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# Formulation Development (Formulation & evaluation cream of *coriander* extract for anti-acne activity).

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**MODULE-1**

## 1.1. Introduction of formulation development :

Pharmaceutical formulation development links the discovery of a new drug substance to the successful development of a commercial drug product. Formulation development scientists must determine the most appropriate route to achieving effective drug delivery based on patient need, then optimize the formulation's characteristics based on a knowledge of the drug product's bioavailability and processing requirements.[1]

## 1.2.Concept of cGMP:

FDA regularly monitors medication manufacturers' compliance with its Current Good Manufacturing Practice (CGMP) requirements to assure the quality of drug products. The minimal standards for the processes, settings, and controls utilized in the creation, processing, and packaging of a drug product are laid forth in the CGMP laws for pharmaceuticals. The rules ensure that a product is safe to use, that it has the components and strength it purports to have, and that it is labelled accurately.

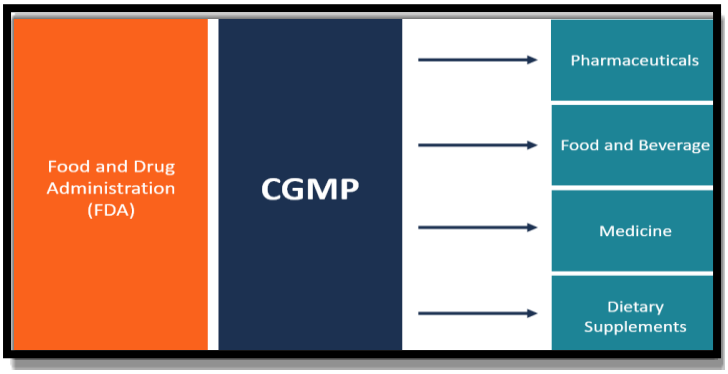



**Fig.No.1: Concept of cGMP**

The FDA's Current Good Manufacturing Practices standards are referred to as "cGMP." Systems for ensuring effective manufacturing process and facility design, monitoring, and control are provided by CGMPs. By ensuring that drug makers properly supervise manufacturing activities, CGMP standards ensure the identification, strength, quality, and purity of drug products. Establishing rigorous operating procedures, acquiring acceptable quality raw materials, identifying and looking into product quality variations, and maintaining trustworthy testing labs are all part of this.

### *1.3. Steps in formulation development :*

**a) Identification & Characterization of Drug:**
The identification and characterisation of drugs are crucial because they have a significant impact on the finished product and have the potential to increase or decrease toxicity.
**b) Excipient compatibility study:**
The more the excipient compatibility with the drug, the greater the likelihood that the medicine will be successfully formulated.
**c) Formulation development:**
The creation of the formulation, which determines which chemicals go with which excipients, is the next stage.

**d) Formulation optimization :**

At this stage, vaccine formulations are produced; these formulations require a significant amount of expertise and more investigations than standard formulations.

**e) Formulation Evaluation:**

By altering components of the formulation, such as the vehicle types, evaluation studies assist in improving the formulation that has previously been created.

**f) Stability study:**

It addresses formulation stability by conducting various tests to boost formulation stability; it also contributes to extending the shelf life of formulation in five key areas: development, quality control, production, distribution, and inspections.[2]

## 1.4. Requirement listing & Procurement

**a) Procurement of drug and excipients required for selected formulation:**

- Procurement is defined as a process of acquiring supplies through purchases from the manufacturer, their agents like distributors or from private or public suppliers.
- The acquisition of raw materials, important intermediates, and excipients is thought to be a complex process that involves numerous routes, calls for trained employees, and requires appropriate validation.

**b) Procurement of equipment and instruments for formulation and analysis:**

The pharmaceutical formulation equipment procurement market report offers in-depth analysis into a range of supplier selection criteria, RFX questions, supplier evaluation metrics, and service level agreements that purchasers should take into account using to realize significant cost savings, streamline the procurement process, and lower category TCO while sourcing for pharmaceutical formulation equipment.[3]

**MODULE-2**

### *2.1. Basic techniques:*

**SOP handling:** **a. Preparation of SOPs for different instrument & equipment.**

Pharmaceutical Standard Operating Procedure (SOP) is a tried, tested, approved, and documented method of carrying out operations that form the foundation of the pharmaceutical sector. Provides staff with step-by-step instructions for carrying out a given process.

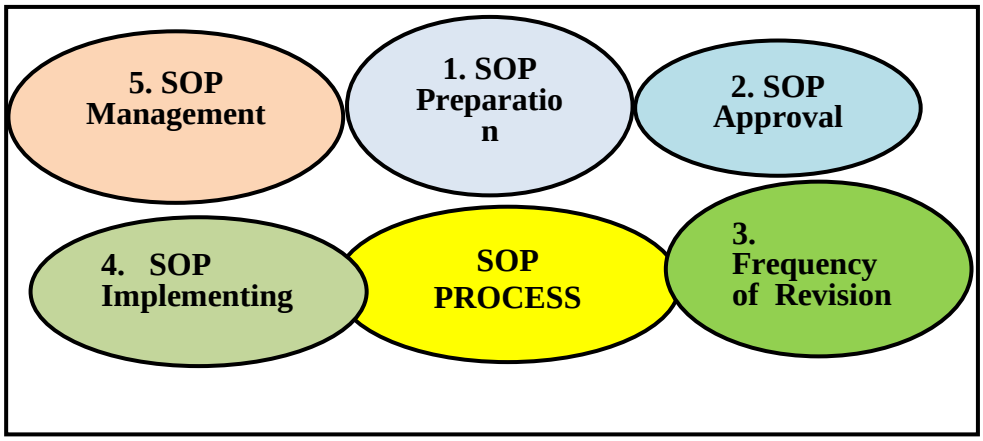



**Table. No. 01: SOP Process**

SOP is a written step-by-step document that describes how to perform the actions required to complete a task. These steps must be followed by everyone involved. SOPs are used in all types of industries, rules and regulations, government laws, and organizations to operate their own businesses.

**Some reasons for writing SOPs:**

1. To arm those who conduct operations with the necessary operational, environmental, safety, and health knowledge to do their
2. To safe guard both the environment and the health and well-being of workers.
3. To keep the neighbourhood safe.
4. To make certain that procedures are followed consistently in order to keep process and product quality under control.
5. To ensure that processes continue and completed on a prescribed schedule.
6. To make sure that procedures continue and are finished according to a set timeline.
7. Preventing any manufacturing and associated process failures that might damage staff members or anybody in the neighbourhood.
8. To be used as a training manual to instruct users on a procedure.
1. 9. To guarantee compliance with corporate and governmental requirements and the execution of approved processes.[4]

<table>
<tr><td>SOPs No.</td><td>MWIT 01</td><td>Effective Date:</td><td></td><td>PreparedBy:<br>Sunil Dudhkawade, Shraddha Baswante</td><td></td></tr>
<tr><td>Instrument Dead Stock No.</td><td></td><td>Review Period:</td><td>Biannual</td><td>Approved By:</td><td></td></tr>
<tr><td>Department</td><td colspan="2">Chemistry</td><td colspan="2">Principal</td><td></td></tr>
<tr><td>OBJECTIVE</td><td colspan="2">To describe the procedure for operation of pH meter</td><td colspan="3" rowspan="3"> 
</td></tr>
<tr><td>SCOPE</td><td colspan="2">This SOP is applicable for the operation of pH meter</td></tr>
<tr><td>RESPONSIBILITY</td><td colspan="2">Instrument in-charge & H.O.D.</td></tr>
</table>

***2.2. Various equipment and instruments handling:***

**A. Tablet Compression Machine:**

Tablet Compression Machine or rotary tablet compression machine is designed to compress tablet from granulated powders. Hydraulic pressure is the fundamental basis of tablet compression machines. The static fluid transmits this pressure without lowering it, Fig. No. 2 tablet compressor

**B. Tablet coater:**

Tablet coating is the technique of applying a dry, outer layer of coating material to the surface of a tablet to provide unique benefits over the uncoated type. Coatings used on a variety of oral dosage forms, including particles, powders, granules, crystals, pellets, and tablets.

**Fig. No.3: Tablet Coater Machine**

**C. Capsule filling machine:**

Capsule filling machine is the one which is used in the pharmaceutical industries for filling the empty capsules. Capsule filler machine is also known as encapsulation. Capsule filler machine is available in different types like automatic, semi-automatic, and manual capsule filling machines. The capsule filling machine, also known as a capsule filler,


**Fig. No.4: Capsule filling Machine**

**D. Fluidized bed dryer :**

Fluidized bed dryer (also called fluid bed dryer) is a kind of equipment extensively in the pharmaceutical industries to reduce the moisture content of pharmaceutical powder and granules. The equipment works on a principle of fluidization of the feed material.

FBD works on the fluidization principle. A high-pressure Hot air from the supply is passed through the perforated container containing wet granules. As the hot air passes through container granules start to suspend in the air to become dry, the process is called fluidization.

**E. Extruder & Spheronizer:**

One of the most effective methods for producing pellets is agglomeration via extrusion and spherization. The ratio of liquid to solid material, as well as the size of the extruder holes, might influence the quality of the extrudates. The pellet hardness is ensured by the final drying. Extrusion is the process of applying pressure to a prepared plastic mass until it flows out through an opening to produce extrudates.

Extrusion is a process in which pharmaceutical material or other material is forced through a series of dies to create desired shapes. (Pallets)

**F. Other**

**Soxhlet appratus:**

Soxhlet extractor extracts the components using the condensed vapors of the solvent. The condensed vapors come in contact with the sample powder and the soluble part in the powder gets mixed with the solvent. A fat extractor (Soxhlet extractor) is used in the laboratory for extraction.[5]

**Fig. No.5: Soxhlet apparatus**

**MODULE-3**

***3.1. Preformulation studies and preparation of preformulation data sheet:***

**A. Introduction to preformulation, goals & objectives, study of physiochemical characteristics of drug substances.**

**Preformulation** is the stage of development during which the physicochemical properties of the drug substance are characterised and established. Knowledge of the relevant physiochemical and biopharmaceutical properties determines the appropriate formulation. Pre formulation studies are laboratory investigations conducted to evaluate the properties of active substances and excipients that may influence formulation, process design, and performance.

***Goals & Objectives:***

1) Determine product stability and compatibility with common excipients.
2) To provide insight into how pharmaceutical items should be prepared and stored to ensure quality.
3) To gather useful information for the development of a medication delivery system with high bioavailability.
4) Create an elegant, stable, effective, and safe dosage form.
5) To create important data for the development of safe dosage forms that can be produced on a commercial basis.
6) To improve drug bioavailability & reduce excipient incompatibility.

***Study of physiochemical characteristics of drug substance:***

**1. Organoleptic Properties:**

In organoleptic characters it include colour, odour & taste.

**2. Bulk characterization studies :**

**A. Crystallinity & Polymorphism:**

Crystallinity refers to the structure of a solid compound. Polymorphism refers to a compound's ability to crystallize as more than one distinct crystalline species with different internal lattices and diverse crystal shapes.

**B. Hygroscopicity:**

The term "hygroscopicity" refers to a substance's ability to absorb moisture from its surroundings.

**C. Fine particle Characterization:**

The particle size distribution influences several physical and chemical properties of pharmacological substances, including drug dissolving rate, bioavailability, content homogeneity, taste, texture color, and stability.

**3. Solubility Analysis:**

**a. Intrinsic Solubility:** It is proposed to evaluate inborn dissolvability at two temperatures: 37° C for biopharmaceutical examination and 4-5° C for good real solidity, boosting transient stockpiling and synthetic stability, and providing excellent real solidity until more definitive evidence is available.

**b. Dissociation Constant (Pka):** Numerous medications are either pitifully basic or acidic chemicals that can exist as ionised or unionised entities depending on the pH value. Unionised species are more readily lipid-dissolvable and so maintained. The Henderson-Hasselbatch equation can be used to quickly compute the overall centralizations of a acidic or basic medication in a system at a given pH.

**4. Partition Coefficient:**

The partition coefficient is defined as the ratio of unionized drug distributed between the organic and aqueous phase at equilibrium. Partition constant (the solvent: water quotient of drug distribution) includes a variety of applications which square measure relevant to preformulation.[7]

**B. Identification & Characterization of drug using FTIR, DSC, UV & Drug Excipients Compatibility Study using DSC, FTIR etc. -**

**1. FTIR ( Fourier transform infrared spectroscopy ):**

FTIR are being extensively used to identify the structural groups present in a compound. The aim of the this work is make thorough investigation on vibrational frequencies of sample. In analogy with the vibrational band assignments of related compounds and the magnitudes and relative intensities of the bands.

FTIR Shows the characteristics of broad peaks of FTIR of pure drug & FTIR of physical mixture of drug.

**2. DSC ( Differential Scanning Colorimetry ) :**

DSC has shown to be an important tool to quickly obtain information about possible interactions between the active and the excipients, according to the appearance, shift, or disappearance of endothermic or exothermic peaks.

Differential scanning calorimetry (DSC) is a technique used to measure thermodynamics of solid or liquid phase transitions that produce or absorb heat. DSC is commonly applied in the biopharmaceutical setting for the characterization and engineering of manufacturable drug products.

It is a thermoanalytical technique in which the difference in amount of heat required to increase the temp. of sample and reference is measured as a function of temp.

**3. UV Spectroscopy : (Ultra-visible Spectroscopy)**

Ultra violet visible spectroscopy is a absorption spectroscopy. It has smaller wavelength than the visible light. Comparison of UV-spectra of Sample With standard. The λ max was found to be nm and was found to be identical with sample & standard spectra.

It depends on the Beers and Lamberts Law,

- Beers Law states that the concentration is directly proportional to the absorption.
- Lamberts Law states that the concentration is directly proportional to the path lenght.[8]


**Fig. No.6: Ultra-visible Spectroscopy**

**C. Physical properties : Physical form ( crystal & amorphous ), particle size, shape, flow properties, solubility profile etc.**

**1. Physical Properties:** The physical properties of the candidate drug molecule and excipients, such as color, odour, and taste, can be determined by analyzing them.

2. Physical Forms:

**a. Crystalline:** A crystal, also known as a crystalline solid, is a solid material in which the constituents (atoms, molecules, or ions) are arranged in a highly ordered microscopic structure, forming a crystal lattice that extends in all directions.

**b. Amorphous:** Amorphous solids are similar to liquids in that they lack an ordered structure, or an orderly arrangement of atoms or ions in three dimensions.

**3. Particle shape & Size :** The particle size ensures that the drug content is homogeneous and compressible. manufacturing. Particle form is also linked to contact sites, and thus solubility.

**4. Flow Properties:** Particle size, density, shape, and adsorbed moisture changes that may occur during processing or formulation have a significant impact on flow properties. Because the medicine is only available in small quantities during the preformulation stage, the flow property is dictated by bulk density and angle of repose, hausner ratio, cars index.

| Carr's Index | Hausner's ratio | Angle of repose | Flowability |
|---|---|---|---|
| 5 - 15 | 1.05 - 1.18 | 25 - 30 | Excellent |
| 12 - 16 | 1.14 - 1.20 | 31 - 35 | Good |
| 18 - 21 | 1.22 - 1.26 | 36 - 45 | Fair possible |
| 23 - 35 | 1.30 - 1.54 | 46 - 55 | Poor |
| 33 - 38 | 1.50 - 1.16 | 56 - 65 | Very poor |
| >40 | >1.67 | 66 | Very, very poor |

**Table. No. 02: Flow Properties**

**E. Application of preformulation in dosage form design:**

Scientists can use preformulation to screen lead candidates based on their physicochemical and biological qualities. This information can be used to select novel chemical entities (NCEs) for preclinical efficacy/toxicity investigations, which is a major component of an investigational new drug application. The physicochemical and biological characterisation of NCEs is an important factor in product development.[9]

***3.2. Formulation of conventional or novel drug delivery system:***

**a. Formulation of conventional drug delivery system:**

**1) Tablets:** They are compressed solid dosage form that contain medicaments with or without excipients used to diagnosed or cure the diseases. Ex. compressed tablets, multiple compressed, repeat action delayed release, sugar coated film coated. Machines: single station, multi station, tablet compressing

machines.

**2) Capsule:** It is pharmaceutical dosage forms in which the drug or a mixture of drugs is enclosed in a gelatin Shell or any other suitable material to form various shapes.

Type - hard gelatin, soft gelatin, enteric coating, sustains release, rectal, vaginal.

**3) Oral liquid:** Liquid orals are the homogeneous liquid preparations containing one or more active ingredients with or without additives dissolved in a suitable vehicle, meant for oral administration.

Type: syrups, elixirs, linctus's, mixtures, oral solutions, oral suspensions, emulsion, drops.

**4) Parentereral:** Parenteral dosage is a sterile drug product, which is presented in the form of solution, suspension, emulsion, or reconstituted lyophilized powder, suitable for administration by injection.

Type: liquid, powder, emulsion, suspension , oily, Infusion for injection.

**b. Formulation of novel drug delivery system:**

**1) Controlled drug delivery system:** A controlled drug delivery system is designed to deliver the correct dose of a therapy directly to the intended zone and at the appropriate time.

**2) Nano-carriers:** Nanocarriers are useful in drug delivery because they can carry medications to specific targets, allowing drugs to be given to specific organs or cells but not others.

Ex- liposomes, phytosomes, nanoparticles.

**3) Vesicular drug delivery system:** The vesicular drug delivery system is one of the technologies can improve medication bioavailability and reduce toxicity by delivering the drug to a specific spot.

**4) Gastro retentive drug delivery system:** Gastro retentive delivery systems are designed to be retained in the stomach for an extended period of time and release their active ingredients, allowing for sustained and prolonged drug input to the upper part of the gastrointestinal (GI) tract.

**5) Nose-Brain drug delivery system:** It is an interesting approach to deliver a drug directly in the brain through the nose. Intranasal drug delivery is very beneficial because it avoids first-pass metabolism and achieves a greater concentration of drugs in the central nervous system (CNS) at a low dose.

### *3.3. Evaluation:*

**a. Solid dosage form :**

**1) Dissolution & disintegration test:**

**Dissolution test:** Dissolution is the process by which a solid solute enters a solution. Pharmaceutically, it may be defined as the amount of drug substance that goes into solution per unit time under standardized conditions of liquid/solid interface, temperature and solvent composition.


**Fig. No.7: Dissolution test appratus**

**Disintegration test:** The disintegration test is a measure of the time required under a set of conditions for a group of tablets to disintegrate into particles which will pass through a 10 mesh screen. We use a basket that holds 1 to 6 tablets to perform a tablet disintegration test. This is then elevated and dropped into a beaker of water to imitate stomach. If the tablets or capsules float, perforated plastic disks are placed on top of them to keep them submerged.

**Fig. No.8: Disintegration test appratus**

**2) Friability & hardness test:**

**Friability test:** The Roche Friabillator is used to test the tablet's friability. Before placing the tablets in the device, their initial weight is checked, and batches are separated to check accordingly. The tablet's initial and final weights are measured. Friability testing is frequently associated with hardness testing.


**Fig. No.9: Friability test appratus**

**Hardness test:** It is the amount of force necessary to crush the tablet when it is put on its edge. The test is carried out in order to satisfy the demand for pressure changes on the tableting machine.

Hardness of the tablets can be determined by using following apparatus:

1. pFizer hardness tester.
2. Monsanto hardness tester.

**Fig. No.10A: pFizer hardness tester** **Fig. No.10B: Monsanto hardness tester**

3) Weight variation & content uniformity:

Weight variation test: To determine weight uniformity, a comparison of 20 tablets' average weight is estimated individual weight is performed. Formula= W average – W initial/W average x 100%.

**Content uniformity test:** 10 powdered tablets and 100 mg equivalent powder are dissolved in a suitable solvent to form a 100 ml solution and dilute it 100 times.

**B. Liquid dosage forms:**

A) Leakage & Clarity test:

**Leakage test:** 10 containers filled with liquid dosage form and inverted for 24 hours moreover, check for leakage if the rubber closure is used. Leakage test for ampoules is intended to detect incompletely sealed ampoules so that they discarded in order to maintain the sterile conditions can be medicines.

**Clarity test:** Dilute the preparations and test for cloudiness with clean water as a control. In this test, transparent or white particles were noticed against a black background, while black or dark particles were observed against a white background.

**B) Sterility & Pyrogen test:**

**Sterility test:** Sterility testing attempts to reveal the presence or absence of viable micro organisms in a sample of containers taken from batch of product.

**Pyrogen test:** Limulus Amoebocyte Lysate (LAL) of limulus polymethyls gel is used 0.1 ml sample with the L A L reagent incubation for 1 hr at 37 ºC clot is analysed. Used to detect the presence and concentration of bacterial endotoxins in drugs and biological products.

**C) Semisolid dosage form:**

**Viscosity:** The viscosity is a property of liquid related to resistance to flow. A Brookfield synchrolectric viscometer with a spindle is used to determine viscosity. The formulas were filled in, and the spindle was dropped perpendicularly, taking care not to touch the bottom of the jar. The spindle was rotated in the gel at 0.5, 1, 2.5, and 5 rpm shear rates.

**pH:** The pH is determine by means of the various methods like used of pH meter electrode measures the pH. The pH probe measures the difference between the internal electrode and the reference electrode in a pH probe to generate a voltage from the hydrogen ions, which is then converted into a readable pH value by the pH meter. The range goes from 0 - 14, with 7 being neutral. pHs of less than 7 indicate acidity, whereas a pH of greater than 7 indicates a base.

### *3.4. Labelling and packaging:*

**A) Types of packaging:**

**Defination:** Packaging is the most cost-effective manner of presenting, safeguarding, identifying, informing, containing, making it easy to use, maintaining integrity, and stabilizing a product. Packaging is the science, art, and technology of enclosing or securing commodities for distribution, storage, sale, and use. It also refers to the packaging design, review, and production processes.

**Types:**

**1) Primary Packaging**: Primary packaging is the packaging that's in direct contact with the usable or consumable product you're selling. e.g. Blisters, Vials, etc

**2) Secondary Packaging**: Secondary Packaging is the packaging that pulls together all the primary packaging forms of a single product. e.g. Cartons, paperboard, etc

**3) Tertiary Packaging**: Tertiary Packaging enables more secondary packaging to be handled and moved on mass and at scale. e.g. Cardboard boxes.

**B) Packaging material**s:

**1) Glass**: They are most commonly used for storing pharma products due to superior protecting quality. Borosilicate glass type 1 it contains 80 % silica 10% boric acid small amount of sodium oxide.

**2) Plastic**:

They contains one or more polymer together with additives desired shape can be given easily. Materials used: polyethene, polystyrene, polycarbonate, polyvinyl chloride, polypropylene etc**.**

**3) Metal: :**

Metals are more versatile of the all products that used . Ex: aluminium, tin, Products tablets, blisters, collapsible tubes, cans, sachets, poches, membranes. etc.

**4) Cotton:** It is used for wadding in solid preparations prevent collisional.

**C) Evaluation test for packaging materials:**

**1) Glass:**

Glass is one of the most widely used material for parenteral product, so special care has to be taken in case of the glass.

**Evaluation test for glass containers:**

**Powdered glass test:**

It estimate the amount of alkali leached from the glass powder. It is performed to determine the type of glass used in packaging.

**Water attack test:**

It is performed for the Type-II glass.(treated soda lime) The principle involved in this, whether the alkali leaches from the surface of container. The basic analysis done by using methyl red indicator. 3 or more containers should be rinsed with high quality water. Fill each container to 90% capacity or higher. Cap all flasks and autoclave for 60 minutes. Cool the contents of the 250ml flask to a volume of 100ml after emptying the containers. 5 drops of methyl red solution While warm, titrate with 0.02N Sulphuric acid. Keep track of the amount consumed. Volume should not be exceeded.

**2) Plastic:**

High molecular weight synthetic polymers make up plastic. One or more polymers are combined with certain additives to create plastic. Polyethylene, polypropylene, polyvinyl, and other polymers are often utilized.

**Evaluation test for plastic container:**

**Leakage Test:**

10 water-filled containers with their corresponding lids are used. They are kept inverted at room temperature for 24 hours. The test is considered successful if there are no signs of container leaking. plastic bottles kept upside-down.

**Transparency Test:**

1 g hydrazine sulphate in 100 ml water; leave for 6 hours. Allow 25ml of 10%w/v hexamine to stand in 25ml of this solution for 24 hours. Preparation of the test solution: - Diluting the normal solution 16 times yields the sample. Fill 5 containers till cloudiness is distinguishable from water- filled containers. At 640 nm, the absorbance range is 0.37 to 0.43.

**Collapsibility test**:

This test is applicable to containers which are to be squeezed in order to remove the contents.

**Water vapour permeability test**:

There are several paths for water vapour to take when entering or leaving containers.

**3) Closure:**

Closures are the devices by means of which containers can be opened and closed. A closure is the part of package which prevent the contents from escaping and allow no substance to enter the container.

**Evaluation test for closure materials:**

**Fragmentation Test:**

This test applies to closures that are intended to be pierced by a hypodermic needle. 12 clean vials are filled with 4 ml of water and their lids are screwed on. With a hypodermic needle, 1 ml of water and 1 ml of air are introduced to the vial after 16 hours of standing allowed. This operation is repeated four times, each time with a different needle. The water in the vial is filtered using a filter with 0.5-micron pore size. The maximum number of closing components allowed should be retained.

**D) <u>Labelling for different dosage forms:</u>**

**Label:**

Label means a display of written, printed or graphic matter upon immediate container or the wrapper of a drug package. The term "labelling" refers to all labels and other written, printed, or graphic matter on an article's immediate container, as well as any packaging or wrapper in which it is encased, excluding any exterior shipping container. All guidliness should be followed while labeling a dosage form. Product name, drug facts, table, active ingredients, purpose and use, warnings, directions, allergic reactions, expiration date, date of manufacture, and various types of pharmaceuticals should all be adequately mentioned.

**1) Manufacturer label:**

A label issued by the medicine's maker, packer, or distributor that includes drug information for use by doctors, pharmacists, or nurses.

**2) Dispensing Label**:

A label that includes the patient's name, strength, batch number, and expiration date of the medication, as well as dose and usage directions, delivery date, storage instructions, and the name and address of the pharmacy.

**Functions of Label:**

- For identification of the product
- Provide ingredients information
- Purpose /use of the product
- Child safety
- Other information like maximum retail price (MRP), Batch No, Shelf-life etc.[10]

**MODULE-4**

**Introduction of acne:**

Acne is a skin condition that occurs when the hair follicles plug with oil and dead skin cells. Is can cause irritation, itching to the skin. If it is not treated on time, it cause various skin allergies to skin like sweeling, redness of skin etc.

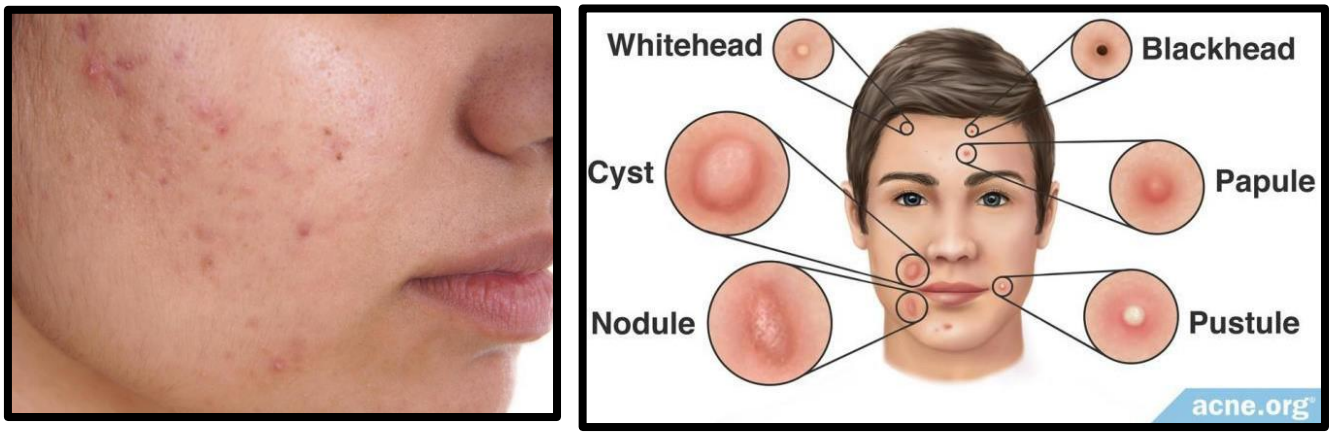



**Fig. No.11: Acne**

**Epidemiology of acne:**

Acne is the most common type of skin condition. It is most widespread among older children, teenagers and young adults. Around 80% of 11 to 30-year-olds are affected by acne. Most acne cases in girls occur between the ages of 14 to 17 and in boys the condition is most common in 16 to 19- year-olds. Most people will experience repeated episodes, or flare-ups, of acne for several years before finding that their symptoms gradually start to improve as they get older. The symptoms of acne usually disappear when a person is in their twenties.[11]

**Cream :**

Creams are the topical preparations which can be applied on the skin. Creams are used for cosmetic purposes such as cleansing, beautifying, improving appearances, protective or for therapeutic function. These topical formulations are used for the localized effect for the delivery of the drug into the underlying layer of the skin or the mucous membrane.

***Ideal Properties of cream :***

1) It easy to apply
2) It spread easily on the skin
3) Less irritation to the skin.[12]

**Aim:** Formulation & evaluation cream of ***coriander*** extract for anti-acne activity.

**Objectives:**

1) To carry out ethanolic extract of ***Coriander*** powder by soxhlet extraction method.
2) To carry out phytochemical screening of ***Coriander*** extract.
3) To formulate ***Coriander*** extract cream.
4) To evaluate the ***coriander extract*** cream.
5) To carry out in-vitro anti-acne activity of ***Coriander*** extract cream.

## Drug Profile :

***Coriander :***

**Fig. No.12: *Coriander***

**Synonyms:** Dhana, Havija, Malli

**Biological Source:** ***Coriander*** is derived from the dried, ripe fruits of ***Coriandrum*** sativum (Apiaceae).

**Chemical constituents:** Linalool, Pinene, Smalll amount of fixed oil and protein.

| **Kingdom** | **Plantae** |
|---|---|
| **Subkingdom** | **Angiospermae** |
| **Order** | **Apiales** |
| **Family** | **Apiaceae** |
| **Species** | ***Coriandrum sativum*** |

**Table. No. 03: Taxonomical character of *Coriander***

**Uses:**

- Anti-inflammatory activity
- Treat skin disease
- Anti-microbial activity.
- Anti-acne. [13]

## Review of literature:[14 15 16]

**Table. No. 04: Review of literature**

| **Name of the author & year** | **Title of the article** | **Conclusion** |
|---|---|---|
| Deepak Kumar Shrivastava 2017 | Phytochemical analysis of a miracle herb Coriander sativum | In the present study, coriander sativum ethanolic extraction method & Phytochemical screening of extract. |
| Mr. Jadhav Narhari Balasaheb 2021 | Formulation and evaluation of herbal cream by using natural ingredients | The study found that formulation of the anti acne cream. |
| Swaranjali G. Shinde 2022 | Formulation and evaluation of Herbal face cream ( Coriander ) | The aim of present study was evaluate the anti acne cream. |

**Preformulation studies :**

Preformulation studies includes the study of physical, chemical properties of the drug substance to develop a safe, effective and stable dosage form. It also include the particle size, shape, odour, colour of the drug used for the formulation.[17]

**Fig. No.13:Preformulation studies of *Coriander***

**Extraction of *coriander* Powder:**

- 25 gm of powder of dried seeds of ***coriander*** is placed in thimble holder.
- About 300 ml of ethanol is filled in the flask.
- The thimble was clogged with cotton in order to avoid transfer of sample particles to the distillation flask.
- The drug was extracted with ethanol in soxhlet apparatus for 3h.
- The etanolic extract is filtered and concentrated to give ethanolic extract.[18]

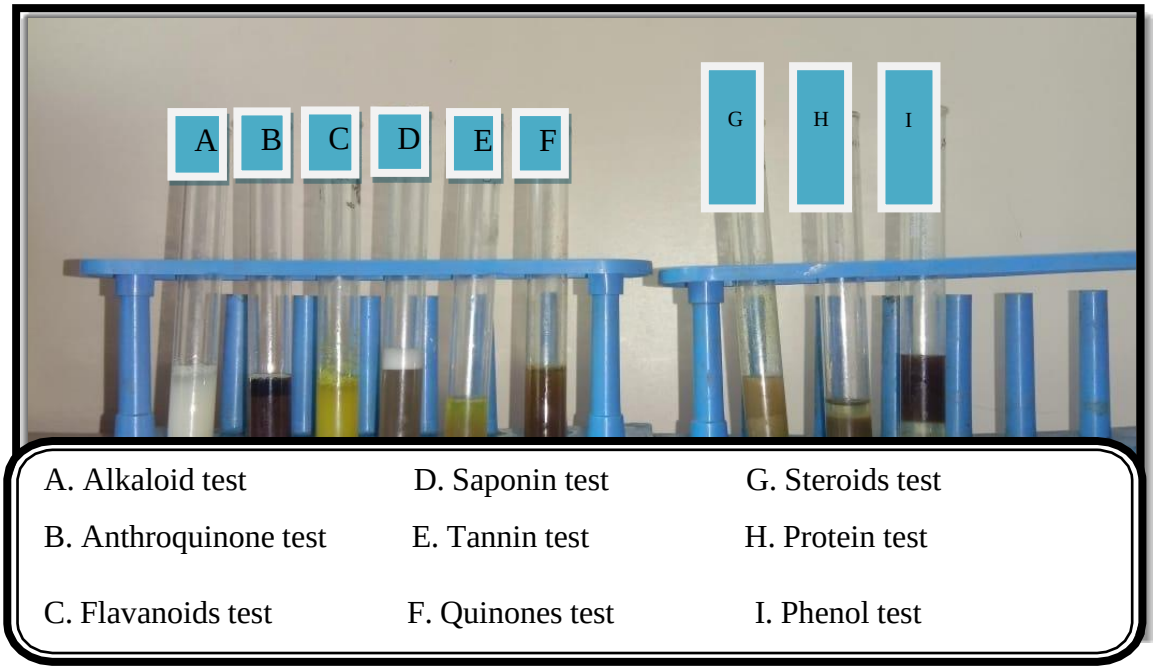
**Fig. No.14:Extraction of Coriander**

***Phytochemical screening of extract:***[19 20 21 22]

| ***Phytochemical test*** | ***Description of test & Observations*** |
|---|---|
| **Alkaloid test** | A fraction of extract was treat with Mayers reagents ( 1.36 gm Mercuric chloride solution & 5 gm potassium iodide ) and formation of white colour ppt. |
| **Tannin test** | The extract was treated with dil. $HNO_3$, The extract turn form reddish to yellow colour ppt. |
| **Phenol test** | The fraction of extract was treated with 5% Ferric chloride and observed for formation of deep or black colour. |
| **Flavonoids test** | A small amount of extract was treated with aqueous aqueous NAOH & HCL formation of yellow orange colour. |
| **Steroids test** | 1 gm extract was treated with chloroform, acetic anhydride and sulphuric acid was added and formation of dark pink or red colour. |
| **Quinones test** | Take few gm of extract and treat with 2 ml of Conc. HCL. And formation of the yellow colour precipitate. |
| **Saponin test** | The extract is treated with vigorously shaken with water and observed for the formation of precipitate form. |
| **Anthraquinone test** | A few gm of extract was heated with 10% ferric chloride solution and 1 ml of Conc. HCL. The extract was cooled, filtered was shaken with diethyl ether. And formation of the pink or deep red colour. |
| **Protein test** | The extract was treated with aqueous ninhydrin and observed for the presence of purple colour indicating the presence of protein. |

**Table. No. 05: Phytochemical screening description**

**Fig. No.15:Phytochemical screening of *Coriander***



***Excipient used in formulation :***[23 24 25]

| Ingredients | Glycerin | Sodium carbonate | Methyl paraben | Beeswax | Isopropyl alcohol |
|---|---|---|---|---|---|
| Mol. Formula | $C_3H_8O_3$ | $NA_2CO_3$ | C8H8O3 | C46H92O2 | $C_3H_8O$ |
| Mol. Weight | 192.9 g/mol | 106 g/mol | 152.15 g/mol | 300 g/mol | 60 g/mol |
| IUPAC Name | Propane-1,2,3-Triol | Disodium Carbonate | Methyl-4- Hydroxy benzoate | Bees wax | 2-propanol |
| Use | Humectant | Cleanser | preservative | Thickener | Astringent |
| pH | 6-7 | 10-11 | 5.8 | 8 | 7 |
| Appearance | Colourless liquid | White powder | Crystal powder | Solid | Clear liquid |
| Odour | Odourless | Odourless | Odourless | Agreeable | Slight |
| Melting point | $18^0$ C | $851^0$ C | 125 $^0$C | 62-65 $^0$C | -89$^0$C |
| Boiling point | $290^0$ C | 1600 $^0$C | 270 $^0$C | 144-147 $^0$C | 82.3 $^0$C |
| Density | 1.26 g/cm$^3$ | 2.54 g/Cm$^3$ | 1.46 g/cm$^3$ | 0.958 g/Cm$^3$ | 0.785 |
| Specific gravity | 1.25 kg m$^{-3}$ | 2.53 kg m$^{-3}$ | 1.36 kg m$^{-3}$ | 0.958 kg m$^{-3}$ | 0.785 kg m$^{-3}$ |

**Table. No. 06: Excipient used in formulation**

**Method of preparation of cream:**[26 27]

| *Ingredients* | *Qty taken For 30 gm* | *Use of ingredients* |
|---|---|---|
| Bees wax | 6.2 gm | Lubricant |
| Potassium hydroxide | 4.8 gm | pH stabilizer |
| Sodium carbonate | 3 gm | Cleanser |
| White Soft Paraffin | 3.6 gm | Moisturizer, treat itching |
| Isopropyl alcohol | 3.6 ml | Astringent |
| Coriander Extract | 1 gm | Main ingredient |
| Glycerin | 2.25 ml | Humectant |
| Distilled water | q.s. | Solvent |
| Methyl Paraben | 3 gm | Preservative |
| Rose oil | 1 ml | Perfume, Emollients |

**Table. No. 07: Quantity of prepare cream**

***Formulation of Cream:***

Weigh accurately all the ingredients

⇩

First oil phase is prepared by the mixture of Bees wax, Potassium hydroxide, Sodium carbonate and White soft paraffin were melted at $70^0$ C in a beaker on a water bath.

After that aqueous phase was prepared of Isopropyl alcohol, Drug extract of ***Coriander*** ( Active drug ), Glycerin, Distilled water were heated at $70^0$ C in another beaker on a water bath.

⇩

The aqueous phase was added to the oil phase at $70^0$ C at continuous stirring.

Then add Perfume ( Rose oil ) and Preservative ( Methyl paraben ) with continuous stirring.The mixture is put in room temperature with

continuous stirring.

⇩

Then formation of cream are produced.

⇩

Finally product is transferred into suitable Container.[28 29]


**Fig. No.16:Formulated cream of *Coriander* with labelling**

***Evaluation test:***

**1) Appearance :** The physical appearance of cream was observed visually. colour, odour and nature were all calculated in this test.
**2) pH :** The auto digital pH meter is used in this method. Firstly Calibrating the pH meter with distilled water. 1.0 gm of cream are dissolved in 10 ml of distilled water and its pH is measure.
**3) Homogeneity:** Homogeneity of the prepared creams was confirm by the visual appearance of touch.
**4) Accelerated stability testing:** The stability of all creams was checked by measuring both pH and spreadability of the prepared creams at three different temperature conditions that is in hot air oven at 50°C, refrigerator at 10°C and at room temperature.
**5) After Feel:** Emolliency, slipperiness and amount of residue left after the application of the fixed amount of cream was found to be good.
**6) Removal test :** The cream formulations are applied on the skin was easily removed by was washing with tap water.
7) Irritancy test : All formulations shows no redness edema inflammation and irritation and during irritancy studies these formulations are found to be safe to use for the skin.
**8) Spreadability test:** Spreadability of formulated cream was measured by placing sample in between two slides then compressed to uniform thickness by placing a definite weight for a definite time. Spreadability was calculated by the following formula:

$$\text{Formula: } S = \frac{m \times l}{t}$$

Where,
S = Spreadability, m= Weight of the upper slide, t = Time taken
l = Length of glass slide t = Time taken.[30 31 32]

## Results & Discussion :

**Table. No.08: Phytochemical screening of extract**

| Sr. No. | Constituents | Coriander extract |
|---|---|---|
| 01 | Alkaloid | + |
| 02 | Tannin | + |
| 03 | Phenols | + |
| 04 | Flavonoids | + |
| 05 | Steroids | + |
| 06 | Quinones | + |
| 07 | Saponin | - |
| 08 | Anthraquinone | + |
| 09 | Proteins | + |


**Fig. No.17:Spreadability test of cream** **Fig. No.18:pH test of cream**

| Sr. No | Test | Observations |
|---|---|---|
| 1 | Colour | Yellowish White |
| 2 | Odour | Characteristics |
| 3 | pH | 5.41 |
| 4 | Removal | Easily removed by tap water |
| 5 | Irritancy test | No irritation on the application, so safe for skin |
| 6 | Homogeneity | Satisfied |
| 7 | After feel | Emollient |
| 8 | Stability test | No seperation occurs so, it's formed to be safe. |
| 9 | Spreadability test | 3.8 |

**Table. No.09: Results**

## Conclusion :

- It is concluded that the prepared formulation showed good Spreadability, no evidence of irritation and good consistency during the study period. From the above study it can be concluded that it is possible to develop creams with herbal extracts.
- The results of different tests of cream showed that the formation could be used topically in order to protect skin against damage and prevent acne.
- It is concluded that the extract of coriander is to get multi purpose effects such as anti wrinkle, anti acne, sunscreen effect of skin, etc.
- The further research of prepared cream will carry out to check scientific action of selected formulation. The studies suggest that composition of extract cream are more stable and safe.

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