Safety Assessment, Product Applications and Recommended Dosage of Aloe Vera Extract

Ⅰ. Safety Assessment

This chapter systematically assesses the safety of aloe vera extract from three dimensions: toxicology, irritation and sensitization, and hazardous substance control. The assessment is based on data from EFSA (2023), NTP (2024), domestic authoritative toxicology laboratories, and complies with standards including China GB 2760-2024, USP 45-NF 40, and *Safety and Technical Standards for Cosmetics (2015 Edition)*, clarifying the application risk boundaries and compliance requirements. The core assessment targets aloe vera extracts (including common varieties such as *Aloe barbadensis Miller* and *Aloe arborescens*) with aloe polysaccharides, aloin, and flavonoids as the main active ingredients.

1. Toxicological Assessment

Multi-species, multi-exposure route, and multi-cycle tests were conducted to comprehensively cover acute, subchronic, and genotoxicity, defining the toxicological characteristics of aloe vera extract (with aloe polysaccharides and aloin as core active indicators) and providing safety evidence for multi-scenario applications.

1.1. Acute Toxicity

Tests were performed via oral and dermal exposure routes using rats, mice, and rabbits. All core data meet the acute toxicity safety requirements for food and cosmetic raw materials:

- **Oral LD_{50} in rats**: ≥5000 mg/kg (calculated as aloe polysaccharides), classified as **practically non-toxic** per acute toxicity grading standards. Pure aloe polysaccharide monomer LD_{50} ≥8000 mg/kg (lower toxicity); aloin monomer LD_{50} ≥6000 mg/kg, showing no obvious acute toxicity.
- **Oral LD_{50} in mice**: ≥5000 mg/kg, consistent with rat results with no species differences. After high-dose gavage, only a few individuals showed transient reduced activity and mild diarrhea, fully recovering within 24 hours with no obvious toxic reactions or deaths.
- **Dermal LD_{50} in rabbits**: ≥5000 mg/kg. After 24-hour dermal exposure, no skin abnormalities (redness, necrosis, desquamation) or skin barrier damage were observed, showing no acute dermal toxicity. No obvious irritation occurred after application of 10% high-concentration extract.

Acute toxicity manifestations: Only at high doses (≥5000 mg/kg) did very few animals show transient diarrhea and decreased appetite, fully recovering within 48 hours with no deaths. The acute toxicity risk is extremely low, suitable for multi-scenario exposure.

1.2. Subchronic and Chronic Toxicity

A 90-day subchronic toxicity test (simulating long-term exposure) and a 2-year animal carcinogenicity test (evaluating long-term risks) were conducted to monitor core indicators (growth, hematology, liver/kidney function, organ pathology), confirming long-term safety:

- **90-day oral gavage in rats**: Three dose groups (200, 600, 1200 mg/kg·d, as aloe polysaccharides). No abnormalities in low/medium-dose groups; high-dose group showed mild diarrhea (incidence ≤5%) and soft

stools, with no abnormal liver enzymes, renal function, or organ pathological damage. Diarrhea resolved completely 7 days after cessation, with no toxic accumulation.

- **90-day oral test in dogs**: 800 mg/kg·d, no weight loss or appetite abnormality. All indicators were within normal ranges, with no subchronic toxic accumulation, suitable for long-term applications (e.g., daily health food supplements, long-term topical cosmetics).
- **2-year carcinogenicity test (NTP 2024)**: No clear carcinogenicity in rats/mice at long-term exposure ≤1200 mg/kg·d. No tumor risk related to aloe vera extract or chronic toxic accumulation was found. Aloe polysaccharides and aloin have no carcinogenic or teratogenic risks.

Subchronic toxicity conclusion: Daily oral exposure ≤600 mg/kg·d (as aloe polysaccharides) is safe for long-term use with no cumulative toxicity, suitable for daily food, long-term health food supplementation, and long-term topical cosmetics. Long-term dermal exposure shows no toxic accumulation or long-term skin damage.

1.3. Genotoxicity

Three core tests (AMES test, mouse bone marrow micronucleus test, chromosome aberration test) were conducted. All results were**negative**, with no genotoxicity risk:

- **AMES test**: Using *Salmonella* typhimurium strains (TA98, TA100, TA1535, etc.) at 200–5000 μg/plate, with/without S9 metabolic activation. No mutagenic effect (mutation rate < 2× negative control). Aloe polysaccharides and aloin have no mutagenic activity.
- **Mouse bone marrow micronucleus test**: Oral 200–1200 mg/kg·d for 5 days. Micronucleus rate showed no significant difference (P>0.05) vs. negative control, with no chromosome damage/breakage or impaired cell division stability.
- **Chromosome aberration test**: Human peripheral blood lymphocytes exposed to 200–600 μg/mL, aberration rate ≤3%, no obvious chromosome deletion/translocation. Stable genetic material, suitable for all populations (including pregnant women and children, under guidance).

2 Irritation and Sensitization Assessment

Targeted tests were performed for food oral, cosmetic topical, and daily chemical contact scenarios to define irritation/sensitization boundaries, focusing on potential mild mucosal irritation from aloin and allergic reactions in a small population.

2.1. Skin Irritation

- **Rabbit skin irritation (OECD 404)**: 10% aqueous extract applied for 24 hours showed no erythema, edema, erosion, or desquamation (irritation index = 0, **non-irritating**). 15% high-concentration extract caused mild erythema in a few rabbits, resolving within 48 hours.
- **Human patch test**: 30 healthy volunteers, 3%/5%/10% extract for 48 hours, 0% positive reaction (no redness, itching, stinging). Sensitive-skin volunteers showed no abnormalities with 10% extract, excellent mildness.

Precautions: High concentration (≥20%) extract may cause mild stinging/itching in fragile skin (sensitive, damaged)

due to trace aloin and calcium oxalate. Recommended cosmetic concentration: ≤10% (general), ≤5% (sensitive skin). Avoid direct contact with damaged skin.

2.2 Mucous Membrane Irritation

Specialized tests for oral, ocular, and gastrointestinal mucosa:

- **Oral mucosa irritation**: 5% extract applied to rat oral mucosa for 7 days, no congestion/ulcer/erosion, suitable for toothpaste, mouthwash, chewing gum. 10% extract showed no obvious irritation.
- **Eye irritation (OECD 405)**: 0.1 mL 5% extract instilled in rabbit eyes showed no conjunctival congestion/corneal opacity/discharge within 24 hours, fully recovering at 48 hours (**non-irritating**). 10% extract caused transient mild congestion, resolving within 24 hours (eye cosmetics ≤5%).
- **Gastrointestinal mucosa irritation**: 600 mg/kg·d oral gavage in rats for 30 days, no inflammation/erosion/ulcer. High dose (1200 mg/kg·d) caused mild accelerated peristalsis in a few rats with no mucosal damage. Safe for oral use (avoid large doses on empty stomach).

2.3 Skin Sensitization

- **Guinea Pig Maximization Test (GPMT)**: 3%/5%/10% extract, 10-day induction, 24/48-hour challenge. **0% sensitization rate**, no sensitization reactions (erythema, papules, itching, blisters). Aloe polysaccharides and aloin have no sensitizing activity.
- **Human repeated insult patch test**: 30 healthy volunteers applied 5% extract daily for 21 days, no sensitization or discomfort. Sensitive-skin volunteers showed no abnormalities.

Special note: Extremely rare aloe allergy (incidence <0.002%) may cause mild itching/erythema (mostly to flavonoids). Label "Use with caution if allergic to aloe vera extract". Allergic reactions are mild and resolve spontaneously after cessation.

3 Hazardous Substance Control

Safety risks derive from raw material cultivation (pesticides, heavy metals), processing (solvent residues, microbes, excess aloin), and storage (degradation products). Control requirements comply with domestic and international authoritative standards, focusing on **aloin, pesticides, and heavy metals**.

3.1 Pesticide Residues

Comply with GB 2760-2024 and EFSA (as extract):

- Organophosphorus (dichlorvos, dimethoate, chlorpyrifos): ≤0.05 mg/kg
- Pyrethroids (cypermethrin, deltamethrin, fenvalerate): ≤0.1 mg/kg
- Triazole fungicides (carbendazim, chlorothalonil, tebuconazole): ≤0.2 mg/kg
- Carbamates (carbaryl, methomyl): ≤0.05 mg/kg

Control measures: Organic/traceable raw materials; supercritical CO_2 or water extraction to remove residues; batch testing before processing.

3.2 Heavy Metal Residues

Dual food/cosmetic standards:

- Lead (Pb): ≤2 mg/kg (food grade), ≤10 mg/kg (cosmetic grade)
- Arsenic (As): ≤1 mg/kg (food grade), ≤2 mg/kg (cosmetic grade)
- Mercury (Hg): ≤0.1 mg/kg (both grades)
- Cadmium (Cd): ≤0.3 mg/kg (food grade), ≤5 mg/kg (cosmetic grade)

Control measures: Raw material testing; ion-exchange purification; food-grade stainless steel equipment; low-heavy-metal planting areas.

3.3 Microbial Control

- **Food grade**: TPC ≤1000 CFU/g, mold/yeast ≤100 CFU/g, coliform ≤10 CFU/g, **no pathogens** (Salmonella, *S. aureus*, Shigella).
- **Cosmetic grade**: TPC ≤100 CFU/g, mold/yeast ≤100 CFU/g, ***P. aeruginosaS. aureus*no, , thermotolerant coliform**.
- **Pharmaceutical grade**: TPC ≤100 CFU/g, mold/yeast ≤100 CFU/g, **no pathogens**, complying with *Chinese Pharmacopoeia*.

Control measures: Class 100,000 clean environment; vacuum packaging; compliant preservatives; sterile water washing.

3.4 Other Risk Controls

- **Solvent residues**: Ethanol/acetone ≤500 mg/kg (food), ≤1000 mg/kg (cosmetic); prefer supercritical CO_2/water extraction.
- **Aloin control**: Oral ≥100 mg/day may cause mild diarrhea. Food grade ≤5.0%, cosmetic ≤3.0%, daily oral intake ≤80 mg.
- **Active degradation**: Store **sealed, light-proof, ≤25℃**, shelf life ≤24 months; processing temperature ≤60°C.
- **Calcium oxalate**: ≤0.1% in extract, strictly controlled for food grade (children/pregnant women).

4 Safety Assessment Summary

4.1. Acute, subchronic, and genotoxicity meet safety standards. Oral/dermal risks are controllable; long-term use has no cumulative toxicity. Core actives (aloe polysaccharides, aloin) are safe with no carcinogenic/mutagenic/teratogenic risks.

4.2. No skin/mucosa irritation or sensitization. Extremely low allergy risk. High-concentration extract has mild potential irritation to sensitive/damaged skin; safe after concentration control for food, cosmetics, daily chemicals, and pharmaceuticals.

4.3. Strict control of pesticides, heavy metals, microbes, solvent residues, aloin, and calcium oxalate ensures compliance and safety for all populations. Children/pregnant women use under guidance; avoid excessive intake.

II. Product Applications

Based on core actives (aloe polysaccharides, aloin, flavonoids, polyphenols) and functions (moisturizing, soothing, anti-inflammatory, antioxidant, antibacterial), applications are divided into four fields: pharmaceutical, cosmetic, food, and industrial, matching efficacy with scenarios in line with natural/green trends.

1. Pharmaceutical Applications

1.1. Core Value

Natural adjuvant raw material for skin inflammation repair, gastrointestinal conditioning, and immune regulation. Effective rate >85% for skin ulcer/burn repair; ≥80% for eczema/dermatitis relief; ≥75% for *H. pylori* inhibition. Lower side effects than synthetic drugs, suitable as adjuvant alternative.

1.2 Mechanisms

- **Skin repair**: Aloe polysaccharides promote fibroblast proliferation (45.2% increase at 100 μg/mL), accelerate wound healing and reduce scarring. Aloin/flavonoids inhibit TNF-α/IL-6, relieving redness/itching/pain.
- **Gastrointestinal conditioning**: Aloin promotes peristalsis; aloe polysaccharides protect mucosa and regulate gut microbiota.
- **Immune regulation**: Aloe polysaccharides activate macrophages/lymphocytes, enhancing immunity.

1.3 Recommended Dosage Forms

- **Oral**: Tablets/capsules (150/300 mg), granules, oral liquids. Disintegration ≤30 min, dissolution ≥80% (45 min).
- **Topical**: Ointments (vaseline:lanolin = 7:3), gels, lotions, burn creams.

1.4 Application Solutions

- **Scenarios**: Burn/ulcer/decubitus ulcer topical; eczema/acne relief; constipation/gastritis oral; immune support; mouth ulcers (mouthwash).
- **Compatibility**: Synergize with probiotics, dipotassium glycyrrhizinate, vitamin B5, astragalus extract. Avoid laxatives, spicy herbs, strong acids/oxidants.
- **Claims**: "Adjuvant skin wound repair", "Gastrointestinal conditioning", "Immune support". Label "Not a replacement for prescription drugs".

2 Cosmetic Applications

2.1 Core Value

Four core effects: moisturizing, soothing, anti-inflammatory repair, mild antioxidant. DPPH scavenging ≥82.3% (0.5 g/L); stratum corneum moisture +≥35% (0.5% extract); redness/stinging relief ≥85%. Replaces 20–30% chemical soothing agents, ideal for sensitive skin.

2.2 Mechanisms

- **Moisturizing**: Aloe polysaccharides form a breathable film, reducing transepidermal water loss.

- **Soothing**: Flavonoids/polyphenols inhibit inflammation, repair barrier, reduce redness.
- **Anti-inflammatory repair**: Inhibits *C. acnes*/*S. aureus*, promotes cell repair.
- **Antioxidant**: Scavenges ROS, inhibits lipid peroxidation, anti-aging.

2.3 Recommended Dosage Forms

- **Liquids**: Toners, essences (pH 4.5–6.5, ≤40℃).
- **Emulsions**: O/W lotions/creams (stable ≥6 months); W/O for dry skin.
- **Others**: Masks, gels, sunscreens.

2.4 Application Solutions

- **Scenarios**: Sensitive/dry/acne/post-sun care; anti-aging; infant care (≤1%).
- **Compatibility**: Synergize with licorice extract, hyaluronic acid, glycerin, ceramides, vitamins. Avoid high-concentration acids, oxidants, formaldehyde releasers, ≥20% alcohol.
- **Claims**: "Moisturizing", "Soothe redness/sensitivity", "Barrier repair", "Mild antioxidant".

3 Food Applications

3.1 Core Value

Natural antioxidant, moisturizing preservative, and functional conditioner, replacing 30–50% synthetic antioxidants (BHA/BHT). Lipid peroxidation inhibition ≥70% (0.1 g/L), extending shelf life.

3.2 Mechanisms

- **Antioxidant**: Flavonoids/polyphenols/aloe polysaccharides scavenge free radicals, inhibiting oxidation.
- **Moisturizing preservation**: Aloe polysaccharides retain moisture, improving texture of baked goods/confections.
- **Functional**: Gut conditioning and immune support in health foods.

3.3 Recommended Dosage Forms

- **Liquids**: Juices, teas, oral liquids (≤60℃).
- **Solids**: Baked goods, nuts, tablets (microencapsulation ≥85%).
- **Oils**: Edible oils, fried foods (mixed with powder).

3.4 Application Solutions

- **Scenarios**: Oil/baked good preservation; beverages; gut/immune health foods; confectionery.
- **Compatibility**: Synergize with vitamin E, tea polyphenols, probiotics, dietary fiber. Avoid high acids, strong flavors, laxatives.
- **Claims**: "Natural antioxidant", "Moisturizing preservation" (regular food); "Gut conditioning", "Immune support" (health food). Label "Health food is not a drug".

4 Industrial and Other Applications

4.1 Core Value

Green, eco-friendly functional enhancer replacing chemical additives. 1–5% extract causes ≥90% wood rot fungi mortality; 0.5% reduces surface tension to 30 mN/m; replaces 20–30% antibiotics in feed.

4.2 Mechanisms

- **Antiseptic**: Inhibits microbes/insects in wood/leather.
- **Surfactant**: Lowers surface tension for emulsification/dispersion.
- **Adsorption**: Removes heavy metals/organic pollutants in wastewater.
- **Feed additive**: Enhances immunity, improves gut health in livestock/aquaculture.
- **Leather/textile conditioning**: Improves flexibility, gloss, antistatic properties.

4.3 Recommended Dosage Forms

Solutions (wood/wastewater), suspensions (leather/textile), premixes (feed), powders (adsorbents/dyes).

4.4 Application Solutions

- **Scenarios**: Wood preservation; leather tanning; wastewater treatment; textile auxiliaries; green feed additives; cosmetic packaging preservation.
- **Compatibility**: Synergize with boric acid, chromium salts, alum, probiotics. Avoid strong oxidants, high alkalis, heavy metal salts (except chromium).
- **Claims**: "Green preservation", "Natural eco-friendly", "Green feed additive", "Wastewater adsorbent".

III. Recommended Dosage

Note: Dosages are based on conventional purity (aloe polysaccharides 5.0–10.0%, aloin 3.0–5.0%, total flavonoids 2.0–5.0%). Reduce proportionally for higher purity. Daily oral aloin intake ≤80 mg to avoid diarrhea.

Core Dosage Summary by Field

- **Pharmaceutical**:

  Oral 150–300 mg/tablet (daily 300–900 mg as polysaccharides);

  Topical 2.0–8.0% (ointment/gel),

  Lotion 1.0–5.0%, burn cream 5.0–10.0%,

  Mouthwash 0.5–2.0%.

- **Cosmetic**:

  Leave-on 0.01–0.5% (sensitive 0.01–0.1%, infant ≤1.0%);

  Rinse-off 0.1–2.0% (max 4.0%);

  Sunscreen 0.5–1.0%;

  Aloe gel 5.0–10.0%.

- **Food**:

  Antioxidant 0.01–0.1% (oil 0.05–0.1%, beverage 0.01–0.05%);

Moisturizing 0.05–0.5% (baked 0.1–0.5%, candy 0.05–0.3%);

Health food 0.5–2.0% (daily ≤500 mg as polysaccharides).

- **Industrial**:

  Wood preservation 1–5%; leather 0.5–2.0%;

  Surfactant 0.1–1.0%, adsorbent 1–10%;

  Textile dye 1–5%, auxiliary 0.1–0.5%;

  Feed 0.1–0.5%; wastewater 5–10%.

Ⅳ. Supplementary Notes

1. **Purity**: Higher purity allows lower dosage. Select products complying with *Chinese Pharmacopoeia* or ISO 22517:2022. Adjust dosage by aloe variety.
2. **Storage**: Sealed, light-proof, cool/dry, shelf life 24 months. Avoid moisture/oxidation; use within 1 month after opening.
3. **Testing**: Test heavy metals, microbes, pesticides, and actives before use; retain batch reports.
4. **Special populations**: Pregnant/lactating women, children, and gastrointestinal-sensitive individuals use under guidance. Avoid excessive intake; allergic individuals prohibited.
5. **Processing**: Control temperature/pH to protect actives. Prefer solvent-free extraction. Microencapsulation improves stability.