POLYSACCHARIDES

- **STARCH**
- **DEXTRAN**
- **GUM**
- **MUCILAGE**
- **CELLULOSE**
- **PECTİN**
- **MUCOPOLYSACCHARIDES**

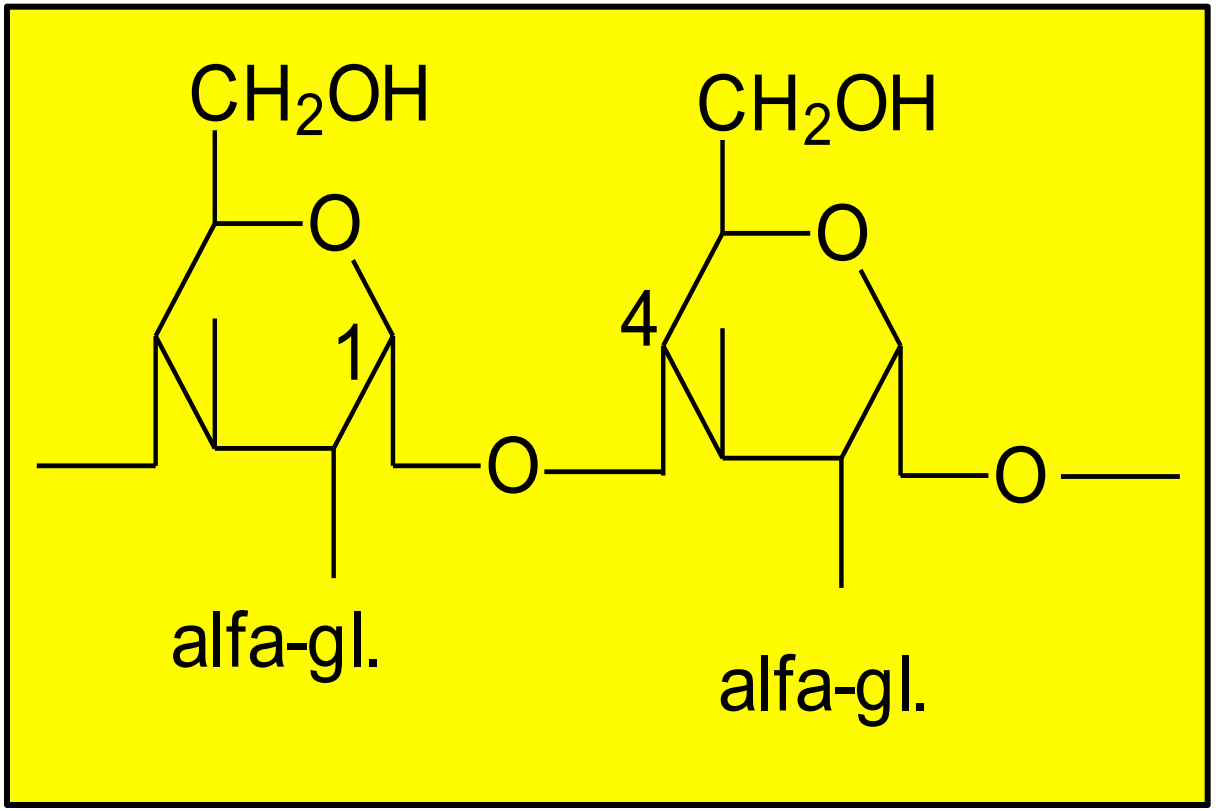
STARCHS

- **The main reserve substance in plants.**
- **These carbohydrates obtained from seeds, roots and fruits**
- **Tubers (Potato), stem (palm), roots (manihot) , rhizome (Maranta) , seed (Leguminosae and Graminae), fruit as reserve substance**
- **Especially found in seed and underground parts**

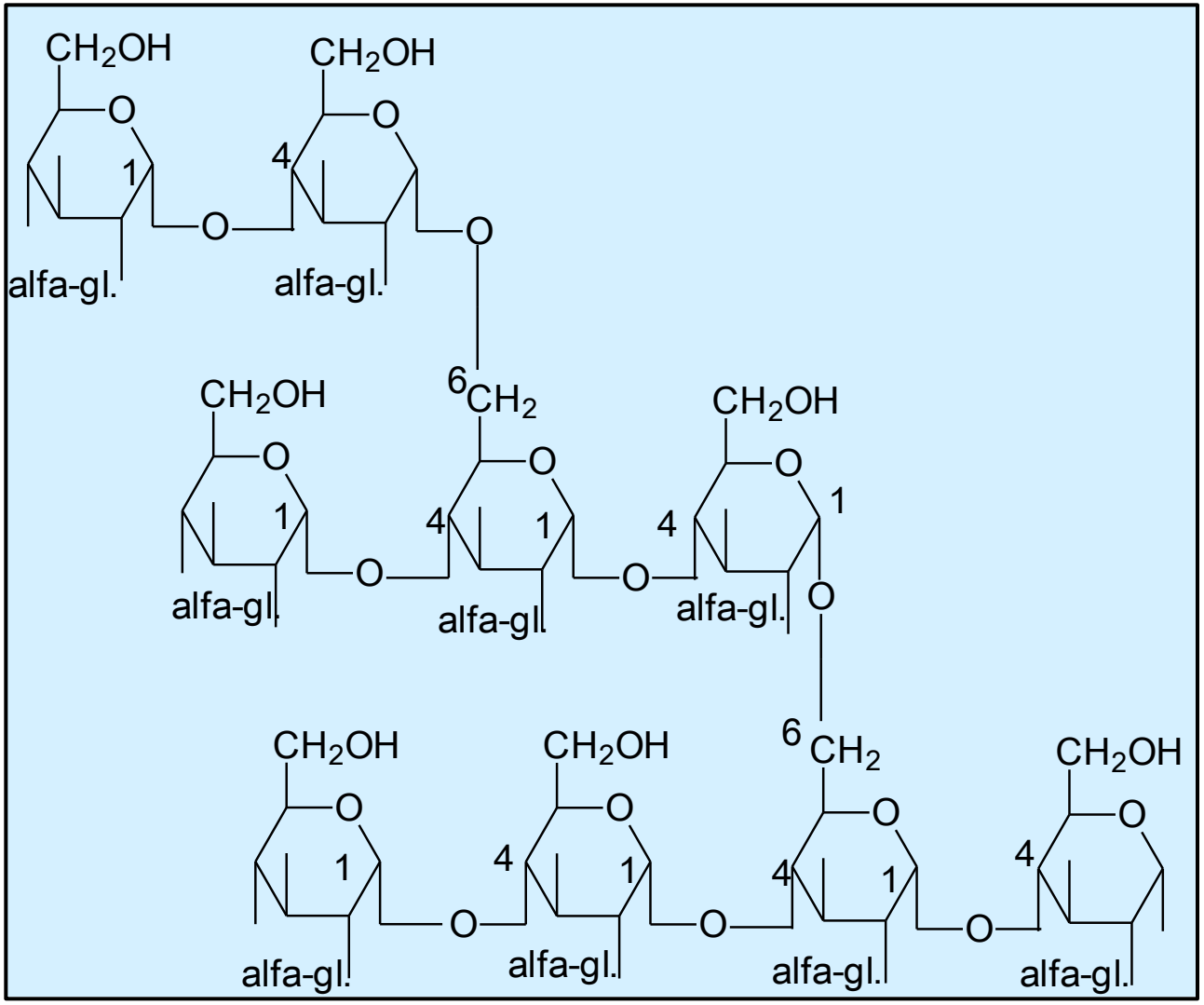
- **MW is in between 50.000-1.000.000**
- **Odourless, tasteless white powder**
- **Insolubile in cold water, dissolve partly in hot water and jellified**
- **Blue colour produce with iodine**
- **Composed almost pure glucose**
- **Hydrolysed with acid or enzymes resulted in glucose**

- **The two main constituents are Amylose and amylopectin**
- **Amylose; solubile part of starch, %10-20 part of starch composed α-D glucose nonbranching helical chain bonded 1-4 glycosidic linkage**
- Produce blue colour with iodine
- **Amylopectin**; insoluble in water, swelling part of starch, %80-90 of starch composed α-D glucose branched chain, 1-4 linkages in the chains and 1-6 linkages at the branch points
- Produce blue-violet colour with iodine

Amylose



Amylopectin



- **2 molecule of α-D glucose bonded 1-4 glycosidic linkage resulted in MALTOSE a disaccharide, occurs. And this molecules are the main structure of starch**
- **Three enzyme hydrolyzed the starch molecules to α-D glucose:**
- **1) α-Amylase: Found in pancreas and saliva in animals. These enzyme induce to hydrolization to maltose and glucose molecules**

NİŞASTALAR

- **2) β-amylase**: Induce hydrolization to maltose
- **3) α-1-6 Glucosidase: Induce breaking up in brached structure of starch**
- **Starch.....diluted HCl....maltose..... α-glucose occurs**

► Identification

- ► I_2, Iodine-KI or iodine-water resulted in blue colour due to amylose structure. Amylopectin gives purple or brown colour with iodine
- ► **Soluble in %50 of cloral hydrate solution**
- ► "Blue value" for starch can be measured and used for identification
- ► Blue value : Absorbtion of blue colour of iodine with starch at 680 nm. Blue value is proportional with amylose content. If amylose content is high blue value is high.

►HILUM

- ►The formation of starch granule starts at a point called the hilum in leucoplast
- ►Some of them are centric placed at the center of granule, some of them are excentric placed out of the center of the granules
- ►They can be so small and is not possible to seen

- Starch granules come in a wide range of shapes, which assists identification , disc, spheres, ovals, elongated, rounded, kidney-shaped, polyhedral and irregular forms are common.
- They can be alone or combined
- Granules of starch jellyfied with water and gel time related to starch source and reaction conditions. These specifications can be determinant for identification of starch
- Gel temperature in water
- Gel time in %10 KOH solution is also important for determinant

► Production of starch

- ► Drug is grained and mixed with water. Upper phase is transferred and lower phase is dried for obtaining starch and grained.
- ► Different sources are used according to the country and geographic places: Wheat, rice, potato, corn, *Maranta arundinacea* (Marantaceae), *Manihot esculenta* (Euphorbiaceae) (Tapioka starch and *Metroxylon* species (Palmae= Arecaceae) (Sago starch)

- ***Oryza sativa* (rice), *Zea mays* (corn) are the main sources for pharmacy**
- **Industry especially rice and wheat also corn are used (yield %65-75)**
- ***Solanum tuberosum* (potato) contains %20 of starch**

►Quantification

- ►**1)Gravimetric**: Obtained and weighed
- ►**2) Titrimetric**: Hydrolysed with acid or enzyme and reducing monosaccharides are quantified by titrimetric method
- ►**3) Colorimetric**: Starch+iodine, blue colour measured by colorimetry
- ►**4) Polarimetric**: Starch hydrolization and occuring monosaccharides are measured by polarimetry

►Specifications of Starch used in Pharmacy

►1) Does not contain oil and impurity

►2) Granules of starch are not deformed

►3) Ash content should be lower than % 0.6

►4) Ash content should be lower than %15

►5) Nitrogen content should be defined

►6) Acidity should be controlled

►7) Microorganisms and fungi are not found

►USAGE

- ►1) Humectant and main component of talc. Used against irritatant and refreshing activity on inflammation
- ►2) Digestable easily therefore used as nutrient for infants and elder patients.
- ►3) Small granule starchs is more suitable for talc such as rice

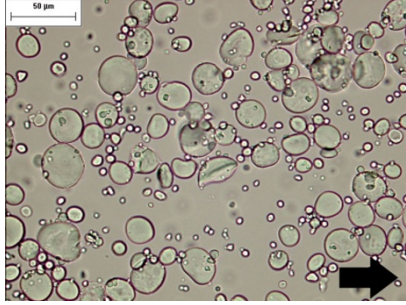
- **4) Diluent in powders and tablets manufacture**
- 5) Starting material for glucose, dextrin and amyl alcohol
- **6) Antidote for iodine poisoning**
- **7) Hydroxy ethyl starch used as %6 solution in isotonic saline solution for treatment of hypovolemic shock**

►PREPARATIONS

►***1) Fresubin diabetes*** **(diet): %70 starch+%30 fructose**

►**2) *Nutrodrip diabetes (*diet):**
Starch+fructose+ medium chain triglyceride

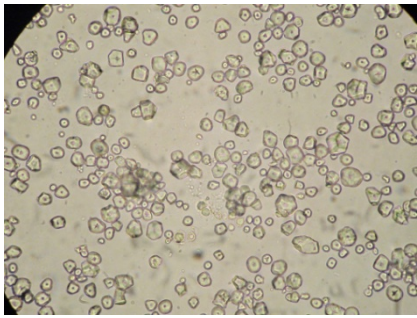
►**3) *Undo talk***



► **1) AMYLUM TRITICI (TF) (Wheat starch):**

► ***Triticum vulgare*** **(*T. sativum*) (Graminae)**

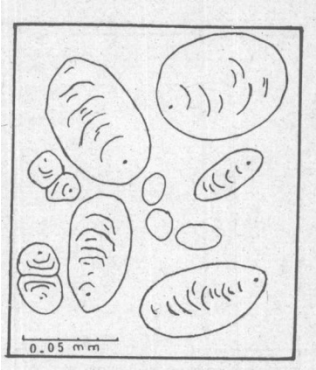
► **Lentiform, 15-45 µm, hilum seen hardly.**



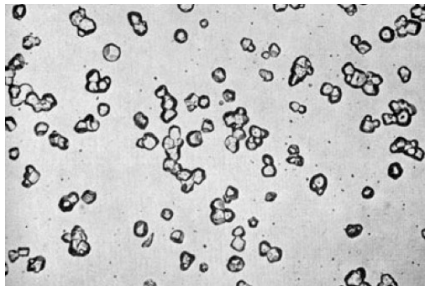
► **2) AMYLUM MAYDIS (Corn starch):**

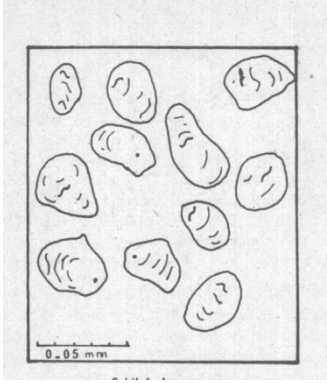
► ***Zea mays*** **L. (Graminae)**

► **Polyangular granules, 10-25 µm,hilum is centric and cracked**



- **3) AMYLUM SOLANI**
- **(Potato starch) (EP):**
- ***Solanum tuberosum* L.** (Solanaceae)
- Ovoid or pear shaped, 15-100 µm
- Two or three granules are combined, hilum excentric
- **4) AMYLUM ORYZAE (TF) (Rice starch):**
- ***Oryza sativa*** L. (Graminae)
- Polyangular shaped, granules are simple or many of them combined, 2-10 µm,
- hilum centric





- **5) ARROWROT (Hararot) (Amylum Maranthae):**
- ***Maranta arudinacea*** **(Maranthaceae) rhizome**
- **Similar to potato starch, 30-40µm**
- ***Curcuma*** **sp. (Zingiberaceae) e.e.**
- ***Manihot utilissima*** **(Euphorbiaceae) tubers**
- **Arrowrot 60^0C soluble, 70^0C completely decomposed.**
- **Used as nutrient for infant food**

- **AMYLUM SOLUBILE (Soluble Starch) (BP 1999):**
- **Starch boiled in long time or**
- **Hydrolized with dil. Acid ….Amylopectin chain is decomposed and more soluble form in water is obtained**
- **7) ULTRA AMYLOPECTIN:**
- **Sodium amylopection gluconate**
- **Disintegrant in tablet manufacture**
- **Supplement material for washable pomade and pasta preparation**
- **Lubricant in pharmaceutical technology**

- **8) AMYLUM NON-MUCILAGINOSUM (ANM): Tetramethylacetylene ether of starch**
- **Excipient for talc, powders and tablets**
- **9)FARİNA: Seed flours which containin starch**
- **Used in pharmaceutical industry.**

DEXTRIN

- **Products obtained by partial hydrolysis of starch**
- **Hydrolization products are; soluble starch, amylodextrine, achrodextrin and maltose**
- **Sweet taste, white/yellow, odourless, amorphous powder**

- Adhesive in pharmaceutical technology (Dissolved in 3 part of boiled water)
- **Agent for emulsion and suspension**
- Manucature of tablets and capsule
- **Costemics**
- Source for saccharides as nutrient.

Does not contain lactose,

Contain low electrolyte

- **Paper, ink, match, fabric and paint industry.**

DEXTRIN

- ***Oryza sativa glutinosa*** **and** ***Sorghum vulgare glutinosa*** **used as sources to obtain**
- **Gives red colour with iodine (Difference between dextrin and amylodextrin)**
- **Starch...dil.acid (HNO_3)....DEXTRIN (Dried at 110-120 ^{0}C White colour)**
- **(Dried at 150-250 ^{0}C Yellow colour) (More hydrolized, contains more maltose molecules)**

CYCLODEXTRINS

- **Cyclic oligosaccharides produced by the enzymatic degredation of starch (generally 6-8).**
- **The enzyme cyclodextrin glycosyl transferase is produced by different *Bacillus* sp.**
- **Degredation by this enzyme is produced**
- **Cyclodextrins are cyclic glucose units and shaped like a torus**

CYCLODEXTRINS

Structurally α-, β-, and γ- cyclodextrins consist of six, seven and eight glucose units respectively linked by α 1-4 bond

α- cyclodextrin (α CD= C 6 A)

- **Cyclohexaglucans**
- **Cyclic structure consisting 6 α-glucopyranose units**

β- cyclodextrin (β CD= C 7 A) (BP/USP/EP)

- Cycloheptaglucans
- Cyclic structure consisting 7 α-glucopyranose units

- **γ- cyclodextrin (γ CD= C 8 A)**
- Cyclooktaglucans
- Cyclic structure consisting 8 α-glucopyranose units

- **Molecular weight and solubility of cyclodextrins in water are different**
- **β- cyclodextrin (β CD) the least dissolved in water**
- **γ- cyclodextrin (γ CD) the most dissolved in water**

USAGE

- **Pharmaceutical technology**
- **1) Excipient (dilüent, to increase solubility, tablet manufacturing)**
- **2) Formulation in oral dosage forms:**
- **a) To prepare crystalline form of liquid compounds**
- **b) To mask taste and smell Kötü koku, tat düzeltici**
- **c) Producing complex of compounds to improve their miscibility.**

- **3) Improving physical and chemical specifications:**
- **a) Increasing stability of volatile compounds**
- **b) Protect compounds against oxidation**
- **c) Prevent decomposition, polymerisation and catalytic reactions**
- **d) Desensitization against light, acidity of stomach and others**

- 4) Improve bioavailability:
- a) Improve solubility in water
- b) Modify serum concentration of hydrophobic compounds as their complex with cyclodextrin after oral administration to decrease their required dosage
- c) Decrease hydrophobicity by producing complex. Increase percutaneous and rectal absorbtion
- d) Prepare of liquid drug formulations (paranteral solutions (injectable), eye drops and others)

►Food Industry

- ►1) Stabilization of taste
- ►2) Protect microbial contamination
- ►3) Mask taste and smell
- ►4) Prevent oxidation, thermal and light decomposition, sublimation and volatility

DEXTRANS

- **Polysaccharides consisting α-D-glucopyranose molecules occured by proliferation of some microorganisms such as *Leuconostoc mesenteroides* in medium containing sucrose.**
- **For usage in pharmacy;**
- ***1) Leuconostoc mesenteroides* NRRLB 512 strain must be used**
- **2) α-glucose molecules must be 1-6 bonded**
- **3) MW should be $100x10^6$ olmalı**

►Production of dextran

- ►Two different method are used in industry:
- ►**1.Method:** %10 sucrose containing sterile medium is used leave for 24 h. **DEXTRAN is obtained by** %50 yielding Ethyl alcohol+CH3COOH+Lactic acid obtained as by-products
- ►Methyl alcohol is added to precipitate **DEXTRAN**
- ►**DEXTRAN** + non pyrogen water dissolved and then precipitate again

- **Partial hydrolysis resulted in desired MW of DEXTRAN as 40.000 and 75.000**
- **After precipitation of methyl alcohol and recrystllization medicinal dextran is obtained**
- **2. Method: Dextran sucrase is an enzyme and production of *Leuconostoc mesenteroides.* *In vitro* dextran sucrase catalyses sucrose solution to production of dextran**

%2 sucrose + %2 corn germ + mineral compounds containing medium used for fermentation with microorganism

at pH=6.7 for 12 h

- **Dextran sucrase enzyme concentration reach to the maximum level,** medium will filtered to remove microorganisms
- pH is adjusted to 5.0 and the tempereatuse is 15 ºC using dextran sucrase enzyme dextran is obtained from sucrose
- Sucrose.....dextran sucrase (*Leuconostoc mesenteroides)*...Glucose+Fructose polymerisation .....higher molecular weight of **DEXTRAN**.....partial hydrolysis.....**DEXTRAN**

► USAGE

- ► 1) Two different type of dextran and their complex and esther forms are used
- ► 2) Dextrans are administered intravenously (infusion) . The viscosity and osmolarity of these solutions are close to plasma
- ► Dextran is nontoxic, neutral serologically , prolonged action and completely eliminated. It is a plasma substitute used for following indications:
- ► For plasma volume expansion in due to hemorrhage, taruma, toxiinfection

- 3) Used in some preparations as stabilizer
- 4) In synthetic tears preparations against xerophthalmia
- (Dextran-70...Tears naturale; Dextran-40.....Clarex drops)

- **Dextran production in desired molecular weight**
- 1) Diluted acid hydrolysis for partial depolymerisation
- **2) Modulated precursor compounds are added (maltose or low molecular weight dextrans)**

- **Different dextrans**
- **Obtained by *Acetobacter*, *Stretobacterium*, *Lactobacillus*, *Streptococcus* strains**
- **1-6, 1-4 and 1-3 bonded. All are glucans or glucose polymers**
- **Molecular weight / degree of polymerisation / viscosity / solubility in water / monosaccharide bonds / polymerisation degree are the differences of dextrans**

DEXTRAN 40, DEKSTRAN 40, GENTRAN 40, RHEOMACRODEX

- **MW approximately 40.000 α 1-6 bonded dextran**
- **In surgery first application of the cardiopulmonary bypass pump**
- **Isotonic solution is used for preventing of agregation of erythrocyte aggregation**
- **Regulation of blood stream by decreasing viscosity**
- **%5 dextrosum solution containing %10 Dextran 40 solution is used in hypovolemic shock**

DEXTRAN 40, DEKSTRAN 40, GENTRAN 40, RHEOMACRODEX

- **It is also indicated that for dehydration and extensive burns**
- **Side effects;**
- **Hypersensitivity reactions are rare but always possible, thus the infusiun must begin very slowly. To prevent or alleviate the anaphylactic reaction first it is preferable to inject a very low molecular weight dextran which block the antigen sites on antibody.**
- **for patients that have kidney problems, polmonary eudema is not suitable**

DEXTRAN 75, DEKSTRAN 75, GENTRAN 75, MACRODEX

- **MW approximately 75.000, α 1-6 bonded dextran**
- **% 6 dextran solution in isotonic saline or %5 glucose(dextrose) is used for plasma volume expansion in surgery and extensive wounds. However if the blood cells are decreasing or in case of lipoproteinemia dextran solution usage is not suitable**
- **Hypovolemic shock**
- **Clinically anticoagulant activity is important. Used against trombosis**

Semi-synthetic derivatives of dextran

► DEXTRAN SULPHATE

- ► H_2SO_4 esther of dextran
- ► Anticoagulant in trombosis and phlebitis as pomade externally

► IRON-DEXTRAN ENJECTABLE SOLUTION

- ► Small MW of dextran (partial hydrolyses of dextran) and $Fe(OH)_3$ colloidal and sterile complex solution
- ► ***Production:*** Dextran water solution+$FeCl_3$ addition.....mixture cooling....centrifuged.....iron content adjusted to %95-105.....concentrated.....filtered and sterilized
- ► Dark brown colour.
- ► Used for anaemia
- ► IM form is easily absorb without irritation

IRON SORBITOL (=JECTOFER)

- **Sterile solution**
- **Fe+Sorbitol+citric acid complex**
- **Used for treatment of anaemia**