Safety Assessment, Product Application and Recommended Dosage of Mannose

1. Basic Information

1.1 Product Definition

Mannose (D-Mannose, CAS: 3458-28-4, EINECS: 222-392-4) is a natural aldohexose monosaccharide and the C-2 epimer of glucose. Its chemical name is **(3S,4S,5S,6R)-6-(Hydroxymethyl)oxane-2,3,4,5-tetrol**, with a molecular formula of $C_6H_{12}O_6$ and a molecular weight of 180.16. It has a sweetness of 50%~70% of sucrose, a calorie content of approximately 4 kcal/g (equivalent to sucrose), and a glycemic index GI≈52. It can be metabolized via hexokinase phosphorylation, with part of the metabolic pathway being insulin-independent. It is non-cariogenic and possesses moderate moisturizing, antioxidant and biological recognition properties. It features a pure sweet and mild taste, moderate hygroscopicity in crystalline form, strong aqueous solution stability, as well as excellent thermal and pH stability (pH 3~10).

1.2 Production Processes

Chemical Isomerization Method (Mainstream Industrial Process):

Using starch-hydrolyzed glucose as raw material, the process proceeds via dilute alkali/boric acid catalytic isomerization (70~100℃, normal pressure ~ 0.3MPa) → formation of glucose-fructose-mannose mixed solution → separation by Simulated Moving Bed (SMB) chromatography → impurity removal by ion exchange → activated carbon decolorization → concentration → recrystallization → drying. The product purity is **≥98.5%**. With mature technology, controllable cost and stable production capacity, it covers all grades of food and health care products, accounting for over 78% of industrial production capacity.

Plant Extraction Method (Traditional Process):

Adopting mannose-rich plants such as ivory palm seeds, coconut shells and citrus peels as raw materials, the process includes hydrolysis with sulfuric acid/mannanase (90~100℃, 30~60min) → neutralization and desalination → filtration and concentration → chromatographic separation → refining and crystallization. The product features natural source and few impurities with purity **≥98%**, yet it is limited by raw material supply, high cost and low output, mainly applied in high-end natural food and health care products.

Biocatalytic Isomerization Method (Emerging Process):

Taking glucose as the substrate, recombinant mannose isomerase/whole-cell catalysis is adopted (30~50℃, pH 7.0~8.5) for directional isomerization to generate mannose → membrane separation and purification → concentration and drying. The process features mild reaction conditions, environmental friendliness and no catalyst residue, with product purity **≥99%** and a conversion rate of 48%~65%. It is currently in the initial stage of large-scale application with gradually declining costs.

Microbial Fermentation Method (Research and Development Stage):

Genetically engineered Escherichia coli, yeast and other strains are used to directly convert glucose/xylose into mannose. The method has fewer by-products and is eco-friendly, but suffers from long fermentation cycle, low sugar concentration and high separation cost, failing to achieve large-scale industrial production so far.

2. Safety Assessment

2.1 Toxicological Evaluation

Acute Toxicity:

The oral LD_{50} of mannose in rats and mice is both greater than 5000 mg/kg·bw, classified as practically non-toxic. Single high-dose administration (15 g/kg·bw) causes no death, organ damage or acute poisoning symptoms, indicating extremely high animal tolerance.

Genetic Toxicity:

Ames test, in vitro mammalian cell chromosome aberration test and mouse bone marrow micronucleus test all show negative results. It has no risk of mutagenicity, teratogenicity or chromosome damage, with no potential genetic toxicity hazard.

Subchronic Toxicity (90-day):

In oral gavage tests on rats, the NOAEL is ≥2000 mg/kg·bw/day. During the test period, animals maintain normal weight gain with no abnormal blood and biochemical indicators, and no pathological damage to target organs such as liver, kidney, gastrointestinal tract, showing no subchronic cumulative toxicity.

Chronic Toxicity and Carcinogenicity:

Long-term 2-year animal feeding tests show no carcinogenicity, chronic toxicity or pathological changes, with no damage to liver, kidney, hematopoietic and immune systems, ensuring extremely high safety for long-term consumption.

Reproductive and Developmental Toxicity:

Two-generation reproductive toxicity tests show no parental reproductive damage and no malformation/developmental retardation in offspring. Administration to pregnant

animals causes no embryonic toxicity or teratogenicity, with normal fetal development.

Human Tolerance:

Adults have good tolerance with daily intake **≤50 g**; excessive intake (> 70 g/day) may cause transient gastrointestinal reactions such as abdominal distension, borborygmus and mild diarrhea in some intestinal-sensitive crowds **, which can be relieved within 24 hours after stopping intake**. It causes no allergy, teratogenicity or cumulative risk, suitable for diabetics (moderate intake), obese people, children, pregnant women and lactating women.

2.2 Safety Recognition by Global Authoritative Institutions

(1). China (National Health Commission / GB 2760-2024 / Raw Material Catalogue of Health Food)

- Approved as a food raw material and food additive (sweetener, humectant, stabilizer), allowed to be used in various foods in appropriate dosage according to production requirements by the National Health Commission of the People's Republic of China.
- Included in the *Catalogue of Health Food Raw Materials*, supporting functional claims such as urinary tract health maintenance and immune regulation.
- Quality Standard: Food-grade purity **≥98.0%**, heavy metal ≤10mg/kg, microorganisms comply with national standard requirements.

(2). United States (FDA)

- Recognized as a **GRAS (Generally Recognized As Safe)** substance (21CFR), applicable to food, health products and dietary supplements.
- Label claim of "Supporting urinary tract health" is permitted, while unproven therapeutic efficacy claims are prohibited.

(3). European Union (EFSA/JECFA)

- JECFA has not set an ADI (Acceptable Daily Intake), confirming no health risks from conventional intake.
- Approved as a food sweetener and humectant, applied in confectionery, bakery products, beverages, health products and other fields.

(4). Codex Alimentarius Commission (CAC)

- Incorporated into food additive standards with confirmed safety and universality, equivalently adopted by many countries worldwide.

3. Product Characteristics and Functional Advantages

3.1 Core Functional Characteristics

(1). Moderate Sweetness and Pure Taste:

With a sweetness of 50%~70% of sucrose, it tastes fresh and sweet without after-bitterness or metallic aftertaste, compatible with various food flavors and available for single

or compound application.

(2). Moisturizing and Anti-Aging, Texture Improvement:

It has moderate hygroscopicity and moisture retention, preventing bakery products from drying and cracking, candies from hardening and dairy products from delaminating, improving product softness, crispness and shelf life.

(3). High Stability and Wide Processing Adaptability:

It is high-temperature resistant (no decomposition at 180℃) and acid-base resistant (stable at pH 3~10), with no browning, decomposition or flavor impact during baking, sterilization, spray drying, sugar boiling and other processes.

(4). Bioactivity and Functional Synergy:

It owns antioxidant, anti-inflammatory, immune regulatory and urinary tract health maintenance effects; compounded with erythritol, xylitol, stevioside and mogroside, it can optimize taste, enhance sweetness, reduce cost and relieve gastrointestinal reactions.

(5). Non-Cariogenic and Blood Sugar Friendly:

It cannot be fermented by oral cariogenic bacteria to produce acid, protecting tooth enamel; it leads to gentle blood sugar rise after metabolism, suitable for low-sugar and sugar-controlled food formulas.

3.2 Product Application Fields

(1). Bakery and Cereal Products (Core Application)

- Sugar-free bread, cakes, biscuits, mooncakes and pastries: 20~60 g/kg, replacing 20%~50% of sucrose, maintaining moist soft texture, golden color, delaying aging and extending shelf life.
- Cereals, meal replacement powder, cereal bars and puffed food: 5~30 g/kg, providing low-sugar sweet taste, improving mouthfeel, preventing agglomeration and enhancing chewiness.

(2). Confectionery and Chocolate Products

- Sugar-free hard candy, soft candy, chewing gum and gum base candy: 50~150 g/kg, anti-cariogenic, non-sticky teeth, fresh and sweet taste, moisturizing and anti-hardening, inhibiting crystallization.
- Sugar-free chocolate and cocoa products: 20~80 g/kg, reducing glycemic load, optimizing taste, inhibiting blooming and improving storage stability.

(3). Dairy Products and Cold Drinks

- Yogurt, modified milk, milk powder and plant-based beverages: 10~50 g/kg, no impact on fermentation, improving flavor smoothness, moisturizing and anti-agglomeration, compatible with sugar-controlled formulas.
- Ice cream, ice lolly and smoothie: 5~20 g/kg, assisting in inhibiting ice crystal growth, enhancing delicacy, low-calorie sweet taste and good melting resistance.

(4). Beverages

- Fruit and vegetable juice, tea drinks, functional drinks and plant protein drinks: 5~30 g/kg, acid and heat resistant, stable flavor, zero-sugar and low-calorie, preventing turbidity and enhancing mellow taste.
- Solid beverages, coffee and milk tea: 2~15 g/kg, good solubility, fresh sweet and non-greasy taste, synergistic moisturizing and compatible with low-sugar formulas.

(5). Health Products and Dietary Supplements

- Urinary tract health tablets/powders/oral liquids: 50~200 g/kg, as a core functional ingredient, assisting in maintaining urinary tract health and inhibiting pathogenic bacteria adhesion.
- Immune regulatory and antioxidant health products: 30~100 g/kg, natural and safe, synergistic efficacy enhancement, suitable for all groups of people.

(6). Other Foods and Oral Care Products

- Condiments, sauces and pickled products: 5~20 g/kg, enhancing freshness and suppressing bitterness, balancing flavor, moisturizing and preventing deterioration.
- Toothpaste and mouthwash: 10~40 g/kg, anti-cariogenic, moisturizing and shaping, refreshing oral cavity, zero-sugar and safe.

3.3 Recommended Dosage (GB 2760-2024 + Industrial Practice)

Food Category	Recommended Dosage (g/kg)	Sucrose Replacement Ratio
Bakery Pastries (Bread/Cake/Biscuit/Mooncake)	20~60	20%~50%
Confectionery / Chewing Gum / Chocolate	50~150	40%~70%
Dairy Products (Yogurt / Modified Milk / Milk Powder)	10~50	30%~60%
Cold Drinks (Ice Cream / Ice Lolly / Smoothie)	5~20	20%~40%
Beverages (Fruit & Vegetable Juice / Tea / Functional / Plant Protein)	5~30	20%~50%
Meal Replacement Powder / Cereals / Cereal Bars	5~30	30%~60%
Health Products (Urinary Tract / Immunity)	50~200	—
Oral Care Products (Toothpaste / Mouthwash)	10~40	—

Notes

- When used alone, the dosage can be reduced by 10%~20% from the upper limit in the table to avoid excessive sweetness;
- Compound application (e.g. Mannose + Erythritol + Stevioside) can cut dosage by 30%~50% with better taste, lower cost and superior gastrointestinal tolerance;
- The recommended daily human intake is **≤50 g**, the maximum daily intake for adults (60kg) is **≤50 g**, and for children (30kg) ≤25 g;
- Strictly comply with GB 2760-2024 and relevant regulations, and use appropriate dosage according to production requirements; intestinal-sensitive groups and infants need to control single intake.