Course Title: Biochemistry I
Summer Semester
Instructor: Sana khan
Student Name:
Student ID:

Max Marks: 30

Note: **There are FIVE questions, each carry 6 mark with grand total of 30 marks**
ATTEMPT all questions
Avoid copy paste material, as it may deduct your marks

Q1: Write down the points of cell theory.

Q2: Classify monosaccharides on the basis of number of C-atom along with example.

Q3: Briefly discuss the function of Macromolecules found in Cell Membrane.

Q4: Discuss amino acids on the basis of requirement in protein synthesis.

Q5: Explain Digestion and Absorption of Carbohydrate.

Name… Tahsin kamal

ID..16131

Section.. A

Q1…

Ans…CELL THEORY… In **biology**, **cell theory** is the historic **scientific theory**, now universally accepted, that living organisms are made up of **cells**, that they are the basic structural/organizational unit of all organisms, and that all cells come from pre-existing cells. Cells are the basic unit of structure in all organisms and also the basic unit of reproduction.

The three tenets to the cell theory are as described below:

1…All living organisms are composed of one or more cells.

2.. The cell is the basic unit of structure and organization in organisms.

3… Cells arise from pre-existing cells.

There is no universally accepted definition of **life**. Some biologists consider **non-cellular entities** such as **viruses** living organisms, and thus reasonably disagree with the first tenet..

- All cells arise only from pre-existing cells
- The cell is the most basic unit of life
- All living organisms are composed of one or more cells

Q2..

Ans…monosaccharides… Monosaccharides are the simplest carbohydrates in that they cannot be hydrolyzed to smaller carbohydrates. They are basic units of Carbohydrates. They are made up of only one carbohydrate moiety. The general chemical formula of an unmodified monosaccharide is $(C{\bullet}H_2O)_n$, literally a “carbon hydrate”. This is termed as the empirical formula.
In this formula, the “n” varies from 3-6 and rarely seven. This implies that in nature no. of carbon atoms found in monosaccharide varies from minimum 3 to maximum 7.

The smallest monosaccharides (for which n = 3) are dihydroxyacetone and glyceraldehyde. However, not all carbohydrates conform to this precise stoichiometric definition (e.g., uronic acids, deoxy-sugars such as fucose), nor are all chemicals that do conform to this definition automatically classified as carbohydrates.

Monosaccharides Classification

1. Placement of its carbonyl group,
2. Number of carbon atoms it contains, and
3. Its chiral handedness.

Number of Carbon Atoms

Monosaccharides with three carbon atoms are called trioses, those with four are called tetroses, five are called pentoses, six are hexoses, and so on. These two systems of classification are often combined. For example, glucose is an aldohexose (a six-carbon aldehyde), ribose is an aldopentose (a five-carbon aldehyde), and fructose is a ketohexose (a six-carbon ketone). Various examples of other monosaccharide are given in the following table.

Trioses.. A triose is a monosaccharide containing *three carbon atoms*. The general formula is C3H6O3. There are only two trioses, an aldotriose (glyceraldehyde) and a ketotriose (dihydroxyacetone). Trioses are important in respiration. Namely, lactic acid and pyruvic acid are derived from aldotriose and ketotriose, respectively.

Tetroses.. *A tetrose is a monosaccharide containing four carbon atoms. The general formula is* $C_4H_8O_4$. Example:*D- Erythrose-4-P is an intermediate in hexosemonophosphate shunt which is an alternative of glucose oxidation.*

Pentoses.. *A pentose is a monosaccharide containing five carbon atoms. The general formula is* $C_5H_{10}O_5$.

Example of Pentoses are

- D- ribose is a constituent of RNA and many co-enzymes e.g. FAD, NAD.
- D-2 deoxy is a constituent of DNA component of DNA.
- D-Lyxose is a constituent of lyxoflavin found in the human heart.
- D- arabinose is a constituent of plant cell wall
- Phosphate esters of D- Ribulose and D- xylose occurs as an intermediate in the HMP pathway

Hexoses

A Hexose is a monosaccharide containing six carbon atoms. The general formula is $C_6H_{12}O_6$

D- Glucose

It is the chief physiological sugar present in human blood. Its values are regulated between 70-110 mg/dl of blood by a pancreatic hormone Insulin and Glucagon. Increase in blood sugar levels leads to Diabetes. All tissues utilize glucose for energy. Brain and Erythrocytes depend exclusively on glucose. Its polymeric form glycogen is used as energy storage material in animals. Its polymeric form starch is used as energy storage material in plants.

D-Galactose

seldom found free in nature occurs as a constituent of milk sugar lactose and in tissues as galactolipids and glycoproteins.

D-Mannose

It is used to stamp proteins by the process of glucosylation. It does not occur free in nature but is widely distributed in combination as the polysaccharide mannan, e.g.- ivory nut. It is also found as the constituent of glycoproteins

D- Fructose

it is a ketohexose and is commonly called the fruit sugar, as it occurs in fruit. It is a sweet sugar sweeter than glucose and sucrose. It is found in honey as laevulose. In the seminal fluid of man fructose is the chief source of energy for sperms.

Heptoses

A heptode is a monosaccharide containing seven carbon atoms. The general formula is $C_7H_{14}O_7$. Examples are Sedoheptulose It is a keto-heptulose found in plants of the sedum family. (most of the aldoses end in "**-oses**" and ketoses end in "-**uloses**" e.g. erythrose and erythrulose).

Q3…

Ans…Cell membrane.. The **cell membrane** (also known as the **plasma membrane** (**PM**) or **cytoplasmic membrane,** and historically referred to as the **plasmalemma**) is a biological membrane that separates the interior of all cells from the outside environment (the extracellular space) which protects the cell from its environment. The cell membrane consists of a lipid bilayer, including cholesterols (a lipid component) that sit between phospholipids to maintain their fluidity at various temperatures. The membrane also contains membrane proteins, including integral proteins that go across the membrane serving as membrane transporters, and peripheral proteins that loosely attach to the outer (peripheral) side of the cell membrane, acting as enzymes shaping the cell The cell membrane controls the movement of substances in and out of cells and organelles. In this way, it is selectively permeable to ions and organic molecules. In addition, cell membranes are involved in a variety of cellular processes such as cell adhesion, ion conductivity and cell signalling and serve as the attachment surface for several extracellular structures, including the cell wall, the carbohydrate layer called the glycocalyx, and the intracellular network of protein fibers called the cytoskeleton. In the field of synthetic biology, cell membranes can be artificially reassembled.

Prelude to Biological Macromolecules.. Food provides the body with the nutrients it needs to survive. Many of these critical nutrients are biological macromolecules, or large molecules, necessary for life. These macromolecules (polymers) are built from different combinations of smaller organic molecules (monomers). What specific types of biological macromolecules do living things require? How are these molecules formed? What functions do they serve? In this chapter, these questions will be explored.

: Synthesis of Biological Macromolecules.. Biological macromolecules are large molecules, necessary for life, that are built from smaller organic molecules. There are four major classes of biological macromolecules (carbohydrates, lipids, proteins, and nucleic acids); each is an important cell component and performs a wide array of functions. Combined, these molecules make up the majority of a cell's dry mass (recall that water makes up the majority of its complete mass).

Carbohydrates.. Carbohydrates are made up of monosaccharides (sugars), and their polymers. The monosaccharides bond together to form polysaccharides, which are the polymers of carbohydrates. The most common monosaccharide is glucose, which is one of the most valuable sugars for all animals and plants. The function of carbohydrates is to act as an energy source for storage and structure for all living things. For plants, starch is the chief energy source and cellulose is what provides structure and support. For animals, glycogen supplies energy and chitin provides the structure and support.

Lipids… Lipids come in three forms -- fats, steroids and phospholipids. The main function of these lipids is energy and insulation. Fats come in either saturated or unsaturated forms, and are insoluble and therefore, buoyant. Saturated fats are found in animals and are solids at room temperature; unsaturated fats are found in plants and are liquids or oils at room temperature. Lipids, in the form of phospholipids, are also important elements in membranes.

Protein.. Proteins are very important macromolecules; they have many levels of structure and a number of functions. Every cell in the human body contains proteins and most bodily fluids contain proteins as well. Proteins make up a large part of human skin, organs, muscles and glands. Proteins assist the body in repairing cells and making new ones, and are an important dietary and energy requirement, especially for growing adolescents and expectant mothers.

Nucleic Acids

Nucleic acids include the all-important DNA and RNA. DNA is the blueprint for genetic development for all life-forms; it holds the necessary information required for protein synthesis. RNA is the carrier of this information to the actual site of protein production. The body is made up of hundreds of thousands of proteins and each has to act in a specific way to function properly. Nucleic acids contain the information necessary for these proteins to develop and act the way they are supposed to.

Q4…

Ans.. amino acids on the basis of requirement in protein synthesis.

Protein biosynthesis (or **protein synthesis**) is a core biological process, occurring inside **cells**, **balancing** the loss of cellular **proteins** (via **degradation** or **export**) through the production of new proteins. Proteins perform a variety of critical functions as **enzymes**, structural proteins or **hormones** and therefore, are crucial biological components. Protein synthesis is a very similar process for both **prokaryotes** and **eukaryotes** but there are some distinct differences.

Protein synthesis can be divided broadly into two phases - **transcription** and **translation**. During transcription, a section of **DNA** encoding a protein, known as a **gene**, is converted into a template molecule called **messenger RNA**. This conversion is carried out by enzymes, known as **RNA polymerases**, in the nucleus of the cell. In eukaryotes, this messenger RNA (mRNA) is initially produced in a premature form (pre-mRNA) which undergoes post-transcriptional modifications to produce mature mRNA. The mature mRNA is exported from the **nucleus** via **nuclear pores** to the **cytoplasm** of the cell for translation to occur. During translation, the mRNA is read by **ribosomes** which use the **nucleotide** sequence of the mRNA to determine the sequence of **amino acids**. The ribosomes catalyse the formation of **covalent peptide bonds** between the encoded amino acids to form a polypeptide chain.

Following translation the polypeptide chain must fold to form a functional protein, for example, to function as an enzyme the polypeptide chain must fold correctly to produce a functional **active site**. In order to adopt a functional three-dimensional (3D) shape, the polypeptide chain must first form a series of smaller underlying structures called **secondary structures**. The polypeptide chain in these secondary structures then folds to produce the overall 3D **tertiary structure**. Once correctly folded, the protein can undergo further maturation through different **post-translational modifications**. Post-translational modifications can alter the protein's ability to function, where it is located within the cell (e.g. cytoplasm or nucleus) and the protein's ability to **interact with other proteins**.

Protein biosynthesis has a key role in disease as changes and errors in this process, through underlying **DNA mutations** or protein misfolding, are often the underlying causes of a disease. DNA mutations change the subsequent mRNA sequence, which then alters the mRNA encoded amino acid sequence. **Mutations can cause the polypeptide chain to be shorter** by generating a **stop sequence** which causes early termination of translation. Alternatively, a mutation in the mRNA sequence **changes the specific amino acid encoded at that position** in the polypeptide chain. This amino acid change can impact the proteins ability to function or to fold correctly.[4] Misfolded proteins are often implicated in disease as improperly folded proteins have a tendency to stick together to form **dense protein clumps**. These clumps are linked to a range of diseases, often **neurological**, including **Alzheimer's disease** and **Parkinson's disease**.

Q5…

Ans.. Digestion:

The goal of carbohydrate digestion is to break down all disaccharides and complex

carbohydrates into monosaccharides for absorption, although not all are completely absorbed in

the small intestine (e.g., fiber). Digestion begins in the mouth with salivary amylase released

during the process of chewing. There is a positive feedback loop resulting in increased oral

amylase secretion in people consuming diets high in carbohydrates. The amylase is synthesized

in the serous cells of the salivary glands. Amylase breaks starches into maltose and

polysaccharides. Amylase is sensitive to pH and thus is inhibited in the acidic environment of

the stomach. Only 5% of starch is broken down by salivary amylase due to limited

exposure. Salivary amylase has increased importance in two groups; infants with decreased

pancreatic amylase production in the first 9 months and children with pancreatic insufficiency

from cystic fibrosis or other etiologies.

Minimal carbohydrate digestion occurs in the stomach due to the inactivation of amylase in the

acidic environment. Pancreatic amylase is released from acinar cells into the small intestine in

concert with other enzymes under the stimulus of secretin and CCK and continues the process of

carbohydrate digestion. Amylase targets the α-1,4 bonds of complex carbohydrates and is unable

to break terminal bonds or α-1,6 bonds. Starch is digested in the small intestine to simple

components derived from branched amylopectin (maltose, maltotriose and α-limit dextrins). Oligosaccharides and disaccharides are digested by specific enzymes in the microvillus membrane (brush border). Brush border enzymes are synthesized in the endoplasmic reticulum and glycosylated in the Golgi apparatus of the enterocyte. They are then trafficked to the apical membrane where they are anchored at the surface by a transmembrane segment. The anchored enzymes are active following cleavage of a small residue at the extracellular N-terminal end. Disaccharidases are protected from proteolysis by glycosylation and are found in higher concentration in villus enterocytes of the proximal small bowel. These enzymes include maltase (digests maltose to glucose and glucose), sucrase (digests sucrose to fructose and glucose), trehalase (digests trehalose to glucose and glucose), lactase (digests lactose to galactose and glucose) and isomaltase (de-branching enzyme digests α1,6 bonds of limit dextrin to produce glucose). Glucose does not require any additional digestion. The rate limiting step for absorption differs among the carbohydrates. Sucrose uptake is regulated after hydrolysis by the apical membrane uptake rate of fructose and glucose, whereas lactose absorption is limited by the rate of hydrolysis.(See Figure 2)

Humans born full-term have a full complement of disaccharidases at delivery. However, disaccharidase levels vary during gestation: sucrase appears early (by about 20 weeks), while lactase does not achieve “normal” levels until the 3rd trimester. In most humans, lactase

decreases with age starting at about 3-5 years or earlier depending on the population. This

pattern has been termed lactase non-persistence. However, in people of Northern European

ancestry and other population groups in small areas elsewhere in the world, lactase activity

remains at the infantile level. This is termed lactase persistence. Lactase non-persistence is

found in the United States mainly in African-Americans, Asians, and Native Americans,

although people of Southern European ancestry can also exhibit lactase non-

persistence. Lactase activity is “hard wired” genetically; lactase is not inducible, and lactose

restriction does not lower lactase levels. Carbohydrates not digested in the small intestine pass

into the large intestine where they are digested by colonic bacteria. This results in the release of

short chain fatty acids (SCFA) (propionate, butyrate and acetate) along with methane. The

SCFA provide vital nutrition to colonocytes, but excess volumes induce diarrhea and abdominal

cramping.

Clinical correlation - Disaccharide deficiency results in symptoms due to an increased osmotic

load in the small intestine and frequently elevated short chain fatty acid (SCFA) production in

the colon. The presence of SCFA and their contribution to colonocyte health must also be

remembered in children with diversion colitis, which is due to an absence of SCFA.

Absorption:

Once carbohydrates are digested, the products must be absorbed and transported to the portal

circulation. Digestion and absorption are typically coupled, with the enzymes closely located to

the appropriate transporters. Glucose absorption occurs in the small intestine via the SGLT-1

transporter (sodium glucose co-transporter). Fructose absorption is completed via the GLUT5

transporter by facilitated diffusion. (See Figure 3)

Glucose and galactose are actively transported from the small intestine lumen by the sodium

glucose transporter (SGLT-1) located in the brush border of the small intestine. The transporter

is more prevalent in the duodenum and jejunum. Glucose transport is driven by a sodium

gradient across the apical cell membrane generated by the Na+

,K+

-ATPase pump located in the basolateral membrane of the enterocyte. The Na+

,K+

-ATPase pump creates a low intracellular

sodium concentration by transporting 3 Na+

ions out of the cell and 2 K+

ions into the cell. The

SGLT-1 transporter utilizes the sodium gradient. Two Na+

ions bind to the outer face of the

SGLT-1 transporter which results in a conformational change permitting subsequent glucose

binding. The two Na+

ions and the glucose molecule are then transferred to the cytoplasmic side

of the membrane following another conformational change that involves rotation of the receptor.

The glucose is released first followed by the sodium ions. The sodium is transported from high

to low concentration (with concentration gradient) and at the same time allows the carrier to

transport glucose against its concentration gradient. The Na+

ion is subsequently expelled by

Na+

,K+

-ATPase pump to maintain the gradient. The SGLT-1 transporter undergoes another

conformational change resulting in the binding sites again being exposed at the apical surface.

This action can occur one thousand times per second. Much of the glucose transported into the

cell passes out of the cell at basolateral surface by facilitated diffusion via GLUT-2. Sodium

ions and accompanying anions and water follow the glucose, maintaining iso-osmolarity. A

small portion of the glucose is utilized by the cell.

Facilitated diffusion is the mechanism for fructose transport. Facilitated diffusion utilizes a

carrier protein to achieve transport at rates greater than simple diffusion and does not rely on

concentration gradients. GLUT-5 is present on the apical membrane of the brush border

throughout the small intestine with increased density in the proximal small intestine. Little

fructose is metabolized in the cell. Both GLUT-2 and GLUT-5 are present at the basolateral

membrane to transport fructose to the portal circulation. Fructose malabsorption can be minimized by simultaneous glucose administration suggesting there is another glucose responsive system in the enterocytes.

There continues to be debate about passive glucose absorption. Recent data suggests passive glucose absorption does exist, but that it is a facilitated system mediated by glucose-dependent activation. The GLUT-2 facilitative glucose transporter can be recruited to the brush border membrane to assist with glucose transport.

Disaccharidase Regulation

Sucrase-isomaltase (SI) and maltase-glucoamylase levels increase in response to high carbohydrate intake, suggesting a transcriptional regulation mechanism. SI is encoded for by a gene located on chromosome 3. The 5' flanking region of the SI gene has several DNA regulatory regions that control the initiation of gene transcription. Three different transcriptional proteins are involved in SI transcription promotion including; hepatocyte nuclear factor (HNF-1), GATA-type zinc finger transcription factors, and caudal-related homeodomain proteins (Cdx). There are also promoter regions that down-regulate SI transcription. Down regulation of SI occurs in the presence of glucose. Hormonal influences have also been proposed and are currently being studied further.

Unlike SI, lactase production is not affected by diet. The lactase gene is located on chromosome

2. Studies have demonstrated that Cdx, HNF-1 and GATA 5, along with other transcription

factors all interact with the proximal promoter region and result in transcription initiation. A

distal promoter region has been identified and is currently being characterized. It has also been proposed that a repressor region exists that down regulates lactase expression. It has been

hypothesized that lactase persistent people fail to bind this repressor due to single nucleotide

polymorphisms (SNPs) These SNPs are currently under investigation.

Clinical Correlations:

• Lactose Intolerance

– See above for lactose intolerance clinical presentation and natural history

– Management of lactose intolerance per the 2010 NIH Consensus Guidelines

(http://consensus.nih.gov/2010/lactosestatement.htm)

• Limit lactose to 12 grams (approx. 1 cup) and titrate for symptoms

• Recommend lactose be taken with other foods

• Evaluate diet for adequate nutrition, particularly calcium and Vitamin

D

• Studies are currently lacking to support use of probiotics or

supplemental lactase.

• Congenital Sucrase-Isomaltase Deficiency

– Autosomal recessive disease due to homozygous or heterozygous mutations in

the SI gene resulting in maldigestion of sucrose. Found in 1 in 5,000 North

Americans, but more significant in Artic indigenous peoples with 10% of

Eskimos affected. Presents with osmotic diarrhea, abdominal pain and FTT.

Treatment requires dietary elimination of sucrose and occasionally initially a starch free diet. Once the child is sucrose free, starch may be slowly reintroduced. There is a supplement for sucrase, Sucraid®
, available.

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• Small Bowel Bacterial Overgrowth

– Increased bacteria in the small bowel due to dysmotility, infection or medication exposures. The bacteria present in SBBO result in increased fermentation of sugars. Diagnosis may be made by clinical history and supported by breath testing, although the sensitivity and specificity of this test is approximately 60%. In this test, malabsorption of the test sugar results in increased breath H+…

THE END…