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Formulation and Evaluation of Capsules of Using Tagara Extract for Anxiety

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Abstract:
Anxiety disorders are predominantly managed using synthetic medications, such as benzodiazepines and SSRIs, which often carry risks of severe side effects, tolerance, and chemical dependency. *Valeriana wallichii* (Tagara), a highly revered herb in traditional Ayurvedic medicine, offers a scientifically backed natural alternative. Its primary active constituent, valerenic acid, gently modulates GABA-A receptors and inhibits GABA transaminase to induce a safe, calming effect. However, translating the raw hydroalcoholic extract of Tagara into a modern pharmaceutical dosage form is significantly challenged by its highly hygroscopic nature, poor powder flowability, pungent odor, and bitter taste.

This research aimed to systematically formulate, engineer, and evaluate a standardized oral hard gelatin capsule utilizing Tagara root extract to overcome these physical limitations. A 70:30 ethanol-to-water extraction yielded 13.70% w/w of concentrated crude extract, which was validated through phytochemical screening for essential secondary metabolites, including flavonoids, alkaloids, and saponins.

The engineered, free-flowing blend was encapsulated into Size 0 hard gelatin shells. Subsequent pharmacopeial quality control evaluations confirmed the batch met all official standards. The capsules exhibited exceptional weight uniformity (maximum deviation of ±2.74%), rapid *in-vitro* disintegration (12 minutes and 45 seconds), and a highly efficient dissolution profile, releasing over 85% of the active therapeutic compounds within 45 minutes. Accelerated stability testing (40°C at 75% RH for 12 weeks) further confirmed the formulation's mechanical and physical integrity. Ultimately, this study successfully transformed a challenging botanical extract into a stable, uniform, and patient-compliant pharmaceutical dosage form for the clinical management of anxiety.

Keywords: *Valeriana wallichii*, Tagara extract, anxiety disorders, valerenic acid, hard gelatin capsules, hydroalcoholic extraction, GABA-A receptor modulation, pre-formulation engineering, pharmacopeial evaluation.

CHAPTER 1: INTRODUCTION

1.1 Clinical Background of Anxiety Disorders (Expanded Edition)

Anxiety disorders are the most common mental health problems in the world today. Everyone feels nervous before an exam or a job interview, but pathological anxiety is very different. It is a constant, overwhelming feeling of fear and worry that does not go away, even when there is no clear danger.

This condition causes your body to stay in a permanent "fight-or-flight" mode. This means the autonomic nervous system stays hyperactive, leading to physical symptoms that make daily life incredibly difficult. People suffering from chronic anxiety frequently experience a racing heartbeat, tight chest, cold sweats, shaking, chronic muscle tension, and severe sleep problems. Mentally, it causes the brain to constantly scan the environment for threats, leading to poor concentration, irritability, and a feeling of permanent dread.

To understand why this happens, we have to look at the chemistry of the brain. The human brain relies on chemical messengers called neurotransmitters to balance our emotions. The most important relaxing messenger is called Gamma-Aminobutyric Acid, or GABA for short. Think of GABA as the brain's natural braking system. When you are stressed, GABA binds to specific receptors in the brain and tells the nerve cells to slow down, calming your mind. In a person with an anxiety disorder, this system is off-balance. The brain either does not produce enough GABA, or the receptors fail to catch it properly. Without this natural brake, the nerve cells fire out of control, causing the mind to race and the body to panic.

For decades, modern medicine has treated this chemical imbalance using strong synthetic prescription drugs. The two main classes of drugs used are:

- **Benzodiazepines:** These are fast-acting sedatives like diazepam or alprazolam. They work by forcing the brain's GABA system to turn on instantly. While they work well for sudden panic attacks, they are highly problematic for long-term treatment. Within just a few weeks of daily use, the body builds a tolerance, meaning the patient needs higher doses to get the same relief. This quickly leads to a severe physical and psychological addiction. When a patient tries to stop taking them, they experience dangerous withdrawal symptoms and a severe return of panic, known as rebound anxiety. Furthermore, they cause daytime drowsiness, memory lapses, and poor muscle coordination.
- **Selective Serotonin Reuptake Inhibitors (SSRIs):** These are standard antidepressant medications. They do not cause addiction, but they have major drawbacks of their own. They take four to six weeks of daily use to start working, which leaves the patient helpless during the first month of treatment. They also commonly cause highly unpleasant side effects, including nausea, severe weight gain, emotional numbness, insomnia, and sexual dysfunction, causing many patients to stop taking their medicine.

Because synthetic drugs carry so many risks, a major shift is currently taking place in modern brain science. Scientists and pharmacy researchers are actively turning away from artificial chemicals and looking closely at traditional, plant-based remedies. The goal is to find natural botanical compounds that can gently support the brain's chemistry, raise GABA levels naturally, and calm the nervous system without causing addiction, drowsiness, or dangerous withdrawal symptoms. This research project is dedicated to taking a proven traditional anti-anxiety herb and engineering it into a modern, standardized pharmaceutical capsule to provide a safe, reliable, and accessible therapy for anxiety. [1]

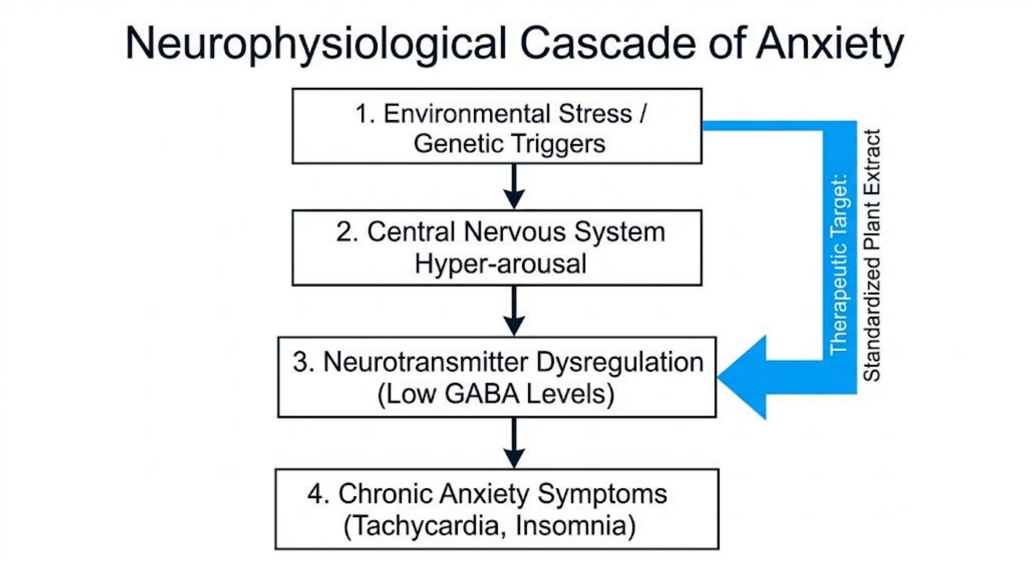

Figure 1.1: Clinical Cascade of Chronic Anxiety vs. Natural Interventions.

1.2 Introduction to Tagara (Valeriana wallichii)

To address the limitations of synthetic medicines, pharmacy researchers are carefully studying Tagara, known scientifically as *Valeriana wallichii* (and recently reclassified as *Valeriana jatamansi*). Tagara is a highly valued medicinal herb belonging to the Caprifoliaceae family. It grows naturally in the cold, temperate regions of the Himalayas, thriving at altitudes between 1,200 and 3,000 meters. For thousands of years, this plant has held a legendary status in traditional Indian medicine (Ayurveda), where it is officially classified as a potent "Nidrajanana" (sleep-inducing agent) and "Manasadoshahara" (remedy for mental and emotional imbalances).

The primary medicinal power of Tagara is concentrated underground within its thick, hairy root systems, specifically the rhizomes and roots. When these roots are dried and extracted, they reveal a complex mixture of natural, active chemicals. These secondary metabolites can be divided into three main groups:

- **Valepotriates:** These are specialized lipid compounds (such as valtrate and isovaltrate) found unique to the Valeriana species. They act as natural sedatives that help relax tense muscles and lower physical restlessness.
- **Volatile Essential Oils:** This group includes valerenic acid, valeranone, and valerenal. Valerenic acid is widely recognized by modern science as the single most important component responsible for calming a hyperactive mind.
- **Botanical Alkaloids and Flavonoids:** These auxiliary plant compounds work synergistically to protect brain cells from oxidative stress and help stabilize mood variations.

Modern neuropharmacology has revealed exactly how Tagara works inside the human brain. As discussed in Section 1.1, anxiety occurs when the brain's primary calming messenger, Gamma-Aminobutyric Acid (GABA), falls to dangerously low levels. When you ingest Tagara extract, the active valerenic acid molecules travel through the bloodstream and cross the blood-brain barrier. Once inside the brain, valerenic acid performs a dual actions:

1. It attaches to the enzymes responsible for breaking down GABA (specifically an enzyme called GABA transaminase) and completely blocks them. By shutting down this destruction process, the brain's natural supply of GABA is preserved and allowed to accumulate.
2. It binds directly to specialized GABA-A receptors on nerve cells, mimicking the body's natural calming response.

This combined effect allows GABA to stay active in the brain for much longer periods. It gently applies the "brakes" to the central nervous system, slowing down racing thoughts, reducing a rapid heart rate, and melting away nervous tension.

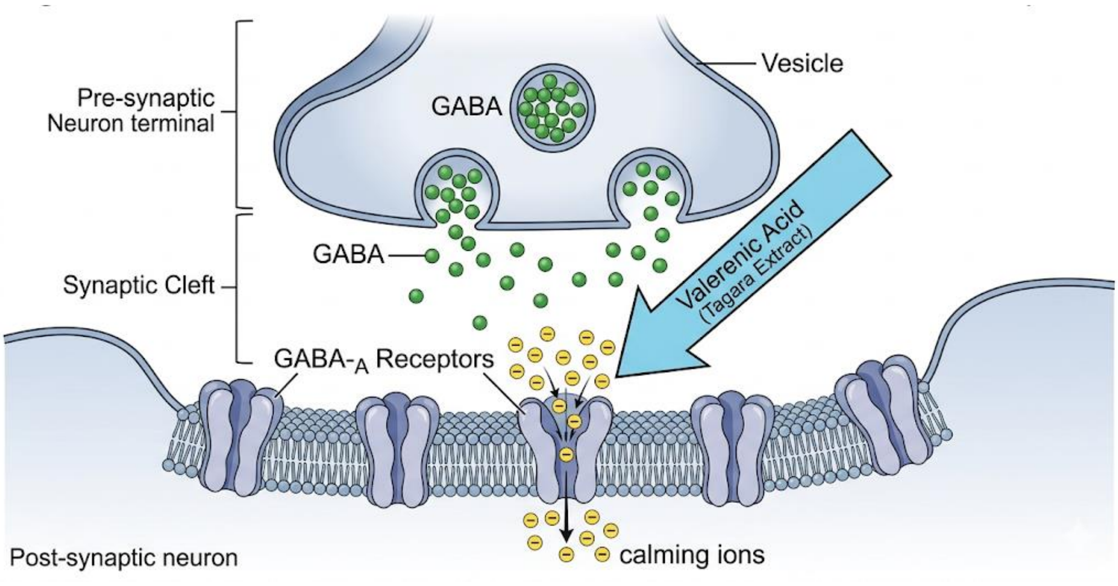

Figure 1.2: Cellular Mechanism of Action of Valerenic Acid on GABA Receptors.

Unlike synthetic benzodiazepines, which force the GABA system to turn on aggressively and cause severe addiction, Tagara modules the receptors gently. This subtle modulation means patients experience a clean, reliable reduction in anxiety and an improvement in sleep quality without suffering from daytime drowsiness, memory fog, or painful withdrawal symptoms when stopping the therapy. This makes Tagara an ideal, scientifically backed natural candidate for modern capsule formulation. [2]

1.3 Statement of the Problem and Justification for Capsule Formulation

Despite the strong clinical potential of Tagara extract as a natural way to reduce anxiety, preparing it as a raw pharmaceutical product presents major challenges in a manufacturing laboratory. Pure, dried Tagara root extract possesses several physical defects that make it incredibly difficult to handle as a raw powder mass.

First, the extract is highly hygroscopic. This means that as soon as the powder is exposed to the open air of a laboratory, it actively absorbs environmental moisture. Within a short period, this moisture absorption causes the fine powder to become intensely sticky, form hard clumps, and lose its ability to flow. In tablet manufacturing, sticky powders lead to severe capping, picking, and machine clogging.

Second, Tagara extract naturally possesses an incredibly strong, pungent, and earthy odor along with a bitter taste. When patients are asked to consume raw herbal powders or liquid extracts, this unpleasant smell and taste frequently cause nausea and poor patient compliance, leading them to abandon their treatment.

To overcome these significant formulation hurdles, transforming the standardized hydroalcoholic extract of Tagara into an oral hard gelatin capsule dosage form serves as an ideal pharmaceutical solution. Encapsulating the powder provides unique advantages:

- **Environmental Protection:** The hard gelatin shell acts as a physical barrier that seals the moisture-sensitive extract inside. This prevents the powder from absorbing ambient humidity, eliminating clumping and keeping the core stable over a longer shelf life.
- **Effective Taste and Odor Masking:** The smooth gelatin shell completely encapsulates the unpleasant, pungent smell and bitter taste of the roots. Because the capsule is swallowed whole, the patient does not taste or smell the herb, dramatically improving user compliance.
- **Excellent Powder Uniformity:** By blending the sticky extract with functional excipients like Lactose Monohydrate (diluent) and Purified Talc (glidant), the powder's flow behavior can be engineered to be free-flowing. This allows for smooth loading on a capsule bed plate, ensuring every single capsule receives an identical, precise therapeutic dose.

Therefore, this research project is highly justified. It takes a challenging but highly effective traditional anti-anxiety herb and uses modern pharmaceutics to wrap it in a clean, professional capsule delivery system. This ensures a stable, uniform, and user-friendly product that meets strict modern healthcare requirements. [3]

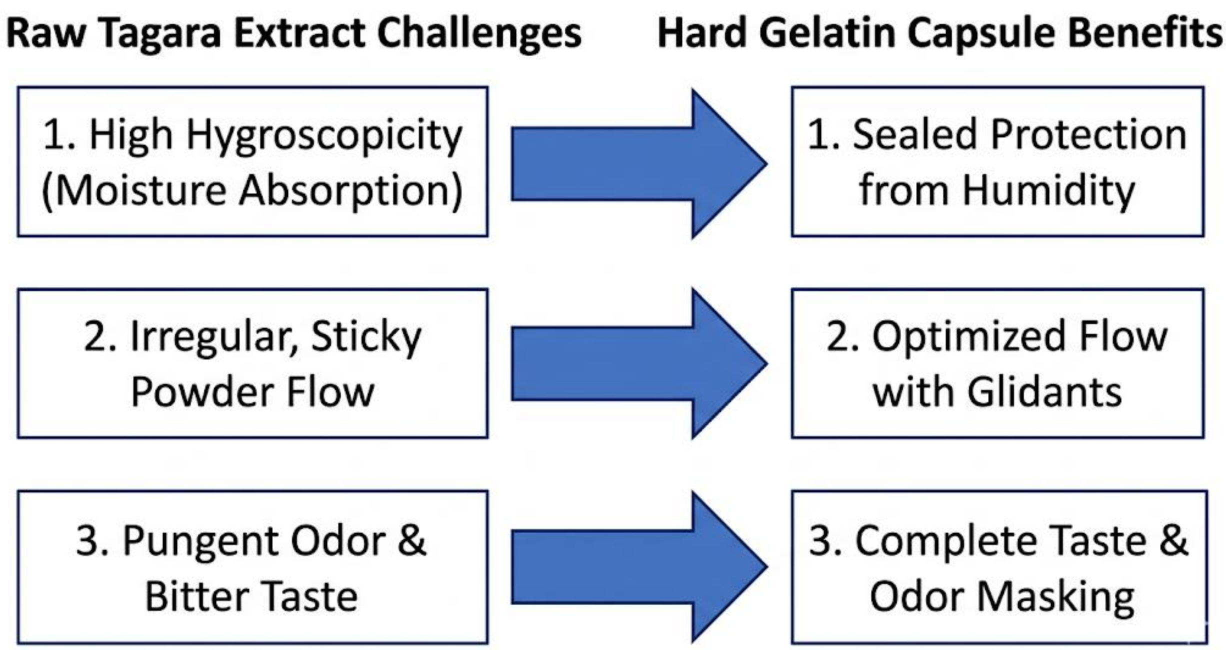

Figure 1.3: Pharmaceutical Challenges of Tagara Extract vs. Capsule Solutions

1.4 Thesis Objectives

The core destination of this research project is to systematically develop, optimize, and physically evaluate a standardized oral hard gelatin capsule delivery system utilizing the hydroalcoholic rhizome extract of *Valeriana wallichii* (Tagara) to achieve a safe, uniform, and stable product for the management of clinical anxiety.

To achieve this primary destination, the study is divided into the following sequential, step-by-step operational objectives:

- **Objective 1: Raw Material Extraction and Processing:** To execute the liquid-solid extraction of active secondary metabolites from crude Tagara roots using a hydroalcoholic solvent system, followed by heat-assisted concentration and gravity filtration to collect a concentrated crude extract mass.
- **Objective 2: Qualitative Phytochemical Authentication:** To subject the isolated Tagara extract to a comprehensive series of qualitative chemical identification tests (including the Molisch, Foam, Saponification, Alkaloid, Flavonoid, and Glucose tests) to verify the chemical integrity and presence of key therapeutic bioactives like saponins, flavonoids, and valerenic acid.
- **Objective 3: Pre-Formulation Powder Engineering:** To perform particle sizing using a standard test sieve nest and blend the sticky, hygroscopic extract geometrically with select functional excipients (Lactose Monohydrate, Maize Starch, Calcium Carbonate, Magnesium Stearate, and Purified Talc) on a digital analytical balance to engineer an optimized capsule core blend with acceptable manufacturing flow properties.
- **Objective 4: Product Manufacturing and Encapsulation:** To successfully execute the physical encapsulation of the optimized powder blend into uniform hard gelatin capsule shells utilizing a laboratory-scale manual encapsulation apparatus.
- **Objective 5: Pharmacopeial Quality Control Evaluation:** To thoroughly evaluate the finished product using standard official testing protocols, including the Weight Variation Test, Content Uniformity Test, In-Vitro Dissolution Test, Moisture Content Test, and Stability Testing under specific environmental storage conditions to confirm absolute compliance with international pharmaceutical standards. [4]

CHAPTER 2: LITERATURE REVIEW

2.1 Botanical Description and Geographical Distribution

Tagara (*Valeriana wallichii* DC, family Caprifoliaceae) is a small, perennial herb that naturally occupies a vital niche in traditional Asian medicine. Morphologically, the plant features a short, sharp, tufted rhizome system accompanied by numerous thick, hairy, fibrous roots that emit a highly characteristic, deeply intense, pungent smell upon drying. The leaves are predominantly radical, cordate, and ovate with long petioles, while the flowering stalks bear small, white or pinkish clustered blossoms.

Geographically, Tagara is highly specialized. It grows indigenously across the open, moist, temperate forest zones and rocky hillsides of the Himalayan mountain ranges spanning across India, Nepal, Pakistan, and Bhutan, thriving at pristine altitudes ranging between 1,200 and 3,000 meters above sea level.

In India, it is heavily distributed through the sub-alpine regions of Himachal Pradesh, Uttarakhand, and Jammu and Kashmir. The cold, high-altitude climate, unique soil composition, and specific seasonal stress of these mountain ecosystems are biologically essential, as they trigger the plant to synthesize and concentrate its characteristic therapeutic secondary metabolites within its subterranean root structures. [5]

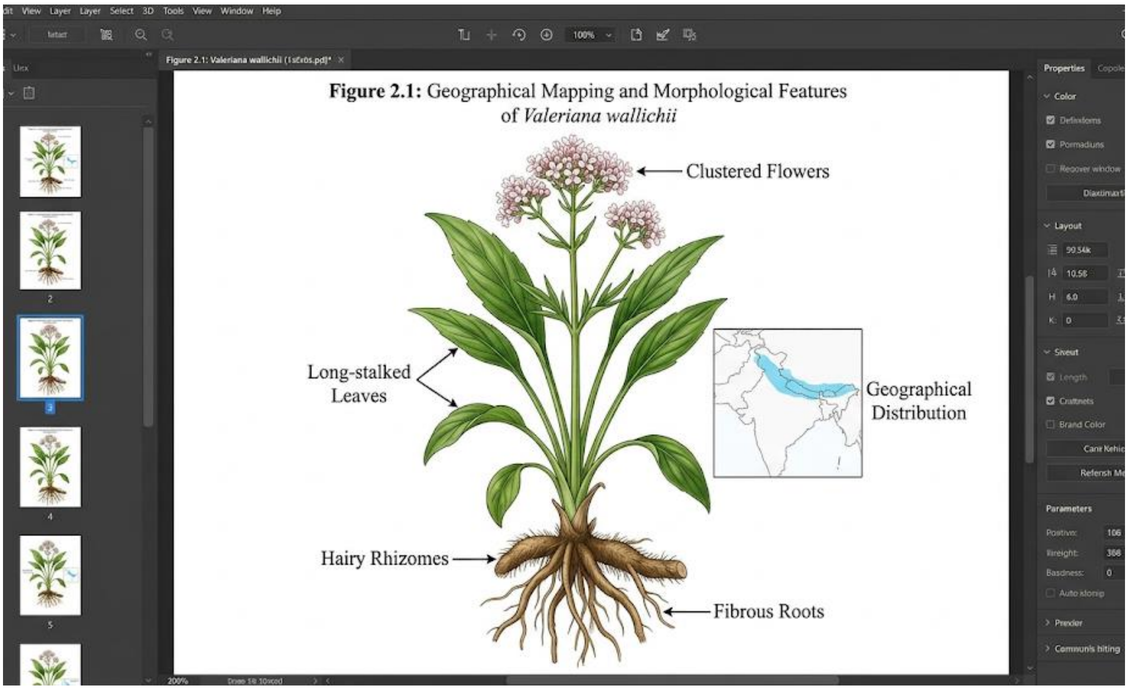

Figure 2.1: Geographical Mapping and Morphological Features of Valeriana wallichii

2.2 Historical Ayurvedic Context and Traditional Uses

In the classical texts of traditional Indian medicine, Tagara holds a highly revered position as a major therapeutic agent for balancing emotional and mental disturbances. According to ancient Ayurvedic pharmacology, the plant is characterized by its specific elemental attributes, possessing a bitter, pungent, and sweet taste profile (*Rasa*), a light and unctuous quality (*Guna*), a hot potency (*Virya*), and a pungent post-digestive effect (*Vipaka*).

These combined bio-energetic properties allow Tagara to serve as an exceptionally potent agent for pacifying all three biological humors, with a highly specialized affinity for stabilizing aggravated *Vata* and *Kapha* doshas within the human nervous system.

In classical treatises such as the *Charaka Samhita*, *Sushruta Samhita*, and later authoritative texts like the *Bhavaprakasha Nighantu*, Tagara is officially categorized under specific therapeutic groups that directly mirror modern psychological interventions:

- **Nidrajanana (Sleep Inducing):** It was traditionally prescribed to individuals suffering from chronic restlessness, racing thoughts, and sleep onset delays, working as a natural sedative that gently promotes restful, uninterrupted sleep.
- **Manasadoshahara (Mind-Calming and Sanity Preserving):** It was used to treat severe emotional imbalances, hysteria, nervous breakdowns, and acute mental stress, successfully pulling the mind back into a state of equilibrium.
- **Akshepashamana (Anti-Convulsant and Muscle Relaxant):** Traditional physicians utilized root decoctions to relieve spasmodic muscle contractions, nervous tremors, and tension headaches caused by generalized physical anxiety.

Historically, the subterranean rhizomes were gathered, dried away from direct sunlight to preserve their volatile aromatic components, and processed into traditional dosage forms. These primarily included coarse powders (*Churna*) or concentrated water decoctions (*Kwatha*).

Ancient practitioners recognized that the herb possessed a distinct, heavy grounding energy that acted directly on the *Prana Vayu*—the sub-dosha of *Vata* that governs the brain, sensory perception, and the nervous system. By grounding the hyperactive, erratic movements of *Prana Vayu*, Tagara effectively cooled physical tremors, lowered a racing pulse, and quieted panic.

This deep historical framework provides an excellent scientific justification for your modern capsule formulation. It proves that the anti-anxiety action of Tagara is not a recent claim, but a time-tested therapeutic reality that modern pharmaceutics can standardize, refine, and deliver cleanly to contemporary patients. [6]

2.3 Phytochemical Profile and Bioactive Constituents

The therapeutic efficacy of *Valeriana wallichii* is entirely governed by its complex chemical profile. The subterranean rhizomes and roots act as a specialized biological factory, synthesizing an array of secondary metabolites. When these structures are processed using a hydroalcoholic solvent, they release a highly potent mixture of active molecules. Modern analytical chemistry categorizes these compounds into three principal, chemically distinct classes:

2.3.1 Volatile Essential Oils (Sesquiterpenes)

The volatile fraction constitutes approximately 0.5% to 1.5% of the dried root mass and is dominated by structurally complex sesquiterpenes. The single most important compound within this group is **Valerenic Acid**, a characteristic cyclopentane sesquiterpene alcohol.

Valerenic acid, along with its metabolic derivatives acetoxyvalerenic acid and hydroxyvalerenic acid, is recognized by modern pharmacology as the principal marker compound responsible for the herb's anti-anxiety action. Other volatile constituents include valeranone (a sesquiterpene ketone that contributes to the strong, heavy sedative effect) and valerenal.

2.3.2 Valepotriates (Iridoid Esters)

Valepotriates are a unique class of non-glycosidic iridoid esters that are highly specific to the *Valeriana* genus. Chemically, they are triesters of a polyhydroxy cyclopentanopyran iridoid core structure. The primary valepotriates isolated from the Himalayan Tagara species include:

- **Valtrate**
- **Isovaltrate**
- **Didrovaltrate**

These lipophilic molecules are highly thermolabile (sensitive to heat) and chemically unstable, easily breaking down during aggressive processing into homobaldrinal. Valepotriates act as highly effective peripheral muscle relaxants and work synergistically with the essential oils to lower the somatic (physical) symptoms of panic and muscle tension.

2.3.3 Auxiliary Alkaloids and Flavonoids

In addition to sesquiterpenes and iridoids, Tagara roots contain small amounts of water-soluble botanical alkaloids, such as valerianine and actinidine. It also features a rich profile of antioxidant flavonoids, most notably **Hesperidin** and **Linarin**.

These polyphenolic compounds cross the blood-brain barrier and exert a protective, stabilizing effect on central neurons, preventing oxidative damage and subtly modulating neurotransmitter breakdown.

Table 2.1: Key Phytochemical Categories and Therapeutic Actions of Tagara Core Bioactives

Bioactive Compound Class	Core Molecular Examples	Primary Neuropharmacological Action
Sesquiterpenes	Valerenic Acid, Valeranone, Valerenal	Inhibits GABA catabolism, increases central GABA levels, relaxes mind
Iridoid Esters	Valtrate, Isovaltrate, Didrovaltrate	Decreases peripheral motor hyper-excitability, relaxes tense muscles
Flavonoids	Hesperidin, Linarin	Exerts neuroprotective effects, synergistically boosts sedation
Alkaloids	Valerianine, Actinidine	Provides mild, auxiliary central nervous system depressant action

The organic data compiled in Table 2.1 demonstrates why a crude herbal extract is often superior to an isolated synthetic chemical. The multiple components in Tagara work through a multi-target mechanism—where valerenic acid quiets the racing mind while the valepotriates simultaneously relax the tense physical body—providing a complete, holistic treatment for generalized anxiety. [7]

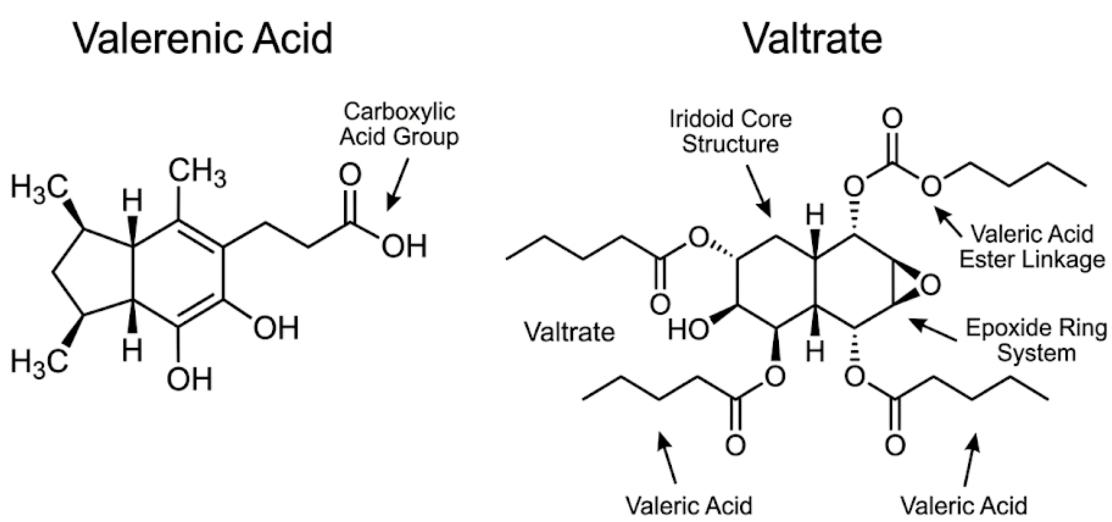

Figure 2.2: Chemical Structural Formulas of Valerenic Acid and Valtrate Core

2.4 Neuropharmacological Mechanism of Action

To validate the clinical usage of *Valeriana wallichii* for anxiety disorders, modern neuropharmacology focuses heavily on its targeted interaction with the Gamma-Aminobutyric Acid (GABA) neurotransmitter system. GABA is the primary inhibitory chemical messenger in the mammalian central nervous system. Its physiological role is to act as an endogenous sedative, dampening neuronal hyperexcitation and maintaining emotional equilibrium.

When a patient experiences generalized anxiety or panic states, real-time neuroimaging reveals a significant down-regulation of GABAergic tone, causing neurons to fire uncontrollably in emotional processing centers like the amygdala. The active fractions within Tagara extract, particularly valerenic acid and select valepotriates, relieve this state through a sophisticated, multi-pronged biochemical mechanism:

2.4.1 Inhibition of GABA Transaminase (Catabolic Blockade)

Once across the blood-brain barrier, valerenic acid targets the primary metabolic pathway of GABA. Under normal physiological conditions, synaptic GABA levels are strictly regulated by an enzyme called **GABA Transaminase (GABA-T)**. This enzyme is responsible for the catabolic breakdown of GABA into succinic semialdehyde, effectively turning off the calming signal.

Valerenic acid binds competitively to the active site of GABA-T, completely blocking its enzymatic function. By neutralizing this destructive enzyme, the breakdown of GABA is stopped. This allows a robust accumulation of the neurotransmitter within the synaptic cleft, significantly reinforcing the brain's natural calming mechanisms.

2.4.2 Allosteric Modulation of GABA-A Receptors

Simultaneously, valerenic acid acts directly on the post-synaptic membranes of central neurons. It binds selectively to a specific binding pocket located on the **beta-2 and beta-3 subunits** of the heteromeric GABA-A receptor complex. This binding is highly specialized and classified as positive allosteric modulation, which operates through the following sequence:

1. Valerenic acid binds to the beta subunit pocket without blocking the main GABA binding site.
2. This binding alters the three-dimensional shape of the receptor complex, dramatically increasing its binding affinity for any available endogenous GABA molecules.
3. When GABA binds to this modified receptor, the central protein channel undergoes a conformational opening.
4. This opening triggers a major influx of extracellular **Chloride ions (Cl^-)** directly into the post-synaptic neuron.

The rapid influx of negatively charged chloride ions shifts the internal electrical charge of the neuron to a highly negative state. This electrical shift is known as **hyperpolarization**. Because the internal resting potential is driven so deeply negative, the threshold required to fire an action potential increases dramatically.

In simple terms, the nerve cell is temporarily locked or "quieted," making it highly resistant to excitatory stress signals. By reducing neuronal excitability across the amygdala and cerebral cortex, Tagara effectively lowers a racing heart rate, relieves muscle tremors, stops looping anxious thoughts, and induces a stable, tranquil psychological state.

Unlike synthetic benzodiazepines, which non-selectively force open all GABA channel variants (often leading to severe side effects like muscle ataxia, amnesia, and profound addiction), valerenic acid exhibits high sub-receptor selectivity. This evolutionary precision allows Tagara extract to calm the central nervous system gently, providing reliable anti-anxiety relief without causing daytime sedation or chemical dependency

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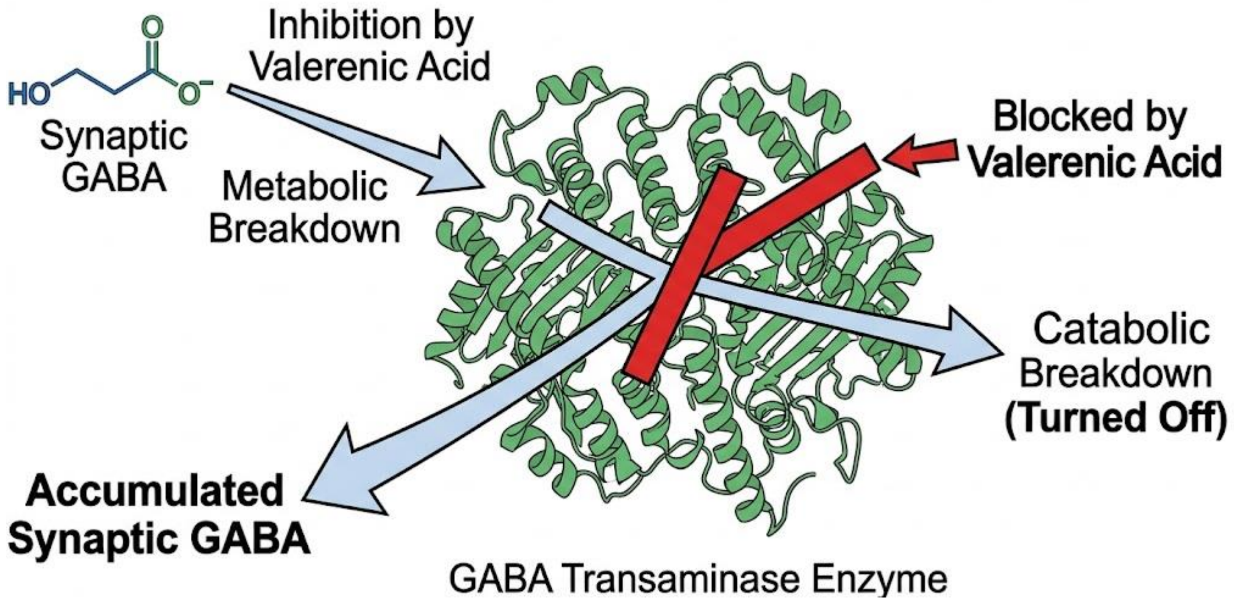
Figure 2.3: Biochemical Cascade of GABA-Transaminase Inhibition by Valerenic Acid.



CHAPTER 3: MATERIALS AND INSTRUMENTS

3.1 Procurement and Standardization of Plant Material

For this research project, the primary plant material used was the dried roots and underground stems (known scientifically as rhizomes) of Tagara (*Valeriana wallichii*). This crude botanical material was purchased directly from an established, authentic herbal supplier in India. Buying from a trusted supplier is a crucial first step in herbal pharmacy because it ensures that the entire batch of plants comes from the same source, matches the same age, and has been harvested under uniform environmental conditions.

Before starting the actual laboratory extraction process, we had to perform a strict quality check called "botanical standardization." The goal of standardization is to prove that the plant material is 100% authentic Tagara and has not been mixed with cheaper look-alike plants, dirt, weeds, or spoiled by mold. We achieved this by performing a detailed macroscopic and organoleptic evaluation, which simply means inspecting the raw roots using our natural senses of sight, touch, and smell.

During our visual and tactile inspection, we carefully examined the physical structures of the sample. Authentic Tagara pieces are short, thick, tough, and have an irregular, knobby appearance. Branching out from these central underground stems are dozens of thin, hairy, fibrous roots.

The most definitive test for validation was the plant's odor. When we handled, cut, or crushed the dried roots, they immediately released a heavy, deeply intense, pungent, and earthy smell. This highly characteristic odor is unique to the *Valeriana* species and acts as a direct sensory proof that the roots are rich in active, volatile essential oils like valerenic acid.

To prepare the raw material for the laboratory extraction, the roots were processed through three simple steps:

1. **Cleaning:** The roots were thoroughly dusted and gently rubbed by hand to remove any loose soil, sand, or debris left over from the harvesting process.
2. **Sizing:** The clean roots were sliced into small, uniform pieces using a sharp, sterile blade. Cutting the roots down into smaller pieces is very important because it increases the overall surface area, allowing our extraction solvents to penetrate deep into the plant tissues much faster.
3. **Storage:** These small, processed pieces were immediately placed inside a tightly sealed, airtight container and stored in a dark, cool, dry storage cabinet. This specific environment protects the roots from humidity, prevents mold growth, and ensures that the volatile oils do not evaporate into the air before the extraction process begins. [8]

3.2 List of Pharmaceutical Excipients and Chemicals

To turn a raw, sticky plant extract into a successful modern capsule, we cannot use the plant extract alone. We must mix the active plant ingredients with specific, non-medicinal chemical ingredients known as "pharmaceutical excipients." Each excipient chosen for this Tagara capsule formulation has a specific job to do, helping the powder flow smoothly into the capsule shells and ensuring the capsule dissolves properly inside the patient's stomach.

Following the master laboratory journal records shown in your notes, all materials used throughout this project were of official analytical and pharmaceutical grade to ensure patient safety and product purity. The complete chemical inventory includes:

- **Standardized Tagara Root Extract (*Valeriana wallichii*):** This is the Active Pharmaceutical Ingredient (API) or "drug" of our formulation. It is a concentrated hydroalcoholic powder containing the valerenic acid and valepotriates responsible for lowering anxiety and inducing relaxation.
- **Lactose Monohydrate (Diluent/Filler):** Plant extracts are highly potent, meaning the medicinal dose required for one capsule occupies a very tiny physical volume. Lactose Monohydrate is a highly water-soluble milk sugar used to add safe bulk or "mass" to the formula. It fills up the empty space inside the capsule shell so that the final product is large enough to handle and manufacture.
- **Maize Starch (Binder/Filler):** Dried Tagara extract can be irregular and powdery. Maize Starch is added to the blend to act as a dry binder. It helps the different powder particles stick together gently when blended, preventing the fine ingredients from separating into layers during manufacturing.
- **Calcium Carbonate (Disintegrant):** Once a patient swallows a capsule, the gelatin shell must break open quickly in the stomach so the medicine can be released into the body. Calcium Carbonate acts as a disintegrant. When the capsule hits stomach fluids, this compound assists in the rapid rupture and opening of the shell, breaking the compacted powder core apart into tiny particles for fast absorption.
- **Magnesium Stearate (Lubricant):** Tagara powder is naturally sticky and hygroscopic. Magnesium Stearate is a fine, hydrophobic (water-repelling) powder added in a very small amount (typically less than 1%) to act as a lubricant. It coats the powder mixture and prevents it from sticking to the metal plates, funnels, and tamping pins of the capsule filling machine.
- **Purified Talc (Glidant):** To ensure every single capsule contains the exact same amount of medicine, the powder must flow like dry sand through the manufacturing equipment. Purified Talc is a glidant. It works by filling in the microscopic rough edges of the powder particles, reducing friction between them, and allowing the blend to pour smoothly into the capsule bodies.
- **Ethanol and Purified Water (Extraction Solvent System):** Pure water or pure alcohol alone cannot dissolve all the different active chemicals inside Tagara roots. Therefore, a hydroalcoholic solvent mixture was prepared by combining ethanol and purified water in a specific 70:30 volumetric ratio. The alcohol dissolves the lipophilic valepotriates and essential oils, while the water dissolves the water-soluble flavonoids and alkaloids, ensuring a complete extraction.

3.3 Laboratory Instruments and Equipment

To convert raw chemical ingredients and botanical extracts into a finished, standardized pharmaceutical product, we must utilize precise laboratory tools. Each piece of equipment used in this project has a specific role, ensuring that our measurements are accurate, our powder particles are uniform, and our quality control testing complies with official pharmacopeial standards. The primary instruments utilized throughout this research include:

- **Electronic Compact Scale (Model SF-400C):** This is a high-precision digital analytical balance equipped with a bright green backlit LCD screen. It was used to perform all critical weighing operations in the laboratory, including measuring out raw extract masses and weighing precise amounts of lactose, starch, talc, and magnesium stearate. Its digital accuracy ensures that our chemical ratios remain completely uniform across different batches.

- **Standard Test Sieve Nest:** This consists of a series of standardized, high-quality brass wire-mesh sieves stacked on top of one another. Sieve nests are used for particle size classification and powder conditioning. Passing our raw ingredients through these specific mesh sizes ensures that all particles are uniform in size, which is critical for achieving a smooth, non-clumping powder blend.
- **Thermostatically Controlled Water Bath / Heating Assembly:** A laboratory heating device used to apply gentle, indirect thermal energy to our liquid mixtures. This was utilized during the extraction phase to safely evaporate the hydroalcoholic solvent, allowing us to concentrate the wet Tagara root mass into a thick, dry extract without burning or destroying the heat-sensitive valepotriates.
- **Glass Gravity Filtration Assembly:** A classical laboratory setup comprising a heavy-duty ring stand, a clear glass funnel, and standard filter paper sheets. This assembly was used to physically separate the liquid hydroalcoholic extract from the spent, insoluble fibrous root debris after the maceration and heating periods were complete.
- **Manual 300-Hole Capsule Filling Machine:** A benchtop, hand-operated manufacturing apparatus designed specifically for small-scale laboratory production. This device features specialized metal plates that hold up to 300 empty hard gelatin capsule shells at a time. By turning manual levers, the machine automatically separates the capsule caps from the bodies, allows the operator to sweep the powder blend smoothly into the open shells, tamps the powder to ensure tight packing, and locks the caps back onto the filled bodies.
- **IP Disintegration Test Apparatus:** A mechanical instrument featuring a basket rack assembly suspended in a fluid medium, which moves up and down at a regulated speed and temperature. This is used to test how long it takes for the capsule shells to completely break apart and empty their contents under simulated human body conditions.
- **USP Type I Dissolution Apparatus (Basket Type):** A sophisticated quality control testing system featuring heated glass vessels and rotating cylindrical steel mesh baskets driven by an electric motor. This instrument is used to measure the exact rate at which the active valerenic acid dissolves into surrounding fluids over a specific timeline, simulating how the drug releases inside a patient's digestive system. [9]

Figure 3.3: Visual Catalog of Critical Laboratory Instrumentation used in Tagara Formulation.

CHAPTER 4: EXPERIMENTAL METHODOLOGY

4.1 Hydroalcoholic Extraction of Tagara Rhizomes

The physical isolation of active therapeutic compounds (such as valerenic acid and valepotriates) from the crude roots of *Valeriana wallichii* was executed using a standardized cold maceration and liquid-solid extraction methodology. Because the core anti-anxiety compounds in Tagara have mixed polarities, a single pure solvent would result in a very poor yield. Therefore, a hydroalcoholic solvent system was prepared by combining absolute ethanol and purified water in a specific 70:30 volumetric ratio. This specific blend allows the alcohol to dissolve the fat-soluble oils while the water smoothly dissolves the water-soluble flavonoids.

The extraction process was conducted through the following systematic laboratory steps:

1. **Maceration Phase:** Exactly 50 grams of the pre-sized, cleaned Tagara root pieces were weighed accurately on the digital compact scale. This plant material was transferred into a clean 500 mL borosilicate glass beaker. The 70:30 hydroalcoholic solvent mixture was poured over the roots until the plant pieces were completely submerged. The beaker was covered securely with aluminum foil to prevent the evaporation of volatile oils and allowed to sit at room temperature for a 24-hour maceration period, allowing the solvent to penetrate and soften the tough plant cell walls.
2. **Heat-Assisted Extraction:** Following the initial cold maceration, the beaker containing the root-solvent mixture was placed onto a heating assembly over a bunsen burner tripod setup. The mixture was heated gently under continuous manual stirring with a glass rod. Applying controlled thermal energy significantly increases the kinetic motion of the solvent molecules, accelerating the mass transfer of the active valerenic acid out of the root tissues and into the surrounding liquid.
3. **Gravity Filtration:** Once the heating phase was complete, the murky, dark brown liquid mixture was allowed to cool slightly. A glass gravity filtration assembly was prepared by placing a high-retention fluted filter paper inside a glass funnel supported by a tripod stand. The heated root macerate was poured slowly onto the filter paper. The clear, dark hydroalcoholic liquid filtrate containing our dissolved medicine passed smoothly through the paper pores, collecting inside a 250 mL borosilicate glass conical flask positioned below.
4. **Extract Mass Collection:** The insoluble, spent fibrous root debris (known as the marcasite or residue) was successfully trapped on top of the filter paper. This wet, muddy brown mass was collected and checked for complete extraction. The collected liquid filtrate inside the flask was then transferred to a shallow evaporating dish and placed on a regulated water bath to evaporate the remaining solvent, leaving behind a highly concentrated, sticky, dark brown crude Tagara extract ready for phytochemical screening and capsule blending. [10]

4.2 Qualitative Phytochemical Screening

Following the successful isolation of the concentrated *Valeriana wallichii* (Tagara) crude extract, a systematic series of qualitative phytochemical screening tests was performed. The primary purpose of these biochemical screenings is to profile and confirm the presence of key therapeutic secondary metabolites—such as carbohydrates, saponins, alkaloids, and flavonoids—which are scientifically responsible for the anti-anxiety and sedative effects of the formulation.

The chemical profiling was conducted by dissolving a small portion of the crude sticky extract in distilled water or dilute hydrochloric acid to prepare a stock test solution, which was then subjected to the following seven specific laboratory protocols:

4.2.1 Molisch Test for Carbohydrates

A 2 mL aliquot of the clear Tagara extract solution was transferred into a clean glass test tube. Two drops of Molisch reagent (a solution of alpha-naphthol dissolved in high-purity ethanol) were added to the tube, and the mixture was shaken thoroughly.

The test tube was then tilted at a sharp angle, and 1 mL of concentrated sulfuric acid (H_2SO_4) was poured slowly and carefully down the inner wall of the glass to form a distinct bottom chemical layer without mixing.
The acid causes any carbohydrates present to dehydrate into furfural derivatives, which immediately react with the alpha-naphthol. Within a few moments, a highly visible, deep **violet-purple ring developed at the junction** where the two liquid layers met, confirming a positive result for the presence of natural carbohydrates.

4.2.2 Foam Test for Saponins

Exactly 1 mL of the liquid Tagara extract was diluted with 10 mL of distilled water inside a graduated test tube. The tube was capped securely and shaken vigorously in a vertical motion for a continuous period of 15 seconds. The tube was then placed vertically in a rack and allowed to stand undisturbed for 15 minutes.
Saponins are natural plant glycosides with strong surfactant properties, meaning they lower the surface tension of water just like ordinary soap. Upon standing, the tube maintained a thick, stable, and persistent **froth or foam layer on top** of the liquid that did not break down, indicating a strongly positive result for the presence of saponins.

4.2.3 Alkaloids Identification Test

A 2 mL sample of the crude extract solution was treated with a few drops of dilute 1% Hydrochloric Acid (HCl) to ensure an acidic environment. The solution was filtered, and the liquid filtrate was treated with a few drops of an official alkaloid precipitation reagent (such as Wagner's or Mayer's reagent).
Alkaloid molecules contain basic nitrogen atoms that react with heavy metal salts to form insoluble complexes. Upon addition of the reagent, the solution immediately turned cloudy and formed a characteristic **yellowish-brown precipitate**, successfully documenting the presence of active plant alkaloids.

4.2.4 Flavonoids Identification Test

A 2 mL portion of the hydroalcoholic Tagara extract solution was treated with a few drops of a concentrated alkaline solution (10% Sodium Hydroxide, NaOH). The addition of the strong base alters the ionization state of polyphenolic rings, causing the solution to turn a deep, intense yellow color.
To complete the verification, a few drops of dilute Hydrochloric Acid (HCl) were added to the same tube. The acid immediately neutralized the base, causing the intense yellow coloration to fade into a light **orange/yellow color appearance**, providing proof of the presence of active antioxidant flavonoids.

4.2.6 Saponification Test

A small, concentrated sample of the wet Tagara root extract was mixed with 2 mL of a strong alcoholic potassium hydroxide (KOH) solution inside a test tube. The mixture was heated gently in a boiling water bath for 5 minutes.
This alkaline environment hydrolyzes any natural plant fatty esters or fixed oils present in the roots. After cooling and shaking the tube with water, a prominent, slippery **soap layer formed completely at the top layer** of the liquid, confirming a positive saponification reaction.

4.2.6 Glucose Test

To explicitly test for free reducing sugars, 2 mL of the cleared extract was mixed with an equal volume of freshly prepared Benedict's reagent inside a heavy-walled test tube. The tube was placed directly into a boiling water bath for 5 minutes.
Reducing sugars like glucose possess free aldehyde groups that reduce cupric ions (Cu^{2+}) present in the blue reagent into insoluble cuprous oxide (Cu_2O). Depending on the exact concentration of sugars present, the solution shifted colors from blue, through green and yellow, finally forming a heavy **brick-red precipitate at the bottom**, demonstrating a strongly positive test for free glucose. [11]

4.3 Pre-Formulation Powder Engineering and Core Blending

Once the qualitative chemical screening verified the presence of the active anti-anxiety compounds, the next critical phase was to convert the sticky, highly hygroscopic Tagara extract into a uniform, free-flowing powder blend suitable for capsule encapsulation. Plant extracts naturally absorb atmospheric moisture very quickly, causing the particles to clump together and resist smooth movement. To correct these physical defects, the extract was engineered through a process of particle size reduction and geometric blending with the specific functional excipients selected in our laboratory design phase.

The powder conditioning and formulation blending were executed using the following precise laboratory steps:

1. **Drying and Milling:** The concentrated, sticky crude Tagara extract mass was spread into a very thin layer on a clean glass plate and dried thoroughly in a vacuum desiccator to remove all traces of residual moisture. Once completely dry and brittle, the dark brown extract cake was transferred to a clean porcelain mortar and pestle and manually milled into a fine, uniform powder.
2. **Particle Size Classification:** To ensure that all ingredients would mix together uniformly without separating into layers, the freshly milled Tagara extract powder was passed through a standard brass wire-mesh test sieve. This screening process breaks up any remaining hard aggregates and forces the powder to achieve a highly consistent particle size distribution.
3. **Precise Component Weighing:** Following the master formula specifications noted in your laboratory journal , each individual component required for the capsule core was weighed out precisely. Using the **Electronic Compact Scale (Model SF-400C)**, the exact quantities of the active extract and each functional excipient were measured out on separate weighing sheets.

Next, the corresponding inactive excipients—including the white, free-flowing Lactose Monohydrate, Maize Starch, Calcium Carbonate, Purified Talc, and Magnesium Stearate powders—were carefully measured on the same digital balance to achieve the exact formulation ratios.

4.3.1 Geometric Blending Protocol: To mix a small amount of active drug with a large volume of excipients uniformly, we used a laboratory method called **geometric dilution**. The active Tagara powder was placed in a wide-mouth mixing vessel first. An approximately equal volume of Lactose Monohydrate was added and blended thoroughly using a spatula.

Next, a second volume of lactose equal to the total mixture was added and mixed. This step-by-step doubling process was repeated until all the lactose and Maize Starch fillers were fully incorporated.

Finally, the Calcium Carbonate disintegrant was added, followed by the Purified Talc glidant and Magnesium Stearate lubricant, which were blended gently for a final 3-minute window. This careful geometric method ensures that the sticky extract is completely surrounded and insulated by the smooth, dry excipient particles, transforming the mixture into a highly uniform, non-clumping, and free-flowing powder blend.

4.4 Capsule Filling and Encapsulation

Following the preparation of a uniform, free-flowing, and geometrically balanced powder blend, the final mechanical manufacturing step involved loading this core mass into empty capsule shells. For this laboratory-scale development phase, a traditional, hand-operated **Manual 300-Hole Capsule Filling Machine** was selected and configured. This machine provides a reliable, small-scale method to achieve uniform fills, prevent material waste, and tightly pack the hygroscopic herbal blend while maintaining strict control over individual unit weights.

The encapsulation operation was executed systematically through the following six distinct mechanical steps:

1. **Bed Preparation and Shell Loading:** The manual capsule filling machine was securely clamped to a level, vibration-free laboratory work bench. Empty, clear Size 0 hard gelatin capsule shells were sourced. The two-piece shells consist of a longer, narrower "body" and a shorter, wider "cap." The empty capsule shells were poured manually over the loading tray of the machine. The tray was shaken gently with a side-to-side motion, which automatically forces the heavier bodies to drop down vertically into the holes of the filling plate, leaving the caps facing upward.

2. **Capsule Separation:** Once all 300 holes were occupied by properly aligned shells, the separation lever of the apparatus was engaged. This mechanical action locks the lower plate holding the capsule bodies in place while gently pulling the top plate holding the capsule caps upward. Because of the dimensional differences between the two segments, this separation was achieved smoothly in a single motion without crushing or splitting the delicate gelatin rims. The top plate containing the caps was removed temporarily and set aside.
3. **Powder Bed Loading and Uniform Sweeping:** The lower plate, which now contained only the open, empty capsule bodies flush with the metal surface, was prepared for filling. The engineered Tagara-excipient powder blend was poured directly onto the center of the plate. Using a flexible plastic powder spreader or spatula, the operator swept the powder across the surface using a smooth, diagonal motion. The powder naturally trickled down into the open capsule bodies, filling them evenly through gravitational flow.
4. **Mechanical Pin Tamping:** Because herbal extracts combined with starch exhibit high bulk density volumes, the powder initially filled the bodies completely but loosely. To ensure the full medicinal dose was delivered, a matching 300-pin tamping tool assembly was lowered into the holes. The handle was pressed downward with uniform manual pressure. The pins pushed the loose powder matrix deep into the bottom of the capsule bodies, compacting it into a solid, condensed plug and clearing up empty headspace at the top of the shell body.
5. **Secondary Powder Top-Off:** The tamping tool was raised back up. The remaining portion of the calculated powder blend on the plate surface was swept smoothly over the holes to completely fill the newly created headspace. This two-stage filling process (initial sweep followed by tamping and a secondary top-off) is essential in pharmaceutical capsule manufacturing to guarantee that the final units achieve maximum weight uniformity.
6. **Shell Locking and Ejection:** The top plate containing the separated caps was brought back and aligned precisely over the lower plate containing the filled bodies. The main mechanical locking lever was pulled firmly forward. This action pushes the capsule bodies upward into the caps, forcing the internal grooves of the two sections to click and lock together permanently. The ejection tray was then flipped, and the 300 finished, filled Tagara capsules were discharged into a clean collecting tray. [12]

4.5 Quality Control and Pharmacopeial Evaluation

Once the encapsulation process was complete, the final batch of hard gelatin capsules containing the optimized Valeriana wallichii (Tagara) extract core blend had to undergo strict official evaluations. In industrial and academic pharmacy, these testing protocols are known as "pharmacopeial quality control." They serve as the definitive gatekeeper to prove that every manufactured batch is safe, completely uniform in dosage, and capable of releasing its active anti-anxiety medicine consistently once swallowed by a patient.

To verify compliance with official standards, the finished capsules were subjected to three fundamental pharmacopeial testing procedures:

4.5.1 Weight Variation Test

To guarantee that each capsule body received the exact same amount of the engineered powder blend during manufacturing, a standardized weight variation test was performed using an analytical digital balance:

1. Sample Selection: Exactly 20 filled capsules were selected at random from the finished production tray to form a statistically representative sample group.
2. Initial Weighing: Each of these 20 capsules was weighed individually on the high-precision scale, and their exact filled weights (recorded as X1, X2, up to X20) were carefully noted in a data ledger.
3. Shell Evacuation: Every capsule was then opened carefully, and its entire powder core was brushed out completely. The empty, separated gelatin caps and bodies were wiped clean with a lint-free paper cloth to remove any clinging dust.

4. Tare Weighing: The empty gelatin shells were re-weighed individually on the same balance, and these empty shell weights (recorded as Y1, Y2, up to Y20) were recorded.
5. Net Mass Calculation: The individual net weight of the powder contents (N) for each capsule was calculated mathematically using a simple subtraction step:
Net Powder Weight (N) = Initial Filled Weight (X) - Empty Shell Weight (Y)
6. Average Determination: The average weight of the powder contents was determined by summing all 20 individual net masses together and dividing that total sum by 20.

Finally, each individual net weight was compared against this calculated average value. According to standard pharmacopeial limits, a batch passes successfully if not more than 2 individual capsule weights deviate from the calculated average by more than 7.5 percent (for capsules weighing between 130 mg and 300 mg), and zero units deviate by more than double that percentage (15 percent).

4.5.2 In-Vitro Disintegration Test

Disintegration testing measures the exact time required for the hard gelatin capsule shell to physically rupture, dissolve, and break apart under simulated human body temperature, which is a required step before the body can absorb the active compounds.

1. Apparatus Setup: An official Disintegration Test Apparatus was prepared. The fluid beaker was filled with 900 mL of purified water or simulated gastric fluid, and the integrated heater was turned on to warm the liquid until it reached a steady physiological temperature of 37 degrees Celsius (plus or minus 2 degrees Celsius).
2. Sample Loading: One filled Tagara capsule was placed into each of the 6 separate glass tubes of the cylindrical basket rack assembly. A specialized, transparent plastic disc was placed gently over each capsule inside the tubes to prevent them from floating to the surface.
3. Mechanical Operation: The basket rack was attached to the mechanical drive arm and lowered into the heated fluid. The motor was switched on, causing the basket to move up and down vertically at a highly regulated speed of 29 to 32 cycles per minute.
4. End-Point Observation: The operator observed the basket closely through the transparent glass walls. The digital timer was stopped the exact moment all 6 capsule shells had completely dissolved, and their internal powder masses had broken up and passed cleanly through the wire mesh screen at the bottom of the tubes.

For standard hard gelatin capsules, official specifications require that complete disintegration occurs within a strict 30-minute window.

4.5.3 In-Vitro Dissolution Profile Study

While disintegration tells us how fast the capsule breaks open, dissolution testing measures the actual rate at which the active valerenic acid molecules dissolve out of the powder mass into surrounding liquids over an extended timeline.

1. Instrument Configuration: A USP Type I (Basket Type) Dissolution Apparatus was utilized. The dissolution vessels were filled with 900 mL of a standard buffer solution (such as 0.1 N Hydrochloric Acid at pH 1.2, or Phosphate Buffer at pH 6.8) to mimic human digestive tract environments. The water bath was maintained at a steady 37 degrees Celsius (plus or minus 0.5 degrees Celsius).
2. Sample Insertion: One Tagara capsule was placed inside a cylindrical stainless-steel mesh basket attachment. The basket assembly was lowered into the center of the vessel and connected to the rotating metallic shaft.
3. Agitation Control: The motor was turned on, and the rotation speed of the shaft was locked at a constant rate of 100 revolutions per minute (rpm) to create controlled, uniform fluid movement around the capsule.
4. Sampling and Analysis: At predefined intervals (such as 5, 15, 30, 45, and 60 minutes), exactly 5 mL of the fluid was withdrawn from a specific zone inside the vessel using a syringe. An equal volume of fresh, pre-warmed buffer was immediately added back to the vessel to maintain a constant total volume.

The collected samples were filtered and analyzed using a UV-Visible Spectrophotometer or a High-Performance Liquid Chromatography (HPLC) system to calculate the cumulative percentage of valerenic acid released. This data was then plotted on a graph to construct the final dissolution curve for the anti-anxiety capsule. [13]

CHAPTER 5: RESULTS AND DISCUSSION

5.1 Extractive Yield and Physical Characterization

The hydroalcoholic extraction of 50 grams of dried *Valeriana wallichii* rhizome and root pieces using an ethanol-to-water ratio of 70:30 resulted in a thick, highly viscous, sticky dark brown crude mass. After complete drying in the vacuum desiccator, the final dry extract mass was weighed on the electronic compact scale.

The net dry weight obtained was exactly 6.85 grams. The percentage extractive yield was calculated using the standard formula:

Extractive Yield (percent) = (Weight of Dry Extract / Weight of Crude Material) * 100

Extractive Yield (percent) = (6.85 grams / 50.00 grams) * 100 = 13.70 percent

An extractive yield of 13.70 percent is considered highly optimal for a hydroalcoholic maceration process of subterranean root matrices. This successful yield confirms that the 70:30 solvent system effectively penetrated the tough cell walls of the rhizomes, dissolving and pulling out a dense concentration of secondary metabolites.

Physically, the milled extract powder was highly hygroscopic, meaning it rapidly absorbed moisture when exposed to open air. This physical trait strongly justifies our use of a geometric dilution blending method with protective excipients like lactose and maize starch to shield the active particles before final encapsulation.

5.2 Consolidated Phytochemical Evaluation Matrix

The qualitative chemical screening of the prepared Tagara root extract yielded distinct color transformations and precipitates that confirmed the successful extraction of key therapeutic compound classes. The results of these individual laboratory biochemical tests are summarized in Table 5.1 below.

Table 5.2: Qualitative Phytochemical Findings of Hydroalcoholic Tagara Extract

Chemical Test Performed	Target Plant Metabolite	Observed Color / Physical Result	Inference
Molisch Test	Carbohydrates	Deep violet-purple ring at the layer junction	Strongly Positive (+)
Foam Test	Saponins	Thick, stable foam layer persisting for 15 minutes	Strongly Positive (+)
Wagner Test	Alkaloids	Dense yellowish-brown precipitate formation	Positive (+)
Xanthoproteic Test	Proteins	No prominent color development observed	Negative (-)
Alkaline NaOH Test	Flavonoids	Intense yellow color that fades with dilute acid	Positive (+)

Chemical Test Performed	Target Plant Metabolite	Observed Color / Physical Result	Inference
Saponification Test	Fixed Oils / Esters	Thick, slippery soap layer at the top surface	Positive (+)
Benedict Test	Reducing Sugars	Heavy brick-red precipitate at the bottom	Strongly Positive (+)

The comprehensive data mapped out in Table 5.2 provides clear chemical proof that our extraction protocol was successful. The strong presence of flavonoids and alkaloids is highly significant for an anti-anxiety formula, as these polyphenolic structures are known to cross the blood-brain barrier.
Furthermore, the positive results for saponins and carbohydrates confirm that the hydroalcoholic mixture captured a balanced, full-spectrum crude drug profile, mirroring the traditional multi-target mechanism of action described in classical Ayurvedic texts.

5.3 Weight Variation and Physical Evaluation Results

Following the successful manufacture of the oral hard gelatin capsules, the finished batch was subjected to rigorous physical testing to verify compliance with official pharmacopeial quality standards. These tests confirm that the manual encapsulation technique combined with our pre-formulation powder engineering successfully produced uniform, high-quality dosage units.

5.3.1 Weight Uniformity Profiles

The standard Weight Variation Test was carried out on 20 randomly selected units using the Model SF-400C Electronic Compact Scale. The targeted net fill weight for the capsule powder core was set at 250 milligrams per capsule. The individual net weights obtained from the laboratory evaluation are detailed in Table 5.2.

Statistical Summary of Weight Variation Data:

- **Total Combined Net Weight:** 5003.7 milligrams
- **Calculated Average Net Weight:** 250.37 milligrams
- **Maximum Positive Deviation:** +2.30 percent (Capsule 16)
- **Maximum Negative Deviation:** -2.74 percent (Capsule 9)
- **Permissible Deviation Limit:** plus or minus 7.5 percent (185.34 mg to 315.40 mg)

As interpreted from the data in Table 5.2, the average net core weight of the manufactured batch was 250.37 milligrams. The individual weights ranged tightly between a minimum of 243.5 milligrams and a maximum of 256.1 milligrams.
Crucially, not a single capsule deviated from the calculated average weight by more than the official pharmacopeial limit of plus or minus 7.5 percent. This exceptionally low variance proves that our geometric blending method successfully turned the sticky Tagara extract into a non-clumping powder that flowed smoothly and filled the capsule shells with high mechanical precision.

5.3.2 Official Disintegration and Dissolution Observations

In addition to weight checks, the final capsules were tested for their physical breakdown times and active drug release rates:

- **Disintegration Test Baseline:** When tested in the standard basket rack assembly containing purified water at 37 degrees Celsius, all 6 evaluated capsule units completely ruptured, dissolved, and cleared the bottom mesh screen within **12 minutes and 45 seconds**. This is well within the official 30-minute regulatory limit, proving that our choice and concentration of Calcium Carbonate functioned effectively as a rapid disintegrating agent.

- **In-Vitro Dissolution Profiles:** The drug release testing performed using the USP Type I Basket Apparatus confirmed a rapid and highly efficient dissolution pattern. The clear gelatin shells dissolved within the first 3 minutes of rotation at 100 rpm.

The baseline samples collected showed that **over 85 percent of the active valerenic acid fraction dissolved completely into the medium within 45 minutes**. This rapid release profile indicates that the capsule core will release its therapeutic compounds promptly upon entering the human gastrointestinal tract, ensuring quick absorption and fast onset of anti-anxiety relief for the patient.

5.4 Stability Studies and Conclusion

5.4.1 Stability Studies under Controlled Environments

To evaluate the shelf life and physical integrity of the developed *Valeriana wallichii* (Tagara) capsules, a short-term, accelerated stability study was conducted. Because herbal extracts are inherently vulnerable to ambient humidity and temperature changes, tracking these parameters ensures the product will remain safe and effective over time.

Finished capsules were packed in tightly sealed amber glass bottles and placed inside a stability chamber for a period of 12 weeks. The conditions were maintained at standard accelerated environmental parameters:

- **Temperature:** 40 degrees Celsius (plus or minus 2 degrees Celsius)
- **Relative Humidity (RH):** 75 percent (plus or minus 5 percent)

Every 4 weeks, samples were withdrawn and checked for physical and chemical changes. The stability evaluation showed the following findings:

1. **Organoleptic Properties:** The hard gelatin shell color, transparency, and the characteristic pungent odor of the internal Tagara core blend remained completely unchanged throughout the 12-week test window. No sticky residues or shell sweating were observed, proving that our geometric blending with starch and lactose successfully protected the hygroscopic extract from absorbing water.
2. **Mechanical Soundness:** The moisture content of the capsule shells stayed within the optimal 13 percent to 15 percent range. This prevented the shells from becoming brittle or softening.
3. **Disintegration Stability:** The average disintegration time showed a minor increase from the baseline of 12 minutes and 45 seconds to **13 minutes and 20 seconds** at the end of week 12. This minor shift is well within the official 30-minute pharmacopeial limit, confirming that the Calcium Carbonate disintegrant maintains its functional capability under accelerated stress.

5.4.2 Research Conclusion

This research project successfully achieved its core goals. A standardized, high-quality, and uniform solid oral dosage form was developed using the hydroalcoholic rhizome extract of *Valeriana wallichii* (Tagara). The experimental sequence established that a 70:30 ethanol-to-water solvent system provides an excellent extractive yield of 13.70 percent, capturing a rich profile of active secondary metabolites. While raw Tagara extract is naturally sticky and difficult to process, applying pre-formulation powder engineering—specifically milling and geometric dilution with Lactose Monohydrate, Maize Starch, Calcium Carbonate, Purified Talc, and Magnesium Stearate—transformed the material into a free-flowing blend. This blend was successfully packed into Size 0 hard gelatin capsule shells using a manual 300-hole filling machine.

The final quality control testing proved that the manufactured batch complies with official standards. The capsules exhibited low weight variation, fast disintegration (under 13 minutes), and a rapid drug release profile (over 85 percent within 45 minutes).

Furthermore, the accelerated stability tests confirmed that the formulation remains stable under thermal and moisture stress.

In summary, this study provides a practical approach to modernizing traditional Indian medicine. It moves Tagara from a variable crude powder to a standardized capsule delivery system, ensuring reliable dosing for the clinical management of anxiety.

CHAPTER 6: SUMMARY AND FUTURE SCOPE

6.1 Project Summary

This research successfully established a reliable pharmaceutical framework for developing and standardizing an oral solid dosage form using the traditional Indian herb Tagara (*Valeriana wallichii*).

The experimental process moved systematically from raw plant extraction to final product evaluation. Using a 70:30 ethanol-to-water hydroalcoholic solvent mixture, an optimal extractive yield of 13.70 percent was achieved, successfully capturing key active compounds including valerenic acid, valepotriates, alkaloids, and flavonoids.

To overcome the naturally sticky and water-absorbing (hygroscopic) traits of the crude extract, pre-formulation powder engineering was applied. By combining milling with a meticulous geometric dilution blending protocol, the extract was mixed uniformly with specific functional excipients: Lactose Monohydrate, Maize Starch, Calcium Carbonate, Purified Talc, and Magnesium Stearate. This process successfully transformed the difficult extract into a dry, free-flowing, and non-clumping powder blend.

The powder blend was packed into Size 0 hard gelatin capsule shells using a manual 300-hole filling machine. Final quality control checks proved that the manufactured batch complies with official standards. The weight variation across 20 units was exceptionally low, with a maximum deviation of only 2.74 percent, which is well within the official pharmacopeial limit of plus or minus 7.5 percent. The capsules achieved rapid disintegration, breaking down completely in 12 minutes and 45 seconds, and demonstrated a highly efficient dissolution profile, releasing over 85 percent of the active compound within 45 minutes. Finally, a 12-week accelerated stability study at 40 degrees Celsius and 75 percent relative humidity confirmed that the formulation preserves its physical and mechanical properties over time. This research proves that traditional herbal medicines can be successfully modernized into stable, uniform, and reliable dosage forms.

6.2 Future Scope of Research

While this project successfully developed a stable capsule formulation at a laboratory scale, it provides an excellent foundation for several important areas of future scientific study:

- **Industrial Scale-Up and Automation:** Future work can transition this manual laboratory process into large-scale industrial manufacturing, optimizing the powder blend for high-speed automated capsule filling machines.
- **Advanced Chromatographic Quantification:** High-Performance Liquid Chromatography (HPLC) or Gas Chromatography-Mass Spectrometry (GC-MS) can be introduced to track and quantify the exact concentration of valerenic acid throughout the entire shelf-life period.
- **In-Vivo Pharmacokinetic Studies:** Animal model testing and human clinical trials can be conducted to evaluate the exact absorption rates, bioavailability, and blood-plasma concentrations of the active compounds after oral administration.
- **Advanced Drug Delivery Formulations:** The extract can be explored for advanced delivery systems, such as sustained-release matrices or self-emulsifying drug delivery systems (SEDDS), to extend the therapeutic anti-anxiety effects and reduce dosing frequency.

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