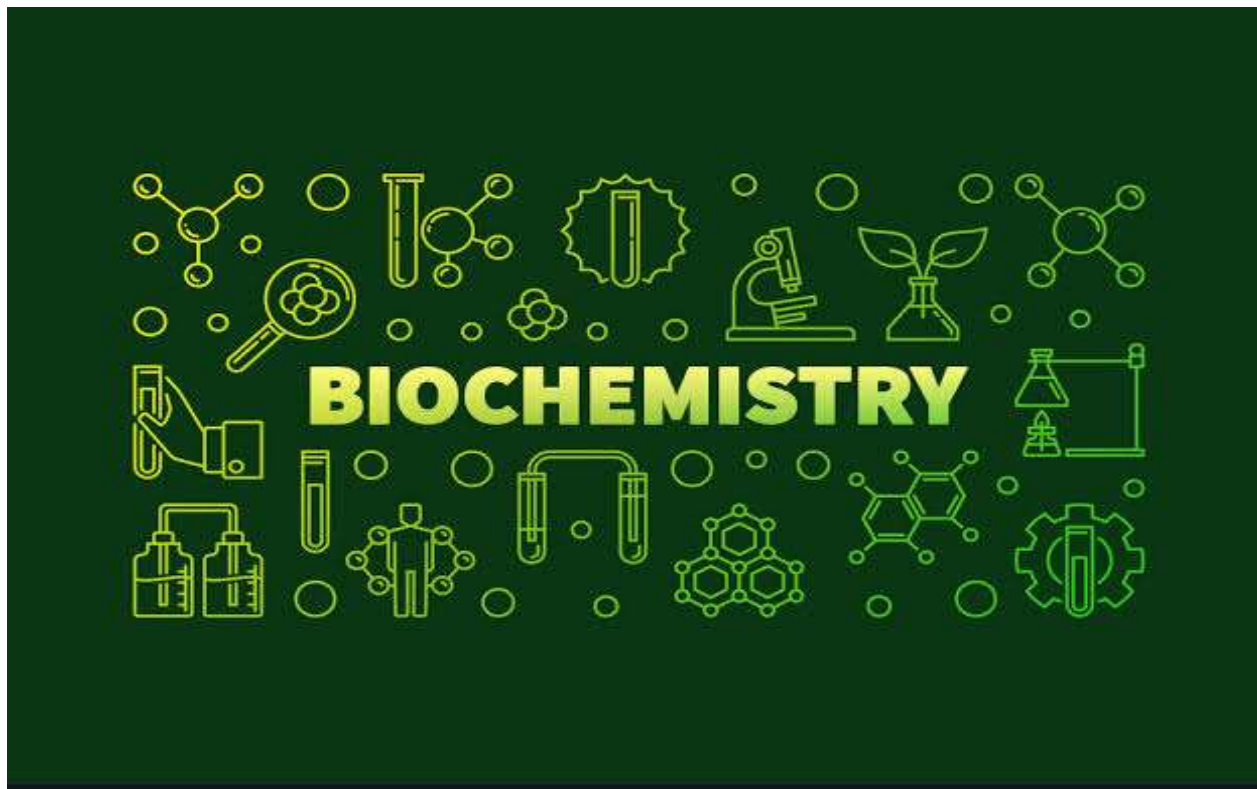




Chemistry of Carbohydrates

BC 3.1



- SLO 3.1.7 Student should be able to explain briefly
3.1.8 Polysacharides of biological significance

Polysaccharides

- Polysaccharides are polymers of monosaccharide units. (>10)
- Macromolecules of colloidal dimensions.
- Hydrolysed by mineral acids/ enzymes to monomeric units.
- Resistant to alkaline hydrolysis.

Polysaccharides

- Homopolysaccharides : If the monomeric units of a polysaccharide are all the same.

Examples- Starch, Glycogen, Dextrins, Cellulose

- Heteropolysaccharides: If contains different sugar units.

Glycosamino glycans

Polysaccharides

- In some, the monomeric units are modified monosaccharides –amino sugars, N- acetylated amino sugars etc.
- Polysaccharides differ in the composition of the monomeric unit, the linkages between them.

Homoglycans

Name	Monomers	Linkage
Glycogen	D Glucose	1>4, 1>6 branches
Starch-----Amylopectin Amylose	D Glucose D Glucose	1>4, 1>6 branches 1>4
Cellulose	D-Glucose	beta 1>4
Chitin	N-Acetyl-D-glucosamine	beta 1>4
Inulin	D Fructose	beta 1-4 linkages
Dextran (High mol wt)	Glucose from microorganisms	Glucose 1>6, 1>4, 1>3

- DEXTROSE
- DEXTRIN
- DEXTRAN

- INULIN
- INSULIN

- Cellobiase enzyme

Biologically important Polysaccharides

Heteropolysaccharides

- A. Agar, Agarose
- B. Carbohydrate moiety of Proteoglycans & Glycoproteins
- C. Blood group antigens

Biologically important Polysaccharides

A. Agar and Agarose

Agar

- Prepared from sea weeds.
- Contains Glc, Gal and other sugars
- Used as a supporting media for electrophoresis and immunodiffusion
- Used to prepare culture media

Agarose

- Galactose and 3,6 anhydrous Galactose
- Used for electrophoresis

Biologically important Polysaccharides

B. Proteoglycans and Glycoproteins

Carbohydrates with Proteins

- Oligosaccharides are covalently linked to polypeptide chain by **O- Glycosidic bonds** with OH gp of Ser or **N Glycosidic bonds** of Asn.
- Glycoproteins - <4 % of CHO
- Proteoglycans - >4 % of CHO

Biologically important Polysaccharides

Proteoglycans:

- Principal structural component of ground substance.
- Structural elements of tissues like bone, cartilage, connective tissue, cornea and synovial fluid.
- **Carbohydrate moiety** of proteoglycans are called

Glycosaminoglycans(GAG)

Biologically important Polysaccharides

Proteoglycans:

Glycosaminoglycans

- Previously called as **Mucopolysaccharides** because they were isolated from mucous secretions.

Biologically important Polysaccharides

GAGs(Mucopolysacharides)

Classification:

- Non Sulfated -Hyaluronic acid
- Sulfated- Chondroitin Sulfate
Keratan Sulfate
Dermatan Sulfate
Heparin
Heparan Sulfate

Biologically important Polysaccharides

Glycosaminoglycans:

- Contain **repeating disaccharide units**
- One of the sugar residue is **Glc NAc** or **Gal NAc**
- 2nd sugar residue is a **uronic acid** – GlcUA or L IdUA – Exception **Keratan Sulfate**
- Most of the residues **contain sulphuric acid** esters either O-esters or N-esters. Exception **Hyaluronic acid**

Biologically important Polysaccharides

Hyaluronic acid

- First found in the vitreous humor of eye.
- Present in Synovial fluid, tendons, umbilical cord, loose connective tissue etc.

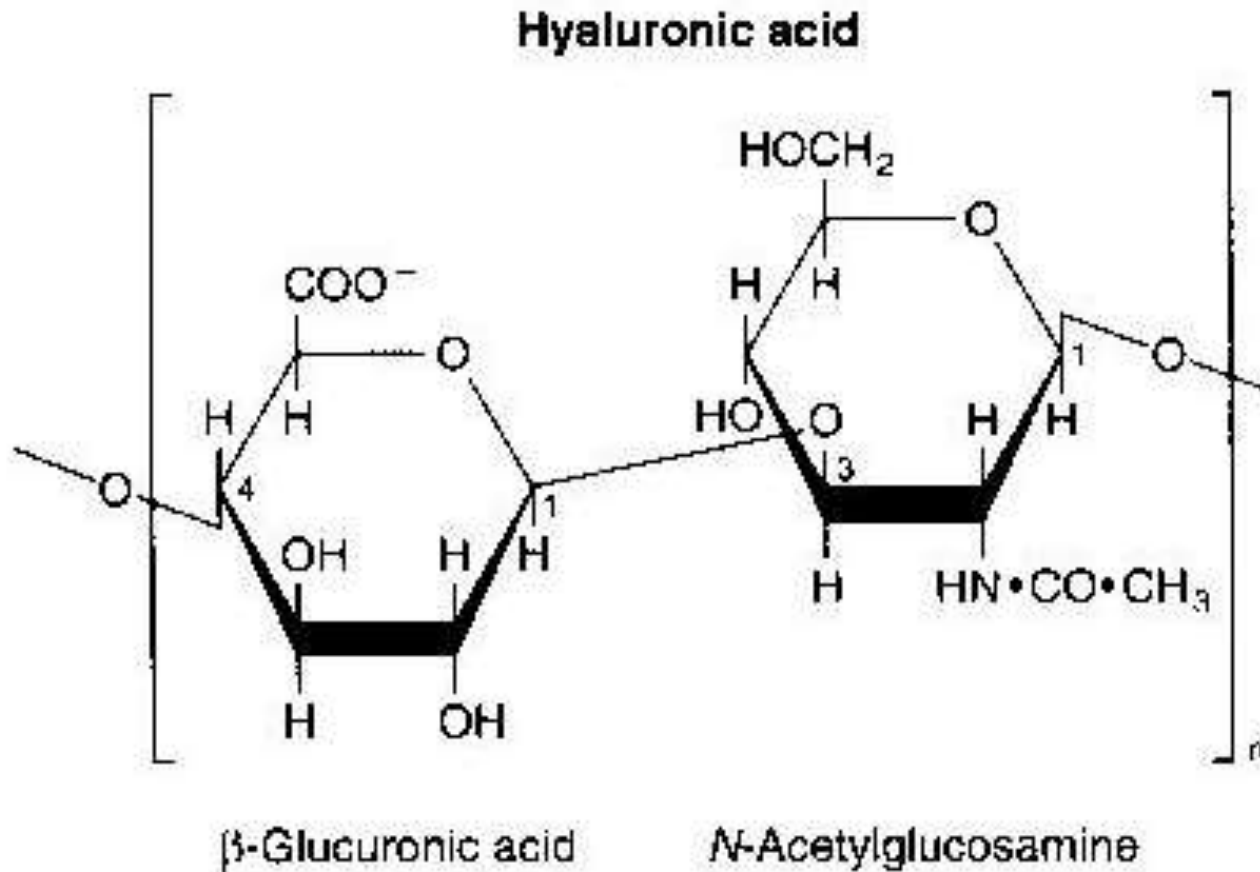
Chemistry : **Non sulfated**

- Repeating disaccharide unit



Biologically important Polysaccharides

Hyaluronic acid



Biologically important Polysaccharides

Chondroitin

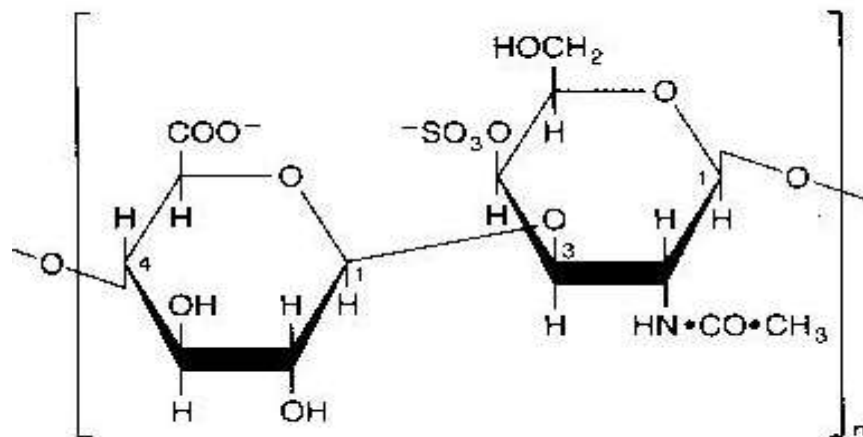
- Present in cartilage, bone, tendons, Cornea



Biologically important Polysaccharides

Chondroitin Sulfate:

- **Chondroitin sulfate A** – Cartilage, bone, cornea

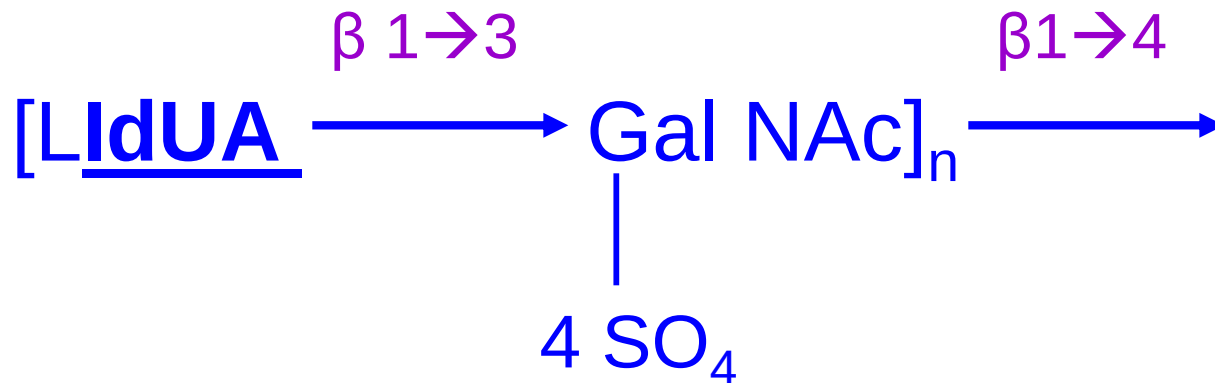


β -Glucuronic acid N-Acetylglactosamine sulfate

Biologically important Polysaccharides

Chondroitin Sulfate:

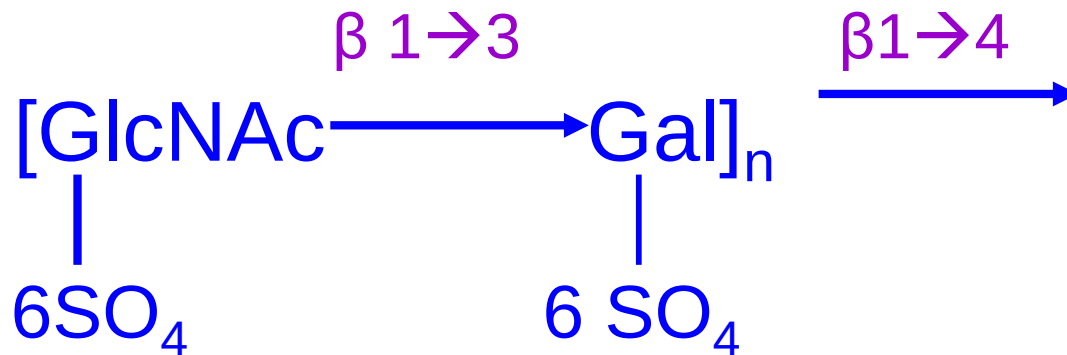
- Chondroitin Sulfate B (Dermatan Sulfate)
- Skin, tendon, cardiac valves, blood vessels, lung parenchyma, heart valves



Biologically important Polysaccharides

Keratan Sulfate:

- Present in Cornea and tendons
- **No Uronic acid residue**
- Defect in sulphation can cause corneal dystrophy & Keratoconus



Keratoconus



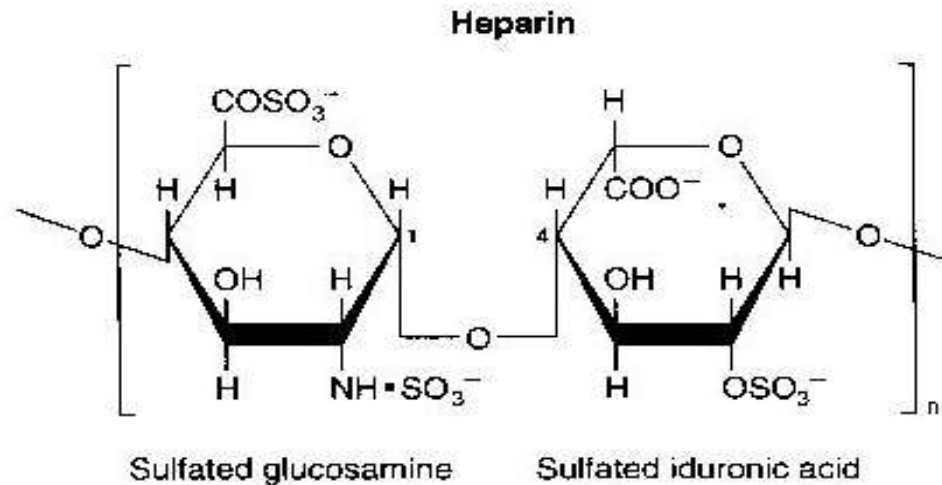
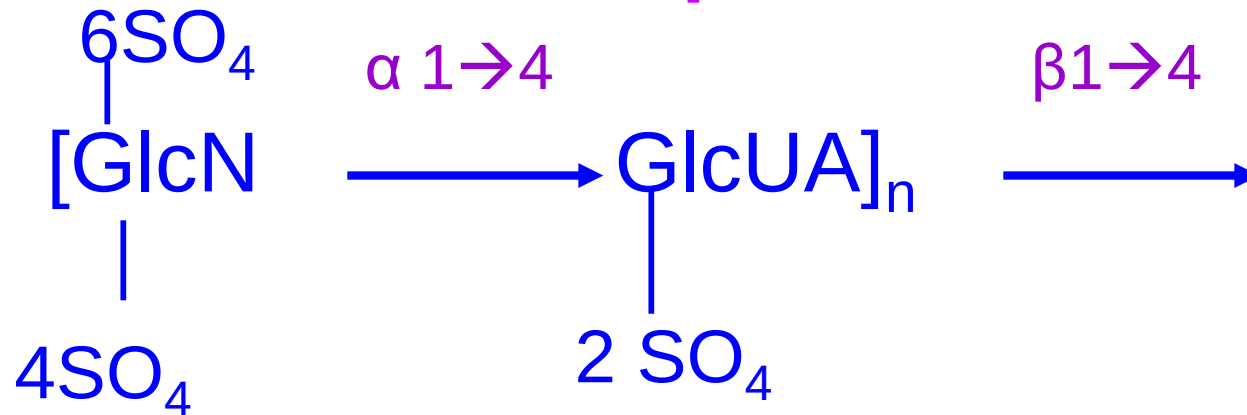
Biologically important Polysaccharides

Heparin

- **Anticoagulant** (in vitro & in vivo)
- Found in Thymus, spleen, walls of large arteries and small amounts in blood
- **Highly sulfated**
- **Commercial preparation from animal lung tissue**
- Contains IdUA

Biologically important Polysaccharides

Heparin



Properties of Glycosaminoglycans

- Polyanionic due to acidic sulfate and carboxylic acid groups.
- The properties and functions of the GAG depends on these negatively charged groups

Functions of Glycosaminoglycans

- 1)Structural components of extra cellular and ground substances in association with other structural elements- collagen and elastin.
- 2)Due to the large number of negatively charged groups, polysaccharide chains are kept apart, hence can hold large amount of water and occupying space which attribute the cushioning and lubricating effect . Eg. Hyaluronic acid present in synovial fluid .

Functions of Glycosaminoglycans

- 3) Poly anions can bind with cations and absorb water by osmosis.
- 4) Because of the long extended nature and gel like consistency acts as a sieve or barrier permitting entry of nutrients and resisting entry of bacteria.

Functions of Glycosaminoglycans

- 5) High concentration of **Hyaluronic acid and chondroitin in tissue constitute compressibility to cartilage.**
- 6) Proteoglycans located in certain neurons may **provide endoskeletal structure** helping to maintain their shape. eg. Chondroitin sulfate.

Functions of Glycosaminoglycans

- 7)Keratan Sulfate present in cornea in between collagen fibres play a role in corneal transparency.
- 8)Dermatan sulfate in sclera play an important role in maintaining the overall shape of the eye.

Functions of Glycosaminoglycans

- 9) Due to the presence of polyvalent anions, GAG can interact with both extra and intra cellular molecules. Eg. **Heparin** binds with factor IX and XI and plasma antithrombin III, which inactivate thrombin.
- **10) Heparan Sulfate** which is present cell wall serves as receptors for macromolecules.

Functions of Glycosaminoglycans

- 11) **GAGs** have got an important role in cell growth, mediate cell to cell recognition and help cell migration. Eg. Hyaluronic acid in embryonic tissue is responsible for cell migration during morphogenesis and wound repair.
- 12) Have got an effect on protein synthesis and intra nuclear functions.

Functions of Glycosaminoglycans

- 13) Numerous **storage granules** such as **chromaffin granules** in adrenal medulla , basophilic granules of mast cells contain GAGs , so it is believed to have a role in **synthesis of biological amines.**

Functions of Glycosaminoglycans

- 14) **Hyaluronic acid** is important in permitting **tumor cells to migrate** through the extra cellular matrix.
- 15) Tumor cells induce fibroblasts to synthesize large amount of GAG and **facilitate metastasis.**

Functions of Glycosaminoglycans

16) Role in Disease and Ageing:

- **High amount of GAG (DS)** is present in arterial walls. They get bound to LDL and play a role in development of atherosclerosis.
- 17) **Proteoglycans** have got a role in development of arthritis. They act as auto-antigens and contribute to pathology.

Functions of Glycosaminoglycans

- **Chondroitin sulfate in cartilage**
decreases with age where as Keratan Sulfate and Hyaluronidic acid increases.
These changes **contribute to**
Osteoarthritis.
- Changes in concentration of **GAGs in skin** are seen with **ageing.**

Synthesis of Glycosaminoglycans.

- Core protein is synthesized in ER and the oligosaccharide moiety is added in Golgi.
- Enzymes responsible for chain elongation are highly specific.

Degradation of Glycosaminoglycans

- GAGs are degraded by specific **hydrolytic enzymes in lysosomes**. Both exo and endo glycosidases degrade GAGs.
- GAGs generally exhibit slow turn over in the order of days and weeks.

Clinical Significance

Mucopolysaccharidoses

- Are a group of disorders characterized by accumulation of substrates in organs due to the **deficiency of degrading enzymes**.
- This results in enlargement of organs, disturbances in structure of bone, skin etc.

Mucopolysaccharidoses

- Included in **Lysosomal Storage disorders**.

Disease is characterized by

- Coarse features,
- Thick skin,
- Corneal opacities,
- Mental retardation,
- Excretion of **MPS in urine**

Mucopolysaccharidoses – Hurler

A four year old boy presenting with

- Delayed milestones,
- Hepatomegaly
- Short stature
- Enlarged tongue
- Nasal discharge
- Hydrocephalus



The disease was progressive and at the age of 8 he died of respiratory arrest.

Mucopolysaccharidoses – Hunter's
6 year old boy diagnosed of having severe
MPS II at the age of one. Presented with

- Hepatomegaly
- Joint stiffness
- Umbilical hernia
- Severe hearing loss
- Developmental delay
- Recurrent ear infections
- Hyperactive



The disease was progressive and at the age of 20,
he died.

Mucopolysaccharidoses – Hunter's

A 48 year old man, suffering from
mild MPS II

- At the age of 13, diagnosis was made.
- He had joint stiffness, coarse facial features, heart murmur but with normal intelligence.
- He has a good career and married and has 2 healthy daughters.
- His maternal uncle and a nephew also have Hunter's.
- Mode of inheritance- X linked recessive



Mucopolysaccharidoses

Diagnosis

- Screening test in urine – Dip a filter paper in Toluidine blue of pH 2. wash with 95% ethanol – **Purple Spot + ve**
- - **Amniocentesis**

Treatment

- **Gene Therapy**

Glycoproteins - Mucoproteins

Differ from Gag by

- Do not contain repeating disaccharide unit.
- Do not contain uronic acid residues
- Sugar residues present are Man, Gal, Xyl, Glc NAc, Gal NAc, Arabinose, L Fucose, Sialic acid
- CHO residue < 4%

Glycoproteins

- Carbohydrate residues are attached to polypeptide chains covalently by N or O glycosidic bonds.
- Present in most organisms, plants, bacteria, virus.
- Most of the membrane proteins and secretory proteins are Glycoproteins.

- 5% Weight of cell membrane is CHO cover entire surface of cell membrane called as **Glycocalyx**

Major membrane glycoprotein of Erythrocytes is **Glycophorin(trans membrane protein)**

- Bacterial cell wall contain heteropolysacharides, repeating units are **NAcMuramic acid(NAM) & Glc NAc** which give mechanical strength
- Penicillin blocks the synthesis of this complex polysacharide. **(Bactericidal action of penicillin)**

Glycoproteins

Functions:

- Structural molecules of cell wall. Eg. Collagen, elastin, fibrin.
- Present in mucin and mucous secretions. Acts as lubricant and protective agent.
- Almost all the plasma proteins, except albumin are glycoproteins.

Glycoproteins

- Act as **transporters** of vitamins, minerals, hormones, drugs etc.
Ceruloplasmin- Copper, Transferrin - Iron
- Constituent of **Immunoglobulins, Complements** etc.
- Many of the Hormones and enzymes are Glycoproteins.
eg.- **Chorionic gonadotropin, TSH**

C.Blood Group Substances

- Human blood is classified into 4 main groups - **A, B, AB and O**
- This classification depends on the presence or absence of blood group substances present on the RBC membrane.

Blood Group Substances

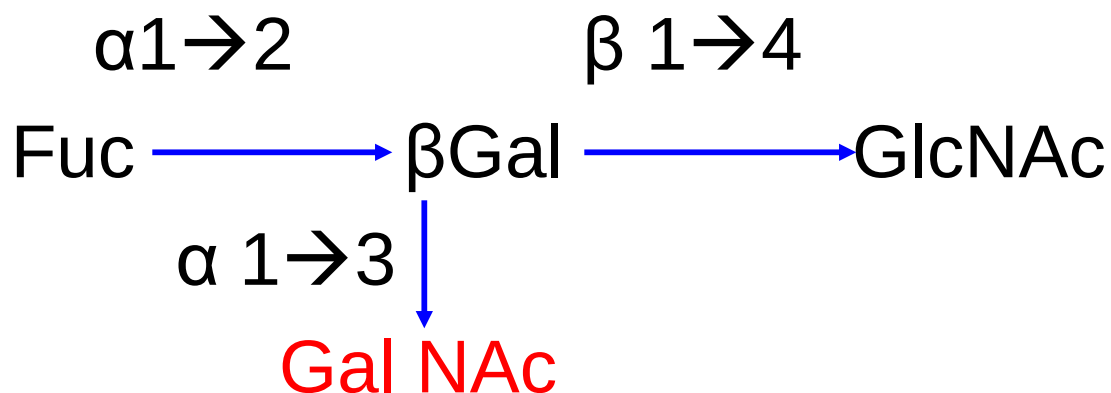
- Blood group substance contain 4 types of monosaccharides.
 - L Fucose (6Deoxy Galactose)
 - Galactose
 - N-acetyl Galactosamine (NAc Gal)
 - N- acetyl Glucosamine (NAc Glc)
-
- Difference in A gp and B gp depends on the Oligosaccharide unit.

Blood Group Substances

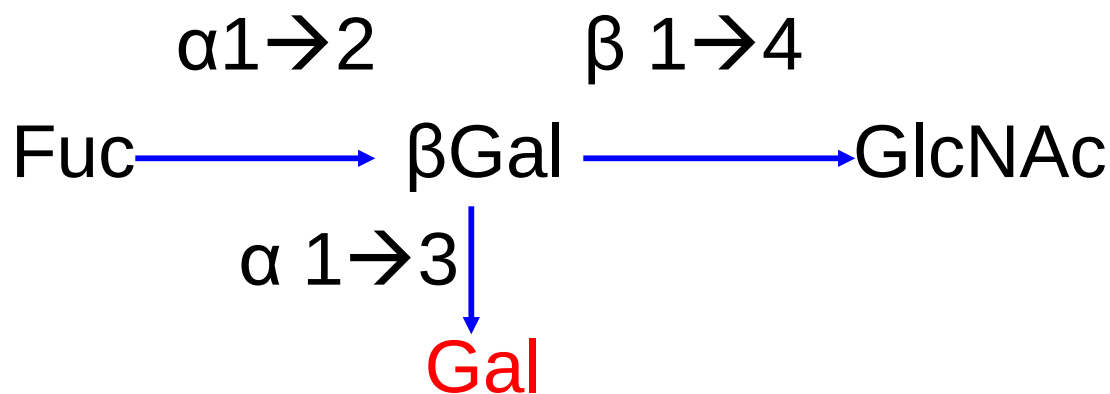
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Blood Group Substances

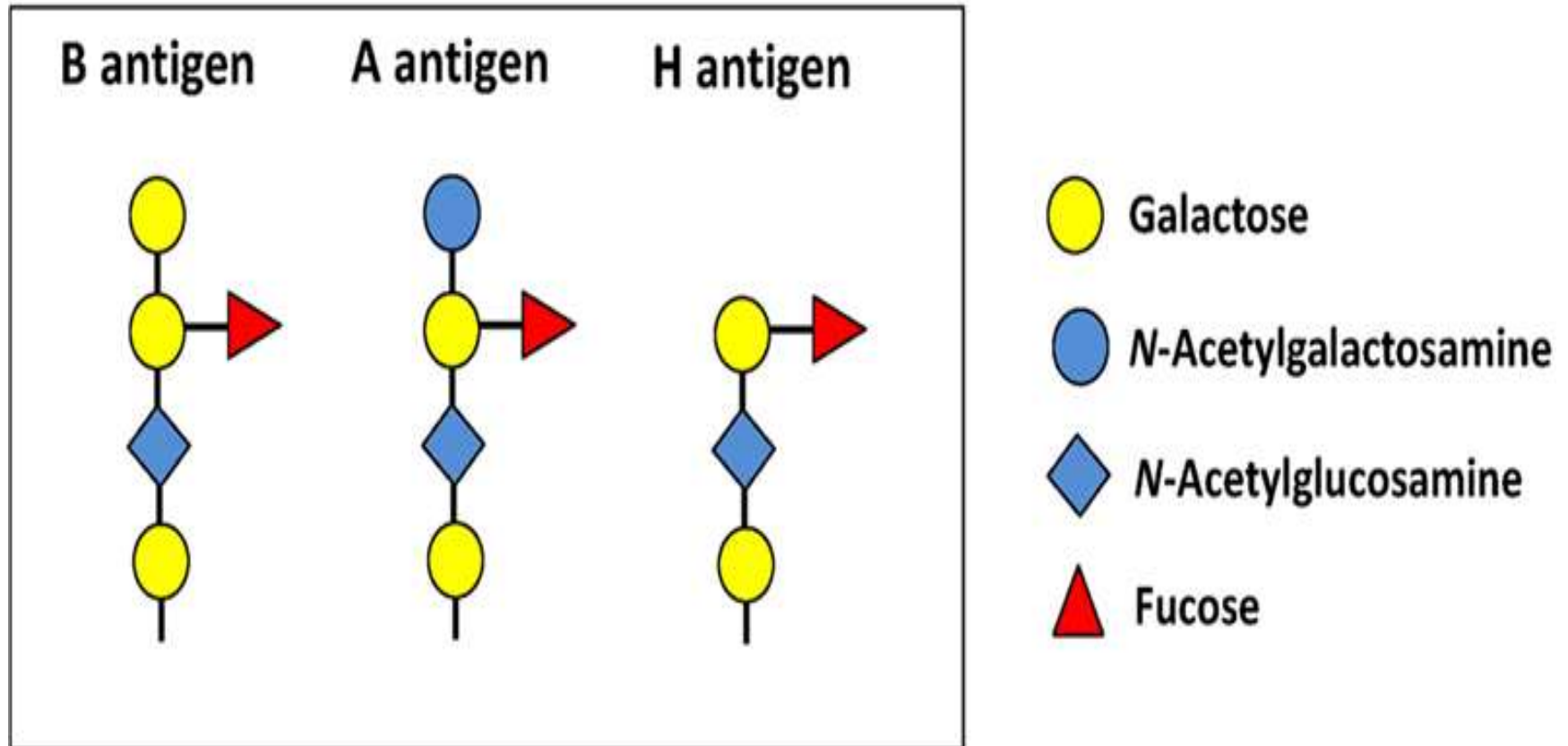
A Group



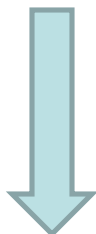
B Group



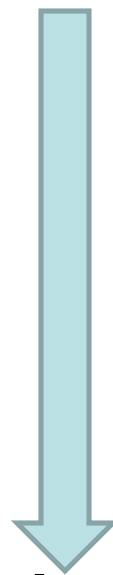
ABO antigens



Polysacharides



Homopoly sacharides



Heteropolysacharides

Homoglycans

Name	Monomers	Linkage
Glycogen	D Glucose	1>4, 1>6 branches
Starch-----Amylopectin Amylose	D Glucose D Glucose	1>4, 1>6 branches 1>4
Cellulose	D-Glucose	beta 1>4
Chitin	N-Acetyl-D-glucosamine	beta 1>4
Inulin	D Fructose	beta 1-4 linkages
Dextran (High mol wt)	Glucose from microorganisms	Glucose 1>6, 1>4, 1>3

Heteroglycans

Name	Repeating units
Agar	Galactose, glucose
Agarose	Galactose , anhydrous galactose
Hyaluronic acid	GlcUA, Glc NAc
Heparin	Sulphated glucosamine, & LIduronic acid
Chondroitin sulphate	GlcUA, Gal NAc
Keratan sulphate	Galactose, Gal NAc
Dermatan sulphate	L-iduronic acid , GalNAc

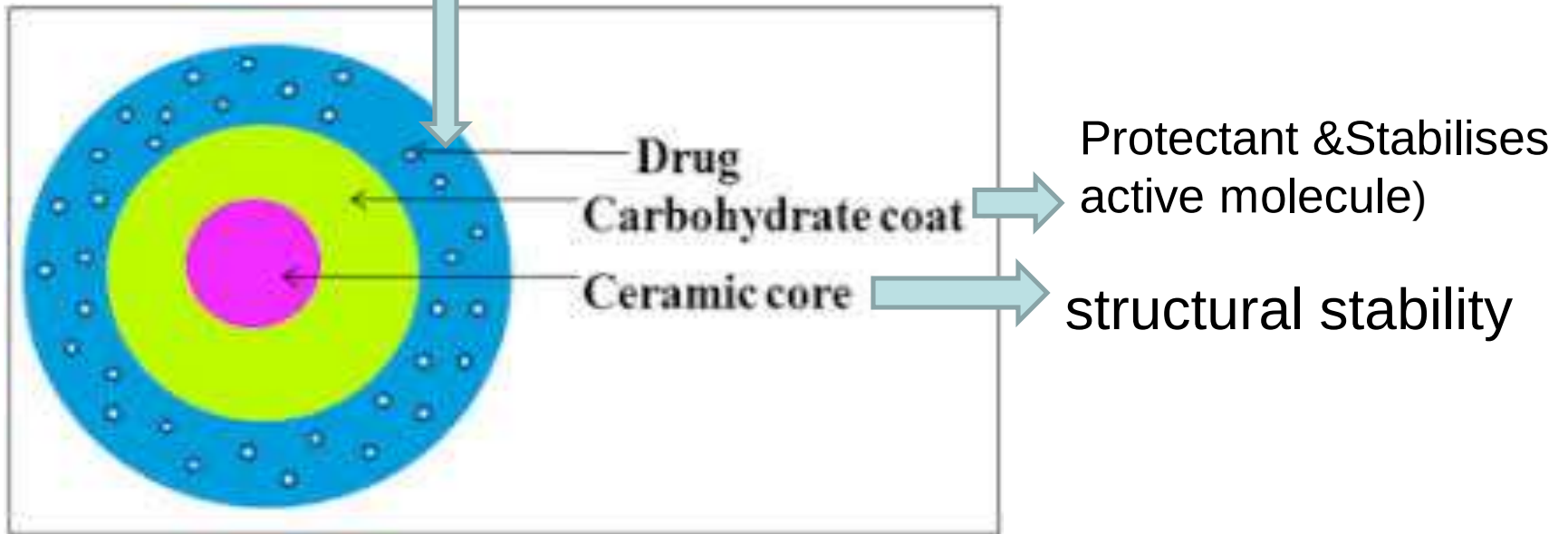
Dietary fibre

- Unavailable CHO in diet
- Form bulk & **help in normal bowel movements**
- Glycans which form dietary fibre are **Cellulose, hemicellulose, pectin, gums**
- Cellulose(homoglycan in bran, flour, tubers)
- Pectin from apples, berries

Aquasomes

- Aquasomes are a **drug delivery system** that **use nanoparticles** to carry bioactive molecules **to specific sites** in the body:
- Spherical nanoparticles with three layers: a ceramic core, an oligomer coat, and a biochemically active molecule.

Biochemically active molecule adsorbed



Aquasomes

- Recently developed delivery system for peptide based pharmaceuticals(egs:Insulin,Hb, peptide, protein, hormones,serratiopeptidase, antigens and genes to specific sites)

Sugar substitutes

Artificial sweeteners

- Acesulphame-potassium
- Aspartame
- Sucralose
- Cyclamate
- Sacharin
- Stevia

Glycomics

- Study of structure& functions of Glycome.
- Glycome refers to all Carbohydrates in an organism



**May Success
be with you,
always.**

All The Best.

