JHARKHAND
Rai University
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# PRACTICAL LAB MANUAL

## INDUSTRIAL PHARMACY - I

## B.Pharm V$^{th}$ Semester

# EXPERIMENT NO: 01

## PREFORMULATION STUDY FOR PREPARED GRANULES

**AIM:** To perform different preformulation studies of prepared granules.

**REQUIREMENTS:** Measuring Cylinder, Funnel, Sieves, Mortar & Pestle, Spatula.

**PRINCIPLE:** Preformulation is defined as the phase of research and development in which preformulation studies characterize physical and chemical properties of a drug molecule in order to develop safe, effective and stable dosage form. The Objective of preformulation study is to develop the elegant, stable, effective and safe dosage form by establishing kinetic rate profile, compatibility with the other ingredients and establish Physico-chemical parameter of new drug substances. The major preformulation studies/parameters of granules are as follows:

1. **Bulk density:** It is defined as ratio of total mass of the powder to the bulk volume of powder. It gives an idea about tablet porosity and its relationship with disintegration time and hardness of a tablet. It is measured by pouring weighed powder into a measuring cylinder and the volume is noted down. It is expressed in gm/ml and is given by

   $D_b = M/V_o$

   Where,

   M= Mass of powder,

   $V_o$ = Bulk volume of powder

2. **Tapped density:** It is defined as ratio of total mass of the powder to the tapped volume of powder. Tapped volume is measured by tapping the powder to constant volume. It is expressed in gm/ml and is given by:

   $$D_t = M/V_t$$

   Where,

   M= Mass of powder,

   $V_t$ = Tapped volume of powder

3. **Angle of repose (Θ):** It is the maximum angle possible between surface of pile of powder and the horizontal plane, can be used to measure frictional forces in a powder.

   $$\Theta = \tan^{-1}(h/r)$$

   Where,

Θ= angle of repose

H height of the powder in cm, R is the radius of heap of powder.

**Relationship between Angle of reposes and flow property**

| **Angle of repose(θ)** | **Type of flow** |
|---|---|
| <25 | Excellent |
| 25-30 | Good |
| 30-40 | Passable |
| >40 | Very poor |

1. **Carr's Compressibility Index:** It indicates the ease with which a material can be induced to flow; it is expressed as a percentage and is given by I = (Dt-Db)/Dt ×100

Where,

D is the tapped density of the powder.

Db is the bulk density of the powder.

**Relationship between Carr's index and flow property**

| Carr's index | Type of flow |
|---|---|
| 5-15 | Excellent |
| 12-15 | Good |
| 15-22 | Fair |
| 23-30 | Poor |
| 33-38 | Very poor |
| >40 | Extremely poor |

2. **Hausner's ratio:** It indicates the flow properties of the powder and is measured by the ratio of tapped density to the bulk density.

Hausner's ratio = (Tapped density)/ (Bulk density) ×100

Values of Hausner's ratio :< 1.25: good flow and > 1.25: poor flow

If Hausner's ratio is between 1.25-1.5, flow property can be improved by addition of glidants.

1. **Measurement Techniques: Size and Size Distribution Analysis:** The particle-size distribution (PSD) of a powder, or granular material, is a list of values or a mathematical function that defines the relative amount, (typically by mass) of particles present according to size.

   The size and shape distribution of the metal particles impacts powder behaviour during die filling, compaction, and sintering, and therefore influences the physical properties of the parts created. In the pharmaceutical industry the size of active ingredients influences critical characteristics including content uniformity, dissolution and absorption rates.

   1. Sieve Analysis
   2. Air elutriation analysis
   3. Photo analysis
   4. Optical counting methods
   5. Electro resistance counting methods
   6. Sedimentation techniques
   7. Laser diffraction methods

The way PSD is usually defined by the method by which it is determined. The most easily understood method of determination is sieve analysis, where powder is separated on sieves of different sizes. Thus, the PSD is defined in terms of discrete size ranges: e.g. "% of sample between 45 μm and 53 μm", when sieves of these sizes are used. The PSD is usually determined over a list of size ranges that covers nearly all the sizes present in the sample. However, the idea of the notional "sieve", that "retains" particles above a certain size, and "passes" particles below that size, is universally used in presenting PSD data of all kinds.

The PSD may be expressed as a "range" analysis, in which the amount in each size range is listed in order. It may also be presented in "cumulative" form, in which the total of all sizes "retained" or "passed" by a single notional "sieve" is given for a range of sizes. Range analysis is suitable when a particular ideal mid-range particle size is being sought, while cumulative analysis is used where the amount of "under-size" or "over-size" must be controlled.

**PROCEDURE:**

**Bulk density and tapped density:** Pass a quantity of sample sufficient to complete the test through a sieve, if necessary, to break up agglomerates. Into a measuring cylinder of 100 ml,

gently introduce, without compacting, approximately 15g of the test sample and weighed. Carefully level the powder without compacting, if necessary, and read the unsettled apparent volume to the nearest graduated unit. Calculate the bulk density by applying the above formula. The tapped volume is obtained by mechanically tapping the measuring cylinder containing the sample of 15 gm with a fixed drop of 14±2 mm at a nominal rate of 300 drops per mins until a constant volume is observed. Then calculate the tapped density by using the above formula.

After getting the value of bulk density and tapped density, **Carr's Compressibility Index and Hausner's ratio** is calculated by using the formula.

**Angle of repose:** The static angle of repose was measured according to the fixed funnel and free standing cone method. A funnel was clamped with its tip 2cm above a graph paper placed on a flat horizontal surface. The powders were carefully poured through the funnel. Block the orifice of the funnel by thumb. Fill the powder in the funnel and remove the thumb immediately. After emptying the powder from the funnel, measure the height of the pile and diameter.

**Size and Size Distribution Analysis:** Arrange all the sieves on the shaker one above the other in increasing opening order i.e. decreasing sieve number, the one with powder sample occupying the upper most position. Weigh about 50g (W) of given sample and place it over the top sieve(Lowest sieve number).Shake the sieve either mechanically or electrically for a period of half an hour. The powder retained on each sieve is collected and weighed separately. The percentage weight retained on each sieve is calculated by,

Percentage powder retained=

$$\frac{\text{Weight of powder that have retained over the sieve}}{\text{weight of total powder taken for experiment}} \times 100$$

**OBSERVATIONS:**

| S. No | Sieve number passed or retained | Arthematic mean size of opening(μm) | Average size of the particle | Weight retained on a sieve(gm) | %weight retained | Cumulative percentage of oversized particles | Cumulative percentage of undersized |
|---|---|---|---|---|---|---|---|
| | | | | | | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 1 | 10/16 | 1350 | | $W_1$ | | | |
| 2 | 16/22 | 855 | | $W_2$ | | | |
| 3 | 22/40 | 517.5 | | $W_3$ | | | |
| 4 | 40/60 | 287.5 | | $W_4$ | | | |
| 5 | 60/85 | 142.5 | | $W_5$ | | | |
| 6 | 85/100 | 27.5 | | W6 | | | |

**REPORT**:

**The preformulation parameters of the prepared granules were found to be:**

**Bulk density:**

**Tapped density:**

**Carr's Compressibility Index:**

**Hausner's ratio:**

**Angle of repose:**

**Size distribution analysis**: The given sample is size separated by the sieves.

Their frequency distribution curve of the particle was plotted.

The average particle size----µm were found to be maximum of ---%. The average particle size----- µm were found to be minimum of ---------- %

The cumulative size distribution curve were also plotted and the total average particle size is found to be----------µm.

## EXPERIMENT NO: 2

## PREPARATION OF PARACETOMOL TABLETS

**AIM**: To prepare and submit 10 paracetamol (100 mg) tablets by wet granulation method.

**REQUIREMENTS:** Mortar and pestle, spatula, beaker, Sieve

**PRINCIPLE:** Tablet is an important solid dosage form which is usually prepared with the aid of suitable pharmaceutical excipients. Tablets may vary with size, shape, cut, hardness, thickness. Their disintegration and dissolution characteristics and other aspects change depending on their intended use and method of manufacturing.

Compressed tablets are mainly prepared by 3 basic methods

- Wet granulation
- Dry granulation
- Direct compression

Wet granulation is the widely used method for the production of compressed tablets. Steps involved in wet granulation method are

a) Weighing and blending of ingredients
b) Preparing a damp mass by adding wet binder
c) Converting the damp mass into wet granules
d) Drying of granules
e) Sizing the granules by dry screening
f) Addition of lubricants
g) Formation of tablets by compression

During the preparation process each step may influence the quality of tablet produced. In this preparation paracetamol used as API (antipyretic), lactose as adjuvant, starch (purified) as binding agent, starch monohydrate as disintegrant, magnesium stearate as lubricant and talc as Glidant.

**Ingredients table (Formula):**

| S. NO | INGREDIENTS | 1 TABLET | 10 TABLETS | PURPOSE |
|---|---|---|---|---|
| 1 | PARACETAMOL(API) | | | Analgesic & Antipyretic |
| 2 | STARCH (PURIFIED) | | | Binding agent |
| 3 | LACTOSE MONOHYDRATE | | | Diluent |
| 4 | STRARCH MONOHYDRATE | | | Disintegrant |

| | | | | |
|---|---|---|---|---|
| **5** | TALC | | | Glidant |
| **6** | MG.STEARATE | | | Lubricant |

**PROCEDURE:**

a) **Preparation of starch mucilage**: Dissolve 5mg of starch in 100ml of distilled water then resulting mixture is heated on a water bath until the starch is gelatinized by the formation of mucilage.

b) Divide disintegrating agent (starch monohydrate) into 2 portions to incorporate during wet granulation and after drying of granules to act as an intragranular and extra granular disintegrant.

c) **Wet Granulation**: Accurately weigh and mix the specified amount of paracetamol and other excipients (except half of the disintegrating agent and lubricant) until uniform powder is formed by geometric mixing.

d) A damp mass of the mixture is prepared by adding appropriate amount of the 5% starch mucilage and kneading by hand.

e) Wet mass is subsequently passes through a 6/10 mesh sieve/screen to form wet granules. Resulted granules are spread evenly on a large piece of paper in a tray and dried at 40℃-60℃ for 30min in an oven.

f) Dried granules are passed through a sieve 16 or 20 # and mixed with remaining half of the disintegrating agent and lubricant.

g) Resulting granules mixture is compressed in a tablet compression machine to obtain tablets.

h) Prepared tablets are stored properly for further evaluation.

**REPORT**: Paracetamol tablets were prepared by wet granulation method and submitted.

# EXPERIMENT NO: 03

## EVALUATION OF PARACETOMOL TABLETS

**AIM:** To evaluate prepared paracetamol tablets. **REQUIREMENTS:**

Beaker, Test tubes, Test apparatuses **PRINCIPLE:**

Evaluation parameters of tablets:

**APPEARANCE:**

Tablet from each formulation were randomly selected and organoleptic properties such as color, taste, and shape were evaluated.

**HARDNESS TEST:**

The tablet hardness is defined as the force required to break a tablet in a diametric direction. A tablet was placed between two anvils. Force was applied to anvils and crushing strength that causes the tablet to break was recorded. The hardness was measured using Monsanto hardness tester.

**THICKNESS:**

The thickness of tablets was determined using a Vernier calliper. Three tablets from each batch were used, and average values were calculated.

**FRIABILITY TEST:**

The friability of tablets was determined using Roche Friabilator. It is express in percentage (%). Ten or twenty tablets were initially weighed and revolved at 25 rpm for 4 min. The tablets were then reweighed after removal of fines and the percentage of weight loss was calculated. The % friability was then calculated by,

$F = (W_{initial} - W_{fiinal}) \times 100 / W_{initial}$

Acceptance criteria for % friability % weight loss should be less than 1%.

**WEIGHT VARIATION TEST:**

Twenty tablets were selected randomly from each batch and weighed individually on electronic balance. The individual weighed is then compared with average weight for the weight variations. The following percentage deviation in weight variation is allowed (U.S.P).

| Average weight | % difference |
|---|---|
| 130 mg or less | 10 |

| | |
|---|---|
| 130 – 324 mg | 7.5 |
| More than 324 mg | 5 |

**DISINTEGRATION TIME TESTING:**

It was determine using USP tablet disintegration test apparatus, using 900 ml of distilled water without disk at room temperature. Test was performed on 6 tablets. One tablet each is kept in all six tubes. The tubes travel upward and downward in water at 37°C±2°C. The time taken for all the six tablets to break down and pass through the mesh at the bottom of the tube is noted. The tablets pass the test if all the six tablets disintegrate within the prescribed time ( Less than 30 mins for uncoated tablets as per U.S.P).

**IN VITRO DRUG RELEASE STUDY:** The release rate of paracetamol from tablets was determined using United States Pharmacopeia (USP) Dissolution Testing Apparatus Type-II. The dissolution test was performed using 900ml of 5.8pH phosphate buffer, at 37°C±0.5°C and 50 rpm. A sample (10ml) of the solution was withdrawn from the dissolution apparatus hourly and the samples were replaced with fresh dissolution medium. The samples were filtered through a 0.45µ membrane filter. Absorbance of these solutions was measured at 243 nm using a Thermospectronic-1 UV/V double-beam spectrophotometer. Cumulative percentage drug release was calculated using an equation obtained from a standard curve.

**REPORT:** The evaluation tests are performed and all the tablets are found to be in the acceptable limits.

# EXPERIMENT NO: 04

## PREPARATION OF ASPIRIN TABLETS

**AIM**: To prepare and submit 10 Aspirin (100 mg) tablets by wet granulation method.

**REQUIREMENTS:** Mortar and pestle, spatula, beaker, Sieve

**PRINCIPLE**: Tablet is an important solid dosage form which is usually prepared with the aid of suitable pharmaceutical excipients. Tablets may vary with size, shape, cut, hardness, thickness. Their disintegration and dissolution characteristics and other aspects change depending on their intended use and method of manufacturing.

Compressed tablets are mainly prepared by 3 basic methods

- Wet granulation
- Dry granulation
- Direct compression

Wet granulation is the widely used method for the production of compressed tablets. Steps involved in wet granulation method are

h) Weighing and blending of ingredients
i) Preparing a damp mass by adding wet binder
j) Converting the damp mass into wet granules
k) Drying of granules
l) Sizing the granules by dry screening
m) Addition of lubricants
n) Formation of tablets by compression

During the preparation process each step may influence the quality of tablet produced. In this preparation Aspirin used as API (Aspirin, also known as acetylsalicylic acid, is a medication used to treat pain, fever, or inflammation), lactose as adjuvant, acacia as binding agent, starch monohydrate as disintegrant, magnesium stearate as lubricant and talc as Glidant.

**Ingredients table (Formula):**

| S.NO | INGREDIENTS | 1 TABLET | 10 TABLETS | PURPOSE |
|---|---|---|---|---|
| 1 | ASPIRIN (API) | | | Treat Pain, Fever, Or Inflammation |

| | | | | |
|---|---|---|---|---|
| **2** | ACACIA | | | Binding agent |
| **3** | LACTOSE MONOHYDRATE | | | Diluent |
| **4** | STRARCH MONOHYDRATE | | | Disintegrant |
| **5** | TALC | | | Glidant |
| **6** | MG.STEARATE | | | Lubricant |

**PROCEDURE:**

a) Divide disintegrating agent (starch monohydrate) into 2 portions to incorporate during wet granulation and after drying of granules to act as an intragranular and extra granular disintegrant.

b) **Wet Granulation**: Accurately weigh and mix the specified amount of Aspirin and other excipients (except half of the disintegrating agent and lubricant) until uniform powder is formed by geometric mixing.

c) A damp mass of the mixture is prepared by adding appropriate amount of the acacia and drop wise addition of water.

d) Wet mass is subsequently passes through a 6/10 mesh sieve/screen to form wet granules. Resulted granules are spread evenly on a large piece of paper in a tray and dried at 40ºC-60ºC for 30min in an oven.

e) Dried granules are passed through a sieve 16 or 20 # and mixed with remaining half of the disintegrating agent and lubricant.

f) Resulting granules mixture is compressed in a tablet compression machine to obtain tablets.

g) Prepared tablets are stored properly for further evaluation.

**REPORT**: Aspirin tablets were prepared by wet granulation method and submitted.

# EXPERIMENT NO: 05
# EVALUATION OF ASPIRIN TABLETS

**AIM:** To evaluate prepared Aspirin tablets.

**REQUIREMENTS:** Beaker, Test tubes, Test apparatuses **Evaluation parameters of tablets:**

**APPEARANCE:**

Tablet from each formulation were randomly selected and organoleptic properties such as color, taste, and shape were evaluated.

**HARDNESS TEST:**

The tablet hardness is defined as the force required to break a tablet in a diametric direction. A tablet was placed between two anvils. Force was applied to anvils and crushing strength that causes the tablet to break was recorded. The hardness was measured using Monsanto hardness tester.

**THICKNESS:**

The thickness of tablets was determined using a Vernier caliper. Three tablets from each batch were used, and average values were calculated.

**FRIABILITY TEST:**

The friability of tablets was determined using Roche Friabilator. It is express in percentage (%). Ten or twenty tablets were initially weighed and revolved at 25 rpm for 4 min. The tablets were then reweighed after removal of fines and the percentage of weight loss was calculated. The % friability was then calculated by,

$$F = (W_{initial} - W_{fiinal}) \times 100 / W_{initial}$$

Acceptance criteria for % friability % weight loss should be less than 1%.

**WEIGHT VARIATION TEST:**

Twenty tablets were selected randomly from each batch and weighed individually on electronic balance. The individual weighed is then compared with average weight for the weight variations. The following percentage deviation in weight variation is allowed (U.S.P).

| Average weight | % difference |
|---|---|
| 130 mg or less | 10 |
| 130 – 324 mg | 7.5 |
| More than 324 mg | 5 |

**DISINTEGRATION TIME TESTING:**

It was determine using USP tablet disintegration test apparatus, using 900 ml of distilled water without disk at room temperature. Test was performed on 6 tablets. One tablet each is kept in all six tubes. The tubes travel upward and downward in water at 37°C±2°C. The time taken for all the six tablets to break down and pass through the mesh at the bottom of the tube is noted. The tablets pass the test if all the six tablets disintegrate within the prescribed time ( Less than 30 mins for uncoated tablets as per U.S.P).

**IN VITRO DRUG RELEASE STUDY:**

The release rate of Aspirin from tablets was determined using United States Pharmacopeia (USP) Dissolution Testing Apparatus Type-II. The dissolution test was performed using 900ml of 5.8pH phosphate buffer, at 37°C±0.5°C and 50 rpm. A sample (10ml) of the solution was withdrawn from the dissolution apparatus hourly and the samples were replaced with fresh dissolution medium. The samples were filtered through a 0.45µ membrane filter. Absorbance of these solutions was measured at 265 nm using a Thermospectronic-1 UV/V double-beam spectrophotometer. Cumulative percentage drug release was calculated using an equation obtained from a standard curve.

**REPORT:** The evaluation tests are performed and all the tablets are found to be in the acceptable limits.

# EXPERIMENT NO: 06

## FORMULATION OF FILM COATED TABLETS OF PARACETAMOL

**AIM:** To prepare 10 tablets of paracetamol film coated tablets.

**REQUIREMENTS:** Mortar and pestle, Sieve, Beaker, Glass rod

**PRINCIPLE:** All drugs have their own characteristic, like some drugs are bitter in taste or have an unpleasant odor, some are sensitive to light or oxides, some are hygroscopic in nature. Because of this reasons, tablet coating is the choice of option to solve such problems in conventional dosage form. Tablet film coating is performed by two types, one is aqueous film coating (generally water is used as a solvent) and non-aqueous film coating (generally organic solvents are used). Some problems are associated with the non-aqueous film coating like safety of employees (as most of the solvents are dangerous, smell, and they are not good to breathe), atmospheric pollution etc. But key problem is with the approval of the regulatory authority. High quality aqueous film coating must be smooth, uniform and adhere satisfactorily to the tablet surface and ensure chemical stability of a drug. Coating may be applied to a wide range of oral solid dosage forms, including tablets, capsules, and multiparticulate and drug crystals. When coating composition is applied to a batch of tablets in a coating pan, the tablet surfaces become covered with a tacky polymeric film. Before the tablet surface dries, the applied coating changes from a sticky liquid to tacky semisolid and eventually to a non-stick dry surface. The entire coating process is conducted in a series of mechanically operated acorn-shaped coating pans of galvanized iron stainless steel or copper. The smaller pans are used for experimental, developmental, and pilot plant operations, while the larger pans for industrial production.

**Necessity of Tablet Coating:**

- A number of reasons can be suggested, like: The core contains a material which has a bitter taste in the mouth or has an unpleasant odour. Coating will protect the drug from the surroundings with a view to improve its stability.
- Coating will increase the ease by which a tablet can be ingested by the patient.
- Coating will develop the mechanical integrity; means coated products are more resistant to mishandling (abrasion, attrition, etc.)
- The core contains a substance which is incompatible in the presence of light and subject to atmospheric oxidation, i.e. a coating is added to improve stability.

- The coated tablets are packed on high-speed packaging machine. Coating reduces friction and increases packaging rate.
- Coating can modify the drug release profile, e.g., enteric coating, osmotic pump, pulsatile delivery.

**Ingredients table (Formula):**

| Name of the ingredient | Quantity (%w/w) |
|---|---|
| Cellulose acetate | 6.3 |
| PEG 400 | 0.7 |
| Acetone | 89 |
| Deionized water | 4 |

**PROCEDURE:** Paracetamol uncoated tablets are prepared by wet granulation method. The prepared tablets are then coated with film coating solution prepared as below.

**Film coating solution preparation:** The coating solution was prepared by dissolving PEG in water followed by addition of this solution to acetone. Cellulose acetate was then added to the above mixture and stirred to achieve a clear solution.

The coating process was performed in a Vector Hi-Coater LDCS (batch size, 1.5 kg, with inclusion of placebo tablets) at a product temperature of 28ºC. Coated tablets were dried in a vacuum drying oven at 40ºC for 24 hours to remove residual solvent and moisture.

**REPORT:** 10 tablets of paracetamol film coated tablets are prepared and submitted.

# EXPERIMENT NO: 07

## PREPARATION AND EVALUATION OF HARD GELATIN CAPSULES OF TETRACYCLINE HYDROCHLORIDE

**AIM:** To prepare and evaluate hard gelatin capsules of tetracycline hydrochloride.

**REQUIREMENTS:** Mortar and pestle, beaker, test tubes, spatula, glass rod, Test apparatuses

**PRINCIPLE:** Hard gelatin capsule shells are used in most commercial medicated capsules. The community pharmacist also uses hard gelatin capsules in the extemporaneous compounding of prescriptions. The empty capsule shells are made of gelatin, sugar, and water. As such, they can be clear, colourless, and essentially tasteless; or they may be colored with various dyes and made opaque by adding agents such as titanium dioxide. Most commercially available medicated capsules contain combinations of colorants and opaquants to make them distinctive, many with caps and bodies of different colors. Gelatin is obtained by the partial hydrolysis of collagen obtained from the skin, white connective tissue, and bones of animals. In commerce, it is available in the form of a fine powder, a coarse powder, shreds, flakes, or sheets. Gelatin is soluble in hot water and in warm gastric fluid; a gelatin capsule rapidly dissolves and exposes its contents. Gelatin, being a protein, is digested by proteolytic enzymes and absorbed. Advantages of hard gelatin capsule are rapid drug release possible, flexibility of formulation and sealed HGCs are good barriers to atmospheric oxygen. Disadvantages of this dosage form are very bulky materials are a problem, filling equipment process is slower than tablets, generally more costly than tablets, but must judge on a case-by-case basis; concern over maintaining proper shell moisture content.

Tetracycline is used to treat a wide variety of infections, including acne. It is an antibiotic that works by stopping the growth of bacteria. This antibiotic treats only bacterial infections. It will not work for viral infections (e.g., common cold, flu). First Tetracycline hydrochloride granules are prepared by using wet granulation technique by using required ingredients. Then these granules are filled in the hard gelatin capsule shell

**FORMULA:**

| **Name of the ingredient** | **Quantity (mg)** |
|---|---|
| Tetracycline hydrochloride | 100 |

| | |
|---|---|
| Microcrystalline cellulose | 38 |
| PVPK30 | 6 |
| Magnesium stearate | 4 |
| Talc | 2 |
| Alcohol | q.s |

**PROCEDURE:**

**Formulation of Granules of Tetracycline hydrochloride:**

Tetracycline hydrochloride granules were prepared by wet granulation method. Specified quantity of tetracycline hydrochloride, micro crystalline cellulose and PVP K30 will be weighed and mixed uniformly. Required quantity of alcohol drop wise incorporated to the blend. Wet granules will be passed through sieve #10 & air dried for 15 minutes. The dried granules will then be passed through sieve #22. Required quantity of magnesium stearate & talc were added to the granules. The prepared granules were then added to the Size #3 empty hard gelatin capsule.

**Evaluation of prepared capsule of tetracycline hydrochloride:**

**Weight Variation Test:** Twenty capsules were selected randomly from each batch and weighed individually on electronic balance. The individual weighed is then compared with average weight for the weight variations. The % difference should be 10%.

**Disintegration time Testing:** It was determine using disintegration test apparatus, using 900 ml of distilled water with disk (in case capsule floats) at room temperature. Test was performed on 6 capsules. One capsule each is kept in all six tubes. The tubes travel upward and downward in water at 37°C±2°C. The capsules pass the test if no drug or particles other than capsule fragments remained on the mesh or tube. The time taken for that is considered as disintegration time.

**In vitro drug release study:** The release rate of Tetracycline hydrochloride from capsule was determined using United States Pharmacopeia (USP) Dissolution Testing Apparatus Type-II. The dissolution test was performed using 900ml of 5.8pH phosphate buffer, at 37°C±0.5°C and 50 rpm. A sample (10ml) of the solution was withdrawn from the dissolution apparatus hourly and the sample were replaced with fresh dissolution medium. **The samples were filtered through a 0.45µ membrane filter. Absorbance of this solution was measured at 334 nm using a thermospectronic-1 UV/V double beam spectrophotometer.**

# EXPERIMENT NO: 08

## PREPARATION OF CALCIUM GLUCONATE INJECTION

**AIM:** To prepare and submit 10 ml Calcium gluconate injection.

**REQUIREMENTS:** Beaker, Glass rod, Funnel, Filter paper, Ampoule

**PRINCIPLE:** Injections are sterile solutions, emulsions or suspensions. They are prepared by dissolving, emulsifying or suspending an active ingredient and any other substances in water for injection. Injecting is the act of giving medication by use of syringe and needle to obtain the desired therapeutic effect taking into account the patient's safety and comfort. It is suitable for those drugs that are altered or not absorbed by other methods of administration.

Calcium gluconate is a mineral supplement and medication. As a medication it is used by injection into a vein to treat low blood calcium, high blood potassium, and magnesium toxicity.

Supplementation is generally only required when there is not enough calcium in the diet. Calcium Gluconate is the calcium salt of gluconic acid, an oxidation product of glucose, and contains 9.3% calcium, which is about one-third of the calcium in strength of calcium chloride USP. Since it is soluble to the extent of only one part in 30 parts of cold water, the 10% solution is supersaturated and is stabilized by the addition of calcium saccharate tetrahydrate 0.46% w/v.

**FORMULA:**

| **Ingredients** | **1 ml injection** | **10 ml injection** |
|---|---|---|
| calcium gluconate monohydrate | 98 mg | |
| calcium saccharate tetrahydrate | 4.6 mg | |
| Water for injection upto | 1 ml | |

**PROCEDURE:** calcium gluconate monohydrate and calcium saccharate tetrahydrate are dissolved in water for injection in a beaker and makes upto required volume. Filter it and take 1 ml of the filtrate. Then it is transferred into previously sterilized ampoules, sealed properly and sterilized by autoclaving.

**USE:** It is used as mineral supplement and medication.

**REPORT:**

# EXPERIMENT NO: 09

## PREPARATION OF ASCORBIC ACID INJECTION

**AIM:** To prepare and submit 2 ml ascorbic acid injection.

**REQUIREMENTS:** Beaker, Glass rod, Funnel, Filter paper, Ampoule

**PRINCIPLE:** Injections are sterile solutions, emulsions or suspensions. They are prepared by dissolving, emulsifying or suspending an active ingredient and any other substances in water for injection. Injecting is the act of giving medication by use of syringe and needle to obtain the desired therapeutic effect taking into account the patient's safety and comfort. It is suitable for those drugs that are altered or not absorbed by other methods of administration. Ascorbic Acid (vitamin C) is a water-soluble vitamin. It occurs as a white or slightly yellow crystal or powder with a light acidic taste. It is an antiscorbutic product. Ascorbic Acid injection is a clear, colourless to slightly yellow sterile solution of Ascorbic Acid in Water for Injection, for intravenous, intramuscular or subcutaneous use.

**FORMULA:**

| **Ingredients** | **1 Ampoule** | **2 Ampoules** |
|---|---|---|
| Ascorbic Acid | 0.5 gm | 1 gm |
| Water for injection upto | 2 ml | 4 ml |

**PROCEDURE:** Ascorbic acid is dissolved in water for injection in a beaker and makes upto required volume. Filter it and take 2 ml of the filtrate. Then it is transferred into previously sterilized ampoules, sealed properly and sterilized by autoclaving.

**USE:** It is used as anti-scurvy.

**REPORT:**

# EXPERIMENT NO: 10

## PREPARATION OF PHYSOSTIGMINE EYE DROPS

**AIM:** To prepare and submit 10 ml of Physostigmine eye drop.

**REQUIREMENTS:** Beaker, Glass rod, Measuring cylinder

**PRINCIPLE:** Eye drops are saline-containing drops used as an ocular route to administer. Depending on the condition being treated, they may contain steroids, antihistamines, sympathomimetics, nonsteroidal anti-inflammatory drugs (NSAIDs), antibiotics, antifungal, or topical anesthetics. Eye drops sometimes do not have medications in them and are only lubricating and tear-replacing solutions. Eye drops are also used for stopping itching and redness of the eyes. Physostigmine ophthalmic reduces pressure in the eye by increasing the amount of fluid that drains from the eye. It is used to treat glaucoma by lowering pressure inside the eye. Here benzalkonium chloride is used as bactericide and sodium metabisulphite is used as reducing agent.

**FORMULA:**

| **Ingredients** | **For 100 ml** | **For 10 ml** |
|---|---|---|
| Physostigmine sulphate | 0.5 gm | |
| sodium metabisulphite | 0.2gm | |
| Benzalkonium chloride solution | 0.02 gm | |
| Purified water upto | 100.0 ml | |

**PROCEDURE:** Mix sodium metabisulphite and Benzalkonium chloride solution dissolve the medicament in the mixture and adjust the final volume with purified water. Filter the solution and packed in a previously sterilized suitable container or sterilize it after packing.

**PRECAUTION:** Avoid contamination during use.

**REPORT:**

# EXPERIMENT NO: 11

## PREPARATION OF ATROPINE EYE DROPS

**AIM:** To prepare and submit 10 ml of Atropine eye drop.

**REQUIREMENTS:** Beaker, Glass rod, Measuring cylinder, conical flask

**PRINCIPLE:** Eye drops are saline-containing drops used as an ocular route to administer. Depending on the condition being treated, they may contain steroids, antihistamines, sympathomimetics, nonsteroidal anti-inflammatory drugs (NSAIDs), antibiotics, antifungal, or topical anesthetics. Eye drops sometimes do not have medications in them and are only lubricating and tear-replacing solutions. Eye drops are also used for stopping itching and redness of the eyes. Atropine eye drop is used before eye examinations (e.g., refraction) and to treat certain eye conditions (e.g., uveitis). It belongs to a class of drugs known as anticholinergic. Atropine works by widening (dilating) the pupil of the eye.

**FORMULA:**

| **Ingredients** | **For 100 ml** | **For 10 ml** |
|---|---|---|
| Atropine sulphate | 1 gm | |
| Phenyl mercuric nitrate solution, 0.004% w/v | 50 ml | |
| Purified water upto | 100 ml | |

**PROCEDURE:** Weigh the medicament and dissolve it in the bactericidal solution in a small conical flask. Transfer it to a 10 ml measure, rinse the flask, and adjust the final volume with purified water. Sterilize it by autoclaving at 115$^{o}$C for 30 mins.

**PRECAUTION:** Avoid contamination during use.

**REPORT:**

# EXPERIMENT NO: 12

## PREPARATION OF COLD CREAM

**AIM**: To prepare and submit 10gms of cold cream (w/o type of emulsion) **APPARATUS**: Beaker, glass rod, china dish, mortar and pestle, thermometer.

**PRINCIPLE:** Cold cream is w/o type of emulsion, which when applied to the skin, a cooling effect is produced, due to the slow evaporation of water, present in emulsion. Cold cream is prepared by saponification reaction between and alkali-borax; i.e borax reacts with free fatty acids of bees wax and produce borax soap in-situ (ester of fatty acid). This soap acts as emulsifying agent.

In cold cream, the internal phase is oil and external phase is water, hence it forms o/w type of emulsion. But after application on the skin, water evaporates and leads to phase inversion from o/w type to w/o type emulsion. Therefore oily phase, which is remaining (left) on the skin, gives emollient nature. Liquid paraffin is used as emollient and rose oil is used as perfume, to give a pleasant flavour to the cream. **Ingredients table (Formula):**

| **Ingredients** | **Official formula** | **Working formula** |
|---|---|---|
| White Bees Wax | 16 | |
| Liquid paraffin(emollient) | 50 | |
| Borax | 0.8 | |
| Water | 32.2 | |
| Perfume | q.s | |

**PROCEDURE:**

Since there will be little wastage ((loss) during weighing and preparing, to manipulate these practical losses, calculate the ingredients for at least one or two grams extra, than prescribed.

1) Grate the white beeswax in to small pieces. Weigh the required quantity of white beeswax and liquid paraffin and melt in china dish, by heating on a water bath up to 70°C.
2) In a glass beaker, dissolve borax in water and heat up to 70°C

3) When both oily and aqueous phases reach the same temperature (70°C), gradually add borax solution to the melt of beeswax, with constant stirring.
4) Stir continuously until it becomes cool. When the temperature lowers to 40-45°C, incorporate rose oil and mix uniformly, until a homogenous semi solid mass is obtained.

Dispensing: weigh the prescribed quantity of cream on a butter paper and transfer to an ointment jar or metallic/plastic collapsible tube, close it thoroughly and label.

**DIRECTION**: Apply to skin.

**USES**: Cold cream is used as an emollient for the treatment of dry skin. Hence this becomes quite popular in winter season.

**STORAGE**: Store in a cool place but do not allow to freeze.

Auxiliary label: FOR EXTERNAL USE ONLY **REPORT**:

# EXPERIMENT NO: 13

## PREPARATION OF VANISHING CREAM

**AIM**: - To prepare and submit 10gms of vanishing cream (o/w type).

**APPARATUS**: China dish, glass rod, beaker, Bunsen burner, thermometer

**PRINCIPLE**: Vanishing cream is o/w type of emulsion, which when applied to the skin, it vanishes and leaves an almost invisible layer on it. Hence it is called as 'vanishing cream'. The layer left behind after application, acts as a base or foundation, for facial make up. Hence vanishing creams are also called as 'foundation creams'. Since water is an external phase, it will be quickly washed off with water.

The main ingredients of vanishing creams are stearic acid, alkali and water. Stearic acid gives a pearly white shining appearance to the cream, which on application gives a thin white film of free stearic acid. Soap is prepared in-situ by the chemical reaction between alkali and stearic acid, which is used as emulsifying agent.

Vanishing creams are o/w type emulsion; there is a possibility of evaporation of water from the external phase of emulsion. Therefore, glycerine, polyethylene glycol or alcohol are incorporated as humectants, to prevent the drying out of cream, since external phase of vanishing cream is aqueous, it should be protected from the contamination, from microorganisms by adding suitable preservatives, like methyl paraben or propyl paraben. These creams are also be scented pleasantly, using suitable perfumes in small quantities.

| **Ingredients** | **Official Formula** | **Working Formula** |
|---|---|---|
| Stearic acid | 4GM | |
| Potassium hydroxide | 0.28GM | |
| Glycerine (humectants) | 0.8GM | |
| Methyl paraben | 0.02GM | |
| Water | 14.92GM | |
| Perfume | QS.. | |

**PROCEDURE**:

- Melt stearic acid in china dish on water bath by heating up to $70^0$C.

- In a beaker, Dissolve KOH, and methyl paraben (methyl parahydroxybenzoate) in water, add glycerin to it.
- Heat this aqueous solution up to $70^0$C on water bath.
- When both aqueous and oil phases reaches the same temperature $70^0$C, add aqueous phase to the melted stearic acid with continuous stirring.
- Remove the dish from heat and continue the stirring and when temperature reaches $40^0$C, add perfume.
- Mix uniformly until it becomes cool and homogenous cream is obtained.

**DISPENSING:** Weigh the prescribed quantity of cream on the butter paper and transfer to a wide mouthed, small, screw capped plastic or glass bottle or to collapsible tube, seal and label.

**DIRECTION**: Used for external application. Apply to skin where ever necessary.

**STORAGE**: store in a cool place.

**AUXILIARY LABEL:** FOR EXTERNAL USE ONLY

**USES:** vanishing cream is used as foundation for holding the makeup preparation for longer period.

**REPORT**:

# EXPERIMENT NO: 14

## EVALUATION OF GLASS CONTAINERS (AS PER IP)

**AIM:** To carryout different evaluate tests of glass container as per I.P.

**REQUIREMENTS:** Class container, Beaker, Conical flask, Burette, Mortar and pestle, Sieve

**PRINCIPLE:** Glass containers may be colourless or coloured. Neutral glass is a borosilicate glass containing significant amounts of boric oxide, aluminum oxide, alkali and/or alkaline earth oxides. It has a high hydrolytic resistance and a high thermal shock resistance. Soda-lime- silica glass is a silica glass containing alkali metal oxides, mainly sodium oxide and alkaline earth oxides, mainly calcium oxide. It has only a moderate hydrolytic resistance.

**According to their hydrolytic resistance, glass containers are classified as:**

- Type I glass containers which are of neutral glass, with a high hydrolytic resistance, suitable for most preparations whether or not for parenteral use.
- Type II glass containers which are usually of soda-lime- silica glass with high hydrolytic resistance resulting from suitable treatment of the surface. They are suitable for most acidic and neutral, aqueous preparations whether or not for parenteral use.
- Type III glass containers which are usually of soda- lime-silica glass with only moderate hydrolytic resistance. They are generally suitable for non-aqueous preparations for parenteral use, for powders for parenteral use and for preparations not for parenteral use. Glass containers intended for parenteral preparations may be ampoules, vials or bottles. Glass is a common material to be used in either non sterile or sterile liquid dosage forms. It leaches alkali from its surface. Hence, a limit test for alkalinity is to be performed before using it for a particular product. USP and IP provide two tests to determine the chemical resistance of glass containers.

### 1. Powdered Glass Test

From the glass containers, alkaline constituents (oxides of sodium, potassium, calcium, aluminum, etc.) are leached into purified water under conditions of elevated temperatures. When the glass is powdered the leaching of alkali can be enhanced in the powdered is critical. The principle involved in the powdered glass test in estimate the amount of alkali leached form the glass powder. The amount of acid that is necessary to neutralize the released alkali (a specified limit) is specified in the pharmacopoeia. The basic analysis is acid-base titration using methyl red indicator.

## 2. Water Attack Test

This is only for treated soda lime glass containers under the controlled humidity conditions which neutralize the surface alkali and glass will become chemically more resistant. The principle involved in the water attack test is to determine whether the alkali leached form the surface of a container is within the specified limits or not. Since the inner surface is under test entire container (ampoule) has to be used. The amount of acid that is necessary to neutralize the released alkali from the surface is estimated, the leaching of alkali is accelerated using elevated temperature for a specified time. Methyl red indicator is used to determine the end point. The basic is acid-base titration.

**PROCEDURE:**

**Powdered glass test:**

**Step-1**: **Preparation of glass specimen**: Few containers are rinsed thoroughly with purified water and dried with stream of clean air. Grind the containers in a mortar to a fine powder and pass through sieve no.20 and 50.

**Step-2**: **Washing the specimen**: 10gm of the above specimen is taken into 250 ml conical flask and wash it with 30 ml acetone. Repeat the washing, decant the acetone and dried ate specimen after which it is used within 48hr.

**Step-3**: 10gm sample is added with 50ml of high purity water in a 250ml flask. Place it in an autoclave at 121°C±2°C for 30min.Cool it under running water. Decant the solution into another flask, wash again with 15ml high purity water and again decant. Titrate immediately with 0.02N sulphuric acid using methyl red as an indicator and record the volume.

**Water attack test*:***

Rinse thoroughly with high purity water. Fill each container to 90%of its overflow capacity with water and is autoclaved at 121°C for 30min then it is cooled and the liquid is decanted which is titrated with 0.02N sulphuric acid using methyl red as an indicator. The volume of sulfuric acid consumed is the measure of the amount of alkaline oxides present in the glass containers.

**Limits of alkalinity for glass containers:**

| TESTS | CONTAINER | VOL.OF 0.02N $H_2SO_4$ |
|---|---|---|
| **Powdered glass test** | Type I | 1.0 |
| | Type II | 8.5 |
| | Type III | 15.0 |
| **Water attack test** | Type II(100ml or below) | 0.07 |
| | Type II(above 100ml) | 0.02 |

**REPORT:**