Mucopolysaccharide

→ Glycosaminoglycans (GAG)

- long
- unbranched, Negative charged
- Heteropolysaccharide chain containing Repeated disaccharide unit (Acidic sugar / amino sugar)

Except - Keratan sulfate

galactose than acidic sugar

- Are proteoglycans - >95 % Carbohydrate
  5-10 % protein

Glycoprotein - >95 % protein
5-10 % Carbohydrate
e.g. All protein are glycoprotein except albumin

→ Amino sugar — D-glucosamine or D-galactosamine

Amino group is acetylated

positivity reduced.

(or)

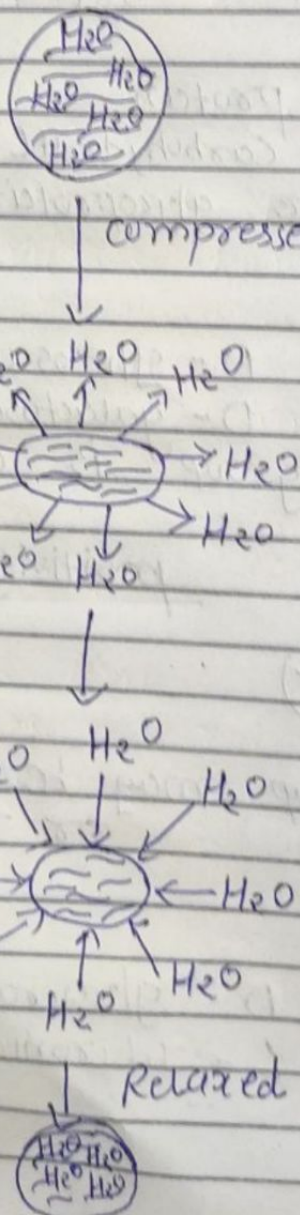
Amino group may be sulfated at C_4 or C_6 or on nonacetylated nitrogen.

→ Acidic sugar (uronic sugar) - D-glucuronic acid or L-Iduronic acid (C_5 epimer of D-glucuronic acid)

- contain carboxy group (COOH)
↓
Negatively charged at physiological pH
↓
with SO_4^{2-} group, make GAG strongly negatively charge

→ Structure-function relationship :-

- makes Synovial fluid & vitreous humor of eye resilience



→ Classification :-

- All are sulfated except hyaluronic acid
- All GAG attached to protein forming proteoglycan monomer.

(1) Chondroitin sulfate

- Disaccharide unit →
- N-acetylgalactosamine ē (5) on C_4 or C_6 + glucuronic acid
- most abundant in body
- found in cartilage
  Tendons
  Ligaments
  Aorta
- Form proteoglycan aggregate through non covalent association with hyaluronic acid
- In cartilage - Bind collagen & hold fiber in tight, strong network

(2) Keratan sulfate (Ks) I & II

- Disaccharide unit
  ↓
  N-Acetylglucosamine & galactose
- most heterogenous - Addition monosaccharide like mannose, N-acetyl neuraminic acid, L-fucose present.

- KS I - present in cornea

- KS II - In loose connective tissue proteoglycan aggregates with chondroitin sulfate

(3) Hyaluronic acid

- Disaccharide unit
  N-acetylglucosamine &
  glucuronic acid

- Non Sulfated
- Not covalently attached to protein
- Also present in bacteria

- Serve as a lubricant & shock absorber

- Found in - Synovial fluid of joints,
  vitreous humor of eye,
  Umbilical cord
  Cartilage
  Loose connective tissue

(4) Dermatan Sulfate

- Disaccharide unit
  N-acetylgalactosamine &
  L-Iduronic acid (variable amount of glucuronic acid)

- Present - Skin
  Blood vessels
  Heart valves

(5) Heparin

- Disaccharide unit
  ↓
  Glucosamine & glucuronic acid or iduronic acid
- most glucosamine residues are bound in Sulfamide linkages.
- α Linkage join sugar
- Intracellular component of mast cells that line arteries especially in skin, liver & lungs.
- serve as anticoagulant.

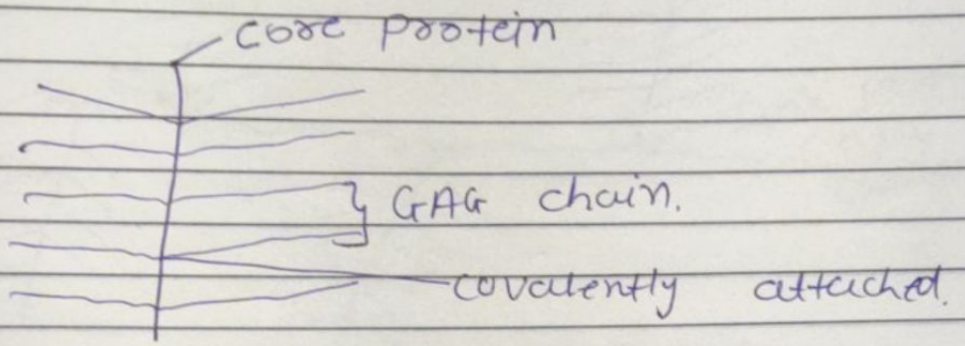
(6) Heparan sulfate

- Disaccharide unit
  ↓
  Glucosamine & glucuronic acid or iduronic acid.
- some glucosamines are acetylated &
- Fewer
- Extracellular GAG.
- present in - Basement membrane & as a ubiquitous component of cell surfaces.

- Proteoglycans

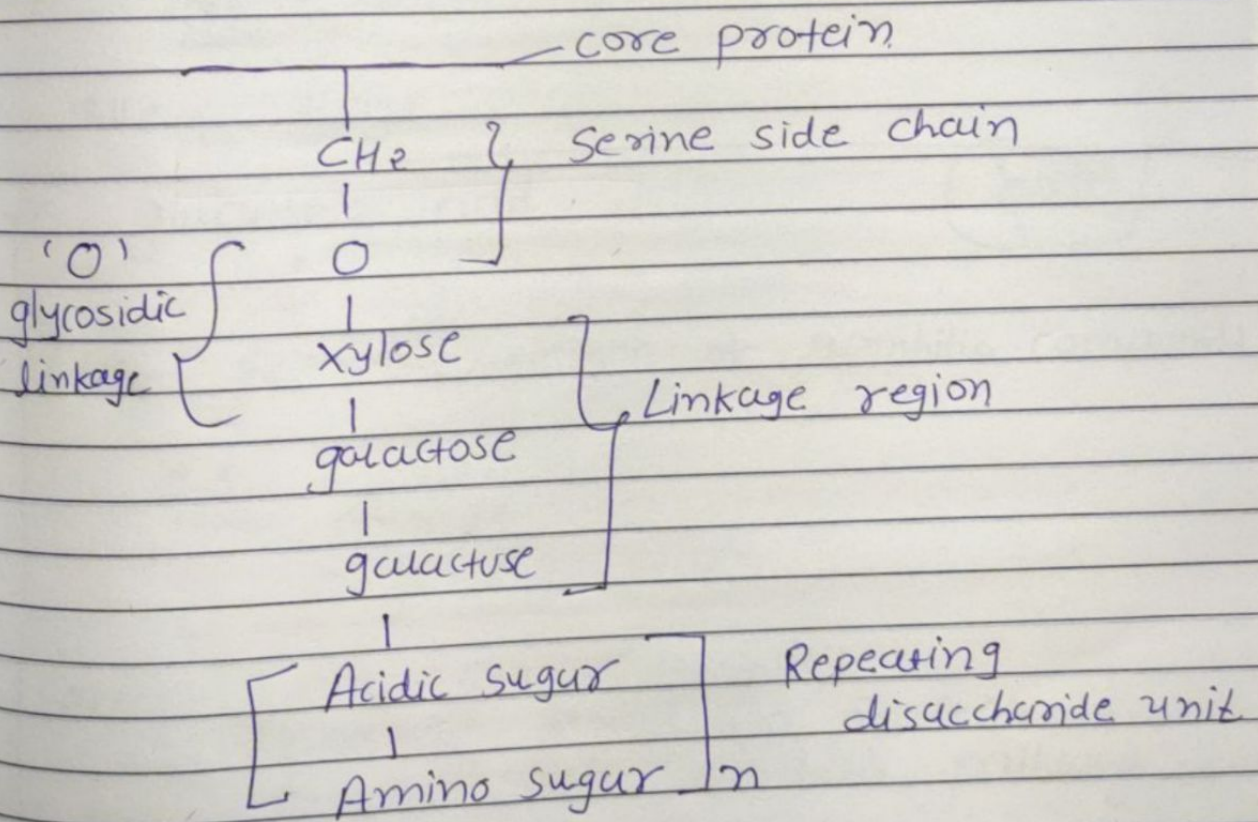
- found in ECM & on outer surface of cells

① Monomer structure

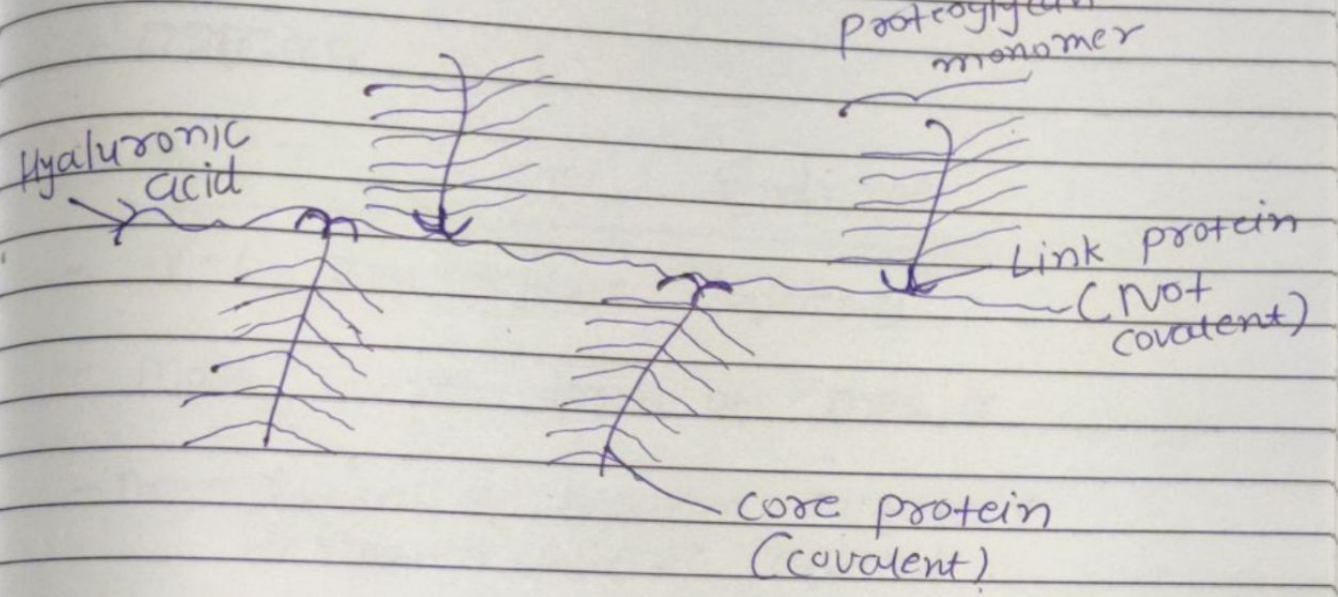


looks like bottle brush

② GAG - protein linkage



③ Aggregate formation



→ Synthesis:-

Site - golgi

↳ glucuronic acid (Extra)

↓

Required for detoxification of lipophilic compounds

e.g. bilirubin
steroids
Drugs e.g. statin

Source - Diet - small quantity
Lysosomal degradation of GAG
Uronic acid synthesis pathway

Mucopolysaccharidoses (MPS)

- Hereditary disease
- ~~Deficiency~~

(1) MPS I - Hurler Syndrome

- α-L- Iduronidase deficiency
- Most severe form of MPS I
- Degradation of heparan sulfate & dermatan sulfate affected
- Deposition ~~of~~ in Coronary artery
  ↓
  ischaemia & early death.
- Rx. → Bone marrow or Cord blood transplantation before age ~~18~~ months.
  - Enzyme replacement therapy

(2) MPS II - Hunter Syndrome

- Iduronate sulfatase deficiency
- X linked deficiency.
- wide range of severity
- No corneal clouding

Rx - Enzyme replacement therapy.
- Degradation of dermatan sulfate & heparan sulfate affected.

(3) MPS III (Sanfilippo Syndrome)

- (4) enzymatic steps necessary for removal of N-sulfated or N-acetylated glucosamine residues from heparan sulfate

Type A - Heparan sulfatase deficiency

Type B - N-Acetylglucosaminidase deficiency

Type C - Acetyl CoA: α-glucosaminide acetyltransferase deficiency

Type D - N-Acetylglucosamine 6-Sulfatase deficiency

- Severe nervous system disorders > developmental disability.

(4) MPS VII (SLY Syndrome)

- β glucuronidase deficiency

- Degradation of dermatan sulfate & heparan sulfate affected.