to A. While osmotic pressure is a pulling pressure, which in this case is exerted by the solute which pulls the water from A to B. When the pushing and pulling pressure become equal, there is no further movement of water. Finally, to summarize *osmosis is the net movement of water from a region of high water concentration across a selectively permeable membrane to a region of low water concentration, driven by a difference in solute concentrations on the two sides of the membrane.* Figure 8.7 illustrates the osmosis process.

We have looked at diffusion, osmosis and the facilitative diffusion process so far. We shall also look at the processes of ultrafiltration which is included under the passive transport system.

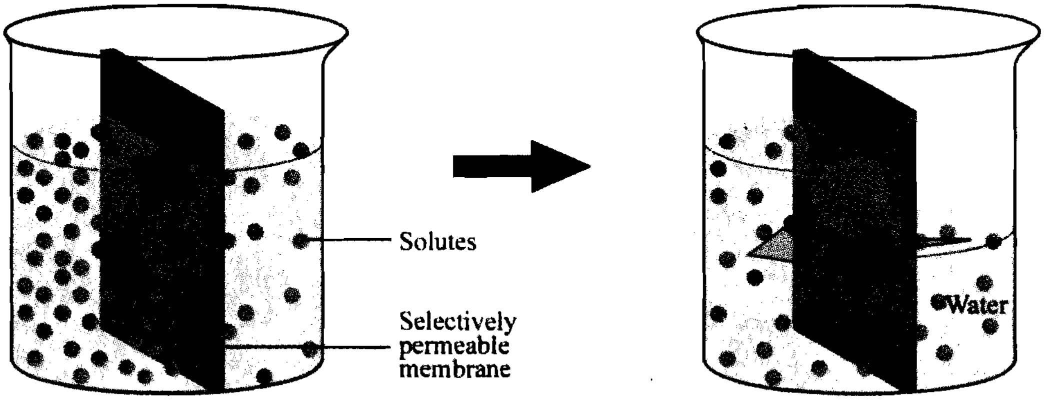


**Figure 8.7: The osmosis process**

D) *Ultrafiltration*

As the name suggests, ultrafiltration is *a process of filtration*. If we try to pass a solution through a filter, the solvent and other small molecules in the solution pass through while large molecules stay on the filter. Whether the given substance will pass through a filter or not, depends on the relative size of its molecules and on the process of the filter. The rate of filtration can be increased by applying pressure. For e.g. hydrostatic pressure in renal glomeruli is higher than any other capillaries of the body. As a result, water and small molecules filter through the glomeruli rapidly while proteins and blood cells do not.

Filtration under pressure, therefore, is known as *ultrafiltration*.

With this, we end our discussion on passive transport systems. Before moving on to the next mode of transport, let us check what we have learnt so far.

**Check Your Progress Exercise 2**

1) Define the following terms:

a) Diffusion

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b) Facilitated diffusion

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c) Dialysis

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2) Fill in the blanks:

a) ................................, ..............................., ......................................

and ......................................... are the substances which cannot pass through the semi-permeable membrane.

b) The transport across cell membranes driven by the kinetic energy of the molecules being transported is referred to as .......................... .

c) Various modes of passive transport are .........................., .........., ................................ and ..................................

d) Substances diffuse through the membranes by becoming dissolved in and through minute ....................................... .

e) The process of filtration under pressure is termed as ............................

3) What are the factors that influence 'facilitated diffusion'?

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Now, let us learn about active transport – what does it mean, how is it different from passive transport, its role, significance and factors inhibiting the transport in the biological systems.

### 8.5.2 Active Transport

Active transport is the mediated transport of biochemicals, and other molecular substances, across membranes. Unlike passive transport, this process requires chemical energy. In this form of transport, molecules move against either an electrical or concentration gradient (collectively termed as electrochemical gradient). This is achieved by either altering the affinity of the binding site or altering the rate at which the protein changes conformations.

Active transport, so we know now involves the utilization of energy. Depending on the source of energy, the active transport can be differentiated as:

- primary transport
- secondary transport

*Primary transport* uses energy directly, light or chemical energy is converted to electrochemical energy as electrochemical potential of the substances to be transported. This category comprises photosynthetic electron transport, light driven ion pumps, redox energy – dependent respiratory chains, transport ATPases and sodium pumps utilizing decarboxylation energy. Unlike primary transport, in *secondary transport,* the electrochemical energy originates from the electrochemical potential of another substance that is used up in *symport* (the transport of two different molecules or ions in the same direction through a membrane using a common carrier mechanism).

Next, let us get to understand where active transport is utilized in our body.

Active transport is required for maintaining the difference in the electrolyte composition between the intracellular and extracellular fluids. Inside the cell, the sodium ion concentration is much lower than outside, opposite is the situation in case of potassium ions. Active transport is also of special significance for the transport of several nutrients in the gastrointestinal tract. The absorption of nutrients should obviously continue until the luminal concentration has dropped to negligibly low levels even when the sizeable concentrations have built up in the enterocytes. This is possible only through active transport.

Since active transport needs metabolic energy, often a specific ATPase is present in the membrane of actively transporting cells. Active transport may be inhibited by the inhibitors of ATPase e.g. digitalis, which specifically inhibits the $Na^+$ – $K^+$ ATPase in cardiac muscle and omeprazole, which specifically inhibits the $H^+$– $K^+$ ATPase in the gastric parietal cells.

Active transport may also be non-specifically inhibited by dinitrophenol (DNP), which uncouples oxidation and phosphorylation in biological oxidation, by cyanide, which poisons the electron transport chain, and by fluoride or iodoacetate because these cells derive energy only from anaerobic glycolysis.

Having looked at the active transport, next we shall look at the secondary active transport operational in our body.

*Secondary Active Transport:* In secondary active transport, there is no direct coupling of ATP, instead the electrochemical potential difference created by pumping ions out of the cells is used.

This is an ingenious device used by the cells to utilize the active transport of one substance to drive the uphill transport of one or more other substances as well. A few types of secondary active transport are as follows:

a) *Coupled transport:* The transport of two substances may be coupled to each other because they bind to the same carrier in the cell membrane.

b) *Co-transport:* If the two substances whose transport is coupled, move in the same direction, the phenomenon is called as *co-transport* or *symport* for e.g. in the small intestine, absorption of sodium ions is coupled with that of glucose, because they bind to the same carrier in the enterocyte membrane.

c) *Counter transport:* If the two substances whose transport is coupled, move in opposite directions, the phenomenon is called *counter transport* or *antiport*, e.g., in proximal convoluted tubules of kidneys, sodium is actively reabsorbed. Simultaneously, for each sodium ion reabsorbed, one hydrogen ion is transported by the same carrier into the lumen of the tubule.

Some examples of transport by solute-solvent interactions are secondary to the active transport of some substance. Let us get to know about solute-solvent interaction next.

## 8.6 SOLUTE-SOLVENT INTERACTION

A solution, as you may already know, is a mixture of *solute* (present in small amount) and *solvent* (present in large amount).

The interaction between solute-solvent inside the cell and outside the cell is governed by many physical factors like concentration gradient, electrical gradient, osmotic pressure difference and the characteristics of the membrane. Some molecules come out of the membrane through it gates and for others selective transport through these gates is permissible. But for all living excitable cells, there is a potential difference during the resting state which is always negative towards inside the cell. When the cell becomes active, this potential difference is reversed and this is called *action potential.* So this interaction of solutes-solvent outside and inside maintain this important cell activity i.e., excitability. The main factors given below are responsible for this activity. Let us read about them.

*Osmosis*

We have earlier studied about osmosis and the role of hydrostatic pressure in the osmotic process. Here, we shall see how osmosis acts as secondary phenomenon to the active transport. Entry of solute into a cell by active transport increases the osmotic pressure within the cell. Hence, water also enters the cell by osmosis. Reabsorption of water from the gut takes place by this mechanism.

*Solvent Drag*

This is a process, which may be further secondary to the osmotic movement of water. Along with water, some substances dissolved in water may move in the same direction by bulk flow. This is known as *solvent drag.*

*Gibbs-Donnan Equilibrium*

Let us consider a situation in which a semipermeable membrane separates two electrolyte solutions, only one of which contains an ion to which the membrane is not permeable.

Let us imagine that the concentrations are as follows:

| A | B |
|---|---|
| $Na^+$ 30<br>$P^-$ 30 | $Na^+$ 30<br>$Cl^-$ 30 |

This situation cannot last very long, however,

where : $Na^+$ 30 is the concentration of Sodium ion = 30

$Cl^-$ 30 is the concentration of Chloride ion = 30

$P^-$ is Proteins which are negatively charged non-diffusable.

| A | B |
|---|---|
| ← | $Cl^-$ |
| ← | $Na^+$ |

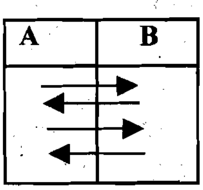
The concentration gradient would lead to a diffusion of $Cl^-$ from compartment B to A. However, that would create an electrical gradient, which would lead to a diffusion of $Na^+$ also from B to A.

| A | B |
|---|---|
| $Na^+$45<br>$Cl^-$ 15<br>$P^-$ 30 | $Na^+$15<br>$Cl^-$ 15 |

In effect, each $Cl^-$ would be accompanied by $Na^+$, leading to the situation as shown in the box alongside. This is also an unstable situation because the concentration of $Na^+$ is higher in A than in B.

Hence, $Na^+$ will diffuse from A to B and to maintain neutrality, $Cl^-$ will accompany $Na^+$. However, this does not go on indefinitely.

| A | B |
|---|---|
| $Na^+$ | → |
| $Cl^-$ | → |




Diffusion of $Na^+$ from A to B creates positivity on side B so that an equilibrium is reached when the concentration gradient from A to B exactly matches the electrical gradient.

| A | B |
|---|---|
| $Na^+$ 40 – | + $Na^+$ 20 |
| – | + |
| $Cl^-$ 10 – | + |
| – | + |
| P 30 – | + $Cl^-$ 20 |

In the same way, for $Cl^-$, the concentration gradient from B to A exactly balances the electrical gradient from A to B. As a result, the membrane will develop potential difference between its two surfaces, side B being positive as compared to A. The positivity on side B will prevent further diffusion of $Na^+$ and the negativity on side A will prevent further diffusion of $Cl^-$.

Thus the end result will be a higher concentration of $Na^+$ in A, a higher concentration of $Cl^-$ in B and a membrane potential across the semipermeable membrane.

In a body, a situation like this develops across the capillaries. The capillary endothelium is permeable to electrolytes but not to proteins, and the capillaries contain plasma proteins which are negatively charged at a physiological pH. As a result, the sodium concentration is higher in the plasma than the interstitial fluid. The chloride and bicarbonate concentrations are the other way round, and there is a membrane potential (about 1 mV) across the capillary, the positivity being towards the interstitial fluid.

The concentration at which equilibrium is achieved in situations like this, are predictable and follow a mathematical relationship known as the *Gibbs-Donnan equation*. According to this equation,

$$[Na^+]_A \times [Cl^-]_A = [Na^+]_B \times [Cl^-]_B$$

OR

$$\frac{[Na^+]_A}{[Na^+]_B} = \frac{[Cl^-]_B}{[Cl^-]_A} = r$$

where 'r' is known as the Gibbs-Donnan ratio.

**Check Your Progress Exercise 3**

1) How is active transport system different from passive transport system?

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2) What are the two different active transport systems?

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3) What is a 'solvent drag'?

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4) What are the different types of secondary active transport systems? Explain.

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5) Explain Gibbs-Donnan equilibrium.

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## 8.7 LET US SUM UP

In this unit, we studied about homeostasis. A variety of fluids such as intracellular, extracellular fluids as well as transport systems help in maintaining homeostasis. The unit focused on these fluids and the transport systems. A brief discussion on the body fluids and measurement techniques of various types of fluids was included.

The transport systems, we learnt are of two types, passive and active. Passive transport involves simple diffusion, facilitated diffusion, osmosis, ultra filtration. The active transport can be primary or secondary transport. The secondary active transport, we learnt, includes solute-solvent interaction which further involves osmosis, solvent drag, etc. Gibbs-Donnan equilibrium, which helps to understand the mechanisms involved in maintaining the concentration gradient.

## 8.8 GLOSSARY

**Antiport** : the movement of two substances in opposite directions.

**Competitive block** : blockage of facilitated transport by a specific agent having a high affinity for the transport protein/carrier.

**Hydrostatic pressure** : pressure which is exerted on a portion of a column of fluid as a result of the weight of the fluid above it.

**Mediated transport** : transport mediated by a transport protein.

**Non-competitive block:** blockage of facilitated transport – where in the blocking agent binds to the carrier but does not get transported and blocks the carrier reversibly.

**Osmolality** : a measure of moles of solute per kg of water. Osmolality basically measures the concentration of particles in a solution.

**Polycythemia** : an abnormally large number of red blood cells in the blood stream.

**Potential space** : a space in the body that normally contains little fluid but under special conditions can become filled with large amounts.

**Symport** : the movement of two substances in the same direction.

**Vital dye** : a dye which has the ability to combine with the proteins.

## 8.9 ANSWERS TO CHECK YOUR PROGRESS EXERCISES

**Check Your Progress Exercise 1**

1) The state of sustained equilibrium in which all cells and all life forms exist is referred to as homeostasis for example, fluid in the blood and lymph vessels, cerebrospinal fluid.

2) The fluid inside the body cells is called as intracellular fluid and the fluid outside the cells is called as extracellular fluids.

3) Radioactive sodium, radioactive chloride, radioactive bromide, thiosulphate ion, thiocyanate ion, inulin and sucrose are the substances that are used to measure extracellular fluid.

4) a) Haematocrit or the percentage of RBCs in the blood can be determined roughly from the levels of the packed cells.

b) RBCs are tagged with radioactive chromium ($^{51}Cr$). The total content of $^{51}Cr$ is then determined with a Geiger or scintillation counter. The radioactive cells are then re-injected in the person and after 10 minutes, radioactivity in this blood is determined.

c) Interstitial fluid volume is determined by measuring the concentration of heavy water in plasma. The measurement can be done quantitatively either by accurate specific gravity measurements of water samples or by infrared spectrophotometry.

d) Blood volume can be approximated by subtracting the plasma volume from the total extracellular fluid volume.

**Check Your Progress Exercise 2**

1) a) Transport across the cell membrane is termed as diffusion.

b) Transport which is carried out by the carrier present in the cell membrane is called facilitated diffusion.

c) Dialysis is corrective procedure in which the principles of diffusion are applied for the treatment of renal failure.

2) a) plasma proteins, erythrocytes, thrombocytes and leukocytes

b) passive transport

c) osmosis, simple diffusion, facilitated transport, ultrafiltration.

d) lipid pores

e) ultrafiltration

3) The factors that influence facilitated diffusion are:

- minor differences in the molecular structure
- substances with a similar molecular structure. These compete with one another for transport, and
- specific agents which can block transport.

**Check Your Progress Exercise 3**

1) Active transport system involves the utilization of energy which makes it possible to transport a substance at a faster rate and against an electrochemical gradient. While passive transport doesn't require input of energy and transport occurs along the concentration gradient.

2) Primary transport and secondary transport are the two different types of active transport.

3) Solvent drag is a process secondary to the osmotic movement of water. In this, along with water, some substances dissolved in water may move in the same direction by bulk flow.

4) Coupled transport, co-transport and counter transport are the types of secondary transport.

Coupled transport is the transport of two substances which are coupled to each other because they bind to the same carrier in the cell membrane. Co-transport is the movement of the two substances whose transport is coupled, in the same direction. Counter transport is the movement of the two substances whose transport is coupled, in opposite directions.

5) Gibbs-Donnan equilibrium: A semi-permeable membrane separating two electrolyte solutions, only one of which contains an ion to which the membrane is impermeable. In such a case, the difference in concentration gradient would lead to diffusion of that ion from one solution to gradient and hence an unstable situation. The diffusion continues till the concentration gradient of both solutions matches and develops a potential difference. The concentration at which equilibrium is achieved and follow a mathematical relationship is known as the 'Gibbs-Donnan' equation. This equation is represented as:

$$[Na^+]_A \times [Cl^-]_A = [Na^+]_B \times [Cl^-]_B$$

OR

$$\frac{[Na^+]_A}{[Na^+]_B} = \frac{[Cl^-]_B}{[Cl^-]_A} = r$$

Where 'r' is known as the Gibbs-Donnan ratio.