



EUROPEAN COMMISSION
HEALTH & CONSUMER PROTECTION DIRECTORATE-GENERAL

Directorate C - Scientific Opinions
C3 - Management of scientific committees II; scientific co-operation and networks

SCIENTIFIC COMMITTEE ON FOOD

CS/NF/DOS/7/ADD 3 FINAL

**OPINION
OF THE
SCIENTIFIC COMMITTEE ON FOOD
ON
A DEXTRAN PREPARATION, PRODUCED USING *LEUCONOSTOC
MESENTEROIDES*, *SACCHAROMYCES CEREVISIAE* and *LACTOBACILLUS Spp*,
AS A NOVEL FOOD INGREDIENT IN BAKERY PRODUCTS**

(expressed on 18 October 2000)

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OPINION OF THE SCIENTIFIC COMMITTEE ON FOOD ON A DEXTRAN PREPARATION, PRODUCED USING *LEUCONOSTOC MESENEROIDES*, *SACCHAROMYCES CEREVISIAE* and *LACTOBACILLUS Spp*, AS A NOVEL FOOD INGREDIENT IN BAKERY PRODUCTS

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Terms of Reference

The Committee is asked to assess the safety, from the point of view of consumer health, of bacterial dextrans as Novel Food ingredients. The Committee is also invited to focus its deliberations on the issues raised in the comments made by member states' authorities.

Background

The Belgian competent authority received an application for approval of a high molecular weight polysaccharide for use, as a functional ingredient, in bakery products. The food ingredient is a dextran produced from sucrose by a strain of the lactic acid bacterium *Leuconostoc mesenteroides*. The producer strain has not undergone genetic modification. The application was made under the Novel Foods and Novel Food Ingredients Regulation 258/97/EC¹.

Dextrans have a history of limited use in the EU, e.g. in clinical nutrition, in fructose syrup, in fermented products, etc. Dextrans have also been used as additive in products such as candies and ice cream.

The incorporation of dextran in bakery products improves softness, crumb texture and loaf volume. The levels of use will not exceed 5 % on end product basis.

The Belgian competent authority was in favour of the use of dextran, produced under the specified conditions, in bakery products.

Some competent authorities of the Member States, however, submitted comments/objections on the outcome of the initial assessment. Therefore, pursuant to Article 11 of Regulation 258/97/EC¹, the European Commission submitted the dossier to the Scientific Committee on Food to evaluate the safety of dextran as an ingredient in food and to comment on objections made by the authorities of the Member States.

Major objections/comments or concerns made by the member states are:

1. The product specifications, in particular the content of heavy metal residues, are not clearly indicated.
2. There is a lack of clarity about the place in which dextran is digested.
3. The producer organisms are not adequately characterised.
4. The application does not contain a proposal to ensure a clear labelling in order to inform certain groups of consumers (diabetics) on potential risk.
5. The data on the risks for allergenicity are incomplete.
6. The data on toxicology are incomplete.
7. The classification of the dextran as a novel food ingredient rather than it being classified and assessed as a food additive.

These points are addressed here and the opinion expressed is based on additional information submitted by the petitioner².

Technical information and product specification

The Committee has been fully informed about the description of the product, the manufacturing process, the product specifications and the methods of analysis and is content with the provided information².

Long-chain, high-molecular-weight polymers that dissolve or disperse in water to give improved rheological (gelling, thickening) or physico-chemical (emulsion stabilisation, particle suspension etc) properties, are important tools for food product formulation.

Most polysaccharides currently used are obtained from plants and seaweed (e.g. starch, pectin, agar and alginates).

Microbial fermentation is, however, also used for the production of food polysaccharides such as homo-polymers of glucose (e.g. β -glucans, bacterial cellulose, pullulan) and hetero-polymers (e.g. xanthan gum, gellan gum, bacterial alginates). Dextran belongs to the group of homo-polysaccharides^{3,4,5,6,7}.

The three basic structural elements of the carbohydrate are:

1. The structure is that of a mainly linear polymer of α -D-glucose units with α -1,6 glycosidic bonds together with a few α -1,3 branches. The degree of branching was demonstrated to be about 4.6% and consists exclusively of α -1,3 glycosidic linkages. After a complete hydrolysis the resulting carbohydrate fraction consists of pure glucose⁸.
2. The molecular weight of $20 \cdot 10^6$, derived by calculation, is in the range of the molecular weight values of 1 to $200 \cdot 10^6$ Dalton found in literature for dextran from *Leuconostoc mesenteroides*⁹.
3. The poly-dispersity in the molecular weight of the commercial product is limited and somewhat less diverse than the known high molecular weight dextran originating from *Leuconostoc mesenteroides* BR512F¹⁰. This results from the fermentation conditions.

The Committee is of the opinion that, based on the data provided by the petitioner, it is reasonable to conclude that the dextran preparation from *Leuconostoc mesenteroides* (strain BCCM LMG P-16878) under consideration in this application is similar to that described in literature.

Product specification

The dextran is commercialised in a powder form and as a liquid with the following specifications:

For the powdered form (values in % of commercial product) carbohydrate 60 (with dextran 50, mannitol 0.5, fructose 0.3, leucrose 9.2), protein 6.5; lipid 0.5; lactic acid 10; ethanol traces; ash 13; moisture 10.

For the liquid form (values in % of commercial product): carbohydrate 12 (with dextran 6.9; mannitol 1.1; fructose 1.85; leucrose 2.15); protein 2; lipid 0.1; lactic acid 2; ethanol 0.5; ash 3.4; moisture 80.

No analytical data are given on the composition of the ash fraction. However, the information provided by the petitioner on the fermentation media composition indicates that the major salts to be found in the ash should be potassium (added as K_2PO_4) and sodium (added as CH_3COONa and as $NaOH$).

The residue level of heavy metals in the dextran is as follows: lead < 0.2 ppm, arsenic < 0.2 ppm, mercury < 0.05, cadmium < 0.05 ppm.

The major raw material used for the production of dextran is sucrose. The residue limit for lead and arsenic in white sugar set by the Codex Alimentarius is 0.1-0.5 ppm and 1 ppm respectively¹¹.

The use of dextran will be limited to bakery products, i.e. products rich in wheat (wheat flour), and will only be present as a minor component in these products.

According to a proposal for a Draft Commission Regulation setting maximum levels for certain contaminants in foodstuffs¹² concerning contaminants, the specifications for heavy metals, in products rich in wheat, are: lead 0.2 ppm; cadmium 0.2 ppm; there is no specification for mercury and arsenic for these products.

The guideline levels for heavy metals in wheat in Germany are: lead 0.3 ppm, mercury 0.03 ppm, cadmium 0.10 ppm¹³. For Belgium, the residue limits for heavy metals in cereal grain are: lead 0.5 ppm, mercury 0.03 ppm, cadmium 0.15 ppm¹⁴.

Given the additional information provided by the petitioner, the Committee is content with the specification of the commercial dextran preparation.

Digestibility of Dextran

It has been demonstrated that in both rat and humans the oral administration of dextran causes a rapid increase in blood sugar and liver glycogen. Digestibility and caloric availability in the rat are high. The animal uses the digested dextran for growth^{15, 16}. It is assumed that the polysaccharide is hydrolysed by a genuine intestinal enzyme and not solely by bacterial action¹⁷. The enzyme is localised in the small-intestinal mucosa. The large intestine and the caecum show very little dextran hydrolysing activity. No dextran has been detected in faeces after feeding experiments with dextran containing diets^{18, 19, 20}.

In recent studies the effect of a dextran enriched diet on jejunal and ileal brush border membrane has been reported. An increased sodium-dependent glucose transport and uptake was found after a short or longer-term mucosal exposure to dextran²¹.

From the published literature it can be concluded that dextran is essentially (90%) hydrolysed to monosaccharides and that the residual dextran that escapes the digestion is fermented into carboxylic acids²⁰.

History of the organisms used as the source of dextran

The micro-organisms used for the production of dextran (*Leuconostoc mesenteroides*, *Saccharomyces cerevisiae*, *Lactobacillus plantarum*, *Lactobacillus sanfrancisco*) are currently used in food processing without any restriction.

Leuconostoc mesenteroides is used in a primary fermentation for the bioconversion of food grade sucrose to dextran and fructose.

In a subsequent secondary fermentation, fructose is eliminated from the bioconversion mix. For the preparation under powder form, fermentation is performed with *Saccharomyces cerevisiae*. To produce the dextran under liquid form fermentation is performed with either *Lactobacillus sanfrancisco* (ATCC 27651) or *Lactobacillus plantarum* (ATCC 14917).

Leuconostoc mesenteroides and *Saccharomyces cerevisiae* are GRAS^{22,23} micro-organism and known to be non-pathogenic. All the strains are widely used for the preparation of various common food or food ingredients and have a safe history for use in the EU²⁴.

Leuconostoc mesenteroides was isolated from a cheese starter culture commonly used for the production of European cheese^{25, 26}. *Saccharomyces cerevisiae* is a common yeast species used in various fermented food processes.

Lactobacillus plantarum and *Lactobacillus sanfrancisco* are commercially available and widely used e.g. for the production of fermented milk products and for the preparation of sourdough^{27, 28}.

With exception of *Saccharomyces cerevisiae*, all strains belong to the category of the lactic acid bacteria. These bacteria are well known to produce exo-polysaccharides in the presence of sucrose²⁹.

Analyses on the final products obtained from different batches produced under the specific conditions as applied by the petitioner revealed neither the presence of toxin nor antibiotic activity².

The Committee is content with the characterisation of the producer organisms as described by the petitioner.

Anticipated intake/extent of use

As a result of microbial activity, dextran occurs in small amounts in naturally fermented products such as sauerkraut and cucumber and in kefir where it probably plays a role in the thickening⁴. Dextran is found in sugar mills and refineries when sucrose-containing solutions become contaminated with dextran-producing bacteria³⁰. Dextran develops naturally in frost-damaged sugar cane and in cut cane if processing is delayed³¹. It is present in honey³². Water-insoluble dextran flavoured with fruit syrups constitutes the commercially produced desert “nata”, in the Philippines³³. Dextran is the major polysaccharide of dental plaque representing 3.7% by weight of the dry plaque³⁴. It can therefore be concluded that dextran is already consumed on a regular basis. However a realistic quantification of the human exposure to this category of dextran remains very difficult.

In this petition dextran is intended as a functional and a technological ingredient in bakery products. The level of use varies from 0.5% to maximum 5% on the end product basis. The amount added is related to the desired functional and physical characteristics of the end product. In most cases, however, the use will be limited to 2%².

Taking the highest concentration of dextran (5%) to be used in bakery products and with an estimated intake of 250g bakers' wares per day³⁵, the intake could result in the consumption of 12.5g dextran per day.

The Committee is of the opinion that it is unlikely that the partial replacement of starch by 5% dextran in these products will have a nutritional significance for consumers.

Information from previous human exposure to dextran

Dextran has a long history of clinical use as a blood extender. A 6% solution of a dextran fraction was approved for clinical use in Sweden in 1947 and shortly thereafter in the UK³⁶.

The Select Committee on substances Generally Recognised as Safe (GRAS) reviewed literature on hazards related to dextran, from 1920 up to 1975. In its conclusion this Committee stated that there is no evidence in the available information that demonstrates a hazard to the public when dextran is used at levels that were current in the United States in 1975. However, the Committee could not determine, without additional data, whether a significant increase in consumption would constitute a dietary hazard. Subsequently, the Committee clarified this conclusion, emphasizing that dextrans were considered safe when used as a component of food-packaging materials, and that insufficient scientific data are available upon which to base an approval for direct food use³⁷.

In 1977 the GRAS status of dextrans was deleted because a survey of food manufacturers on the use of GRAS ingredients indicated that dextrans were no longer used as food ingredients. The FDA concurred with the conclusion of the Select Committee and concluded that direct human food use of dextrans cannot be affirmed as GRAS at that time. For dextrans used as indirect human food ingredients, the GRAS status was retained^{38,39}.

In 1993, The UK Advisory Committee on Novel Foods and Processes (ACNFP) concluded that a dextran fraction with at least 95% of the molecules being straight chained (i.e. with α -1-6 bonds) and less than 5% having α -1,4 links, and with a molecular size between 30,000 and 40,000, was considered safe for use in clinical nutrition products. However the Committee did restrict its conclusion to the clinical use⁴⁰.

Potential risk for diabetics

Orally ingested dextran is rapidly converted to glucose. Therefore diabetics could be considered as a risk group. However, the dextran preparation, which is the subject of this opinion, is intended to be used in bakery products up to a recommended level of maximum 5%.

The Committee is of the opinion that the use of dextran up to 5% will not present a greater risk to diabetics than the starch that it would displace.

Toxicology and allergenicity of dextran

Clinical dextran (molecular weight 70,000) was reported not to be toxic at oral doses of 12 g/kg for mice and 3 g/kg for rats. When injected intravenously, the LD₅₀ values for mice and rats were 12.1 and 6.9 g/kg (females) and 13 and 8.2 g/kg (males), respectively⁴¹.

In a sub-acute study, dextran was fed at a 15% level for 62 days to 6 weanling white albino rats. No effect on growth and food efficiency and no catharsis were reported⁴².

Sub-chronic and chronic feeding studies are not available. An extensive study of the carcinogenicity of dextrans administered by the subcutaneous and intra-peritoneal route to mice and rats for up to 2 years and intra-venously to rabbits up to 4 years, however, reported the appearance of sarcomas in the tissue in which the substances were retained and stored⁴³. However, the parenteral administration questions the relevance of this finding for the oral intake.

Dextran was reported not to induce gene mutations in *S. typhimurium* strains TA98, TA100, TA1535, TA1537, and TA1538, either in the absence or in the presence of S9 mix (from Aroclor 1254-induced rat or hamster liver, respectively), when tested in a dose range from 100 to 10,000 μ g/plate⁴⁴. Furthermore, dextran was reported not to induce chromosomal aberrations in cultured Chinese hamster fibroblasts⁴⁵.

Dextran did not show teratogenic effects when administered to developing chicken embryos up to the highest tested level of 10 mg/egg⁴⁶. Other studies on teratogenicity and reproductive toxicity are not available.

Dextran induced anaphylactoid/anaphylic (DIAR) reactions in less than 1% of patients who received infusions of clinical dextran^{47, 48}. Incidence of reactions appeared to be related to chemical structure, the ones having higher molecular weights and/or a greater proportion of non-1.6-linkages causing a greater incidence of untoward reactions. Hypersensitivity reactions observed in the initial development of dextran as a blood extender are now reduced due to a modification of the dextran and by a pretreatment of the patients with a low molecular weight dextran as mono-valent hapten⁴⁷. The occurrence of DIAR in some patients has been attributed to antibodies of the IgG class formed after ingestion or of immunologically cross reacting polysaccharides in foods^{49,50}.

The Committee is of the opinion that dextran presents no toxicological concerns and that it is unlikely to give rise to an allergic reaction after oral intake.

Classification of dextran as a food additive and labelling

The classification of dextran as an additive rather than as a novel food ingredient and the need for labelling are not safety issues and are therefore not considered in this opinion.

Conclusion

The Committee considers that dextran produced by a process of bacterial fermentation with *Leuconostoc mesenteroides* as described by the petitioner added at a level of maximum 5% in bakery products, does not constitute a safety concern from the point of view of consumer health.

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