# Formulaite Enhancement Report

Generated: November 30, 2025 at 3:43 PM

172 scientific papers analyzed, 212 corroborating papers found

## Formulation Details

**Current Formulation:** Ashwagandha Withania Sofnifera Std. Ext. 100 mg. Tagar Valeriana Wallichi Std. Ext. 100 mg. Jatamansi Nardostachys Jatamansi 100 mg. Shankhpushpi Convolvulus Pluricaulis 75 mg. Bramhi Bacopa Monnieri 50 mg. Vacha Acorus Calamus 50 mg

**Delivery Type:** Capsule

**Requirements:** Only ayurvedic ingredients

**Desired Benefits:** Promotes Restful Sleep, Relieves Anxiety & Mental Stress

## Summary

*This formulation enhancement includes 1 new ingredient addition, 2 ingredient replacements, and 3 dosage adjustments. Piperine (10mg) is added to enhance bioavailability of co-administered herbs, while Saffron (14mg) replaces Shankhpushpi and Centella asiatica (100mg) replaces Vacha to provide superior clinical evidence for anxiety and mood support. Key dosage increases include Ashwagandha (100mg to 200mg), Brahmi (50mg to 150mg), and Jatamansi (100mg to 125mg) to align with clinically validated therapeutic doses. These evidence-based modifications collectively target improved sleep quality, reduced anxiety and mental stress, enhanced cognitive function, and optimized bioavailability of all active compounds.*

## Final Formulation Ingredients

**Ingredients:** Ashwagandha Withania Somnifera Std. Ext., Tagar Valeriana Wallichi Std. Ext., Jatamansi Nardostachys Jatamansi, Bramhi Bacopa Monnieri, Saffron Crocus sativus standardized extract, Centella asiatica Mandukparni, Piperine from Piper nigrum Black Pepper

## Enhancement Suggestions

### 1. Brahmi (Bacopa monnieri)

## DOSAGE ADJUSTMENT

**Dosage:** Current 50 mg per capsule -> Recommended 150 mg per capsule

**Benefit:** Improved cognitive performance and reduced anxiety and depression

**Preparation:** Use a standardized Bacopa monnieri whole plant extract (standardized to bacosides). Blend the powdered extract uniformly with other herbal ingredients in the capsule fill to ensure consistent dosing per capsule unit.

**Dosage Adjustment Reasoning:** The current 50 mg dosage is below the clinically validated therapeutic dose for chronic supplementation. The cited study demonstrated that 300 mg total daily dose of standardized Bacopa monnieri extract administered over 12 weeks produced significant improvements in cognitive function and reductions in anxiety and depression in elderly participants. At 150 mg per capsule, this dosage represents half of the 300 mg daily dose validated in this chronic supplementation trial. This dosage aligns with established chronic dosing protocols for sustained cognitive and anxiolytic benefits, and works synergistically with other adaptogenic herbs in the formulation (Ashwagandha, Valerian, Jatamansi, Saffron) to address the formulation's goals of promoting restful sleep and relieving anxiety and mental stress.

**Ayurvedic Basis:** According to the Astangahrdaya, Uttarasthana, Adhyaya 6, Brahmi Ghrita is specifically formulated for conditions including unmada (mental disorders), apasmara (loss of memory/epilepsy), and buddhi daurbalya (intellectual weakness). Brahmi is incorporated into this medicated ghee preparation where it is combined with other supportive ingredients, indicating its traditional use for addressing disorders affecting mental faculties and consciousness. The formulation emphasizes Brahmi's role in supporting clarity of mind and mental function through its inclusion in therapeutic preparations designed for medhya (intellect-promoting) purposes. In traditional Ayurvedic formulations documented in the Bhaisajyaratnavali, Tagara (Valeriana Wallichii) is frequently paired with other calming herbs in rasayana formulations, and Ashwagandha (Withania somnifera) appears in Puga Khanda alongside Tagara, suggesting established synergistic combinations for mental wellness.

**Scientific Basis:** A randomized, double-blind, placebo-controlled trial with 54 elderly participants (mean age 73.5 years) demonstrated that 300 mg daily of standardized Bacopa monnieri extract administered for 12 weeks significantly improved cognitive function (particularly delayed recall scores on the Rey Auditory Verbal Learning Test) and reduced anxiety and depression compared to placebo. The study used a whole plant standardized dry extract given as a single daily dose over the 12-week treatment period. The mechanism involves modulation of cholinergic neurotransmission and antioxidant neuroprotection during chronic supplementation.

**Primary Reference:** 10.1089/acm.2008.0018

**Additional Supporting Studies:**

- https://doi.org/10.1016/j.jep.2025.120633: Studies Bacopa monnieri preventing cognitive deficits and neuroinflammation in AD mouse model, corroborates cognitive benefits.

• https://doi.org/10.1007/s40261-025-01492-1: RCT of Bacopa monnieri extract for memory and cognitive function in adults, directly corroborates main study.

• https://doi.org/10.3390/children12091142: Reviews herbal medicines including Bacopa for mental health symptoms in youth, corroborates anxiety/mood benefits.

• https://doi.org/10.1007/s12035-024-04392-1: Bacopa monnieri extract shows neuroprotective effects on memory in Parkinson's model, supports cognitive benefits.

• https://doi.org/10.1208/s12249-024-02870-2: Develops Bacoside A nasal formulation for epilepsy but confirms Brahmi's cognitive enhancement benefits.

• https://doi.org/10.1016/j.explore.2024.02.008: RCT shows Bacopa monnieri improves cognitive performance and sleep in mild cognitive impairment patients.

• https://doi.org/10.1016/j.jep.2024.117899: Investigates Bacopa monnieri's mechanisms for ameliorating oxidative stress in neuronal cells, supports neuroprotection.

• https://doi.org/10.2174/0115672050361294241211071813: Reviews natural compounds including Bacopa for Alzheimer's disease pathogenesis, supports cognitive/neuroprotective benefits.

• https://doi.org/10.1080/10408398.2021.2021137: Systematic review of plant-derived nootropics including Bacopa on human cognition in health and disease.

**Corroborating Evidence:** Backed by **53 additional studies**

## 2. Piperine (from Piper nigrum - Black Pepper)

NEW INGREDIENT

**Dosage:** 10 mg per capsule

**Benefit:** Enhanced bioavailability of co-administered herbal compounds through inhibition of hepatic and intestinal glucuronidation

**Preparation:** Incorporate standardized black pepper extract powder (standardized to ≥95% piperine) during the final blending phase of capsule preparation. Mix thoroughly with the existing herbal extract powders to ensure uniform distribution throughout the batch before encapsulation.

**Ayurvedic Basis:** Black pepper (Marica) functions as a bioenhancer within traditional Ayurvedic formulations designed to support restful sleep and mental wellbeing. According to the Sarngadhara Samhita (Madhyamakhanda, Adhyaya 10; 28-32), Piperine from black pepper is formulated alongside Tagara (Valeriana Wallichi), Jatamansi (Nardostachys Jatamansi), and Saffron (Nagakesara) in the Pippalyadyasava preparation. According to the Astangahrdaya (Uttarasthana, Adhyaya 3; 93-97), black pepper appears in a traditional formulation that includes Tagara, with warm milk as the recommended vehicle for administration—a traditional practice supporting relaxation. According to the Sahasrayoga and other classical preparations, black pepper is consistently paired with Brahmi (Bacopa Monnieri), Jatamansi, and other nervine herbs in formulations addressing mental tranquility. The pairing of these ingredients demonstrates black

pepper's role in enhancing the bioavailability and efficacy of calming botanicals within traditional sleep and stress-relief preparations.

**Scientific Basis:** A landmark human clinical study demonstrated that concomitant administration of piperine 20 mg with curcumin 2 g produced significantly higher serum concentrations and increased bioavailability by 2000% compared to curcumin alone, where serum levels were either undetectable or very low. The mechanism involves piperine's inhibition of hepatic and intestinal glucuronidation, significantly increasing time to maximum concentration ($P<0.02$) while significantly decreasing elimination half-life and clearance ($P<0.02$). At 10 mg per capsule (providing 20 mg daily with twice-daily administration), this dosage exactly matches the clinically validated dose that demonstrated dramatic bioavailability enhancement in human volunteers. Piperine functions as a bioenhancer by inhibiting CYP3A4 and P-glycoprotein drug transporters, thereby improving absorption and systemic availability of co-administered herbal compounds including the ashwagandha, brahmi, valerian, and other adaptogenic herbs in this formulation.

**Primary Reference:** 10.1055/s-2006-957450

**Additional Supporting Studies:**

- https://doi.org/10.1007/s11095-025-03920-5: Directly discusses piperine's bioenhancing potential through metabolic enzyme and transporter inhibition
- https://doi.org/10.1093/chromsci/bmaf036: Confirms piperine as bioavailability enhancer by stopping CYP enzyme activity
- https://doi.org/10.1371/journal.pone.0317899: Black pepper used to enhance curcumin bioavailability in formulation
- https://doi.org/10.1007/s12672-024-01716-4: Piperine demonstrated significant anticancer properties and potential for chemotherapy enhancement
- https://doi.org/10.1080/13880209.2024.2311201: Piperine used as bioenhancer to improve andrographolide pharmacokinetics and bioavailability
- https://doi.org/10.1016/j.lfs.2024.122943: Discusses piperine's role in chemosensitization and overcoming drug resistance mechanisms
- https://doi.org/10.3390/molecules28186569: Reviews clinical evidence of black pepper's metabolic benefits and bioavailability enhancement
- https://doi.org/10.1016/j.freeradbiomed.2022.11.008: Clinical trial showing piperine enhances turmeric's biological effects through bioavailability enhancement
- https://doi.org/10.17219/pim/145512: Reviews piperine extraction and pharmacological activities including bioavailability enhancement

**Corroborating Evidence:** Backed by **49 additional studies**

## 3. Ashwagandha (Withania somnifera)

## DOSAGE ADJUSTMENT

**Dosage:** Current 100 mg per capsule -> Recommended 200 mg per capsule

**Benefit:** Improved sleep quality and reduced anxiety in healthy subjects and insomnia patients

**Preparation:** Use a standardized full-spectrum root extract containing withanolides. Mix the powdered extract uniformly into the capsule blend to ensure consistent distribution across all capsules.

**Dosage Adjustment Reasoning:** Increasing from 100 mg to 200 mg per capsule provides a meaningful therapeutic enhancement while respecting capsule capacity constraints with multiple herbal ingredients. At 200 mg per capsule, this dosage provides a meaningful therapeutic level that remains conservative compared to study protocols. The cited study demonstrated significant improvements in sleep quality and anxiety reduction in both healthy subjects and insomnia patients. This moderate increase works synergistically with other adaptogenic herbs in the formulation (Valerian, Jatamansi, Brahmi, and others) to address the formulation's primary goals of promoting restful sleep and relieving anxiety without overloading the capsule capacity.

**Ayurvedic Basis:** Ashwagandha is synergistic with Tagar (Valeriana Wallichii) in the Sadbindu Taila formulation documented in Bhaisajyaratnavali, Sirorogadhikara, where both ingredients support therapeutic outcomes when combined in oil preparations. Within sleep-supporting formulations, Ashwagandha works synergistically with herbs like Tagara and Jatamansi, as these ingredients are traditionally paired in Ayurvedic texts for promoting restful sleep and relieving mental tension. In Ayurvedic rasayana theory, Ashwagandha promotes longevity and supports mental faculties.

**Scientific Basis:** A randomized, double-blind, placebo-controlled study with 80 participants (40 healthy, 40 with insomnia) demonstrated that Ashwagandha root extract administered for 8 weeks significantly improved sleep parameters including Sleep Onset Latency, Total Sleep Time, Wake After Sleep Onset, and Sleep Efficiency in both healthy subjects and insomnia patients. The study also showed significant improvements in Pittsburgh Sleep Quality Index scores and Hamilton Anxiety Scale scores. The mechanism involves sleep-inducing effects through GABAergic modulation and reduction of cortisol levels, promoting relaxation and facilitating the transition to sleep while reducing anxiety symptoms.

**Primary Reference:** 10.1016/j.jep.2020.113276

**Additional Supporting Studies:**

- https://doi.org/10.1007/s12325-025-03327-z: RCT showing Ashwagandha formulation improves stress, anxiety, mood, and sleep quality - directly corroborates
- https://doi.org/10.3390/nu17132143: Focuses on mental health and sleep quality with Ashwagandha - directly relevant benefits
- https://doi.org/10.3390/clockssleep6030028: RCT showing milk enriched with ashwagandha extract improves subjective sleep quality
- https://doi.org/10.1002/hup.2911: Systematic review and meta-analysis on Withania somnifera for

anxiety and insomnia - directly corroborates

• https://pubmed.ncbi.nlm.nih.gov/39759822/: Evaluates anxiolytic and antidepressant effects of standardized Ashwagandha - related anxiety benefit

• https://doi.org/10.38212/2224-6614.3456: Sleep-promoting activity of Ashwagandha root extract via GABA receptors - directly corroborates

• https://doi.org/10.2147/JEP.S407906: Depression and anxiety efficacy of Ashwagandha formulation - directly corroborates anxiety benefit

• https://doi.org/10.1080/17512433.2022.2121699: Review of pharmacotherapeutic properties including stress, anxiety, and sleep effects - corroborates

• https://doi.org/10.1089/jmf.2022.0042: Ashwagandha impact on stress, sleep quality, and mental clarity in students - directly corroborates

**Corroborating Evidence:** Backed by **28 additional studies**

## 4. Saffron (Crocus sativus) standardized extract

REPLACES: Shankhpushpi (Convolvulus Pluricaulis)

**Dosage:** 14 mg per capsule

**Benefit:** Improved mood, reduced anxiety, and enhanced psychological well-being in adults with subclinical mood symptoms

**Preparation:** Incorporate standardized saffron extract powder (affron® or equivalent, standardized to ≥3.5% lepticrosalides including crocin and safranal) during the capsule blending phase. Mix thoroughly with the other powdered herbal extracts before encapsulation to ensure uniform distribution throughout the batch.

**Replacement Reasoning:** Replacing Shankhpushpi with Saffron provides superior clinical evidence for anxiety and stress-related symptoms with a well-validated standardized extract tested in healthy adults. At 14 mg per capsule (providing 28 mg daily with twice-daily administration), this dosage exactly matches the clinically validated dose that demonstrated significant improvements in mood and psychological well-being in the Lopresti et al. 2022 study. Saffron has demonstrated significant benefits in multiple controlled human trials for mood regulation and anxiety relief, offering stronger evidence-based support for the formulation's primary benefits of promoting restful sleep and relieving anxiety compared to Shankhpushpi. This replacement reduces total formulation mass (replacing 75 mg Shankhpushpi with 14 mg Saffron saves 61 mg), bringing the total to approximately 867 mg per capsule, which is well within size 000 capsule capacity while upgrading to an ingredient with robust clinical evidence. The 14 mg per capsule dosage stays well under the 30 mg limit specified in user feedback.

**Ayurvedic Basis:** According to classical Ayurvedic formulations documented in the Sahasrayoga and Astangahrdaya, Saffron (Crocus sativus/Kesara/Nagakesara) appears as a component in

several therapeutic preparations. In the Baladhatryadi Taila (Sahasrayoga, Tailaprakarana; 57), Kesara (Naga puspa) is combined with multiple nervine and calming herbs including Jatamansi (Mamsi), Tagara, and Ashwagandha as part of a formulation used externally for vatarakta and raktagata vata. Additionally, Kesara appears in a complex polyherbal formulation documented in Astangahrdaya (Uttarasthana, Adhyaya 3; 93-97) alongside similar nervine herbs including Pippali, Marica, Tvak, Ela, and other ingredients. Kesara functions as part of multi-ingredient synergistic combinations with established nervine herbs like Ashwagandha, Tagara (Valerian family), and Jatamansi to support overall systemic wellness.

**Scientific Basis:** A 6-week randomized, double-blind, placebo-controlled study with 62 recreationally-active healthy adults demonstrated that 28 mg daily of standardized saffron extract (affron®) significantly improved mood states and psychological well-being. The study measured outcomes using the Profile of Mood States and Patient-Reported Outcomes Measurement Information System-29, showing significant improvements in mental health parameters. At 14 mg per capsule, this dosage represents half of the 28 mg daily dose validated in this trial. The mechanism involves modulation of serotonergic, dopaminergic, and glutamatergic neurotransmitter systems through saffron's bioactive compounds crocin and safranal, with the study also measuring changes in brain-derived neurotrophic factor to identify mechanisms of action.

**Primary Reference:** 10.1080/15502783.2022.2083455

**Additional Supporting Studies:**

- https://doi.org/10.7759/cureus.82924: Review on saffron for mood, anxiety, and cognitive symptoms in relevant populations
- https://doi.org/10.1016/j.tjnut.2025.05.024: RCT on saffron extract (affron) for mood and wellbeing in adults with low mood
- https://doi.org/10.3390/nu17050809: RCT examining saffron effects on mood regulation in mild-to-moderate depressive symptoms
- https://doi.org/10.1093/nutrit/nuae076: Meta-analysis comparing saffron versus SSRIs for depression and anxiety treatment
- https://doi.org/10.1002/ptr.8424: Study on saffron extract effects on anhedonia in mild depression, rats and humans
- https://doi.org/10.1155/2024/3661412: RCT on saffron-withania supplement for mild-to-moderate anxiety in women
- https://doi.org/10.1002/ptr.8169: Review on saffron therapeutic potential in brain disorders including mood and anxiety
- https://doi.org/10.59249/XURF4540: Comparative review on saffron as therapeutic agent in depression treatment
- https://doi.org/10.1002/ptr.8110: Systematic review on saffron for depression, anxiety, and other psychiatric disorders

**Corroborating Evidence:** Backed by **27 additional studies**

## 5. Centella asiatica (Mandukparni)

REPLACES: Vacha (Acorus Calamus)

**Dosage:** 100 mg per capsule

**Benefit:** Reduces anxiety and mental stress while improving stress-correlated depression

**Preparation:** Incorporate 70% hydro-ethanolic extract of Centella asiatica in standardized powder form. Mix uniformly with existing herbal powder blend during capsule filling process to ensure homogeneous distribution.

**Replacement Reasoning:** Replacing Vacha with Centella asiatica provides superior clinical evidence for anxiety and stress relief in patients with generalized anxiety disorder, with measurable improvements on validated psychiatric scales. At 150 mg per capsule (providing 300 mg daily with twice-daily administration), this represents 60% of the clinical study dose (500 mg daily) but remains therapeutically meaningful given the synergistic adaptogenic effects of other herbs in the formulation (Ashwagandha 300mg, Brahmi 150mg, Jatamansi 125mg working together). This replacement increases net formulation mass by only 100mg (removing 50mg Vacha, adding 150mg Centella asiatica), bringing total to approximately 950mg per capsule - at the upper limit but feasible for size 000 capsules. Centella asiatica offers stronger evidence-based anxiolytic and stress-reducing benefits compared to Vacha, making it a more effective ingredient for promoting restful sleep and relieving anxiety.

**Ayurvedic Basis:** Centella asiatica (Mandukparni) is referenced in the Charaka Samhita as part of a Medhakara Rasayana, which invigorates the understanding. When the expressed juice of Mandukaparni is used with milk, along with liquorice or Guduchi, these preparations promote longevity, destroy disease, increase strength, and improve digestion, complexion, and voice. They also invigorate the understanding. The expressed juice of Mandukaparni, mixed with milk, should be administered over a month, which is highly conducive to nourishment, longevity, strength, and restoration to health. Ashwagandha appears in various formulations alongside other medhya (intellect-promoting) herbs like Brahmi and Satavari in Sarasvatarista preparation used as a rasayana.

**Scientific Basis:** In a 60-day clinical study with 33 participants (average age 33 years) diagnosed with generalized anxiety disorder, 70% hydro-ethanolic extract of Centella asiatica administered orally in capsule form at 500 mg twice daily significantly attenuated anxiety-related disorders ($p<0.01$), significantly reduced stress phenomenon and its correlated depression ($p<0.01$), and improved willingness assessed through Hamilton's Brief Psychiatric Rating Scale and psychological rating questionnaires at baseline, day 30, and day 60.

**Primary Reference:** PubMed:20677602

**Additional Supporting Studies:**

- https://doi.org/10.1080/07853890.2025.2559122: Reviews neuroprotective properties of CA including

mitigating oxidative stress, inflammation, and neuronal apoptosis mechanisms.

• https://doi.org/10.1016/j.jep.2023.117266: Confirms asiaticoside from Centella asiatica has antidepressant and anxiolytic activities among other pharmacological properties.

• https://doi.org/10.1007/s12035-024-04198-1: Directly demonstrates C. asiatica extract reverses depressive-like behaviors, inflammation and oxidative stress in stress models.

• https://doi.org/10.1016/j.bbr.2024.114976: Specifically explores antidepressant effects of major C. asiatica constituents including asiatic acid and madecassic acid.

• https://doi.org/10.1016/j.neuropharm.2023.109834: Shows madecassoside from C. asiatica reduces anxiety-like behaviors and protects against neurodegeneration.

• https://doi.org/10.1111/jcmm.17635: Reviews asiaticoside and madecassoside from C. asiatica including cognitive and brain function benefits.

• https://doi.org/10.1089/rej.2022.0036: Studies neuroprotective potential of hydroalcoholic extract of C. asiatica in neurodegenerative disease model.

• https://doi.org/10.1007/s11011-022-00998-3: Demonstrates asiatic acid from C. asiatica attenuates behavioral changes and neuronal loss.

• https://doi.org/10.1007/s12011-021-03083-5: Shows Centella asiatica alleviates aluminum-induced neurological disorders through neuroprotective mechanisms.

**Corroborating Evidence:** Backed by **10 additional studies**

# Manufacturing Instructions

## MASTER BATCH RECORD (MBR)

### AYURVEDIC SLEEP & STRESS RELIEF CAPSULES

*BATCH SIZE: 1000 Capsules*

- --

### 1. BILL OF MATERIALS (per 1000 capsules)

*Active Herbal Ingredients:*

- Ashwagandha (Withania somnifera) Std. Extract: 200.0 g
- Tagar (Valeriana wallichii) Std. Extract: 100.0 g
- Jatamansi (Nardostachys jatamansi) Extract: 100.0 g
- Brahmi (Bacopa monnieri) Std. Extract: 150.0 g
- Centella asiatica (Mandukparni) 70% Hydro-ethanolic Extract: 100.0 g
- Saffron (Crocus sativus) Std. Extract (≥3.5% lepticrosalides): 14.0 g
- Piperine (from Piper nigrum) Std. Extract (≥95% piperine): 10.0 g

**Total Active Ingredients: 674.0 g**

*Excipients:*

- Microcrystalline Cellulose (MCC) Ph. Eur.: 276.0 g
- Magnesium Stearate (vegetable source): 10.0 g

**Total Fill Weight per Capsule: 960 mg**

**Total Batch Weight: 960.0 g**

### *Packaging Materials:*

- Vegetable Capsules Size 000 (HPMC or Pullulan): 1000 units
- HDPE Bottles with tamper-evident seals: As required
- Desiccant sachets (silica gel): As required
- Labels: As required
- --

## 2. EQUIPMENT REQUIRED

- Calibrated analytical balance (capacity: 500 g, precision: ±0.01 g)
- Calibrated bulk balance (capacity: 5 kg, precision: ±0.1 g)
- Stainless steel mixing vessels (2 L capacity minimum)
- Planetary mixer or V-blender with intensifier bar
- 40-mesh stainless steel sieve
- Automatic capsule filling machine (or semi-automatic for smaller batches)
- Capsule polisher
- Moisture analyzer
- Particle size analyzer
- Metal detector
- Environmental controls (temperature 20-25°C, relative humidity 35-50%)
- --

## 3. MANUFACTURING PROCEDURE

### *3.1 ENVIRONMENTAL PREPARATION*

Set manufacturing area to controlled conditions: Temperature 20-25°C, Relative Humidity 35-50%. Ensure all equipment is clean, dry, and calibrated per GMP requirements.

### *3.2 RAW MATERIAL VERIFICATION*

Verify all raw materials against specifications. Check Certificates of Analysis for:

- Identity confirmation
- Assay/standardization levels (Saffron ≥3.5% lepticrosalides, Piperine ≥95%, Ashwagandha withanolides, Brahmi bacosides)
- Microbial limits compliance
- Heavy metals compliance
- Moisture content <8% for all herbal extracts

### *3.3 WEIGHING OF MATERIALS*

Using calibrated balances, accurately weigh all ingredients per Bill of Materials. Perform double-check verification for each ingredient. Record actual weights and lot numbers in batch record.

### *3.4 SIEVING OPERATION*

Pass all herbal extracts and excipients through 40-mesh stainless steel sieve separately to break up agglomerates and ensure uniform particle size distribution. Collect sieved materials in labeled stainless steel containers.

### *3.5 GEOMETRIC DILUTION - PHASE 1 (Low-Dose Ingredients)*

**Step 3.5.1:** Transfer Saffron extract (14.0 g) to clean stainless steel mixing vessel. This is Blend A.

**Step 3.5.2:** Add equal weight (14.0 g) of Microcrystalline Cellulose to Blend A. Mix manually with stainless steel spatula for 3 minutes ensuring complete homogeneity. Blend A now contains 28.0 g total.

**Step 3.5.3:** Add Piperine extract (10.0 g) to Blend A (28.0 g). Mix manually for 3 minutes. Blend A now contains 38.0 g total.

**Step 3.5.4:** Add equal weight (38.0 g) of Microcrystalline Cellulose to Blend A. Mix manually for 5 minutes ensuring uniform distribution. Blend A now contains 76.0 g total.

### *3.6 GEOMETRIC DILUTION - PHASE 2 (Medium-Dose Ingredients)*

**Step 3.6.1:** Add Centella asiatica extract (100.0 g) to Blend A (76.0 g). Mix manually for 5 minutes. Blend A now contains 176.0 g total.

**Step 3.6.2:** Add Tagar extract (100.0 g) to Blend A (176.0 g). Mix manually for 5 minutes ensuring complete incorporation. Blend A now contains 276.0 g total.

**Step 3.6.3:** Add Jatamansi extract (100.0 g) to Blend A (276.0 g). Mix manually for 5 minutes. Blend A now contains 376.0 g total.

### *3.7 GEOMETRIC DILUTION - PHASE 3 (High-Dose Ingredients)*

**Step 3.7.1:** Add Brahmi extract (150.0 g) to Blend A (376.0 g). Mix manually for 5 minutes. Blend A now contains 526.0 g total.

**Step 3.7.2:** Add Ashwagandha extract (200.0 g) to Blend A (526.0 g). Mix manually for 7 minutes ensuring thorough distribution. Blend A now contains 726.0 g total.

**Step 3.7.3:** Add remaining Microcrystalline Cellulose (224.0 g) to Blend A (726.0 g). Mix manually for 7 minutes. Blend now contains 950.0 g total.

### *3.8 MECHANICAL BLENDING*

Transfer entire blend (950.0 g) to planetary mixer or V-blender. Blend at 25 RPM for 15 minutes. Stop and scrape down sides. Resume blending for additional 10 minutes at 25 RPM.

### *3.9 IN-PROCESS QUALITY CONTROL - BLEND UNIFORMITY*

Collect 10 samples from different locations in the blend (top, middle, bottom, sides). Test for:

- Blend uniformity (RSD should be <5% for marker compounds)
- Moisture content (should be <8%)
- Bulk density
- Particle size distribution

Record results. Blend passes if uniformity criteria are met.

### *3.10 LUBRICATION*

Add Magnesium Stearate (10.0 g) to the blended powder (950.0 g). Mix in planetary mixer at 15 RPM for 3 minutes only. DO NOT over-mix as this may cause hydrophobic coating and dissolution issues.

**Final Blend Weight: 960.0 g**

### *3.11 FINAL BLEND ANALYSIS*

Perform final quality checks:

- Appearance: Free-flowing powder, uniform color
- Moisture content: <8%
- Bulk density: Record value
- Tapped density: Record value
- Carr's Index: Calculate and record
- Hausner Ratio: Calculate and record

### *3.12 CAPSULE FILLING*

**Step 3.12.1:** Set up automatic capsule filling machine with Size 000 vegetable capsules (HPMC or Pullulan).

**Step 3.12.2:** Calibrate filling machine to deliver 960 mg ± 5% per capsule.

**Step 3.12.3:** Perform initial calibration run with 20 capsules. Weigh each filled capsule, calculate average fill weight and variation. Adjust machine settings if necessary to achieve 960 mg ± 5%.

**Step 3.12.4:** Once calibration is confirmed, proceed with full batch encapsulation of 1000 capsules.

**Step 3.12.5:** Monitor fill weight every 50 capsules during production run. Record weights in batch record.

### *3.13 CAPSULE POLISHING*

Transfer filled capsules to capsule polisher. Polish for 5-7 minutes to remove excess powder from capsule exterior. Inspect for defects.

### *3.14 IN-PROCESS QUALITY CONTROL - FILLED CAPSULES*

Inspect sample of 50 capsules for:

- Locked capsule integrity (pull test)
- Absence of cracks or defects
- Uniform fill appearance
- Weight variation (weigh 20 capsules individually, calculate average and RSD - should meet Ph. Eur. specifications)
- Disintegration time (should be <30 minutes in water at 37°C)

### *3.15 METAL DETECTION*

Pass all filled capsules through calibrated metal detector. Reject any capsules triggering detection. Record results.

### *3.16 FINAL CAPSULE COUNT*

Count and verify total capsule yield. Record actual yield versus theoretical yield (1000 capsules). Investigate if yield is <95%.

- --

## 4. PACKAGING

### *4.1 PRIMARY PACKAGING*

Fill HDPE bottles with appropriate count per container (e.g., 60 capsules per bottle for 30-day supply at 2 capsules daily). Include one silica gel desiccant sachet (2 g) per bottle.

### *4.2 SEALING*

Apply tamper-evident seals to all bottles. Ensure seals are intact and properly adhered.

### *4.3 LABELING*

Apply labels containing:

- Product name
- Ingredient list with quantities per capsule
- Batch number
- Manufacturing date
- Expiry date (24 months from manufacturing)
- Storage conditions
- Dosage instructions
- Regulatory compliance statements
- Allergen information

### *4.4 SECONDARY PACKAGING*

Pack labeled bottles into cartons with appropriate cushioning. Seal cartons and apply batch identification labels.

- --

## 5. QUALITY CONTROL - FINISHED PRODUCT

Retain samples for testing:

- Appearance and organoleptic properties
- Average weight per capsule (n=20)
- Weight variation (Ph. Eur. limits)
- Disintegration time
- Moisture content
- Microbial limits (Total Plate Count, Yeast & Mold, E. coli, Salmonella)
- Heavy metals (Pb, Cd, Hg, As)
- Marker compound assay (withanolides, bacosides, lepticrosalides, piperine)
- Stability indicating parameters
- --

## 6. STORAGE CONDITIONS

**Finished Product Storage:**

- Temperature: 15-25°C
- Relative Humidity: <60%
- Protect from direct sunlight
- Store in original sealed containers

**Shelf Life:** 24 months from date of manufacture when stored under specified conditions.

- --

## 7. DOCUMENTATION

Complete all sections of batch manufacturing record including:

- Material reconciliation
- Equipment cleaning logs
- In-process control results
- Deviation reports (if any)
- Batch yield calculations

- QC test results
- Release authorization signatures
- --

## 8. CRITICAL QUALITY ATTRIBUTES (CQAs)

Monitor throughout manufacturing:

- Blend uniformity (RSD <5%)
- Capsule fill weight (960 mg ± 5%)
- Moisture content (<8%)
- Disintegration time (<30 minutes)
- Microbial limits compliance
- Marker compound content within specifications
- --

END OF MASTER BATCH RECORD