Operating Guidelines for the Addition of Centella Asiatica Extract in Application Fields

I Executive Standards

This guideline strictly complies with the following national and industrial standards to ensure the compliance, safety and standardization of addition operations, and meet the quality requirements of various application fields:

1. Cosmetic field: GB 5296.3-2008 *General Labeling for Cosmetics*, GB 7916-2014 *Safety and Technical Specifications for Cosmetics*, EC 1223/2009 *Regulation of the European Parliament and of the Council on Cosmetic Products*
2. Pharmaceutical field: *Pharmacopoeia of the People's Republic of China (Current Edition)*, GB 15980-1995 *Hygienic Standard for Single-use Medical Products*
3. Food and health product field: GB 2760-2024 *National Food Safety Standard for the Use of Food Additives*, GB 14881-2013 *National Food Safety Standard for General Hygienic Specification of Food Production*, GB 30616-2020 *General Principles for Food Supplements*
4. General standard: GB 5749-2022 *Drinking Water Health Standard* (Applicable to the requirements of dissolved water in all fields)

II Scope of Application

This guideline applies to four core application fields including cosmetics, pharmaceuticals, food and health products, covering the entire process of addition, operation, metering and quality control of food-grade, cosmetic-grade and pharmaceutical-grade Centella Asiatica Extract (main active ingredients: Asiaticoside, Madecassoside, Asiatic acid, Madecassic acid, purity marked as required). It is suitable for three production modes: laboratory sample preparation, small-batch trial production and industrial continuous production.

This guideline is intended for R&D personnel, production operators and quality control personnel in various fields, and can be used as a standardized operation basis for addition operations to ensure the unification of addition processes and controllable results for different production scales and dosage forms.

III Operating Principles

Combined with the physicochemical properties of Centella Asiatica Extract and the compliance requirements of various fields, the addition operation must strictly follow the following six principles, balancing efficacy retention, safety compliance and process adaptability:

1. Accurate Metering Principle: Select metering equipment with appropriate precision

according to the purity of the extract and the requirements of dosage forms, and strictly control the addition amount to avoid efficacy fluctuation, safety risks or compliance issues caused by errors.

2. Uniform Dispersion Principle: The extract shall be pretreated (dissolution, premixing, etc.) to avoid agglomeration and caking caused by direct addition of pure powder, ensuring its homogeneous distribution in the product system.
3. System Adaptation Principle: Select the corresponding addition time, method and dissolution medium according to the product state (liquid, semi-solid, solid), processing technology (hot processing, cold processing) and pH value.
4. Compliance with Limit Principle: Strictly follow the standard limits of various fields, calculate the total content of active ingredients, strictly prohibit over-addition, and take into account the compatibility taboos of various ingredients during compounding.
5. Efficacy Retention Principle: Avoid scenarios such as long-term high-temperature treatment and strong light irradiation, maximize the retention of core active ingredients such as Asiaticoside, and ensure the stable efficacy of the finished product.
6. Safety and Controllability Principle: Control the raw material quality, equipment cleaning and operation specifications throughout the process, avoid cross-contamination, and ensure the finished product meets the safety testing standards of various fields.

IV Core Characteristics of Centella Asiatica Extract

The Centella Asiatica Extract referred to in this guideline is divided into powder form (particle size 80-120 mesh, moisture ≤5.0%) and liquid concentrate (concentration 50%-70%) according to dosage forms. Its core characteristics determine the key points of addition operation and need to be accurately adapted to various application scenarios:

1. Efficacy Stability: The heat resistance temperature of core active ingredients (Asiaticoside, Madecassoside) is ≤120℃ (prone to degradation above 120℃), and the pH tolerance range is 4.0-7.0. Strong light, high temperature and high humidity environments are likely to cause efficacy attenuation, requiring operation away from light and high temperature.
2. Solubility: Easily soluble in hot water (40-50℃ is optimal) and propylene glycol, slightly soluble in ethanol, and hardly soluble in pure oil. Direct addition of pure powder is prone to agglomeration; it is preferred to prepare mother liquor/suspension for use in industrial production.
3. Compatibility: Good compatibility with most commonly used raw materials in cosmetics, food and pharmaceuticals (humectants, emulsifiers, excipients); avoid direct contact with

high-concentration acids (pH < 4.0), alkalis (pH > 7.0) and heavy metal salts; compounding with vitamin C and vitamin E can produce a synergistic effect.

4. Safety: No acute toxicity; skin contact with high-concentration extract may cause mild irritation. The addition of food-grade extract must comply with ADI limits, and pharmaceutical-grade extract must meet the safety requirements of the Pharmacopoeia. It is used with caution by pregnant and lactating women.
5. Hygroscopy: The powder extract has slight hygroscopy and must be stored in a sealed manner. It is prone to hygroscopic agglomeration after opening, which affects the dispersion uniformity and needs to be used as soon as possible.

V General Basic Operation Specifications

5.1 Requirements for Metering Equipment

Select metering equipment with appropriate precision according to the production scale to ensure accurate metering and full traceability:

1. Laboratory sample/small-batch production (≤50kg): Use an electronic analytical balance (precision 0.001g) or a high-precision electronic scale (precision 0.01g), perform zero calibration before use, and remove residual materials on the surface of the equipment.
2. Industrial large-batch production (> 50kg): Use a fully automatic powder metering and adding device (precision 0.1g) or a liquid metering pump (suitable for liquid extract/mother liquor) with an online calibration function, which shall be calibrated at least once a month.
3. All metering equipment shall be used within the validity period of verification. Record the addition amount, equipment number and operator in a timely manner after metering to ensure data traceability.

5.2 Preparation of Extract Preparations

To avoid agglomeration and uneven dispersion of the extract, it is preferred to prepare powdered extract into mother liquor/suspension for use. Pure powder can be added directly for sample tests (premixing required). The specific specifications are as follows:

1. Preparation Concentration: It is recommended to prepare a 5%-10% (w/w) aqueous solution (deionized water/purified water at 40-50℃) or a 5%-8% propylene glycol solution. Excessively high concentration is prone to agglomeration, while excessively low concentration increases the addition volume.
2. Dissolution Medium: Deionized water for cosmetics, sterile purified water for external pharmaceutical use, and purified water complying with GB 5749-2022 for food/health

products; liposome-encapsulated mother liquor shall be prepared for oil-based systems.

3. Preparation Operation: Heat the dissolution medium to 40-50℃ (to accelerate dissolution and avoid high-temperature degradation), add the extract slowly in proportion, stir at a speed of 300-500r/min for 10-15min until there are no visible particles, forming a uniform mother liquor/suspension.
4. Preparation Storage: Store in a sealed stainless steel tank after preparation with a shelf life of 72h at room temperature, which can be extended to 7d at low temperature (5-10℃). Stir again before use to avoid static layering or precipitation.

5.3 Pre-addition Preparation

Complete raw material verification, equipment cleaning and system confirmation before the addition operation to avoid affecting product quality:

1. Raw Material Verification: Confirm the batch number, active ingredient content and production date of Centella Asiatica Extract; check that the powdered extract is free from hygroscopy, agglomeration and mildew, and the liquid extract/mother liquor is free from turbidity, layering and precipitation.
2. Equipment Cleaning: Clean metering scales, dissolution tanks, conveying pipelines, emulsifiers, homogenizers and other equipment with the corresponding dissolution medium (deionized water/purified water) for 3 times to ensure no residue, oil stain or impurity and avoid cross-contamination.
3. System Confirmation: Stir the product base material to a homogeneous state before addition; remove precipitation from liquid base materials and crush solid/semi-solid base materials to a uniform particle size to ensure the dispersion effect of the extract.

VI Addition Operation Methods in Different Application Fields

6.1 Cosmetic Field (Core Application Field)

Applicable Characteristics: Covering dosage forms such as toners, serums, lotions, creams, facial masks and gels, it needs to adapt to the physiological pH of the skin (5.0-6.5) to avoid skin irritation. The core effects are anti-inflammatory and soothing, barrier repair, antioxidant and fine line fading. The addition amount ranges from 0.1% to 5.0% (adjusted according to the purity of the extract).

6.1.1 Addition Time and Method for Different Dosage Forms

1. Aqueous Preparations (Toner, Lotion, Essence Water)
    - Addition Time: Added in the later stage of aqueous phase preparation after the base material is stirred to a homogeneous state.

- Addition Method: Adopt the "room temperature dissolution + stirring dispersion" method. Prepare the extract into a 5%-10% aqueous solution, pour it slowly into the aqueous phase system, stir at a speed of 200-300r/min for 10-15min, adjust the pH to 5.0-6.5, let it stand for 20-30min, and proceed to the filling process after testing for no precipitation.
- Recommended Addition Amount: 0.1%-2.0% (0.1%-0.5% is recommended for purity above 90%).

2. Serums (Essence Liquid, Essential Oil Serum)
   - Addition Time: Aqueous serums are added before the constant volume of the aqueous phase, and oil-based serums are added after the homogenization of the oil phase.
   - Addition Method: The addition method for aqueous serums is the same as that for aqueous preparations, which can be combined with 5%-8% propylene glycol as a cosolvent; for oil-based serums, a liposome-encapsulated mother liquor must be prepared first (mix the extract with phospholipids at a ratio of 1:3-1:5, disperse at 1000-1500r/min for 15-20min), then add it to the oil phase system in proportion and stir at a low speed of 100-200r/min for 10min.
   - Recommended Addition Amount: 0.5%-3.0% for aqueous serums (2.0%-5.0% for functional type), 1.0%-3.0% for oil-based serums.
3. Creams and Lotions (Lotion, Cream)
   - Addition Time: Dissolve in advance in the aqueous phase preparation stage, and confirm uniform dispersion before cooling after emulsification.
   - Addition Method: Add the base material to the aqueous phase pot and heat to 70-75℃, pour the extract mother liquor slowly and stir at 300-400r/min for 5-8min to integrate into the aqueous phase; heat the oil phase to 75-80℃ for dissolution, pour it into the aqueous phase, emulsify at 800-1200r/min for 15-20min, cool to below 45℃ and add preservatives and fragrances.
   - Recommended Addition Amount: 0.3%-2.0%.
4. Facial Masks (Sheet Masks, Smear Masks)
   - Addition Time: Added in the later stage of essence liquid preparation for sheet masks and in the base material mixing stage for smear masks.
   - Addition Method: The addition method for the essence liquid of sheet masks is the same as that for aqueous preparations, and the mask cloth is soaked after the essence liquid is prepared (25-35ml loaded per piece); the addition method for gel-type smear masks is the same as that for aqueous preparations, which

can be combined with carbomer for thickening; for clay masks, stir the extract mother liquor with clay powder at 400-600r/min for 10-15min to ensure no agglomeration.

- Recommended Addition Amount: 0.5%-2.0% for sheet masks, 0.5%-3.0% for smear masks (0.8%-3.0% for gel type, 0.5%-2.0% for clay type).

6.1.2 Special Notes

1. Compatibility: Avoid compounding with high-concentration acids, alkalis and heavy metal salts; conduct sample compatibility tests first when compounding with sunscreens and humectants.
2. Skin Feel Adjustment: For high-concentration addition (> 2.0%), 1%-3% alcohol or 0.5%-1.0% silicone raw materials can be added to improve the sticky feeling.
3. Stability Control: The single heating time during production shall not exceed 20min, and the temperature shall not exceed 80℃. The finished product shall be stored in a sealed manner away from light.

6.2 Pharmaceutical Field

Applicable Characteristics: Mainly used in external preparations (ointments, gels, creams) with core effects of promoting wound healing, anti-inflammatory and detumescence, suitable for burns, scalds, traumatic ulcers, dermatitis, etc. It must strictly follow the Pharmacopoeia standards to ensure accurate dosage and aseptic safety. The addition amount ranges from 1.0% to 10.0% (adjusted according to the preparation type).

6.2.1 Addition Time and Method for Different Dosage Forms

1. Topical Ointments
   - Addition Time: Added when the matrix is cooled to 50-55℃ after melting to avoid damage to active ingredients by high temperature.
   - Addition Method: Adopt the "matrix melting + low-temperature mixing" method. Heat the matrix (vaseline, lanolin, etc.) to 70-80℃ for dissolution, dissolve the extract with anhydrous ethanol 2-3 times its weight into a mother liquor, pour it slowly into the cooled matrix, stir at 300-400r/min for 10-15min, and cool to room temperature for solidification.
   - Recommended Addition Amount: 5.0%-10.0% (Asiaticoside content ⩾1.0%).
2. Topical Gels
   - Addition Time: Added after the complete dissolution of the aqueous phase thickener and before pH adjustment.
   - Addition Method: In an aseptic environment, heat deionized water to 40-50℃, add 0.5%-1.0% carbomer 940 for dissolution, pour in the extract propylene glycol

mother liquor, stir at 300-500r/min for 8-10min, adjust the pH to 6.0-7.0 with triethanolamine, let it stand to remove air bubbles and then perform aseptic packaging.

- Recommended Addition Amount: 1.0%-5.0%.

3. Topical Creams
    - Addition Time: Added in the aqueous phase preparation stage, and confirm uniform dispersion after emulsification and before sterilization.
    - Addition Method: Refer to the method for cosmetic creams and lotions. The raw materials must meet pharmaceutical-grade standards (extract purity ⩾95%), with aseptic operation throughout the process. After emulsification, conduct high-pressure steam sterilization at 121℃ for 15min, and test the retention rate of active ingredients after sterilization.
    - Recommended Addition Amount: 1.0%-3.0% (3.0%-5.0% for burns and scalds).

6.2.2 Special Notes

1. Aseptic Requirements: Aseptic operation throughout the process; the finished product must be tested for sterility (bacterial count ⩽10cfu/g, mold and yeast count ⩽1cfu/g, no pathogenic bacteria detected).
2. Dosage Control: Strictly follow the Pharmacopoeia limits, the addition amount shall not exceed 10.0% to avoid skin irritation caused by excess.
3. Storage Conditions: Store in a sealed, cool and dry place away from light (10-25℃, relative humidity ⩽60%) to avoid degradation due to high temperature and humidity.

6.3 Food and Health Product Field

Applicable Characteristics: Covering dosage forms such as oral liquids, tablets, capsules and solid beverages with core effects of antioxidant, immune regulation and intestinal mucosa protection. It must comply with food safety standards, balancing taste and efficacy stability. The addition amount ranges from 0.01% to 1.0% (adjusted according to the dosage form).

6.3.1 Addition Time and Method for Different Dosage Forms

1. Oral Liquids
    - Addition Time: Added after the flavoring and compounding of the base material and before constant volume and filtration.
    - Addition Method: Adopt the "room temperature dissolution + flavoring compounding" method. Dissolve the extract with purified water at 40-50℃ into a mother liquor, add sweeteners (0.5%-1.0%) and acidulants (0.1%-0.2%) to adjust the taste, filter with a 0.22μm filter membrane after constant volume, and conduct water bath sterilization at 85℃ for 30min.

- Recommended Addition Amount: 0.05%-0.2%.

2. Tablets/Capsules
   - Addition Time: Premixed before granulation for tablets and mixed uniformly before filling for capsules.
   - Addition Method: For tablets: crush the extract to 80-100 mesh, mix with excipients by equal incremental method (200-300r/min for 10-15min), granulate and dry at 60-70℃, control the tablet hardness at 3-5kg during tableting; for capsules: stir the extract with excipients at 300-400r/min for 15-20min, polish and test after filling.
   - Recommended Addition Amount: 0.1%-1.0% for tablets, 0.5%-1.0% for capsules.
3. Solid Beverages
   - Addition Time: Added after the pretreatment of excipients and before mixing and sieving.
   - Addition Method: Crush the extract to 100-120 mesh, stir with excipients (maltodextrin, xylitol, etc.) at 500-600r/min for 20-30min, sieve through a 100-mesh sieve to remove agglomerates, and perform aseptic packaging with marked brewing methods.
   - Recommended Addition Amount: 0.01%-0.1%.

6.3.2 Special Notes

1. Taste Adjustment: Use sweeteners, acidulants and fruit powder to mask the slight bitter taste of the extract and improve palatability.
2. Dosage Limit: The addition amount of food shall not exceed 0.1%, and that of health products shall not exceed 1.0%, strictly complying with food safety standards.
3. Labeling: Clearly mark the extract addition amount, core active ingredients, edible method and inappropriate population (used with caution by pregnant and lactating women).

VII Key Points of Quality Control for Addition Operations

To ensure the qualified quality and stable efficacy of the finished product, the following quality control measures must be implemented throughout the addition operation, adopting the whole-process control of "pre-operation verification, in-operation control and post-operation testing":

1. Metering Review: Implement a double-inspection system of "initial metering by operator, review by quality inspector", record the addition amount, equipment number and operation time to ensure the metering deviation $\leqslant \pm 2\%$.

2. Dispersion Inspection: Randomly sample and test different parts of the system after addition; liquid products shall be free from particles and layering, solid/semi-solid products shall be free from local agglomeration, and the content uniformity RSD ≤3.0%.
3. Efficacy Testing: Detect the content of Asiaticoside and Madecassoside in each batch of finished products by High Performance Liquid Chromatography (HPLC) to ensure the retention rate of active ingredients ≥85% (≥80% for hot-processed products).
4. Microbial Testing: Implemented in accordance with the standards of various fields; the bacterial count of cosmetic-grade products ≤100cfu/g (ml), pharmaceutical-grade ≤10cfu/g, food-grade ≤100cfu/g, with no pathogenic bacteria detected for all.
5. Stability Inspection: Conduct sample retention observation of the finished product; store cosmetic products away from light for 6 months, and pharmaceutical and health products for 12-24 months to confirm no discoloration, precipitation, layering or efficacy attenuation.
6. Compliance Traceability: Retain the third-party test report of raw materials, addition operation records and finished product test reports, with the record retention period ≥ product shelf life + 6 months.

VIII Safety Operation and Equipment Maintenance Requirements

8.1 Safe Operation for Operators

1. Wear a dust mask and disposable gloves when operating powdered extract, keep the operation area ventilated to avoid inhalation of flying powder into the respiratory tract.
2. Avoid contact of the extract and mother liquor with eyes; in case of accidental contact, rinse immediately with a large amount of purified water for 10-15min and seek medical attention if necessary.
3. For aseptic operation in the pharmaceutical field, wear sterile clothing, sterile gloves, masks and hats, and enter the operation area after disinfection.
4. Operators shall take up their posts after training, and be familiar with the compatibility taboos of the extract, emergency treatment methods and operation specifications of various fields.

8.2 Equipment Maintenance and Cleaning

1. Metering Equipment: Wipe with a dry cloth after daily use to remove residual materials, calibrate the precision monthly and send it for external verification annually to avoid the impact of hygroscopic agglomeration of residual powder on metering.
2. Dissolution Tanks and Conveying Pipelines: Clean with purified water for 3 times after each batch of production, drain the accumulated liquid in the pipelines and disinfect

regularly to prevent cross-contamination.

3. Emulsifiers, Homogenizers and Powder Adding Equipment: Inspect the homogenizing head and feeding screw regularly, keep them dry and clean, and clean the residual materials in a timely manner after production to avoid equipment failure.

8.3 Raw Material Storage and Access

1. Raw Material Storage: Store powdered extract in a sealed cool and dry place (≤25℃, relative humidity ＜65%), away from light, high temperature and humidity; store liquid extract in a sealed stainless steel tank at low temperature away from light.
2. Access Specifications: Use up within 72h after opening, reseal and mark the remaining part to avoid hygroscopy and oxidation; prepare the extract mother liquor for immediate use, and store the unused part in a sealed manner at low temperature for use within 7d.
3. Zoned Storage: Store raw materials, semi-finished products and finished products in different zones with clear marks to avoid mixed storage contamination; store the extract separately away from strong oxidants, strong acids and strong alkalis.

IX Handling of Abnormal Conditions

In case of abnormal conditions during the addition operation, stop the machine immediately for processing, isolate the relevant materials, and resume production only after passing the test. The specific treatment plans are as follows:

1. Metering Error: If the addition amount is excessive, dilute the liquid system with base material liquid and add excipients to the solid system for uniform mixing, resume production after the sample test is qualified; if the addition amount is insufficient, make up the extract mother liquor according to the difference to ensure the total addition amount meets the requirements.
2. Uneven Dispersion: Increase the stirring speed (500-800r/min) and extend the stirring time to 15-20min for the liquid system; re-crush and sieve the solid system for mixing, and add a small amount of cosolvent/thickener if necessary.
3. Raw Material Quality Problems: If the extract is found to be hygroscopic and agglomerated, or the mother liquor is turbid and precipitated, stop using it immediately and replace with qualified raw materials, isolate the added materials, and resume production only after passing the quality test.
4. Equipment Failure: In case of failure of metering, emulsification and homogenization equipment, stop the machine immediately for maintenance and replace with standby equipment, store the materials separately during the failure period, and reprocess only

after passing the quality test.

5. Oxidation of Active Ingredients: If the system is discolored or has an unusual odor, investigate whether it is caused by high temperature or strong light, immediately take measures to avoid light and lower the temperature, add a small amount of antioxidants (vitamin C, vitamin E) for remediation, and decide whether to resume production after evaluating the efficacy.
6. Skin Irritation (Cosmetics and Pharmaceutical External Use): Investigate whether it is caused by excessive addition amount or abnormal pH value, reduce the addition amount, adjust the pH to 5.0-6.5, conduct skin irritation test again, and resume production only after passing the test.

X Supplementary Provisions

1. This guideline applies to Centella Asiatica Extract with Asiaticoside and Madecassoside as the main active ingredients. If the specifications and purity of the extract are different, the addition amount and operation parameters can be adjusted appropriately.
2. This guideline shall be used in conjunction with the relevant standards of various fields; if the relevant standards are updated, implement in accordance with the latest standards.
3. This guideline is jointly formulated by the R&D Department and the Production Department, and the company reserves the right of interpretation. Unfinished matters can be supplemented and revised according to the actual production needs.
4. Operators must strictly follow this guideline for operation to ensure the quality, safety and stable efficacy of the product. Relevant responsibilities shall be investigated for non-compliant operations.