Milk Thistle Extract: Safety Assessment + Application Fields + Recommended Addition Levels

I. Core Overview

Milk Thistle Extract(INCI: SILYBUM MARIANUM EXTRACT, CAS: 84604-20-6) is an active ingredient extracted from the seeds of *Silybum marianum* (Asteraceae). Its core active component is **silymarin**, a flavonolignan complex containing silybin, isosilybin, silychristin and other derivatives. Endowed with multiple potent effects including strong antioxidant, anti-inflammatory, hepatoprotective and skin repairing properties, it is widely applied in health food, pharmaceuticals, cosmetics, food additives and other fields, and is recognized worldwide as one of the classic natural functional raw materials.

II. Safety Assessment (Toxicology + Clinical + Regulatory Compliance)

(I) Toxicological Safety

1. **Acute Toxicity**: The oral LD50 is >5000 mg/kg (rat) and the dermal LD50 is >2000 mg/kg (rabbit), classifying it as **practically non-toxic**. No acute poisoning, mortality or obvious organ damage has been observed in relevant tests.
2. **Subchronic/Repeated Dose Toxicity**: Rats administered silymarin via gavage at 1000 mg/kg·d for 90 consecutive days showed no abnormal body weight, organ coefficient changes or pathological damage, with a **NOAEL (No Observed Adverse Effect Level) ≥1000 mg/kg·d**. Dogs receiving long-term administration (500 mg/kg·d for 6 months) only presented mild gastrointestinal discomfort without hepatorenal toxicity.
3. **Genetic Toxicity**: Ames test, mouse bone marrow micronucleus test and chromosomal aberration test all yielded negative results, indicating **no mutagenic or genetic damage risk**.
4. **Reproductive and Developmental Toxicity**: Reprotoxicity tests on rats and rabbits (at the maximum dose of 1000 mg/kg·d) revealed no teratogenicity, abortion or abnormal offspring development, demonstrating **no adverse effects on the reproductive system**.
5. **Chronic Toxicity/Carcinogenicity**: Long-term (2-year) animal tests found no increased tumor incidence, confirming **no carcinogenic risk**. The extract has no bioaccumulation potential, and its metabolites are mainly excreted via bile and urine without residual risks in the body.
6. **Local Toxicity**: It shows no or mild dermal irritation (rabbit), no eye irritation (rabbit) and negative skin sensitization (Guinea Pig Maximization Test). There is **no risk of phototoxicity or photoallergy**.

(II) Clinical Safety

1. **Tolerance at Routine Doses**: Healthy adults taking 140-600 mg of silymarin orally daily for 6-12 months have an adverse reaction rate of <3%, mainly mild and transient gastrointestinal symptoms (nausea, abdominal distension, diarrhea) and dizziness, which do not require drug withdrawal.
2. **Tolerance at High Doses**: In clinical studies, oral administration of 2000-6000 mg of silymarin daily (in 3 divided doses) only caused mild bilirubin elevation and transient ALT increase (Grade 1-2), with no severe toxicity above Grade 3. It maintains good tolerance even at high doses (for specific medical scenarios only, under professional guidance).
3. **Safety in Special Populations**
    - Pregnant/lactating women: Insufficient safety data available, **not recommended for use**.
    - Children: No adequate safety data for children under 12 years old, **prohibited or used with caution**.
    - Patients with hepatic/renal insufficiency: Those with mild dysfunction may use routine doses; those with moderate to severe dysfunction need dose reduction and regular monitoring of liver and kidney functions.
    - Allergic populations: Individuals allergic to Asteraceae plants (ragweed, daisy, dandelion, etc.) may experience allergic reactions such as skin pruritus and rashes, **contraindicated for use**.

(III) Regulatory Safety Recognition

1. **International Regulations**
    - Health Canada approves Silybum marianum seed extract (silymarin) as a dietary supplement ingredient, with a maximum daily intake of 600 mg (calculated as silymarin) for healthy adults.
    - The EU and the US FDA list it as a **GRAS (Generally Recognized As Safe)** substance, permitting its use in health food and dietary supplements.
2. **Chinese Regulations**: It is included in the *Catalogue of Cosmetic Raw Materials in Use (2021 Edition)* (Serial No. 06266) and is not a prohibited substance specified in the *Cosmetic Safety Technical Specification (2015 Edition)*. It can be used as a raw material for health food (approved for liver protection, antioxidant and other functions) and as a natural antioxidant in food additives (in compliance with the requirements of GB 2760).

(IV) Key Risk Control Points

- **Raw Material Quality**: Strictly control heavy metals (Pb ≤2 mg/kg, As ≤1 mg/kg, Hg ≤0.1 mg/kg), microorganisms (total bacterial count ≤1000 CFU/g, mold ≤100 CFU/g) and pesticide residues (in line with GB 2763) to avoid safety risks caused by impurities.
- **Compatibility Contraindications**: Co-administration with anticoagulants (warfarin) or hypoglycemic agents (insulin, metformin) may enhance drug efficacy,

requiring monitoring of coagulation function and blood glucose. Caution is needed when used with hepatotoxic drugs (e.g., some antibiotics, antipyretic and analgesic drugs) to avoid increasing liver burden.

- **Label Warnings**: Mandatorily label warnings such as "Contraindicated for individuals allergic to Asteraceae plants" and "Not suitable for pregnant women, lactating women and children".

III. Application Fields and Core Efficacy

(I) Health Food / Dietary Supplements

1. **Core Efficacy**: Hepatoprotection (repairing hepatic cell membranes, inhibiting hepatocyte apoptosis, promoting hepatocyte regeneration), antioxidant (scavenging free radicals, alleviating oxidative stress damage), anti-inflammatory (inhibiting the release of inflammatory factors), alcohol detoxification and liver protection (accelerating alcohol metabolism, reducing alcoholic liver injury), and blood lipid regulation (lowering triglycerides and cholesterol).
2. **Applicable Scenarios**
    - Daily liver care: Populations with frequent alcohol consumption, staying up late and high-fat diet.
    - Adjuvant repair of liver injury: Adjuvant conditioning for non-alcoholic fatty liver disease, alcoholic liver disease and drug-induced liver injury.
    - Antioxidant and anti-aging: Antioxidant health care for the middle-aged and elderly, and subhealthy populations.
3. **Product Forms**: Soft capsules, tablets, powder, oral liquid (mostly standardized extracts with a silymarin content of 30%-80%).

(II) Pharmaceutical Field

1. **Core Application**: Clinically used as an adjuvant therapy for acute and chronic hepatitis, fatty liver, liver cirrhosis and drug-induced liver injury. Silybin, the core monomer of silymarin, is the main medicinal component, with preparations including silybin capsules and silymarin tablets.
2. **Efficacy Characteristics**: It improves liver function indicators (ALT, AST, bilirubin) and relieves symptoms such as discomfort in the liver area and fatigue by stabilizing hepatic cell membranes, inhibiting the process of liver fibrosis and promoting bile secretion.

(III) Cosmetic Field

1. **Core Efficacy**: Skin antioxidant (scavenging skin free radicals, delaying photoaging), anti-inflammatory and soothing (reducing skin redness and sensitivity), barrier repair (enhancing the integrity of the skin stratum corneum), and skin brightening (inhibiting melanin production).
2. **Applicable Products**
    - Skin care: Antioxidant serums, repairing creams, soothing lotions for sensitive skin, and post-sun repair products.

- Hair and body care: Shampoos and conditioners (repairing perm and dye damage, improving scalp inflammation).
- Oral care: Toothpaste (alleviating gingival inflammation, antioxidant gingival protection).

3. **Regulatory Basis**: Included in the *Catalogue of Cosmetic Raw Materials in Use (2021 Edition)*, it is classified as a skin protectant with no use prohibition, and can be applied in leave-on and rinse-off cosmetic products.

(IV) Food Additive Field

1. **Core Efficacy**: Natural antioxidant (inhibiting oil oxidation, extending food shelf life) and flavor enhancer (imparting a mild herbal aroma to food).
2. **Applicable Foods**: Functional beverages, baked foods, edible oils, meat products, dairy products and infant formula food (in compliance with national standard limits).
3. **Advantages**: It can replace synthetic antioxidants (BHA, BHT), featuring natural safety and meeting consumers' **clean label** demands.

(V) Other Fields

- **Feed Additive**: Used in livestock and poultry breeding to protect animal liver, improve immunity and enhance growth performance.
- **Industrial Application**: Served as an antioxidant stabilizer for dyes and pigments to extend product service life.

IV. Recommended Addition Levels (Field-Specific Precise Reference)

(I) Health Food / Dietary Supplements (calculated as silymarin, standardized extract)

Application Scenario	Daily Recommended Dose (Silymarin)	Notes
Daily liver care / Antioxidant	140-210 mg	Taken once or in 2 divided doses, suitable for daily health care of healthy adults
Adjuvant conditioning of liver injury	210-420 mg	Taken in 2-3 divided doses, suitable for populations with fatty liver or alcoholic liver injury
Clinical adjuvant therapy (Pharmaceuticals)	420-600 mg	Taken in 3 divided doses under medical advice, for patients with mild to moderate liver injury
High-dose clinical research	600-2000 mg	For medical scenarios only, under the guidance of professional doctors, not for self-administration

(II) Cosmetic Field (calculated as dry extract, silymarin content 30%-80%)

Product Type	Recommended Addition Level (Mass Fraction)	Maximum Use Level	Notes
Leave-on skin care products (creams, serums)	0.5%-2%	2.79%	Focus on antioxidant and repair, significant effect at concentration ≥1%
Leave-on eye products (eye creams, eye serums)	0.5%-2.5%	2.5%	Ocular irritation assessment required, recommended concentration ≤2%
Rinse-off products (shampoos, body washes)	0.1%-0.5%	-	Focus on soothing and antioxidant, avoid excessively high concentration
Toothpaste / Oral care products	0.1%-0.3%	-	Focus on gingival repair and anti-inflammation

(III) Food Additive Field (calculated as dry extract, silymarin content 30%-50%)

Food Type	Recommended Addition Level (Mass Fraction)	Notes
Functional beverages / Oral liquid	0.1%-0.5%	Balance antioxidant effect and taste, avoid bitter and astringent flavor
Baked foods (bread, pastries)	0.5%-1.0%	Inhibit oil oxidation and extend shelf life
Edible oils / Meat products	0.1%-0.3%	Replace synthetic antioxidants for natural preservation
Dairy products / Infant formula food	0.05%-0.2%	Comply with GB 2760, strict dose control required

(IV) Feed Additive Field

- **Recommended Addition Level**: 50-200 g per ton of compound feed (10-50 g per ton calculated as silymarin), focusing on protecting the liver of livestock and poultry and improving their anti-stress ability.

V. Usage Notes

1. **Raw Material Selection**: Prioritize **standardized Milk Thistle Extract**(silymarin content ≥30%, silybin content ≥20%) to ensure stable efficacy. Cosmetic raw materials shall comply with the *Cosmetic Safety Technical Specification (2015 Edition)*, and food raw materials shall meet the requirements of GB 2760 and GB 14881.
2. **Compatibility Optimization**: In health food, it can be compounded with antioxidant ingredients such as vitamin E, selenium and glutathione to enhance liver protection effect; in cosmetics, it can be combined with ceramide and hyaluronic acid to improve skin repair capacity.
3. **Dose Control**: The principle of **efficacy and safety** shall be followed in all fields to avoid blind dose increase. The daily intake of silymarin from health food is not recommended to exceed 600 mg for healthy adults, and the addition level in cosmetics shall not exceed the maximum historical use level.
4. **Storage Conditions**: Store in a sealed, light-proof and dry place (temperature ≤25℃, humidity ≤60%) to prevent oxidative degradation of active ingredients; nitrogen-filled packaging is recommended for extract powder to extend shelf life.
5. **Compliant Labeling**: Health food shall be labeled with functional ingredients and their contents, inappropriate populations and recommended intake; cosmetics shall be labeled with INCI names and raw material sources; food shall be labeled with additive names and doses in accordance with label regulatory requirements.

VI. Conclusion

Milk Thistle Extractis a natural functional raw material with **high safety, definite efficacy and wide application**, with silymarin as its core active component. It has irreplaceable advantages in liver protection, antioxidant, skin repair and other fields. Its safety has been verified through multiple toxicological, clinical and regulatory assessments, with no obvious toxicity at routine doses (caution is needed for special populations). The recommended addition levels shall be precisely adjusted according to application fields, product forms and target efficacy. Meanwhile, strict control of raw material quality and compatibility compliance can maximize its efficacy value, meeting the application demands of health food, pharmaceuticals, cosmetics, food and other multiple fields.