Biomedically Important Polysaccharides/Glycans

- **Polysaccharides** are complex class of Carbohydrates,
- Chemically composed of **more than ten,** same or different **Monosaccharide units or their derivatives**
- Repeatedly **linked** by **glycosidic linkages.**
- General Formula of Polysaccharides $(C_6H_{10}O_5)n$
- **Iodine test is a characteristic test for Polysaccharides**

- Iodine test is based on Physical property of adsorption.
- Iodine get adsorbed on complex structure of Polysaccharides to give characteristic color.

Glucosan

- Type of Homopolysaccharide
- Repeating unit,of Glucosan is **Glucose**
- **Glucosan is a Polymer of Glucose.**
- **Starch**
- **Glycogen**
- **Cellulose**
- **Dextrin**
- **Dextran**

Fructosan

- Type of Homopolysaccharide
- Repeating unit in Fructosan is **Fructose.**
- **Fructosan is a Polymer of Fructose.**
- **Inulin**

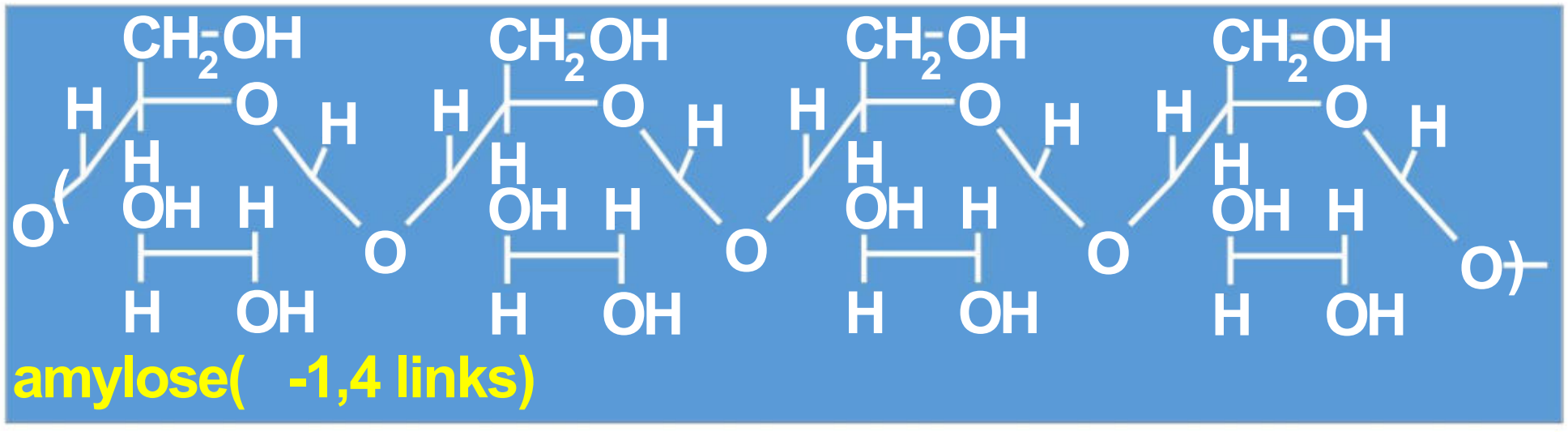
Starch

- Plant Homopolysaccharide
- Starch is Glucosan
- **Repeating Unit** -

  α D Glucose (approx 7000)
- **Components of Starch-**
- Amylose and Amylopectin

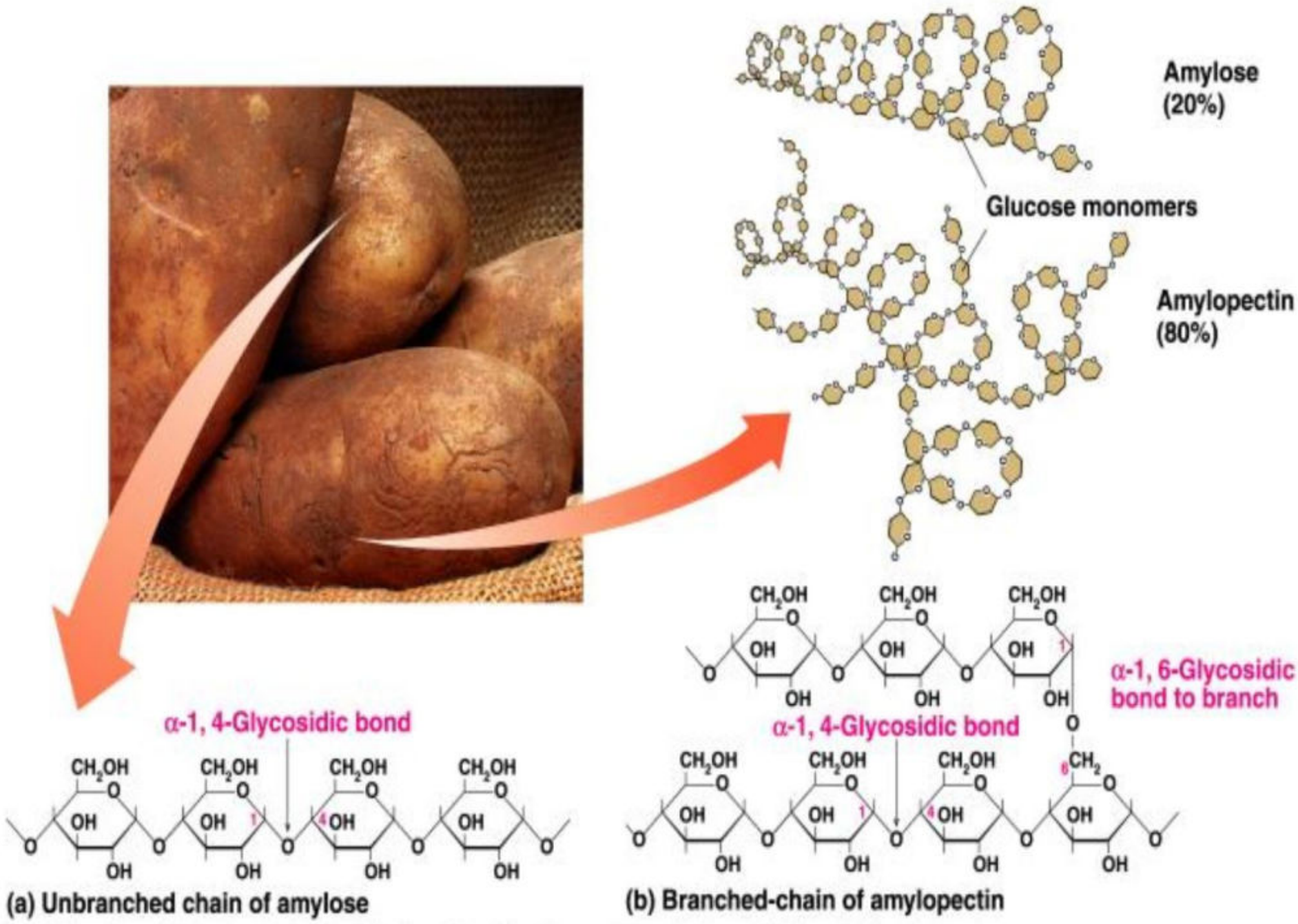
Amylose

- Amylose is 15-20%
- Linear structure
- α D Glucose linked by α (1-4) glycosidic bond.



Amylopectin

- Amylopectin is 80-85 %
- Branched structure
- Branching point appears after every 25-30 Glucose units.
- It has α (1-6) glycosidic bond at branching point.
- α(1-4) glycosidic bonds in linear structure.



- Starch is white ,odourless, tasteless powder .
- Starch is **insoluble in cold** water, but get **solubilized on heating** and form gel /paste.
- Starch is **a non reducing** Carbohydrate.

  Starch -Negative Benedicts Test.
- Starch on **Iodine reaction** gives **blue color.**

Source/Occurrence Of Starch

- Plants- Seeds, Tubers, Roots, Raw fruits.
- **Dietary Sources of Starch.**
- **Grains**- Rice ,Wheat, Jawar, Bajra
- Potatoes
- Beetroot.
- Sago (Tapioca)
- Vermicelli
- Suji.
- Raw Mangoes

Digestion of Starch

- **In mouth-** by salivary **α Amylase**
- **In intestine -**by pancreatic **α Amylase**

- **α Amylase cleaves,** α (1-4) glycosidic bonds of Amylose and Amylopectin and releases **Maltose and Isomaltose.**
- **Maltose** and **Isomaltose** is then **digested by Maltase and Isomaltase** to release free Glucose units.

- Thus Starch on digestion gives **thousands of free Glucose units which have high calorific value.**

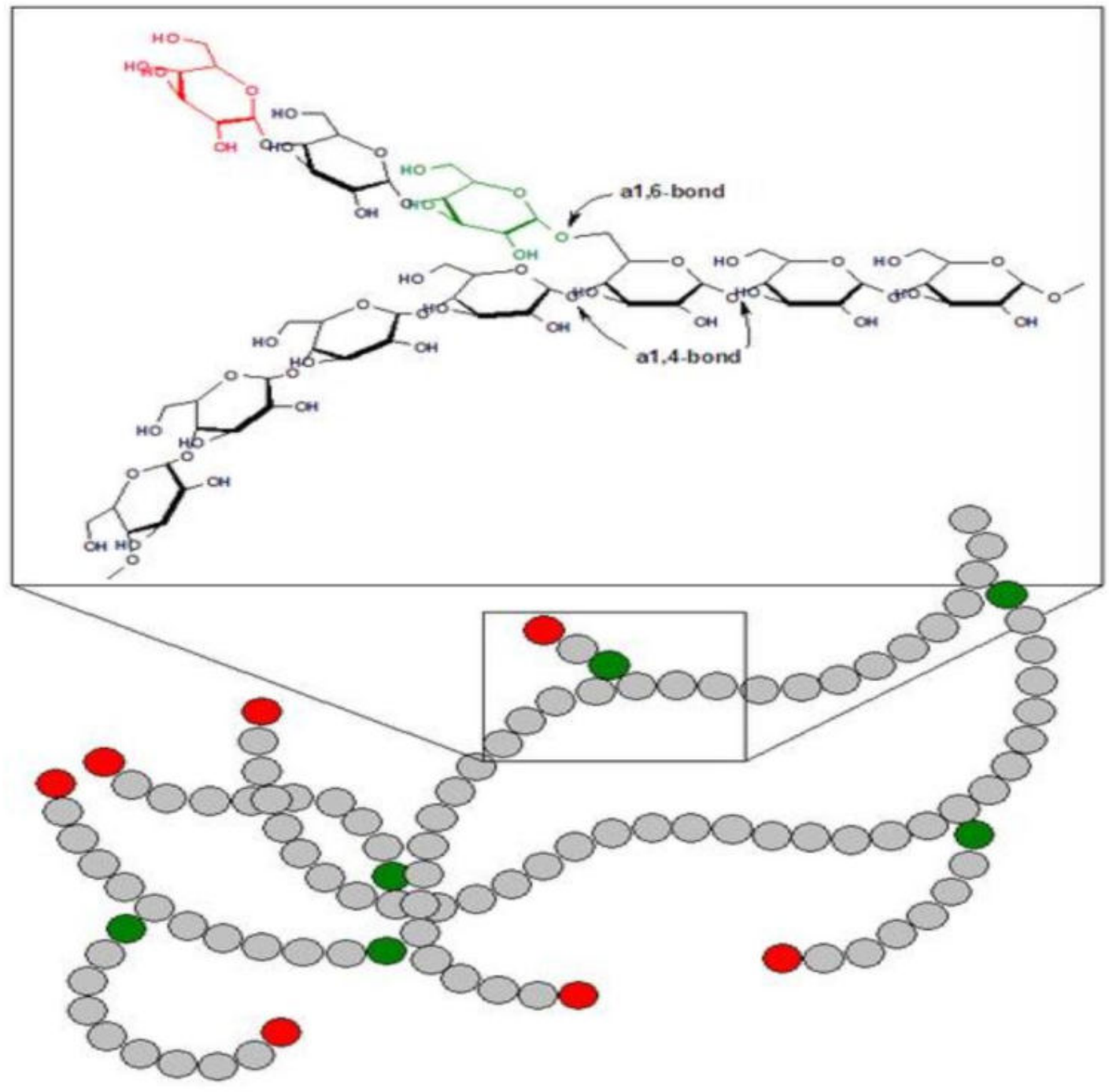
Glycogen

- Animal Homopolysaccharide
- Animal Starch
- Glycogen is chemically Glucosan.
- **Repeating Unit** –

  α D Glucose (25-30 thousand Glucose units)

- **Glycogen** is like Amylopectin structure ,but it is **highly branched**
- **Branching points** appear after every **8-10 Glucose units**, linked by **α (1-6) glycosidic bond.**
- Linear structure has Glucose linked with **α (1-4) glycosidic bond.**
- On Iodine reaction Glycogen gives deep red color.

Glycogen



- Glycogen has **more (1 6) branches**.
- The highly branched structure permits rapid glucose release from glycogen stores, in muscle during exercise.
- Glycogen is present in animal-
  - Liver (75 gm)
  - Muscle (125 gm).

- After well fed condition, free and excess of Glucose is condensed to Glycogen via **Glycogenesis**.

- **Rate of Glycogen synthesis** –
  - **Liver- 6-8 %,**
  - **Muscle 1-2 %**
  - Glycogen is broken down to Glucose via **Glycogenolysis** when body Glucose lowers in fasting and starvation condition.

- Dietary **Glycogen** in GIT is **digested** by **α- Amylase** to Maltose and Isomaltose and finally to thousands of Glucose Units.

Liver Glycogenolysis in Human body **regulates Blood Glucose levels** in fasting condition.

Muscle Glycogenolysis provides **energy** for **muscle activities** in fasting condition.

Sr. No	Starch	Glycogen
1.	Starch is Plant Homopolysaccharide.	Glycogen is animal Homopolysaccharide
2.	Starch is composed of **Amylose** (Linear)&**Amylopectin** (Branched)	Glycogen is highly branched structure with branching points appearing after every 8-10 Glucose residues.
3.	Starch is composed of 4000-7000 Glucose units.	Glycogen is composed of 6000-30,000 Glucose units.
4.	Starch is a storage form of Glucose and reserve food material in plants.	Glycogen is storage form of Glucose and reserve form of energy in animals and human beings.
5.	Starch is stored in roots, tubers, seeds, raw fruits of plants.	Glycogen is stored in Liver and Muscles of animal and human body.
6.	Starch serves as predominant dietary Carbohydrate form in Veg and Nonveg eaters.	Glycogen is dietary form of Carbohydrate only in Non-Veg eaters.
7.	Starch with Iodine test gives deep Blue color.	Glycogen with Iodine test gives deep red color.

Cellulose

- Non digestible carbohydrate

- Cellulose serve as **dietary Fiber.**
- **Cellulose is a Glucosan**
- **Repeating Unit** -**β D Glucose.**
  (approx 2,500- 14,000).

- Cellulose is a **linear ,unbranched** structure where **β D Glucose units** repeatedly linked by **β (1-4) glycosidic bonds**.

Source/Occurrence Of Cellulose

- Cellulose **is an abundant carbohydrate of nature** exclusively present in **Plants cell wall**.

- **Dietary rich sources of Cellulose**
- Whole Grains (outer covering)
- Green leafy vegetables
- Cabbage, Cucumber
- Legumes, Nuts, Beans
- Dates
- Fruits and Vegetable salads.
- In **plants Cellulose** present in cell wall **provides structural and mechanical support.**

Cellulose has Effect on Fecal Mass Formation

- Cellulose acts **as a roughage.**
- It holds water ,helps in **forming soft** and **bulky feces.**
- **Increases intra luminal pressure.**
- **Reduces transit time of feces to remain in gut.**
- **Eliminates daily, metabolic wastes and toxins** out of the body, through feces.
- **Defecation with greater ease and good frequency.**

- **Cellulose prevents constipation,** and **reduces risk of :**
  - colon cancer
  - diverticulosis of intestine
  - hemorrhoids

- Cellulose **reduces** the **absorption** of **:**
  - **Glucose**
  - **Cholesterol**
- Ameliorate the conditions of :
  - **Diabetes mellitus**
  - **Atherosclerosis** respectively.
  - **Cellulose** being **non calorific** and possessing **high satiety value** helps in **managing obesity** in humans.

- For maintenance of good health ingest dietary fibers.

- RDA for dietary fiber to maintain good health:
  - **Adults= 20-25 gm/day.**
  - **Children's= 5-10 gm/day.**
- **Disadvantage** of dietary **Cellulose-**
- **It** decreases absorption of minerals.

Dextrin

- Intermediate hydrolytic product of Starch digestion
- **Dextrin is a Glucosan**
- **Repeating Unit** -α D Glucose.

- Dextrin is less complex than starch structure.
- Dextrin is broken Starch molecule.

Types Of Dextrin

- **Amylodextrin** -Violet to Iodine reaction
- **Erythrodextrin**- Red to Iodine reaction
- **Achrodextrin** -Colorless to Iodine reaction.

Source/Occurrence of Dextrin

- In human GIT **Dextrin** is obtained as an **intermediate hydrolytic product of Starch digestion** by the action of

  α-Amylase activity.

- Dextrin is Present in **commercially** prepared **infant foods**.

Biomedical Importance Of Dextrin

- Dextrin has **mucilage nature(sticky)** hence used as binding and **adhesive agent**.

- Dextrin is used as **infant food.**

Dextran

- Dextran is a Bacterial Homopolysaccharide
- **Dextran is a Glucosan**
- **Repeating Unit** –α D Glucose.

- Highly branched, complex, network like structure Glucose units linked **by**
  α(1-4) ,α(1-6) and α (1-3) glycosidic linkages.
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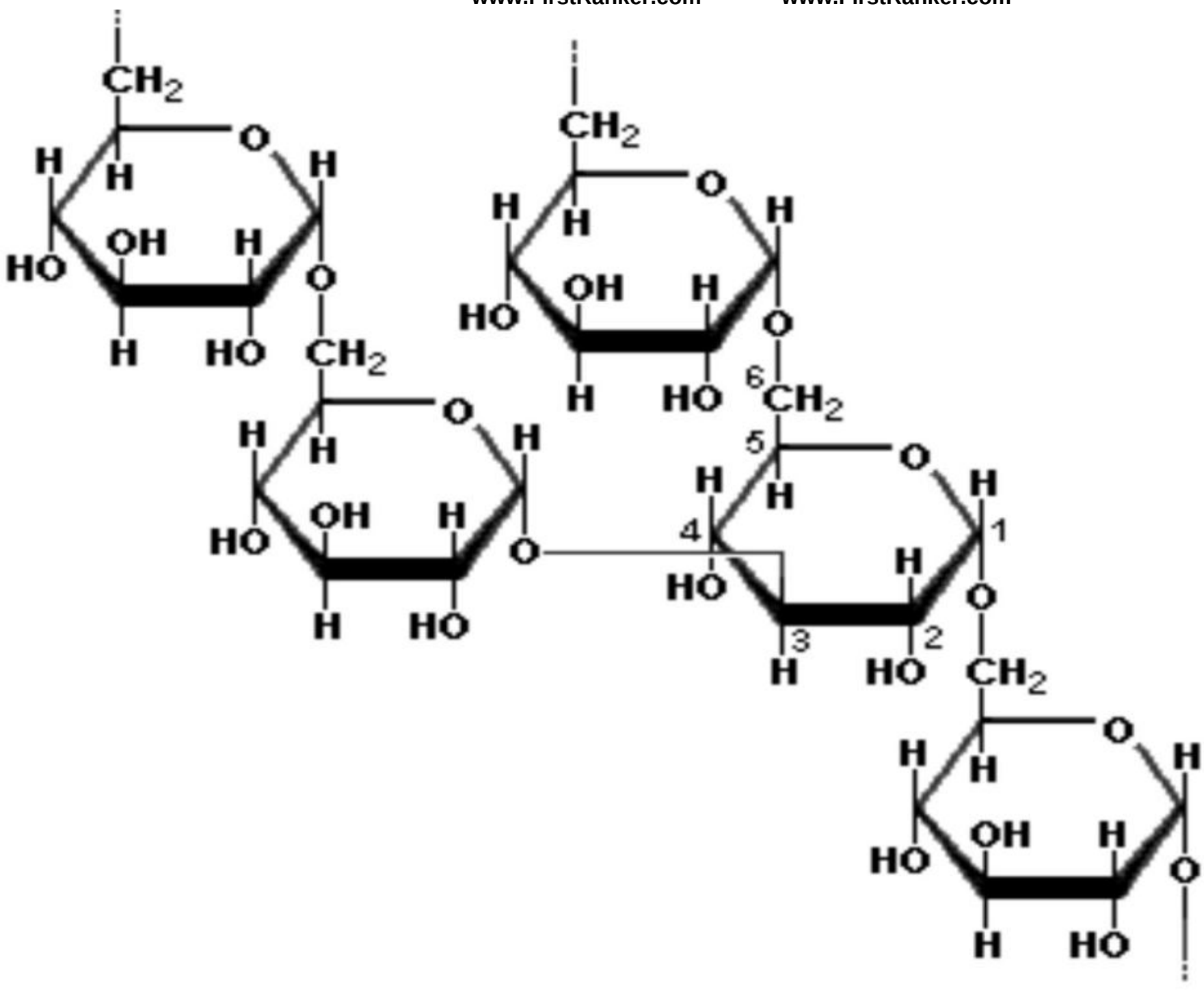


Source/Occurrence Of Dextran

- Dextran is obtained from **Sucrose** solution incubated with bacteria **Leuconostoc mesenteroides**
- Dextran solution is **high molecular weight**, **viscous** solution with **osmotic pressure** equivalent to **plasma Albumin.**
- Dextran **maintains blood volume** and **osmotic pressure.**

- **Dextran solution** is used as
- **Plasma substitute/plasma volume expander**
- Dextran infusion manages a **hemorrhagic case** and **prevent** from **hypovoluemic shock.**

Sr.No	Dextrin	Dextran
1.	Dextrin is plant Homopolysaccharide	Dextran is bacterial Homopolysaccharide.
2.	Dextrin is an intermediary hydrolytic product of Starch digestion.	Dextran is a Glucosan obtained from Sucrose solution incubated with Leuconostoc mesenteroides.
3.	Structure of Dextrin contains α (1-4) & α (1-6) glycosidic bonds.	Structure of Dextran contains α (1-3), α (1-4) & α(1-6) glycosidic bonds.
4.	Dextrin solution is used in commercially prepared infant feedings and mucilage for pasting stamps.	Dextran solution is used as plasma volume expander in relieving hypovoluemic shock in cases of hemorrhage.

Fructosan

- Homopolysaccharide with repeating units as Fructose.

Inulin

- Diagnostic Carbohydrate
- **Diagnoses Kidney Function**- GFR of Kidney.
- Naturally present in Plants
  - **Roots and tubers of Dandelions**
  - **Onion and Garlic bulbs**
  - **Chicory Plant.**

Chemistry Of Inulin

- **Inulin is a Fructosan**
- **Repeating Unit-**
  βD Fructose units (33-35 units)
- Repeatedly linked by
  β (1-2) glycosidic bonds.

- Inulin is non digestible and non absorbable form in human GIT, hence have no calorific value.

- Inulin solution infused intravenously during **Inulin Clearance Test**, **checks Glomerular Filtration Rate** (GFR) of Kidney **(120-125 ml/min).**

Heteropolysaccharides

- Heteropolysaccharides are type of Polysaccharides composed of **more than 10 different**
- **Monosaccharide units or their derivatives** repeatedly linked by glycosidic bonds.

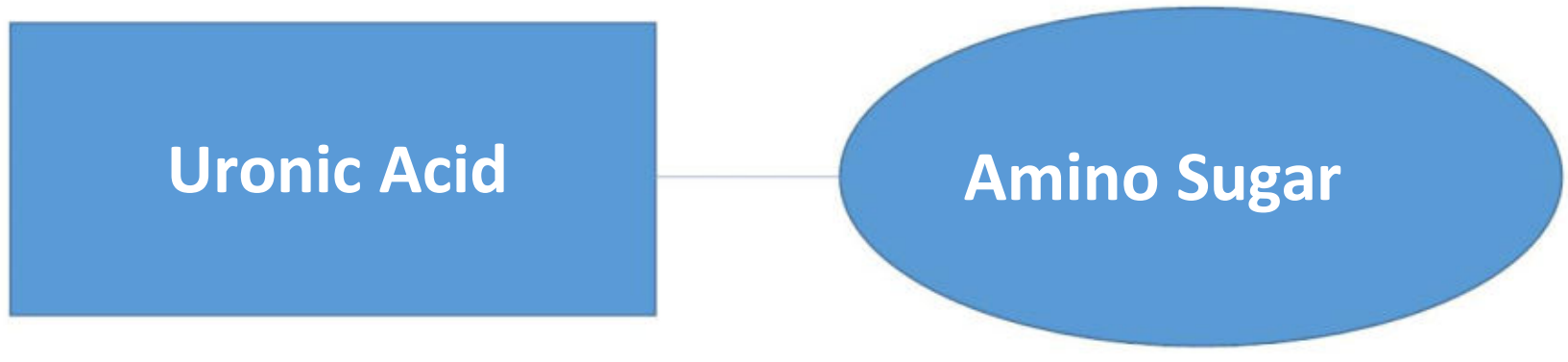
Animal Heteropolysaccharides

Mucopolysaccharides (MPS)

- **Human Heteropolysaccharides**
- **Animal Heteropolysaccharides**
- **Glycosaminoglycans (GAGs)**

- Mucopolysaccharides were first isolated from **Mucin** hence the name **Mucopolysaccharides.**
- Mucopolysaccharides chemically composed of more than 10 Monosaccharide units and its derivatives repeatedly linked by glycosidic bonds.
- Mucopolysaccharides are complex, long, linear, unbranched, polyanionic.

The Glycosaminoglycans has **Disaccharide repeating unit** linked by glycosidic bonds of



- **Uronic Acid** –
  Glucuronic acid /Iduronic acid
  (Iduronic acid is 5’ Epimer of Glucuronic acid)

- **Amino Sugar**-
  Glucosamine / Galactosamine
  (Acetylated or Sulfated or Both)

Jeanloz suggested the term **GAG’s** as these biomolecules has **amino sugars as repeating units.**

Properties of GAG’s

- GAG’s are **polyanionic and acidic** due to presence of
  –COO^- and $SO4^{--}$
- GAG’s are **hydrophillic** and attract water and **helps in distributing water.**
- **MPS due to repulsion of charges:**
- It appear **slippery or sticky** in appearance/mucus like secretions
- It **expand to occupy large space.**

- MPS/GAG's imparts following **physical properties-**
  - **Turgor**
  - **High Viscosity**
  - **High Density**
  - **High Buoyancy.**

Body Mucopolysaccharides

- **Acidic Non Sulfated MPS:**
  - Hyaluronic Acid
- **Acidic Sulfated MPS:**
  - Heparin
  - Heparan Sulfate
  - Chondritin Sulfate
  - Dermatan Sulfate
  - Keratan Sulfate
- **Neutral MPS:**
  - Blood Group Substances

Hyaluronic Acid

- Acidic Non sulfated MPS
- **Repeating Disaccharide Unit**
  - **Glucuronic acid**
  - **NAcetylGlucosamine.**
  - Hyaluronic acid is present as **ground substance/cementing substance** in extra cellular spaces of connective tissue.

- Hyaluronic acid in **synovial fluid of joints** and **vitreous humor** of **eye** serve as lubricant and shock absorbant.
- Hyaluronic acid around ovum gives protection.
- Hyaluronic acid plays role in cell migration during morphogenesis.

- **Enzyme "Hyaluronidase** " hydrolyses Hyaluronic acid.
- **Hylauronidase** present in **head of sperm** , hydrolyzes the Hyaluronic acid present on ovum which **facilitates its penetration and fertilization.**
- **Snake venom** is **rich in Hyaluronidase**, thus snake bite hydrolyzes and liquifies the Hyaluronic acid present in extracellular spaces of cells **(TOXIN)**

Heparin

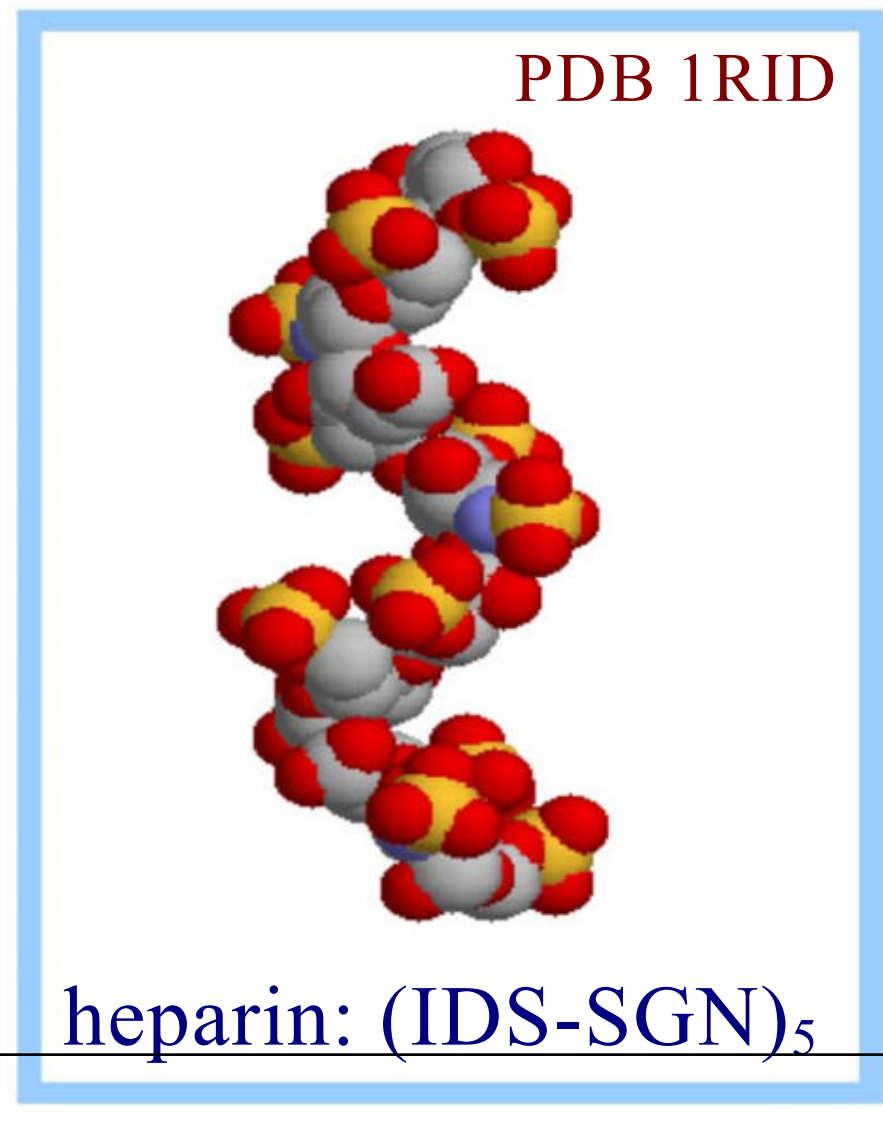
- **Most Acidic Sulfated MPS.**

Disaccharide Repeating Unit:

- Glucuronate sulfate (minor)
- Iduronate sulfate (major)
- N-Glucosamine Sulfate.

- **Heparin**, a soluble glycosaminoglycan found in granules of mast cells and is **highly sulfated**.

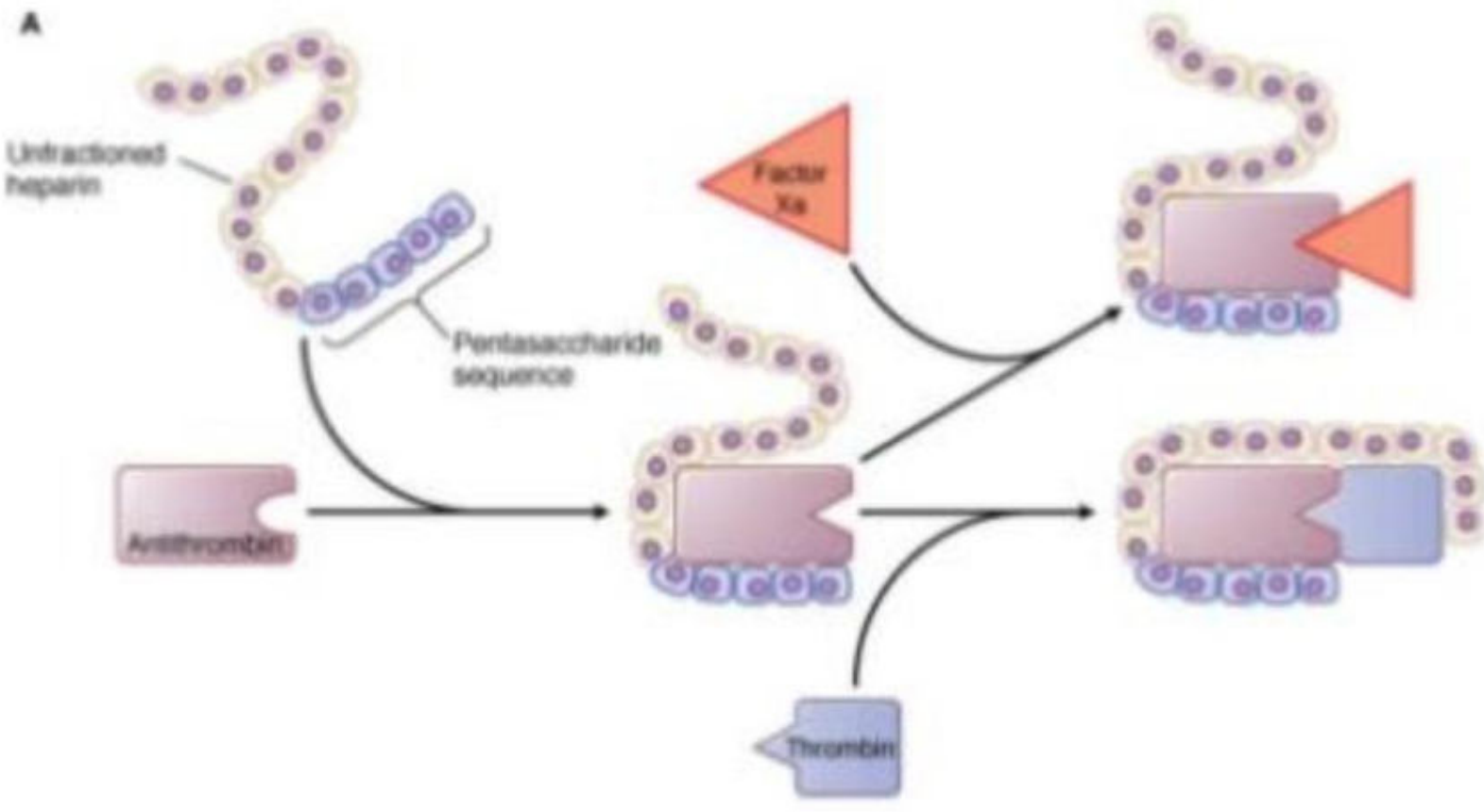
- Heparin has an **extended helical conformation**.



heparin: $(IDS\text{-}SGN)_5$

Actions of Heparin

- UFH works by binding to antithrombin III (AT), throug a key pentasaccharide motif, which catalyses the reaction between AT and thrombin
- AT also inhibits activated factor Xa



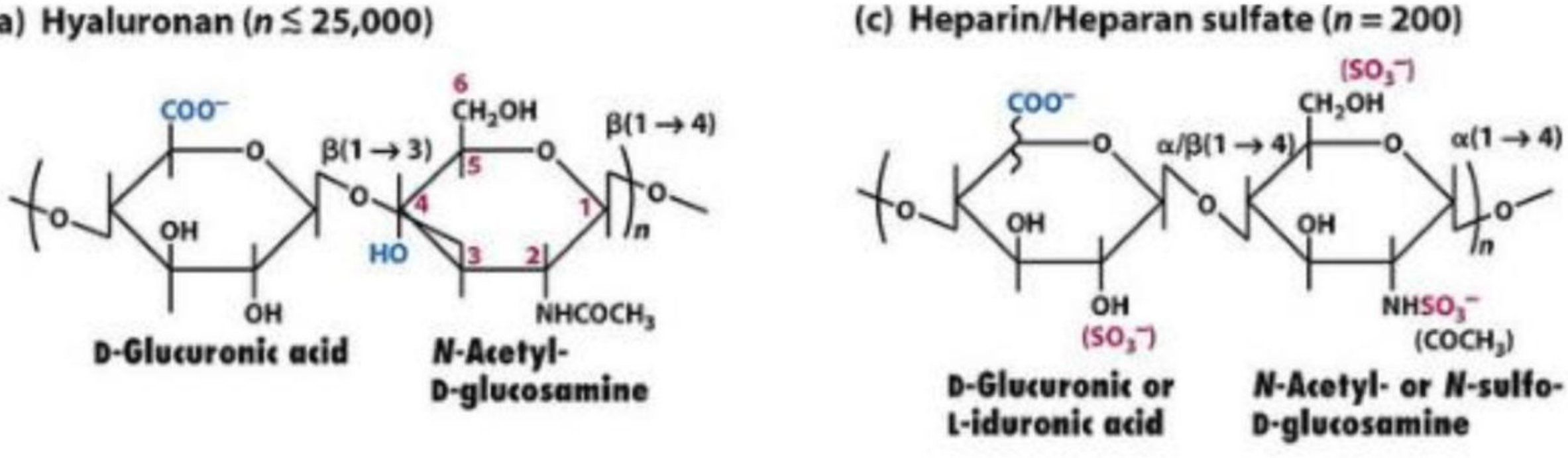
Occurrence and Functions Of Heparin

- Heparin present in blood vessels, Liver, Lung, Spleen and Monocytes
- Natural anticoagulant.
- In blood, it **inhibits clot formation** by interacting with the protein antithrombin.

- Heparin is an indirect Thrombin inhibitor .
- Rapid inactivator of Thrombin.
- Thus antithrombotic agent.
- Prevents intravascular blood clotting.
- Heparin releases enzyme Lipoprotein Lipase from endothelial lining and serve as coenzyme for it. Clearing factor

Therapeutic Use of Heparin

- Heparin is infused to **prevent and treat** thrombous located in vein/artery in MI cases.
- Deep Vein Thrombosis.
- Pulmonary Embolism
- Strokes
- Heparin(LMW Heparin) injections are given to M.I patients
- To liquify blood ,prevent thrombosis and clear blood with lipids.



Heparan Sulfate

- Acidic Sulfated Mucopolysaccharide

- **Disaccharide repeating units**
- Glucuronate Sulfate (major)/ Iduronate Sulfate (minor)-N Acetyl Glucosamine

The difference between heparin and heparan sulfate is quantitative not qualitative

Characteristic	Heparan sulfate	Heparin
Sulfate/hexosamine	0.8 - 1.8	1.8-2.4
GlcN N-sulfates	40-60%	□85%
IdoA content	30-50%	□70%
Solubility in 2 M KAc at ph 5.7, 4ÞC	Yes	No
Site of synthesis	Virtually all cells	Mast cells
Size	10-70 kDa	10-12 kDa
Binding to Antithrombin	0-0.3%	~30%

Occurrence and Functions Of Heparan Sulfate

- **Heparan Sulfate** present on extracellular **cell surfaces** or **plasma membranes** and serves as **receptors**
- **Participate in cell growth, cell adhesion, and cell -cell communication**.
- Heparan sulfate in basement membrane of kidney helps in determining **charge selectiveness of Glomerular filtration.**
- Heparan sulfate are also components of aorta, liver, fibroblasts, synaptic and vesicles.

Chondritin Sulfate

Acidic Sulfated Mucopolysaccharide

- **Disaccharide Repeating Unit**
- Glucuronate-
- N –Acetyl Galactosamine –Sulfated.

- **Chondritin Sulfate A-**4 sulfated.

- **Chondritin sulfate C-**6 sulfated.

Occurrence and Functions Of Chondritin Sulfate

- Chondritin Sulfate is present in connective tissues-bones, cartilage, tendons .
- It gives mechanical strength, compressibility and support to connective tissues.
- Chondritin sulfate present in **cornea** give over all **shape to eye**.

Dermatan Sulfate

- Acidic Sulfated Mucopolysaccharide.
- **Chondritin sulfate-B / β-Heparin**

- **Disaccharide Repeating Unit**
- L-Iduronate-
- N-AcetylGalactosamine-sulfated
- Dermatan sulfate especially present in skin, blood vessels and heart valves gives mechanical strength and structural support to these tissues.

- Dermatan sulfate **plays structural role in sclera of eye.**

Keratan Sulfate

- Acidic Sulfated Mucopolysaccharide
- **Keratan Sulfate** is a MPS **without Uronic acid** instead ~~contains Galactose.~~

- **Disaccharide Repeating Unit**
- Galactose-N-Acetyl Glucosamine –sulfated
- Keratan sulfate present in cartilage, aorta walls, gives structural supports and mechanical strength.

- **Keratan sulfate** present in cornea and lens of eye has **role in lens transparency and shape of eye.**

Applied aspects of Mucopolysaccharides/ GAGs

- On ageing or during pathogenesis the biosynthesis of certain specific Mucopolysaccharide /Glycosaminoglycan is either increased or decreased leading to disorders and manifestations.
- **Tumors cells-**
- **Increased Hyaluronic acid** (Increases cell migration)
- **Decreased Heparan Sulfate** (Decreases cell adhesion)
- **This Increases Metastasis**

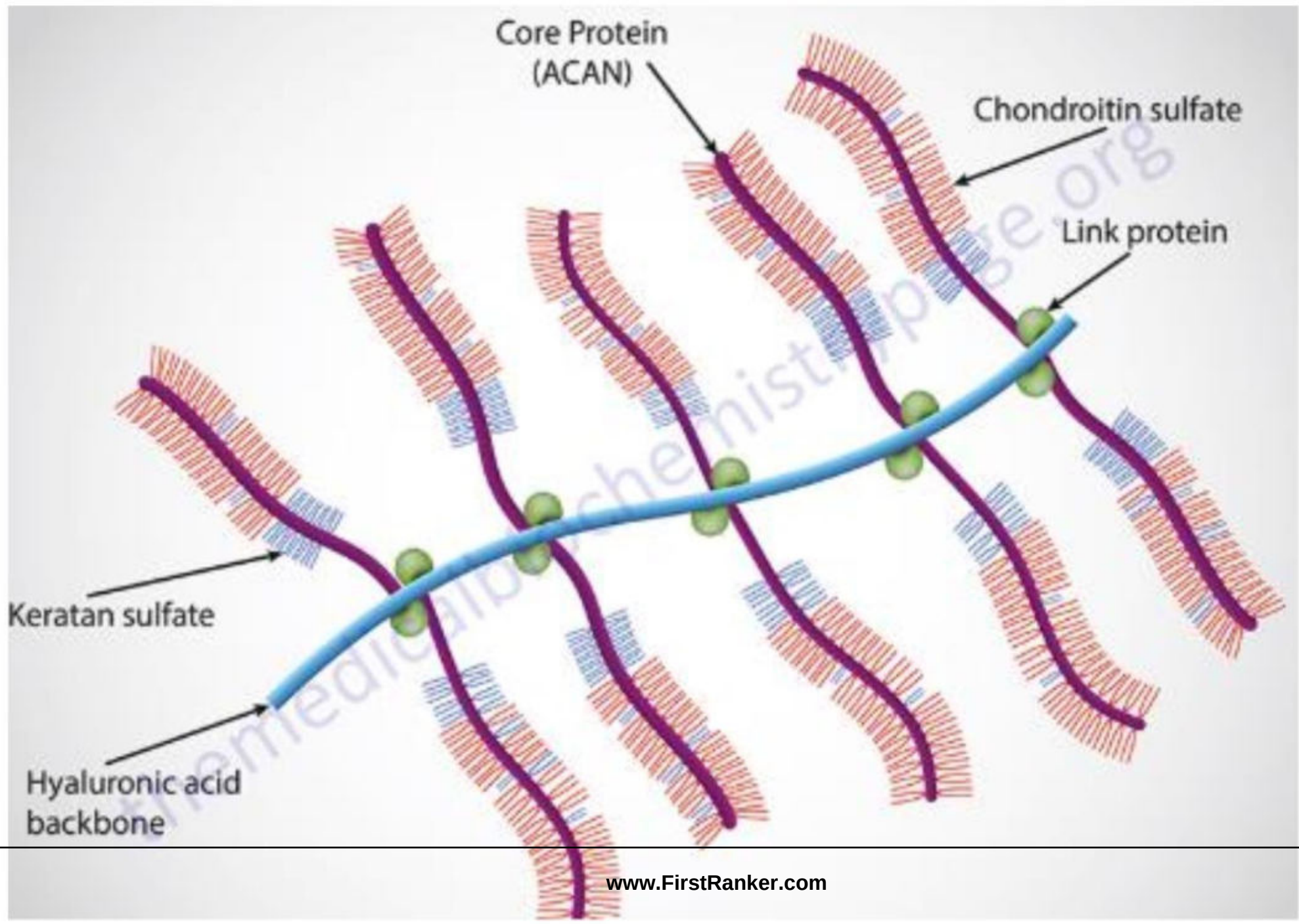
- **Rheumatic Arthritis-**
- Rheumatic nodule shows increased Hyaluronic acid deposition.
- **Atherosclerotic plaque-**
- Excess production of Dermatan Sulfate
- Decreased production of heparin
- **Osteoarthritis-**
- Imbalance biosynthesis of Hyaluronic acid, Chondritin Sulfate and Keratan Sulfate

Glycoprotein Or Proteoglycans

Glycoprotein	Proteoglycan
Primarily protein (Protein + some CHO)	Primarily carbohydrate (CHO + some protein)
CHO chains may be negatively charged	CHO chains always negatively charged
Short chains Branched Neutral or -ve No repeating disaccharide units (Oligosaccharides)	Long chains Linear Negatively charged repeating disaccharide units (Glycosaminoglycans, GAG)

DIFFERENCES BETWEEN GLYCOPROTEIN AND GAG'S

GLYCOPROTEINS	GLYCOSAMINOGLYCANS
Length of carbohydrate chain is short(2-10 sugar units)	Carbohydrate chain is long
No diglucosyl repeated units	Diglucosyl repeated units are present
Chains may or may not be negatively charged	Chains are negatively charged
Carbohydrate contain is variable(4-85%)	Carbohydrate contain is more than 95%
Storage diseases are called oligosaccharidosis	Storage diseases are called mucopolysaccharidosis



- Proteoglycans are composed of as many as 200 GAG chains covalently bonded to a core protein via Serine/ Threonine side chains.
- Molecular weight range: 10^5 – 10^7 Daltons.

- GAG chains linked:

- Hyaluronic acid
- Chondroitin sulfate
- Heparan sulfate
- Dermatan sulfate
- Keratan sulfate

Examples of Proteoglycans

- **Aggrecan (Hyaluronate-Core Protein non covalently linked In Cartilage)**
- **Biglycan**
- **Beta Glycan**
- **Decorin**
- **Serglycin**
- **Syndecan**
- **Perlecan**
- **Versican**

Plant Heteropolysaccharides

Agar-Agar

- Agar is obtained from red algae.(Sea weed)
- Agar is formed of two main components, Agarose and Agaropectin.
- Agarose is a neutral galactose polymer, free from sulfate.
- Agaropectin is formed of galactose and galacturonic acid units partially esterified with sulfuric acid.

Uses of Agar

- Preparation of **bacteriological culture media.**
- **Emulsifier**, thickener for **ice creams,puddings.**
- **Laxative**-for treatment of ulcers and chronic constipation.

Pectin

- Obtained from **apple pomace** and inner portion of **citrus rind**.
- Form viscous solutions in water.
- Composed of **Arabinose, Galactose** and **Galactouronic acid.**
- Average molecular weight 100,000- 250,000.

Uses Of Pectin

- Pectin is **topically applied** as a paste in cases of **burns and ulcers.**
- It acts as a **detoxifying agent** by conjugation with toxins.
- It is of great importance in **treatment of diarrhea and dysentery.**
- It is used as a **gel and emulsion** stabilizer and in **manufacture of jellies and jams.**

Diagnostic Value of Carbohydrate:

- Fructosan **Inulin**, is used to carry out:
- **Inulin Clearance Test**, which checks, Glomerular Filtration Rate of kidney.

Therapeutic Value of Carbohydrates:

- **Cardiac Glycosides Digoxin**- used to treat cardiac insufficiency.
- **Glycosides Ovabain and Phlorizin**- used in treatment of Diabetes mellitus.
- **Glycosides Streptomycin ,Erythromycin** used to treat bacterial infections.

- **Mannitol**- Serve as osmotic diuretic used in treatment of Acute Renal Failure.
- **Lactulose** -Relives Hyperammonaemia in patients of Hepato Encephalopathy.
- **Dextran**- Used as plasma substitute in hemorrhagic cases to prevent hypovoluemic shock.
- **Hyaluronan-** Used to treat osteoarthritis.