World Journal of Pharmaceutical and Life Sciences
WJPLS
www.wjpls.org
SJIF Impact Factor: 7.409

REVIEW ON FORMULATION AND EVALUATION OF HERBAL CAPSULE FROM NATURAL HERBS USED AS RESPIRATORY STIMULANTS

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Article Received on 17/01/2025 **Article Revised on 06/02/2025** **Article Accepted on 26/02/2025**

ABSTRACT
A comprehensive review on the formulation and evaluation of herbal capsules examines the methodologies involved in developing these dosage forms and assesses their quality and efficacy. The review emphasizes the importance of standardizing herbal extracts to ensure consistent potency and safety. It discusses various formulation strategies, including the selection of appropriate excipients, encapsulation techniques, and the optimization of manufacturing processes to maintain the integrity of active compounds. Additionally, the review highlights the significance of rigorous evaluation methods, such as physicochemical testing, stability studies, and in vitro dissolution testing, to ensure the capsules meet established quality standards. By addressing these critical aspects, the review provides valuable insights into the development of effective and reliable herbal capsule formulations.

KEYWORDS: Preformulation, Capsule, Compatibility, Natural herbs, Extraction, % Release.

INTRODUCTION

Polyherbal capsules are a formulation of multiple herbs or plant-based ingredients combined in a single dosage form. These capsules are created with the aim of maximizing the therapeutic benefits by combining the synergistic properties of various herbs, each of which contributes specific medicinal benefits. Herbal medicine has been an integral part of traditional healing systems like Ayurveda, Traditional Chinese Medicine (TCM), and Unani for centuries. In recent years, the demand for herbal supplements, including polyherbal formulations, has significantly increased due to their perceived natural and holistic approach to health and wellness.

A polyherbal capsule consists of a combination of more than one herb or plant-based extract encapsulated into a convenient dosage form. These herbal formulations are intended to enhance health and treat various conditions, often targeting multiple physiological systems at once. The herbs selected for these formulations may act synergistically, improving the overall therapeutic outcome.

The formulation generally contains: Herbal extracts: The concentrated form of active ingredients derived from plants.

Excipients: Non-active ingredients, such as binders, fillers, stabilizers, and preservatives, that helps in the preparation and delivery of the herbal ingredients.

Capsule Shell: The outer shell of the capsule, typically made from gelatin or vegetarian materials (like HPMC - Hydroxypropyl methylcellulose) for vegan-friendly capsules.

Advantages of Polyherbal Capsules

Synergistic Action: When herbs are combined in a formulation, they can produce a synergistic effect, where the combined activity of the herbs is greater than the sum of their individual actions. This can lead to better efficacy with fewer side effects.

Broad-Spectrum Therapeutic Effects: By combining different herbs with complementary actions, polyherbal capsules can target multiple health issues simultaneously. For example, a polyherbal capsule for respiratory health might include herbs that support lung function, reduce inflammation, and boost immunity.

Reduced Side Effects: Herbal combinations can often minimize adverse reactions that may occur when individual herbs are used in higher doses. The safety

profile is usually enhanced when herbs with complementary actions are combined.

Convenient Dosage Form: Polyherbal capsules offer an easy and convenient way to consume a variety of herbal ingredients in a single dose, eliminating the need to consume multiple tablets or extracts.

Natural and Holistic Approach: Polyherbal capsules appeal to individuals seeking natural remedies and those who prefer to avoid synthetic medications.

The **quality** and **effectiveness** of polyherbal capsules depend heavily on the selection and combination of Polyherbal capsules represent an innovative and holistic approach to health and wellness, combining the best of multiple herbs in a single dosage form. These formulations are increasingly favored by those looking for **natural**, **synergistic**, and **effective** alternatives to pharmaceutical drugs. However, their development requires a thorough understanding of herbal properties, appropriate formulation techniques, and robust quality control to ensure safety and effectiveness.

MECHANISM OF HERBAL DRUG RELEASE

The mechanism of herbal drug release from capsules involves various processes that determine how the active compounds from the herbal ingredients are released and absorbed in the body. The mechanism can be influenced by the type of capsule, the herbal formulation, and the excipients used. Here's an overview of the key mechanisms involved.

1. Disintegration

Process: Upon ingestion, the capsule shell (whether hard or soft) disintegrates in the stomach due to the action of gastric fluids (acidic environment, enzymes).
Role: The disintegration allows the herbal contents (powder, granules, or liquid) to be exposed to the gastrointestinal tract, initiating the drug release process.

2. Dissolution

Process: After disintegration, the active herbal ingredients dissolve in the fluid present in the gastrointestinal tract (e.g., stomach acid, bile, digestive juices).
Role: This is a crucial step where the herbal compounds are broken down into smaller particles or dissolved in the fluid to become available for absorption.
Influencing Factors: pH of the gastrointestinal tract, solubility of the herbal compounds, presence of food, and the excipients used (e.g., binders, stabilizers) can affect dissolution rate.

3. Diffusion

Process: The dissolved herbal compounds diffuse across the biological membranes (such as the intestinal wall) into the bloodstream.
Role: This mechanism is responsible for the movement of the active ingredients from the gastrointestinal tract to the systemic circulation, where they can exert their therapeutic effects.
Influencing Factors: The permeability of the intestinal membranes and the molecular size of the herbal active compounds determine how efficiently they diffuse.

4. Controlled or Sustained Release (if applicable)

Process: Some capsules are formulated for controlled or sustained release, meaning the active herbal ingredients are released over an extended period rather than all at once.
Role: This ensures that the herb's effects are prolonged and that the compound is gradually released at a steady rate, which can help maintain therapeutic levels in the bloodstream.
Mechanism: This release is often controlled by specific excipients, such as:
Polymer-based coatings: Used for time-release or enteric-coated capsules that release the contents at specific sites (e.g., the intestines).
Matrix systems: Where the active ingredient is dispersed within a matrix that slowly dissolves, providing controlled release.

5. Errosion/Swelling (for hydrophilic polymers or matrix systems)

Process: Some capsules, especially those made with hydrophilic polymers, may swell or erode upon contact with water in the gastrointestinal tract. This erosion gradually releases the herbal ingredients.
Role: The gradual erosion helps in the controlled release of the active compounds from the herbal formulation, maintaining their therapeutic levels over a longer period.

6. Enzymatic Degradation

Process: In certain cases, the active compounds within the herbal drug may be broken down or activated by enzymes present in the gastrointestinal tract, such as proteases, amylases, or lipases.
Role: Enzymatic activity can enhance or modify the release of certain herbal compounds, especially those that need activation before they become bioavailable.

7. pH Sensitivity

Process: Some capsules are designed to release their contents only when they reach a specific pH (e.g., in the intestines) to prevent premature release in the stomach.
Role: Enteric-coated capsules are designed to withstand the acidic pH of the stomach and only dissolve when they reach the higher pH environment of the small intestine, allowing for targeted release.

Factors Affecting Herbal Drug Release

Herbal Extract Composition: The chemical composition of the herb plays a significant role in its solubility and bioavailability.

Capsule Type: Hard gelatin capsules, soft gelatin capsules, and plant-based capsules (e.g., HPMC) can affect the rate and mechanism of release.

Excipients: Additives like binders, fillers, stabilizers, and disintegrants can influence how quickly or slowly the capsule disintegrates and releases the herbal contents.

Particle Size: Finer particles generally dissolve faster and are absorbed more readily.

The release of herbal drugs from capsules is a complex process involving multiple steps, including disintegration, dissolution, diffusion, and, in some cases, controlled release. The formulation, encapsulation techniques, and specific herbal properties play a crucial role in how quickly and effectively the herbal ingredients are delivered and absorbed in the body.

Herbs used as respiratory stimulant: Several herbs are commonly used as respiratory stimulants, particularly for improving breathing and supporting lung function. Here are some herbs known for their beneficial effects on the respiratory system.

Adhatoda vasica (Vasaka) – Known for its bronchodilator and expectorant properties, it helps in treating cough, asthma, and bronchitis.

Eucalyptus (Eucalyptus globulus) – Its oil is often used for its decongestant and antiseptic properties, which aid in clearing the airways and improving respiration.

Peppermint (Mentha piperita) – Contains menthol, which helps relax the muscles of the respiratory tract, eases breathing, and has soothing properties for the throat.

Ginger (Zingiber officinale) – Known for its anti-inflammatory properties, ginger can help with respiratory infections, reducing inflammation in the airways.

Licorice Root (Glycyrrhiza glabra) – Acts as a soothing agent for sore throats and helps with chronic coughs by clearing mucus and reducing inflammation.

Thyme (Thymus vulgaris) – Contains antimicrobial properties and acts as an expectorant, helping to clear mucus from the lungs.

Honey (not a herb, but often combined with herbs) – Known for its soothing and antimicrobial properties, honey helps in relieving cough and irritation in the throat.

Holy Basil (Ocimum sanctum) – Also known as Tulsi, this herb has anti-inflammatory, antimicrobial, and adaptogenic properties, which support lung health and immunity.

Black Pepper (Piper nigrum) – Contains piperine, which may help in stimulating breathing and relieving congestion.

Mullein (Verbascum thapsus) – Known for its soothing effect on the respiratory tract and used for treating asthma, coughs, and bronchial inflammation.

Cinnamon (Cinnamomum verum) – Helps improve circulation and can ease the discomfort of respiratory issues by acting as an expectorant.

Slippery Elm (Ulmus rubra) – Known for its soothing effects on the mucous membranes, it helps reduce inflammation in the throat and respiratory tract.

These herbs can be used individually or combined in polyherbal formulations to provide respiratory support, especially for conditions like asthma, bronchitis, and coughs. Always consult with a healthcare provider before starting any herbal remedy, especially for those with pre-existing conditions.

Reason behind usage of herbs in capsule forms: Herbs are increasingly being used in capsule form for several reasons, making them a convenient and effective way to deliver their benefits. Here are the key reasons why herbal supplements are commonly found in capsule form.

1. **Convenience and Ease of Use**: Capsules are easy to swallow, and they offer a quick and hassle-free way to consume herbs without the need for preparation (e.g., brewing teas or mixing powders).
   They are portable and can be taken on the go, making it easier for people to incorporate herbal remedies into their daily routine.
2. **Accurate Dosage:** Capsules offer a precise and consistent dose of the herb, which is essential for ensuring effectiveness and safety. Unlike teas or powders, where the concentration can vary depending on preparation methods, capsules provide a controlled amount of active ingredients.
3. **Taste Masking**: Some herbs can have strong, bitter, or unpleasant flavors, making them difficult to consume. Capsules mask the taste, making it more palatable for individuals who would otherwise struggle with the flavor of certain herbs.
4. **Preservation and Stability:** Capsules protect the active compounds in herbs from degradation caused by exposure to air, moisture, or light. This improves the shelf life and stability of the herb's active ingredients, preserving their potency over time.
5. **Targeted Release and Bioavailability**: Modern capsule technologies, such as enteric-coated or time-release capsules, can enhance the bioavailability of herbal compounds, ensuring that they are released at the right time and place in the digestive system for maximum absorption.
6. **Formulation Flexibility**: Capsules can be easily formulated with multiple herbs in combination, making it easier to create polyherbal formulations that target specific health conditions. This is especially useful in creating supplements for respiratory, digestive, or immune system support.

7. **Reduced Risk of Contamination:** Capsules help prevent contamination of the herb by handling, storage, or environmental factors that could affect the raw plant material. They also eliminate the need for potentially harmful additives or chemicals in the preparation process.
8. **Precise Herbal Standardization**: Manufacturers can standardize the amount of active compounds in herbal capsules. This standardization ensures that each capsule contains a consistent amount of the herb's active ingredients, which is essential for safety and efficacy.
9. **Compliance and Preference:** Some individuals prefer capsules over liquid or powder forms of herbal remedies because of ease of use and lack of mess. The capsule form may improve adherence to a treatment plan, as people are more likely to consistently take their supplements when they are convenient.

   In summary, capsules offer a convenient, precise, and stable way to deliver herbal remedies while improving compliance and ease of use for individuals seeking natural health solutions.

Selection of size of capsule for herbal capsule: The size of a capsule used for herbal formulations depends on several factors, including the type of herbal ingredient, the dose required, and the target market. However, **size 00** and **size 0** are the most commonly preferred sizes for herbal capsules. Here's a breakdown of why these sizes are commonly used and when other sizes might be chosen.

1. Size 00 (Most Preferred)

Capacity: Approximately 400-500 mg of powder or granules.

Ideal for most herbal formulations: Size 00 capsules are large enough to accommodate a reasonable amount of herbal powder while remaining easy to swallow for most people.

Common for daily dosages: Many herbal remedies require a higher dosage to be effective, and size 00 can hold enough active ingredients to match those dosages without the need for multiple capsules.

Convenience: It's a good balance between a sufficient dose and ease of swallowing.

2. Size 0

Capacity: Approximately 300-400 mg of powder.

Moderate Dosages: For herbs that require a slightly lower dose, size 0 works well.

Easier to swallow: For individuals who may have difficulty swallowing larger capsules, size 0 is a more comfortable option.

Larger market: It's still a widely used size for herbal supplements.

3. Size 1

Capacity: Approximately 200-300 mg of powder.

Smaller doses: When the herbal formulation requires a smaller dose per capsule, size 1 is suitable.

For blends: Herbal blends that require less of each ingredient may be packaged in size 1 capsules.

For children or people with swallowing difficulties: Size 1 is smaller and easier to swallow for those who have trouble with larger capsules.

4. Size 2

Capacity: Approximately 100-200 mg of powder.

Lower doses: When very small doses are needed, size 2 is appropriate.

For potent herbs: Herbs that are highly concentrated or potent in nature may be placed in smaller capsules to maintain proper dosing.

5. Size 3 (Less Common for Herbal Capsules)

Capacity: Approximately 75-100 mg of powder.

Very small doses: Size 3 is typically used for very concentrated herbs or when a very low dose is required.

Usually for highly potent herbal extracts: When only a small amount of the active compound is needed.

Factors to Consider for Choosing Capsule Size

Herb Dosage Requirements: The required dosage for the herb plays a major role in capsule size selection. If the herb requires a larger dose to be effective, a larger capsule size like 00 will be necessary.

Herb's Density: The density of the herbal powder can impact how much can fit into a given capsule. More compact, concentrated powders may need smaller capsules, while loose powders may need larger capsules.

Swallowing Ability: Some people, especially children or the elderly, may have difficulty swallowing larger capsules, so smaller sizes like 0 or 1 are often preferred for ease of consumption.

Cost and Manufacturing: Larger capsules like size 00 might be more cost-effective for manufacturers because they require fewer capsules per dose, which can reduce packaging costs. However, this must be balanced with the ability of consumers to comfortably swallow them.

Regulatory Guidelines: In some cases, regulatory guidelines may dictate the size of capsules for specific formulations, especially for products intended for mass consumption.

Size 00 is generally the most popular and preferred size for herbal capsules, as it can accommodate a suitable amount of herbal powder while remaining practical for most people to swallow.

Size 0 and **size 1** are also used depending on the dosage and target market.

Compatibility studies of herbs with excipient: The compatibility of herbs with excipients (inactive ingredients used in the formulation of herbal capsules) is crucial to ensure that the active ingredients in the herbs

are effectively delivered and that the product remains stable, safe, and effective over time. Below are the key factors and examples of excipients used in herbal formulations, along with their compatibility considerations.

1. Types of Excipients Used in Herbal Capsule Formulations

Excipients in herbal capsules can be classified into different categories based on their function.

Binders: Help hold the powder together in the capsule. Examples include cellulose, starch, and gum-based excipients.

Disintegrants: Assist in the disintegration of the capsule shell, ensuring that the active ingredients are released effectively. Examples include croscarmellose sodium, sodium starch glycolate.

Fillers (Diluents): Increase the volume of the capsule and provide bulk. Examples include microcrystalline cellulose (MCC), calcium carbonate, or lactose.

Lubricants: Help in smooth capsule filling and prevent sticking during production. Examples include magnesium stearate, stearic acid, or silica.

Glidants: Improve the flowability of the powder mixture. Examples include talc or silicon dioxide.

Coatings: Protect the active ingredient and/or control the release. Examples include gelatin, hydroxypropyl methylcellulose (HPMC), or enteric coatings.

2. Factors Affecting Compatibility

When selecting excipients for herbal formulations, the following factors should be considered:

a) Chemical Stability

Compatibility with Active Compounds: Some herbs contain active compounds that are chemically reactive and may degrade when exposed to certain excipients. For example, flavonoids or alkaloids may degrade in the presence of acidic or alkaline excipients. Therefore, neutral or mild excipients should be chosen to avoid chemical instability.

Oxidation: Some herbs are sensitive to oxidation, and excipients like antioxidants (e.g., ascorbic acid or tocopherols) may be added to prevent the degradation of sensitive compounds.

b) Physical Stability

Moisture Sensitivity: Certain herbs are sensitive to moisture, which can cause degradation or clumping. Excipients like silica or magnesium stearate are often added as desiccants or flow agents to control moisture content.

Temperature Sensitivity: If herbal ingredients are heat-sensitive, excipients should be chosen that do not require high temperatures during the encapsulation process.

c) Bioavailability

Absorption Enhancement: Some excipients can enhance the absorption of herbal compounds. For example, piperine, a compound found in black pepper, is often used in herbal formulations to increase the bioavailability of other active compounds (such as curcumin from turmeric).

Controlled Release: Excipients like hydroxypropyl methylcellulose (HPMC) are used to create controlled-release capsules, ensuring that herbal compounds are released gradually to enhance their therapeutic effects over time.

d) Gelatin vs. Vegetarian Capsules

Gelatin Capsules: Made from animal-derived collagen, gelatin capsules are commonly used but may not be compatible with all herbal formulations, especially for vegan or vegetarian consumers.

Vegetarian Capsules: Made from plant-derived materials like hydroxypropyl methylcellulose (HPMC), these are often preferred for herbal products that need to align with vegetarian or vegan lifestyles. The compatibility of herbal extracts with HPMC capsules is generally good since the material is neutral and does not interfere with most herbal compounds.

3. Examples of Herbal-Excipients Compatibility

a) Herbal Extracts and Cellulose Derivatives

Cellulose (e.g., microcrystalline cellulose, HPMC) is commonly used in herbal formulations as a filler, binder, and capsule shell. It is compatible with most herbal extracts and has minimal impact on bioavailability.

Incompatibilities: Cellulose may not work well with very oily extracts, as it does not dissolve in oil-based formulations.

b) Gums and Mucilages

Gums (e.g., guar gum, xanthan gum) and mucilages (e.g., from slippery elm) are used as binders or stabilizers in herbal formulations. They are generally well-compatible with herbal powders, as they help form a stable capsule matrix.

Incompatibilities: These gums can absorb moisture and may cause clumping, leading to inconsistent dosing. Therefore, moisture-sensitive herbs should be carefully considered when using gums.

c) Magnesium Stearate and Herb Compatibility

Magnesium stearate is a commonly used lubricant that helps prevent capsule contents from sticking to the manufacturing machinery. However, it may interfere with the dissolution of some herbal ingredients, as it forms a coating around the powder. This can slow down the release of active ingredients.

Incompatibilities: Herbs requiring fast release or highly soluble compounds might have reduced bioavailability due to the presence of magnesium stearate.

d) Silicon Dioxide and Flowability

Silicon dioxide (silica) is used to improve powder flowability during encapsulation. It generally has no adverse effects on most herbal ingredients and is often added to ensure uniformity in capsule filling.

Compatibility: Silicon dioxide works well with most herbal powders but should be used in moderation, as excessive amounts could cause the powder to become too dry or dense, impacting dissolution.

4. Potential Herb-Excipient Interactions

Tannins (found in herbs like tea) can interact with excipients like iron salts, reducing the bioavailability of both the herb and the excipient.

Alkaloids (found in herbs like goldenseal or poppy) may interact with excipients like sugars or gums, leading to reduced stability or therapeutic effects.

5. Stability Testing

Before releasing a product into the market, it is important to conduct compatibility testing to ensure that the herbal ingredients and excipients remain stable over time. This includes.

Physicochemical stability testing: Assessing any degradation or interaction between the herb and excipients.

Dissolution studies: Ensuring that the herbal components are released effectively.

Shelf-life studies: Evaluating the product's stability over time under different storage conditions.

The compatibility of herbs with excipients is essential for ensuring the effectiveness, safety, and stability of herbal capsules. Factors such as chemical, physical, and bioavailability considerations must be taken into account when selecting excipients. Conducting thorough compatibility and stability testing is crucial to produce high-quality herbal capsules that deliver the desired therapeutic benefits without compromising the integrity of the active ingredients.

EXTRACTION OF HERBAL DRUGS

The **extraction process of herbs** is essential for obtaining the active ingredients (bioactive compounds) from plant materials to create herbal medicines, supplements, and extracts. The extraction method used can significantly impact the potency, purity, and effectiveness of the final product. There are several methods of extraction, each suited to different types of plant materials and desired compounds. Here's an overview of the most common extraction processes used for herbs.

1. Maceration Extraction: The plant material (fresh or dried) is soaked in a solvent (e.g., water, alcohol, glycerin, or oil) for a prolonged period, typically several hours to days. The solvent dissolves the active ingredients from the plant cells.

2. Infusion: A simple extraction method where hot water is poured over dried herbs (usually in a tea bag or loose) and left to steep. The active compounds are dissolved in the water.

3. Decoction: Similar to infusion, but used for tougher plant parts like **roots**, **barks**, or **seeds** that require more heat and time to release their active ingredients.

4. Percolation: A more advanced method in which the plant material is placed in a vertical column (percolator), and the solvent is passed through it in a continuous flow. The solvent extracts the active compounds, which then drip down and are collected.

5. Soxhlet Extraction: This is a continuous extraction method that uses a specialized apparatus to extract active compounds from plant material using a solvent. The solvent is repeatedly vaporized and condensed to pass through the plant material.

6. Cold Pressing (Used for Oils): This method is commonly used to extract essential oils and other lipophilic (fat-soluble) compounds from plant materials, especially fruits and seeds.

7. **Supercritical Fluid Extraction (SFE**): A high-tech method that uses supercritical CO2 (carbon dioxide) as the solvent. The CO2 is pressurized and heated until it reaches a supercritical state, where it has properties of both a liquid and a gas.

8. Ethanol Extraction (Alcohol Extraction): This is one of the most common methods of extracting herbal compounds. Ethanol or another alcohol (like vodka) is used as the solvent to extract bioactive compounds from the plant material.

9. Steam Distillation (For Essential Oils): Used specifically for extracting essential oils, steam distillation involves passing steam through plant material, causing the essential oils to evaporate. The steam and oil vapors are then condensed and separated.

For instance, **maceration** and **infusion** are simple and suitable for teas, while **supercritical fluid extraction** and steam distillation are used for high-quality essential oils. Cold pressing is ideal for oils, and Soxhlet extraction is effective for more concentrated compounds.

SOLUBILITY CONCERN WITH HERBAL MEDICINE

Solubility is one of the critical factors affecting the bioavailability and overall effectiveness of herbal capsules. The solubility of herbal ingredients determines how well the active compounds in the herbs dissolve and get absorbed in the gastrointestinal (GI) tract. Poor

solubility can result in lower absorption, reducing the therapeutic efficacy of the herbal product.

Solubility Concerns in Herbal Capsules
Low Water Solubility of Active Compounds Many active ingredients in herbs, such as **flavonoids**, **terpenoids**, **alkaloids**, and **polyphenols**, are poorly soluble in water. This low solubility can hinder the absorption of these compounds, especially when they are encapsulated in a solid form like a capsule.

Example: **Curcumin** from turmeric is highly beneficial but poorly soluble in water, which affects its absorption.
Fat-Soluble Compounds Some herbal ingredients contain **lipophilic (fat-soluble)** compounds that are difficult to dissolve in water but dissolve well in fats and oils. These compounds can have poor bioavailability if not properly formulated.

Example: **CBD oil** and **essential oils** are fat-soluble and can be challenging to encapsulate in their pure forms without the aid of an appropriate carrier.

Poor Dissolution Rates If herbal powders are not sufficiently fine or if the encapsulation process isn't optimized, it may result in poor dissolution in the digestive tract. Poor dissolution rates mean that the active compounds do not dissolve efficiently, which limits the body's ability to absorb them.

Example: **Ginseng**, when in large particles, may dissolve too slowly in the stomach, leading to reduced absorption.

Key Factors Affecting Solubility in Herbal Capsules
Particle Size of Herbal Powder The **particle size** of the herbal powder inside the capsule plays a critical role in solubility. Finer particles tend to dissolve faster than larger ones, improving bioavailability. However, finer powders can also cause issues like **clumping** or **caking**.

Excipients Used in Capsule Formulation Excipients can help improve the solubility of herbal ingredients by.
Disintegrants: These help the capsule break apart in the stomach, allowing faster release of active compounds.

Solubilizers: Some excipients, like **cyclodextrins** or **phospholipids**, can enhance the solubility of poorly soluble compounds by forming inclusion complexes or micelles.

Surfactants: Surfactants like **tween** or **lecithin** can increase the solubility of hydrophobic compounds by reducing surface tension and promoting solubilization in the digestive fluids.

Lubricants and Fillers: Certain lubricants (e.g., **magnesium stearate**) or fillers can help optimize the flow and prevent clogging, ensuring the herbal powder is released efficiently.

Formulation of Solid vs. Liquid Fill Herbal powders have limited solubility, but **liquid-filled capsules** (also called soft gels) can encapsulate extracts dissolved in oils or other solvents. This method can enhance solubility for certain active compounds and offer better bioavailability.

Example: Liquid-filled soft gels are commonly used for fat-soluble compounds like **omega-3 fatty acids** or **fish oils**.

Solubility Enhancing Technologies
Nanotechnology: **Nanoemulsions** or **nanoparticles** can be used to reduce the size of herbal ingredients, increasing surface area and improving solubility.

Lipid-based formulations: **Liposomes**, **micelles**, or **solid lipid nanoparticles** are used to increase the solubility and bioavailability of lipophilic (fat-soluble) herbal compounds.

pH and Gastric Environment The solubility of herbal ingredients can vary depending on the **pH** of the stomach and the **digestive enzymes** involved. Some herbal compounds are more soluble in acidic environments, while others require an alkaline environment for better solubility. For example.
Acidic pH in the stomach might help solubilize certain compounds (e.g., **vitamin C**), but others may require an **enteric-coated capsule** to protect the compound from the acidic environment.
Strategies to Overcome Solubility Issues

Formulating with Solubilizers Cyclodextrins: These cyclic oligosaccharides can encapsulate poorly soluble compounds and improve their solubility by forming inclusion complexes. They are often used in the pharmaceutical industry to improve the delivery of poorly soluble compounds.

Phospholipids: Phospholipids like **lecithin** can form liposomes that encapsulate and increase the bioavailability of herbal extracts.

Use of Micronization: Micronization involves reducing the size of the herbal powder particles to the micron level (1-100 microns). This increases the surface area available for dissolution, leading to enhanced solubility.

Using Oils and Fats in Formulations: For fat-soluble herbs, **carrier oils** like **olive oil**, **coconut oil**, or **MCT oil** can be used to encapsulate the active ingredients in liquid-filled capsules. These oils can improve the solubility and absorption of lipophilic compounds.

Nanoformulation and Liposomal Technology: Nanoemulsions can reduce the particle size of herbal ingredients, significantly enhancing their solubility and bioavailability.

Liposomal encapsulation involves encapsulating herbal compounds in lipid-based carriers, which improves the solubility of fat-soluble herbs.

Micelle Formation: Micelles are structures formed by surfactants that can enhance the solubility of hydrophobic substances. Herbal ingredients like curcumin, which are poorly soluble in water, can be made more bioavailable by formulating them into micelles.

Co-Encapsulation: Co-encapsulation involves encapsulating different compounds together, where one compound (such as a surfactant or solubilizer) aids in the solubilization of the other (e.g., an herbal extract). This method is often used for complex herbal formulations that require synergistic action between multiple

SELECTION CRITERIA FOR MAKING CAPSULE FORMULATION

When formulating herbal capsules, it's essential to carefully balance the amount of herbal extract (active ingredient) and excipients (inactive ingredients) to ensure the proper release, absorption, and stability of the final product. The exact percentage of herbs and excipients can vary depending on the type of herbal extract being used, the desired dosage per capsule, and the properties of the herbal material. Here's a general guideline for the percentage breakdown of herbs and excipients in a typical herbal capsule formulation.
Common excipients and their typical percentage in herbal capsules.

Fillers (Diluents) – 10% to 50%: Used to bulk up the formulation, especially when the herb content is not enough to fill the capsule by itself. Eg. Microcrystalline cellulose (MCC), Rice flour, Lactose or starch.

Binders – 1% to 5%: Help hold the ingredients together and ensure that the powder stays compact in the capsule. Eg. Hydroxypropyl methylcellulose (HPMC) (commonly used in vegetarian capsules).
Starch or gum (e.g., gum arabic).

Disintegrants – 2% to 10%: Disintegrants help the capsule break down and release the active ingredient once it reaches the stomach. Sodium starch glycolate, Croscarmellose sodium, Crospovidone.

Lubricants – 0.5% to 2%: Lubricants help prevent the contents from sticking to the capsule machinery and ease the capsule filling process. Magnesium stearate (used in small quantities), Stearic acid. Silicon dioxide.

Glidants – 0.5% to 1%: Improve the flowability of the powder and make the capsule filling process smoother.
Talc. Colloidal silicon dioxide.

Capsule Shell – 10% to 25%: The shell is the outer coating that holds the herbal contents. The capsule shell can be made from gelatin (animal-based) or hydroxypropyl methylcellulose (HPMC) (vegetarian/vegan).
Gelatin capsules: Animal-derived, used widely for encapsulating dry herbs.
HPMC capsules: A plant-based alternative that is more suitable for vegans.

Here's a basic guideline for a typical herbal capsule containing 50% herbal powder and 50% excipients.

Component	% of Total Content
Herbal Powder/Extract	30% - 80%
Fillers (e.g., MCC)	10% - 50%
Binders	1% - 5%
Disintegrants	2% - 10%
Lubricants	0.5% - 2%
Capsule Shell	10% - 25%

SELECTION OF GRANULATION PROCESS FOR HERBAL CAPSULE

When formulating **herbal capsules**, the choice of **granulation method** plays a critical role in ensuring that the active ingredients are effectively encapsulated, are released properly in the gastrointestinal tract, and maintain stability throughout the shelf life of the product. Granulation is the process of forming granules or small, uniform aggregates of powder that facilitate better flowability, compressibility, and uniformity of the final product.

Best Granulation Method for Herbal Capsules
For Moisture-Sensitive or Heat-Sensitive Herbs: **Dry Granulation** is generally the preferred method. It avoids exposure to moisture and heat, making it suitable for delicate herbal compounds like **essential oils** or **volatile compounds**.

For Herbs Requiring Better Binding and Consistency: **Wet Granulation** may be preferred as it results in uniform granules, ensuring better distribution of the herbal active ingredient and improved bioavailability. However, this method must be chosen cautiously for moisture-sensitive herbs.

For High-Quality Granules: **Fluidized Bed Granulation** can offer the best results in terms of granule quality and uniformity but at a higher cost and complexity.

For Simple Formulations with Free-Flowing Herbs: **Direct Compression** is the fastest and simplest method but is generally suitable only for specific herbs that are not prone to clumping or dusting and have good flow properties.

PREFORMULATION STUDY OF HERBAL CAPSULE

1. Physical Characteristics of Granules

Granule Size Distribution: Sieve analysis or laser diffraction.
Limit: Granule size should typically be between 100 µm and 1000 µm, depending on the desired release rate and compression properties. A uniform size distribution is critical for consistent drug release and product uniformity. Granules should have a narrow size distribution, with most granules falling between 250 µm and 850 µm for optimal tableting or encapsulation.
Flowability: Angle of repose, Carr's index, or Hausner ratio.
Angle of repose: Less than 30° indicates good flowability.
Carr's Index: Should be between 15% and 25% for good flowability.
Hausner ratio: Less than 1.25 indicates good flowability.
Bulk Density (Tapped Density): Measured using a graduated cylinder after tapping or vibrating.
Limit: Bulk density should range between 0.3 and 0.6 g/cm³, while tapped density should be around 0.5 to 0.8 g/cm³, depending on the excipients used.
Moisture Content: Oven drying method or Karl Fischer titration.
Limit: Typically between 2% to 5%. High moisture content can promote microbial growth and degradation, while too low may affect the granulation process.
Friability: Friabilator or tablet friability test.
Limit: Less than 1% weight loss, ensuring the granules are not too brittle and will not disintegrate prematurely during handling or storage.

2. Chemical and Active Ingredient Analysis

Phytochemical Profile: High-Performance Liquid Chromatography (HPLC) or Gas Chromatography-Mass Spectrometry (GC-MS). Quantification of active ingredients should meet a specified concentration, based on the therapeutic dose. The amount should be consistent from batch to batch, and the product should contain at least 90% of the labeled content (for the primary active compounds).
Active Compound Stability: Stability study under accelerated conditions (e.g., 40°C and 75% RH for 3–6 months). The degradation of the active ingredient should not exceed 10% of its initial concentration over the product's shelf life.

3. Granulation Process

Binder Concentration: Varying binder concentrations during formulation to achieve the right granule consistency. Typically 2–10% by weight (depending on the type of binder and herbal extract).
Granulation Moisture: Moisture content after wet granulation. Granulation moisture should be within 25% to 30% to ensure good bonding without over-wetting the granules.

4. Disintegration and Dissolution Testing

Disintegration Time: Disintegration test for granules or tablets. Herbal granules should disintegrate within 15–30 minutes, depending on the formulation and desired release rate.
Dissolution Profile: In-vitro dissolution testing using a dissolution apparatus (USP Type II or rotating basket method). The percentage of active compound released should typically be above 80% within 30 minutes for immediate-release formulations. For controlled-release formulations, the release should be sustained over several hours.

5. Stability Testing

Accelerated Stability: Storage at elevated temperature and humidity (e.g., 40°C/75% RH for 3–6 months).
Limit: No significant changes in physical appearance, moisture content, or active ingredient degradation (less than 10% loss).
Long-Term Stability: If available, test at real-time conditions (e.g., 25°C/60% RH for 12–24 months).
Microbial Limit Testing: Microbial content testing (Total Aerobic Microbial Count, Yeast & Mold Count, and testing for specific pathogens like E. coli, Salmonella). No presence of harmful microorganisms like Salmonella or E. coli; total microbial count should typically be under 1000 CFU/g.

6. Excipient Compatibility

Drug-Excipient Interaction: Differential Scanning Calorimetry (DSC), Fourier Transform Infrared Spectroscopy (FTIR), or HPLC. No significant physical or chemical incompatibilities between the active herbal ingredients and excipients.
Excipients Identification and Quality Control

7. Packaging and Storage Conditions

Packaging Integrity:: Sealing integrity, moisture barrier testing, and compatibility with the granules.
Limit: Packaging should protect granules from moisture, air, and light to prevent degradation.
Packaging Material Compatibility: Interaction testing between the granules and the packaging material.
Limit: No chemical interactions or significant changes in the appearance of the granules due to packaging material (e.g., migration of solvents from plastic containers).

EVALUATION PARAMETER FOR HERBAL CAPSULE

Evaluating the quality of **herbal capsules** is essential to ensure their **safety**, **efficacy**, and **consistency** throughout the shelf life. The evaluation of herbal capsules involves a series of tests to assess various **physical**, **chemical**, and

biological properties. Below are the key **evaluation parameters** for herbal capsules.

1. **Appearance and Physical Characteristics**
Capsule Integrity: Ensure that the capsule shells are intact, free from cracks, discoloration, or defects.
Size and Shape: Verify the **capsule size** and ensure that they are uniform in shape and appearance.

Color: Check that the capsules have a consistent color, which should match the specifications for the product.

2. Uniformity of Weight
Weight Variation: Weigh a sample of capsules (usually 20 capsules), and calculate the average weight. The weight variation should be within acceptable limits (e.g., ±10% of the average weight).
USP guidelines: Typically, capsules should meet the following criteria:
If the average weight is ≤ 300 mg: No individual capsule weight should differ by more than ±10% from the average. If the average weight is > 300 mg: The variation should be within ±7.5%.

3. Content Uniformity
This test ensures that the active herbal ingredients are evenly distributed throughout the capsule. It is critical to ensure the efficacy of the herbal preparation.
Uniformity of Active Ingredient: A sample of capsules is analyzed for the **content of the active ingredient(s)**. The active compound(s) should be uniformly distributed across all capsules, and the content in each capsule should fall within the acceptable limits (usually ±10% of the labeled amount).
Testing Method: This can be done using techniques such as **HPLC**, **UV spectroscopy**, or **TLC** to measure the concentration of active compounds in the capsules.

4. Disintegration Test
The **disintegration test** evaluates how quickly and effectively the herbal capsule breaks down in a simulated gastrointestinal environment, which impacts the release of active ingredients.
Disintegration Time: Test how long it takes for the capsule to disintegrate in **simulated gastric fluid** (SGF). The disintegration time should meet the specifications provided for the herbal capsule (typically 30 minutes to 1 hour, depending on the formulation).
USP guidelines: Capsules should disintegrate within 30 minutes, though this can vary based on the type of capsule and release profile.

5. Dissolution Test
Dissolution testing measures how effectively the active herbal ingredients are released from the capsule into solution, which directly affects the **bioavailability**.
Dissolution Profile: Perform the dissolution test using a **USP dissolution apparatus** (typically Apparatus I or II) in **simulated gastric fluid (SGF)** or **simulated intestinal fluid (SIF)**. The herbal active compounds should be released according to the specified dissolution profile.
USP guidelines: A specific percentage (e.g., 80% of the active ingredient) should be released within a defined period (usually 30–60 minutes).
Testing Method: The concentration of active ingredients in the dissolution medium can be determined using **HPLC**, **UV spectrophotometry**, or other analytical methods.

6**. Hardness and Friability:** The hardness and friability of the herbal capsules are important for determining their ability to withstand mechanical stress during handling, transport, and storage.
Hardness: The hardness test measures how resistant the capsule is to breaking when pressure is applied. This is more relevant for **hard gelatin capsules**.
Standard Methods: Use a hardness tester to determine the capsule's resistance to mechanical pressure.
Friability: Friability tests determine the tendency of the capsule to break or crumble. The capsules are subjected to mechanical stress (e.g., rotating drum method), and any weight loss is measured.
Acceptable Limits: Herbal capsules should have a **friability of less than 1%**.

7. Moisture Content
Excess moisture can degrade the herbal ingredients, leading to reduced efficacy, microbial growth, and stability issues. Measure the moisture content of the capsule using a **moisture analyzer** or **Karl Fischer titration**.
Ideal Moisture Content: Capsules typically have a moisture content of **5–10%**, depending on the formulation and the shell material.

8. Microbial Contamination
Herbal capsules should be free from microbial contamination to ensure safety for consumption.
Microbial Testing: Evaluate the **total bacterial count**, **yeast**, and **mold count** to ensure they are within the prescribed limits (usually based on **USP or IP standards**).
Pathogen Testing: Check for the presence of harmful bacteria, such as **Salmonella**, **E. coli**, and **Staphylococcus aureus**.

9. Stability Testing
To ensure that herbal capsules retain their potency and do not degrade over time, stability studies must be conducted under various environmental conditions.
Storage Conditions: Test the capsules under **accelerated** (e.g., 40°C/75% RH) and **long-term** storage conditions (e.g., 25°C/60% RH).
Parameters Measured:
Chemical Stability: The concentration of active herbal ingredients should remain within acceptable limits (usually ±10%) over the product's shelf life.
Physical Stability: Ensure the capsules do not undergo color changes, disintegration failure, or swelling.

Packaging Compatibility: Ensure the capsule packaging protects the product from moisture, air, and light.

10. Tensile Strength (for Hard Gelatin Capsules)
Tensile strength refers to the force required to break or rupture the capsule shell.
Capsule Shell Strength: This can be evaluated using a **tensile strength tester**. The capsule should not break under normal handling conditions.

11. Release Profile (Controlled or Modified Release)
For capsules designed to release the herbal ingredients over time, **controlled-release** or **extended-release** profiles must be evaluated.
Release Rate: Measure how slowly the active ingredient is released over time, ensuring it matches the specified release profile (e.g., slow release over hours).
Comparative Dissolution Studies: If the capsule is designed for controlled or modified release, compare its dissolution profile with the original formulation or a reference product.

12. Labeling Compliance
Ensure that the capsule product is labeled according to regulatory requirements, including the proper dosage, ingredients, and warnings.
Label Information: Check if the label accurately reflects the **active ingredients**, **dosage**, **instructions for use**, **batch number**, **expiry date**, and other relevant details.
Regulatory Compliance: Verify that the product complies with local **pharmacopoeia standards** (e.g., USP, IP, BP) and **regulatory guidelines** for herbal medicines.

13. Pyrogen Testing (Optional)
For some herbal capsules, **pyrogen testing** is essential to ensure that they are free from fever-inducing substances.
Limulus Amebocyte Lysate (LAL) Assay: Used to test for **endotoxins** in the capsules, which can lead to fever or other adverse reactions.

The evaluation of **herbal capsules** is a comprehensive process that ensures the **quality**, **safety**, and **efficacy** of the final product. From **appearance** to **bioavailability**, each parameter plays a crucial role in guaranteeing the desired therapeutic effect and meeting regulatory standards. Consistent and accurate evaluation methods are essential for maintaining the standards of **herbal medicines** in the market.

STABILITY STUDY CRITERIA FOR HERBAL CAPSULE
Stability studies for **herbal capsules** are essential to evaluate their **shelf life**, **safety**, and **efficacy** over time. Stability testing helps ensure that the herbal capsule maintains its **chemical, physical**, and **microbiological** integrity under various storage conditions. Since herbal products are sensitive to factors like **temperature**, **humidity**, and **light**, the stability study is critical for ensuring that the active ingredients, dosage form, and overall product quality remain consistent throughout the shelf life.
Key Parameters in Stability Studies for Herbal Capsules.
Chemical Stability
Active Ingredient Degradation: The main concern for herbal capsules is the stability of the active compounds in the herbal material. Active ingredients, such as **alkaloids**, **flavonoids**, **terpenoids**, and **glycosides**, can degrade over time due to exposure to **light**, **air**, or **moisture**.
Method: **High-performance liquid chromatography (HPLC)**, **UV spectroscopy**, or **gas chromatography (GC)** are commonly used to measure the concentration of the active compounds.
Purpose: To ensure the **potency** of the product is maintained within acceptable limits (typically ±10% of the labeled amount).

Physical Stability
Capsule Appearance: Herbal capsules must retain their **physical characteristics** such as **color**, **shape**, and **integrity**. Capsules should not undergo **swelling**, **brittleness**, **softening**, or **discoloration** during the shelf life.
Disintegration and Dissolution: The **disintegration time** and **dissolution profile** of herbal capsules must remain consistent over time to ensure that the capsules release their active ingredients properly in the gastrointestinal tract.
Hardness and Friability: Capsule **hardness** (resistance to breaking) and **friability** (tendency to crumble) are tested to ensure that the capsules can withstand mechanical stress during handling and transport.
Tests:
Disintegration Test: To ensure capsules break down properly in the digestive system.
Dissolution Test: To ensure the herbal ingredients are released at the correct rate.

Microbiological Stability
Herbal products are particularly prone to microbial contamination, which can lead to spoilage or unsafe consumption. Stability studies should include tests to ensure that the product does not develop **bacterial**, **fungal**, or **mold contamination** during the shelf life.

Testing for Microbial Contamination:
Total bacterial count
Yeast and mold count
Pathogen testing for **Salmonella**, **E. coli**, and other harmful microorganisms.
Microbial Limits: According to **pharmacopoeial standards** (e.g., **USP**, **IP**), herbal capsules should be free from **pathogens** and must not exceed prescribed microbial limits.

Moisture Content
Moisture is a significant factor that affects the stability of herbal capsules. High moisture content can lead to

degradation of the herbal ingredients, microbial growth, or capsule shell **softening**.

Test: **Moisture analysis** should be conducted periodically using methods such as **Karl Fischer titration** or **Loss on Drying** (LOD).

Moisture Content Limits: Typically, herbal capsules should have a moisture content of **5–10%**, depending on the formulation.

Packaging and Environmental Factors

Packaging Materials: The **capsule packaging** must be assessed for its **protective** properties, including resistance to **moisture**, **light**, and **air**. Packaging materials such as **blister packs**, **bottles**, or **foil packs** should be tested for their ability to maintain the stability of the capsules during storage.

Light Sensitivity: Some herbal ingredients are **light-sensitive**, so packaging that protects from light (e.g., **amber-colored bottles** or **opaque blister packs**) is important.

Stability Testing Conditions

International Council for Harmonisation (ICH) guidelines are commonly followed:

Accelerated Stability (usually at **40°C ± 2°C** and **75% RH ± 5%** for 3-6 months):

Helps predict long-term stability and shelf life in a shorter time frame.

Observes degradation or physical changes in the herbal product.

Long-term Stability (usually at **25°C ± 2°C** and **60% RH ± 5%** for **12 months or more**):

Determines the actual shelf life of the herbal capsules.

Provides a more accurate picture of the product's performance over time.

Intermediate Stability (typically at **30°C ± 2°C** and **65% RH ± 5%** for **6 months**):

Ensures the product remains stable under **normal storage conditions**.

Test for Pyrogens (Endotoxins): For herbal capsules intended for long-term use, it is essential to ensure that **pyrogens** (fever-causing substances) are not present in the formulation, as they can cause adverse reactions in consumers. The **Limulus Amebocyte Lysate (LAL) test** is used to detect endotoxins.

Pyrogen Testing: A safety measure to ensure that herbal capsules do not contain harmful endotoxins produced by bacteria during the herbal material's production or storage.

Sensory Evaluation: While not a part of the standard pharmacopoeial tests, **sensory evaluation** is important for consumer acceptance.

Odor, Color, and Texture: Stability testing should include regular checks for any undesirable changes in the sensory attributes, like **odor** (which may indicate spoilage), **color**, or **texture** changes.

Steps in Conducting Stability Studies for Herbal Capsules:

Sample Selection: Select representative samples of the herbal capsule batch that will undergo the stability testing.

Test Time Points: Stability testing is typically conducted at different **time intervals**, such as 0 months, 3 months, 6 months, 9 months, and 12 months.

Test Parameters: Check for the **active ingredient content**, **physical characteristics**, **disintegration**, **dissolution**, **microbial contamination**, **moisture content**, and **packaging integrity** at each time point.

Data Analysis: Analyze data over time to determine **trends** in degradation, **loss of potency**, or other changes. Predict the **shelf life** based on accelerated and long-term data.

Labeling: Based on the results of the stability study, assign an appropriate **expiration date** and ensure proper storage instructions are provided on the product label.

Stability studies for **herbal capsules** are crucial to ensure that the product remains **safe**, **effective**, and of **high quality** throughout its shelf life. These studies help identify potential issues related to **degradation**, **microbial contamination**, **moisture**, and **physical integrity**, allowing for the formulation of stable products that maintain their **therapeutic efficacy**. Proper stability testing also ensures that the **packaging** is appropriate for preserving the capsules' **quality** under various environmental conditions.

CONCLUSION

Polyherbal capsules and formulations have demonstrated promise as respiratory stimulants due to their combined therapeutic effects. However, while preliminary studies are encouraging, comprehensive clinical trials are necessary to establish their efficacy and safety profiles. Individuals considering these supplements should consult healthcare professionals to ensure appropriate use. The poly-herbal combination of chosen plants was tested and found to be good results. It can be utilizing more accurate methodologies is needed to investigate the contents responsible for the action and the mechanism of this activity. The guidance obtained from the review study can be utilized as a reference for setting limits for the reference standards for the quality control and quality assurance of the herbal drugs.

REFERENCES

1. Sumaira Ishaque, Ghazala H. Rizwani, et.al: Research on Formulation and Pharmaceutical evaluation of Polyherbal Capsule (Femitex-SP4) for Treating Menorrhagia, 2011.
2. Bhupendra M. Mahale*, Devendra S. Mahale, Azam Z. Shaikh: Review on Natural Herbs used in Cough and Cold Condition. Research Journals of Pharmacognosy and Phytochemistry, 2022; 14(2): 98-102.
3. Sonali S Gadge: Review on Antiviral and Immunity-modulating Natural Herbs in the Prevention of COVID-19. Research Journal of Pharmacognosy and Phytochemistry, 2021; 13(2): 81-94.

4. Tiwari, R. Shukla, A.K.(2020)Plant metabolites and their role in health benefits: A brief review. Adv. Pharma. J., 2020; 5(2): 47-53.
5. Bajaj, J., Dave. V., Sharma, S., Shukla, A., Chakole, R.D. (2012) Pharmacognostical and Phytochemical Studies on A chyranthesaspera, World J. of Biomed. and Adv. Res., 01(04):1316-1331.
6. Beg MB. Viquar U. Naikodi MAR. Suhail H. Kazmi MH. (2021) Standardization and HPTLC Fingerprinting of a Polyherbal Unani Formulation. Cell Med., 11(1): 1-8.
7. Bhati, Pooja., Shukla, Ajay., Sharma, Maya., Mourya, P. (2014) Hepato protective activity of leaves extracts of carissacarandasl inn.Indo American J. of Pharm Res., 4(11): 1-8.
8. Bisht, A., Dwivedi, H., Rawat, A.K.S. (2021) Development and Evaluation of Polyherbal Formulation for Diabetes. Asian Pac. J. Health Sci., 8(4): 48-54.
9. J. of Medical P'ceutical & Allied Sci., 9(2): 2484- 2491.
10. Ferguson, P.J., Kurowska, E., Freeman, D.J., Chambers, A.F., Koropatnick, D.J. (2004) A flavonoid fraction from cranberry extract inhibits proliferation of human tumor cell lines. J. of Nutrition, **134**: 1529-1535.
11. Garg, K.N., Katara, A., Mathur, M. (2021) Formulation Development, Quality Evaluation and In-Vitro Antioxidant Activity of a Polyherboceutical Composition, Intern. J. of Pharma. Sci. and Drug Res., **13**(2): 190-196.
12. Gupta, A.K., Tandon, N. Review of Indian Medicinal Plants. (2004) Indian Council of Medical Research New Delhi, India.
13. Huai, H. (2010). Ethnomedicinal analysis of toxic plants from five ethnic groups in China. Ethno. Res. and App., **8**: 169-79.
14. Husain, S.Z., Malik, R.N., Javaid, M., Bibi, S. (2008) Ethonobotanical properties and uses of Medicinal plants of Morgah Biodiversity Park, Rawalpindi. Pak. J. of Bot., **40:** 1897-911.
15. Jayachandra, K., Thirugnanasambantham, P., Kumaran, S., Narayanan, N. (2019) Evaluation of in-vitro cytotoxic and anticancer activity of hepato protective poly-herbal formulation in cell line model. Asian J. of Pharma. and Clinical Res., **12**(4): 320-325.
16. Jemal, A., Siegel, R., Ward, E., Murray, T., Xu, J., Smigal, C. et al. (2006) Cancer Statistics. CA: A Cancer Journal for Clinicians, **56**: 106-130.
17. Jo, E .H., Hong, H.D., Ahn, N.C., Jung, J.W., Yang, S.R., Park, J.S. et al. (2004) Modulations of the Bcl-2/ Bax family were involved in the chemo preventive effects of licorice root(Glycyrrhiza uralensis Fisch) in MCF-7 human breast cancer cell. J. of Agr. and Food. Chem., **52**: 1715-1719.
18. Mahto, B.K., Patel, R., Bapna, R., Shukla A.K. (2022) Assessment of antioxidant, anticancer activity of standardized poly-herbal capsule formulation. Neuro Quantology, **20**; 9: 4187-4203.
19. Mourya, Pramod., Shukla, Ajay., Rai,Gopal.,Lodhi, Santram. (2017) Hypoglycemic and hypolipidemic effects of ethanolic and aqueous extracts from Ziziphus oenoplia (L) Millona lloxan-induced diabetic rats. Beni-Suef-University J.of Basic and Appl. Sci., **6**: 1- 9.
20. Mukherjee, A.K., Basu, S., Sarkar, N., Ghosh, A.C. (2001) Advances in cancer therapy with plant based natural products. Curr. Medi. Chem., **8**: 1467-1486.
21. Muthusamy, P. (2014) In-vitro anti-oxidant and anti-arthritic activity of poly-herbal formulation (capsules). American Journal of Pharmacy and Health Research, **2**(3): 66-72.
22. Pandey, P., Garg, A., Shukla, A. (2016) Preliminary phytochemical and physicochemical Investigation and thin layer chromatography of Buteamonosperma flower extract. J. of Med. Pharm. and Allied Sci, 1-10.
23. Pandeya, A.K., Tyagia, C.K., Shah, S.K., Tiwaric, S.M., Rawat, P.K., Sahu, G.D. (2021) Formulation development and evaluation of directly compressed poly-herbal tablets for the management of infections caused by helminthes. Materials today, 1-8.
24. Parasuraman, S., Thing, G.S., Dhanaraj, S.A. (2014). Poly-herbal formulation: Concept of ayurveda. Pharmacognosy Reviews, **8**(16): 73-80.
25. Patil, S.J., Patil, S.D., Pati, lP. B., Patil, P.S., Vambhurkar, G.B., Raut, I.D. (2018) Evaluation of Standardization Parameters of Ayurvedic Marketed Poly-herbal Formulation. Asian J. Pharm. Ana., **8**(4): 220-226.
26. Sharma, P., Pandey, P., Gupta, R., Roshan, S., Jain, A.P., Shukla, A., Shukla, R., Garg, A., Pasi, A. (2013) Development of Quality Control Parameter of Henna Powder, Inter. Journal Pharm. Science Review and Res., **21**(01): 293-295.
27. Sharma, S.K. Medicinal plants used in Ayurveda. National Academy of Ayurveda. Ministry of Health &Family Welfare, Government of India, 1998.
28. Shukla, A.K., Kumar, M., Bishnoi, R.S., Jain C.P. (2019). Development of Natural Gum Based Sustained Release Tablets of Propranolol hydrochloride. Res. J. Pharm. and Tech, 2019: 0974-360X.
29. Shukla, A.K., Kumar, M., Bishnoi, R.S., Jain C.P. (2019). Development of natural and modified gum based sustained-release film-coated tablets containing poorly water-soluble drug. Asian J Pharm Clin Res., 2455-3891.
30. Shukla, A.K., Yadav, A., Vishwakarma, R.K., Mishra, S.K. (2019). Applications, isolation and characterization of fenugreek seed gum as pharmaceutical excipient.