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Preparation and Applications of A Dextrans: Review

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***Abstract* – Dextrans are homopolysaccharides of D-glucose produced by microorganisms.These polysaccharides are synthesized by a number of bacterial species. The synthesis occurs extracellularly and are catalyzed by a species specific enzyme, dextransucrase. Dextran is produced at the industrial level by the fermentation of sucrose rich media. Dextran is commercially available and it is used as drugs, especially as blood plasma volume expander. It has found industrial application in food, pharmaceutical and chemical industries as adjuvant, emulsifier, carrier and stabilizer. In food industry dextran is currently used as thickener for jam and ice-cream. It prevents crystallization of sugar, improves moisture retention and maintains flavor and appearance of various food items.**

***Keywords* – Dextran, Preparation, Dextransucarase, Applications, Lactic Acid Bacteria.**

I. Introduction

Dextran was first isolated in 1861, by the father of microbiology, Louis Pasteur in wine as a microbial product- which is perhaps the most blissful contribution of Pasteur to mankind with a long time impact [1]. Though different varieties of dextran are just simple combinations of glucose molecules with variable glycosidic bonds. Dextran is also the first commercial bacterial exo-polysaccharide [2]. The name dextran was first given Corresponding author. by Scheibler in 1869 as the product showed some similarities with dextrin. He also showed that upon acid hydrolysis, it only produced d-glucose [3]. In 1941 Hehre reported that the first cell-free synthesis of dextran using sucrose as the substrate from enzyme dextransucrase. Dextransucrase (sucrose: 1,6-α- D-glucan 6-α-glucosyltransferase) is the key enzyme that catalyzes the synthesis of dextran from sucrose [4]. Dextran is a complex, branched polysaccharide made of many glucose molecules composed of chains of varying length (from 10 to 150 kilodaltons).The native dextran straight chain consists of alpha α– 1,6 glycosidic linkages between glucose molecules, while branches begin from alpha-1,4 linkage (alpha-1,2 and alpha-1,3 linkages as well)(fig.1). The polyglucans are synthesized from sucrose by many species of the genera Leuconostoc, Lactobacillus and Streptococcus [5].was the first who reported the production of dextran from sucrose by strains of Leuconostoc species [6].reported the formation of dextran from different strains of bacteria that were primarily Leuconostoc strains. Species of bacteria from other genera have been also found to produce dextran. Soluble and insoluble dextran is produced and molecular weights range from 1.5 x 104 to 2 x 107 and higher. The microorganisms used for the production of dextran (Leuconostoc mesenteroides, Saccharomyces cerevisiae, Lactobacillus plantarum, Lactobacillus sanfrancisco) are currently used in food processing without any restriction (U.S. Food and Drug Administration,Code for Food Regulations). Using pure components for the fermentation medium in dextran production imposes high costs on the industry, So the economic production of dextran using local and cheap sources of carbohydrates and nitrogen are investigated. Different concentration of molasses and wheat bran extract are used[7]. Dextrans have been known for their viscosifying, emulsifying, texturizing, stabilizing attributes in food applications. Dextran has the potential to be recruited as a novel ingredient replacing the commercial hydrocolloids in bakery and other food industries. Prebiotic oligosaccharide production by hydrolysis of dextran is a rather new field, garnering research and industrial attention [7]. Also dextran derivatives, dextran conjugates, dextran hydrogel and micelles are extensively used as nanomedicine and nanocarrier because of its simple and nonimmunogenic biopolymeric nature. As of April 2015, Dextran 70 is in WHO model list of essential medicine as blood plasma substitute [1].

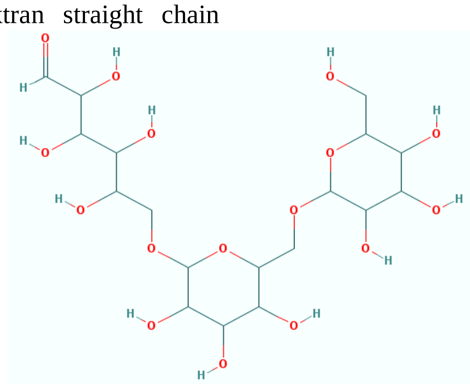

Fig. 1. Structure of Dextran

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II. Sources and Types of Dextran

Dextran occurs naturally in small amounts in foods, such as refined crystalline sugar, maple syrup, sauerkraut juice, and honey, and also as a component of dental plaque. Dextran is synthesized by the action of bacterial enzyme, dextransucrase, on sucrose. Dextransucrase is the sole industrial enzyme used in the commercial production of dextran and is produced by LAB of genera, viz., Leuconostoc, Streptococcus, Lactobacillus, Pediococcus, and Weissella. The structure of each type of dextran depends on the microbial strain and hence on the specific dextransucrase. To date, commercial dextran is produced from Leuconostoc mesenteroides NRRL B- 512F and serves as a model in studying the structure of dextran and the mechanism of its biosynthesis by dextransucrase [8,9].

Table 1 Dextrans with their linkage pattern from different LAB isolated from various food sources.

Microorganism	Source	linkage	Ref.
Leuconostoc Mesenteroides CMG713	Grape	α-(1 → 6) linkages only	[10]
Leuconostoc mesenteroidesAA1	Fermented cabbage	α -(1 → 6) linkages	[11]
Lactobacillus Satsumensis NRRL B-59839	Water kefir grains	44 % α -(1 → 3) and 37 % α -(1 → 6)	[12]
Lactobacillus plantarum DM5	Marcha, fermented Beverage	86.5 % α -(1 → 6) and 13.5 % α -(1 → 3)	[13]
Pediococcus pentosaceus CRAG3	Fermented cucumber	75 % α -(1 →6) and 25 % α -(1 → 3)	[14]
Weissella cibaria CMGDEX3	Cabbage	96.6 % α -(1 → 6) and 3.4 % α -(1 → 3)	[15]
Weissella confusa Cab3	Fermented cabbage	97 % α -(1 → 6) and 3 % α -(1 → 3)	[16]
Weissella cibaria JAG8	Apple peel	93 % α -(1 → 6) and 7 % α -(1 → 3)	[17]

III. Physico-Chemical Properties of Dextrans

Dextran polymers have a remarkable diversity in chain length and in physicochemical properties due to the variation in degree of branching in their glucose backbone. In general, dextran is readily soluble in water, dimethyl sulfoxide, formamide, ethylene glycol, and glycerol but insoluble in monohydric alcohols, e.g., methanol, ethanol, and isopropanol, and also most ketones, e.g., acetone and 2- propanone. However, the water solubility of dextrans depends upon the branched linkage pattern. Linear dextrans have high water solubility, and the aqueous solutions behave as Newtonian fluids. However, some branched dextrans showed shear rate thinning effect, exhibiting non-Newtonian pseudoplastic behavior [13]. Viscosity of dextran solution depends on its concentration, temperature, and molecular weight. As dextran is a neutral polysaccharide, the viscosity is not significantly influenced by changes in pH or salt concentration.Dextrans with>43 % branching through α-(1-3) linkages are water insoluble. Dextrans have molecular weight in the range of 3–500,000 kDa. Dextrans with a molecular weight of 2,000–10,000 kDa exhibit the properties of an expandable coil, and at lower molecular weights (<2,000 kDa), dextran is more rodlike. Low molecular weight dextrans (40, 60, and 70 kDa) are generally preferred in clinical applications [20]. High molecular weight dextrans with few branched linkages are required for the application in sourdough [33].The surface morphological studies of dextran revealed a porous structure [14,13]. The dextran has excellent thermal stability with degradation temperature ~300℃ [13,17]. Dextran was more resistant to hydrolysis by simulated gastric juice and α-amylase than commercial prebiotic inulin. The dextran supported the growth of probiotic bacteria and did not promote the growth of unwanted E. coli [17].

IV. Preparation of Dextran

Dextran is produced commercially by cultivating L. mesenteroides strains in situ in growth medium supplemented with sucrose and in vitro by using purified dextransucrase with sucrose as a substrate [18]. The dextran of desired molecular weight can be achieved by the direct enzymatic synthesis using purified dextransucrase, which allows more control over the reaction conditions as compared with the fermentative synthesis [43]. The production of dextran by dextransucrase from LAB is affected by factors like temperature, aeration, and concentration and type of medium components[44,45;46]. Dextran production is also influenced by solubility, viscosity, nitrogen, phosphorus, and ash content of the medium [47]. The molecular weight of dextran is inversely proportional to the concentration of enzyme and directly proportional to the concentration of sucrose. Moreover, the molecular weight of dextran increases as the temperature increases from 20℃ to 30℃ [43].Several physical and chemical techniques such as UV irradiation [55,59,9].ethyl methanesulfonate [57],and N-methyl-N 0-nitro-N-nitrosoguanidine [48], and site-directed mutagenesis [49] have been used for the enhancement of dextransucrase and dextran production from various LAB. A single dextransucrase can catalyze the synthesis of several types of dextran linkages, thereby permitting the formation of a branched polymer [50,51]. Certain bacterial strains have been shown to produce dextrans of different structures due to the elaboration of different dextransucrases [12,52,51]. Thus, the structure of each dextran is a characteristic of the specific dextransucrase produced by a specific microbial strain [47,53].

V. Characterization of Dextran

The structural characterization of dextran is an important factor for its utilization. A general strategy for dextran characterization is shown in Fig.2

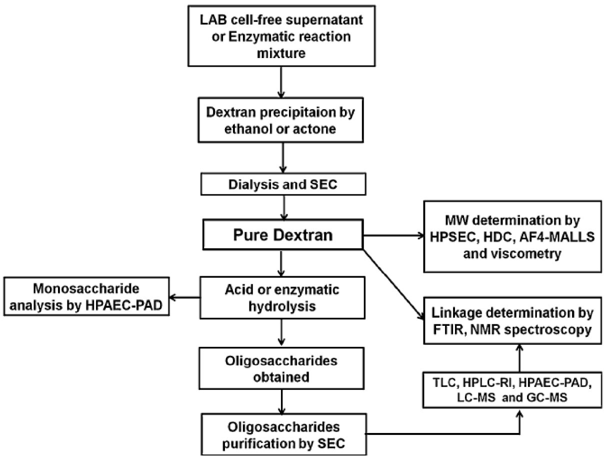

Fig. 2. A general strategy for the characterization of dextran

VI. Isolation of Pure Dextran

The structural analysis of dextran starts with its isolation in pure form in such a way that the chemical and physical properties are not affected [18]. The recovery or purification from culture medium or enzymatic reaction mixture generally involves the following steps:

1) cell removal by centrifugation or filtration in case of culture medium.
2) dextran precipitation from the cell-free supernatant or enzymatic reaction mixture by the addition of water-miscible organic solvents (e.g., ethanol, acetone, etc.).
3) re-precipitation and dialysis of dextran,
4) size exclusion chromatography (SEC) of dextran [19, 16, 17].

The high molecular weight dextran can be purified by SEC, however, low molecular weight dextran can be purified by ultrafiltration.

VII. Applications of Dextran

7.1. *Food Applications of Dextran*

Dextran has been studied as a food ingredient since the 1950s. The US Food and Drug Administration (US FDA) currently lists dextran as GRAS (generally recognized as safe) additive for food and feed applications. In general, dextran is used as gelling, viscosifying, texturing, and emulsifying agent in various food products [18]. Commercial applications of dextran from LAB are generally found in food and pharmaceutical industry, however, dextran also has several potential applications inphotofilm manufacturing, fine chemical, cosmetic, paper, petroleum, and textile industries [20:18]. Due to the heterogeneity of dextran produced by various LAB, their application may depend on well-defined chemical and physicochemical properties. The properties of dextran that are applied in food industry are shown in Table (2). The microorganisms such as Leuconostoc mesenteroides, Saccharomyces cerevisiae, Lactobacillus plantarum, and Lactobacillus sanfranciscoare used for the production of dextran for its application in food processing without any restriction.

Table 2 Food applications of dextran

Applications	The influence	Ref.
Bakery	Improves freshness, mouthfeel, softness, crumb texture, loaf volume, and shelf life	[21]
Confectionary	Improves moisture retention and viscosity and inhibits sugar crystallization and as gelling agents in gum and jelly candies	[22]
Fermented dairy products	Increases viscosity and creaminess and reduces syneresis	[23]
Ice cream	Cryoprotectant	[24]
Cheese making: reduced-fat cheese	Improves water binding and increases moisture content in the nonfat Substance	[25]
Prebiotics	Functional food	[26,27]
Protein-dextran conjugates	Improves emulsifying, foaming, gelling, and solubility attributes of protein by Maillard reaction	[28,29,30]

7.1.1.Bakery

The incorporation of dextran in bread for the improvement of rheological properties and quality is gaining interest [31,32]. The increasing knowledge of sourdough fermentation generates new opportunities for its use in the bakeryfield. In situ dextran production from Weissell asp.and Leuconostoc mesenteroides improved the freshness, mouthfeel, texture, loaf volume, softness, and shelf life of sourdough wheat bread [21,31]. It came forth that dextran should have a high molecular weight and few branched linkages for the application in sourdough [33]. Hence, dextran holds potential application in baking industry for the generation of gluten-free food products for patients suffering from celiac disease [31, 17].

7.1.2. Confectionery

Dextran is used for maintaining flavor, viscosity, moisture, inhibition of sugar crystallization, and as gelling agent in gum and jelly candies in confectioneries [22]. It is also used in soft drinks, flavor extract, milk beverages, and icing.

7.1.3. Ice Cream

Dextran is also used as a cryoprotectant in ice cream [23]. Dextran is bland, odorless, tasteless, and nontoxic and is considered to have many advantages over other ice cream stabilizers. Ice cream mixes containing 2–4 % dextran conferred beneficial properties on viscosity [24].

7.1.4. Fermented Dairy Products

The texture of yogurt and yogurt-like products made from milk by fermentation with LAB can be modified by in situ production of EPS [3,4,35]. EPS produced by LAB, particularly dextran, positively affected the rheological properties of acidified milk gels with enhanced viscosity, creaminess, and reduced syneresis because of its water-binding ability [23].and hence can replace the commercially used texturizers, viz., xanthan, carrageenan, pectin, guar gum, and β-glucan.

7.1.5. Foods

The favorable properties of dextran for stabilizing vacuum, air-dried, and freeze-dried or frozenfoods enable the use of dextran infish products, meat, vegetables, and cheese. Afilm of dextran could protect food from oxidation and other chemical changes and also help to preserve texture and flavor. The increasing demand for fast food in frozen or dried state creates an opportunity for the use of dextran as a preservative, as well as a texture, flavor, and smell enhancer [24].

7.1.6. Reduced-Fat Cheese

The fat reduction in cheese results in many textural and functional defects. The high casein content in reduced-fat cheese imparts afirm and rubbery body and texture. Dextran is a good candidate for making reduced-fat cheese for several reasons. Dextran has the ability to bind water and increase the moisture in the non-fat mass [1].

7.1.7. Prebiotics

In recent years, there is a considerable interest in the use of prebiotics as functional foods in order to modulate the composition of the colonic microbiota to provide health benefits to the host [35]. Foods containing prebiotic have also been associated with the protection against risk of several diseases, viz., bowel cancer, inflammatory bowel disease, diarrhea, coronary heart disease, obesity, osteoporosis, cholesterolemia, and type 2 diabetes. The-(1-6) linkages are known to be resistant to hydrolysis by human intestinal enzymes, which results in the slow digestion of dextran in human. Moreover, α-(1-2) linkages are also highly resistant to the attack of digestive enzymes [58]. Dextran and dextran-derived oligosaccharides have also been reported to increase the fraction of Bifidobacterium species in an in vitro model of the fermentation process in the human colon exhibiting prebiotic activity [26]. A low molecular weight dextran containing α-(1-2)-branched linkages was also reported to act as prebiotic with selective effect on the gut microbiota [27]. This dextran induced the growth of beneficial bacteria such as Bifidobacterium sp. and Lactobacillus sp. Recently, dextrans from Weissella cibariaJAG8 [17] and Lactobacillus plantarumDM5 [13]. showed promising prebiotic potential with very low gut digestibility and selective stimulation of probiotics.

7.1.8. Protein: Dextran Conjugates

Proteins are widely used in the food products such as beverages, yogurt, mayonnaise, and ice creams due to their functional properties, viz., emulsifying, foaming, gelling, and solubility [36, 28]. The functional properties of proteins can be improved by the conjugation of proteins and polysaccharides through Maillard reaction [30]. The Maillard reaction or nonenzymatic browning refers to any chemical reaction involving the interaction between amines and carbonyl compounds. Maillard reaction adds to the aroma, taste, and color of coffee and cocoa beans, bread, cakes, cereals, and meat [59]. Dextran-conjugated proteins have displayed significant improvement in physical and chemical properties of proteins, such as thermal stability, emulsification, and antioxidant properties [37]. The improvement of functional properties of different proteins, such as ova albumin, lysozyme [29], peanut protein [37] soy protein [38], and whey protein [30], after conjugation with dextrans has been studied.

7.2.Medical Uses

7.2.1. Antithrombotic Effect

These agents are used to decrease vascular thrombosis. The antithrombotic effect of dextran is mediated by its binding of erythrocytes, platelets and vascular endothelium, increasing their electronegativity and thus reducing erythrocytes aggregation and platelet adhesiveness. Dextran also reduce the VIII-Ag Von Willebrand factor, thereby decreasing platelet function. Clots formed after administration of dextran are more easily lysed due to an altered thrombus structure. By inhibiting alpha – 2 antiplasmin, dextran serves as a plasminogen activator and therefore possesses thrombolytic features. Apart from these features larger dextrans, which do not pass out of the vessels are potent osmotic agents, and thus have been used to treat hypovolemia. The hemodilution caused by volume expansion with dextran use improves blood flow, thus further improving patency of microanastomoses and reducing thrombosis [7].

7.2.2. Usage in Intravenous Fluids

It is used in some eye drops as a lubricant and in certain intravenous fluids to solubilize other factors. Dextran in intravenous solution provides an osmotically neutral fluid that once in the body is digested by cells into glucose and free water. It is occasionally used to replace lost blood in emergency situations, where replacement blood is not available, but must be used with caution as it does not provide necessary electrolytes and can cause hyponatremia or other electrolyte disturbances [7].

7.2.3. Anticoagulant Activity

Chemically prepared sulphuric esters of polysaccharides are known to have anticoagulant action. One of these is the dextran sulphate. The anticoagulant expressed in units/mg appears to be independent of the molecular weight but depends on a certain minimum number of sulphate groups per glucose units. Clinical grade Dextran are available as Dextran 1,Dextran 40,Dextran 60 and Dextran 70.Solutions of Dextran 40, Dextran 60 and Dextran 70 for injections are commonly used in clinical practice for replacement of blood loss, plasmasubstitution, thrombosis prophylaxis, volume expansion rheological improvement. Administration of Dextran 1 prior to injection of Dextran 40, Dextran 60 and Dextran 70 is known to reduce the adverse reactions significantly. Clinical grade dextran is the safest plasma substitute in clinical use. Clinical grade dextran are used for different purposes example cryopresevation and solutions for storing organs for transplantation and as carriers in vaccines [7].

7.2.4. Iron Dextran

Dextran is an important starting material for Iron dextran synthesis. The iron dextran solution for injection is applied for treatment of human and veterinary anemic deficiency [7].

7.3. In the field of Cosmetics

Dextran and Dextran derivatives have some beneficial applications to the cosmetics as a moisturizer and a thickener, especially Cationic Dextran (CDC) makes complex salts with anionic or amphoteric surfactants, which moderately adsorb to hair and skin to form films having moisturizing effects. CDC is a useful conditioning agents for hair care and skin care products. Dextran sulfate has the following properties which makes it more favorable for its usage in cosmetics(Anti-ageing , Anti-wrinkle effects, Smooth fresh, non-sticky feeling ,Good moisture retention , Increased lipase activity giving weight- reducing effects and supple skin, Anti – inflammatory and anti- allergic, Treating rough, chapped skin) Anti- inflammatory effects of Dextran sulfates have been demonstrated in various studies [40, 41, 42]. Dextran sulfate has been found to reduce lymphoblast extravasation in skin sites inflamed [60]. The osmotic retention of water by Dextran sulfate present in tissue will contribute to the well-being and mechanical properties of the tissue concerned.

7.4. Waste Water Management

Native Dextran finds a wide range of application in waste water management. Dextran offers many useful features like stable alkali and acids at room temperature. It binds metal ions at alkaline pH and is Biodegradable [7].

7.5. Laboratory Uses

• Dextran is used in some size exclusion chromatography matrices e.g.: sephadex It is used to make micro carriers for cell culture.

- Dextran preferentially binds to early endosomes fluorescently labeled dextran can be used to visualize these endosome under a fluorescent microscope.
- Dextran has been used in immobilization in biosensors. It can also be used as a stabilizing coating to protect metal nanoparticles from. Oxidation and improve biocompatibility.
- Dextran coupled with a fluorescent molecule (such as FITC) can be used to create concentration gradients of diffusible molecules for imaging and allow subsequent characterization of gradient slope.
- It can also be used as a stabilizing coating to potent metal nanoparticles from oxidation and improves biocompatibility.
- Dextran is also been used in immobilization in biosensors.
- and in bead form it is used to aid in biosensors applications.

VIII. Conclusion

From the facts outlined of physico-chemical characterization and prebiotic potential of dextran it appears that Dextran hasseveral potential applications in food and many health benefits. And also has contributes to many more applications in technical and pharmaceutical industries too. It has been recognized the necessity to encourage the industrial production of dextran using cheaper substrates considering the economic strategies.

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