TECHNOCRATS

Lab Work Book of

Industrial Pharmacy-I

(BP - 506 P)

Department of Pharmacy

Lab Manual of

Industrial Pharmacy-I

(BP - 506 P)

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PUBLICATIONS

Lab Work Book
of

Industrial Pharmacy I

(BP - 506 P)

Name : .....

Enrollment No. : .....

Institute : .....

Academic Session : .....

Department of Pharmacy

TECHNOCRATS
PUBLICATIONS

Vision of the Institute

To grow as an institute of Excellence for Pharmacy Education and Research and to serve the humanity by sowing the seeds of intellectual, cultural, ethical, and humane sensitivities in the students to develop a scientific temper, and to promote professional and technological expertise.

Mission of the Institute

M 1: To inculcate ethical, moral, cultural and professional values in students

M 2: To provide state of art infrastructure facilities to the staff and students so as to enable them to learn latest technological advancements

M 3: State of art learning of professionalism by the faculty and students

M 4: To produce well learned, devoted and proficient pharmacists

M 5: To make the students competent to meet the professional challenges of future

M 6: To develop entrepreneurship qualities and abilities in the students

PROGRAM OUTCOMES (POs)

1. **Pharmacy Knowledge:** Possess knowledge and comprehension of the core and basic knowledge associated with the profession of pharmacy, including biomedical sciences; pharmaceutical sciences; behavioral, social, and administrative pharmacy sciences; and manufacturing practices.
2. **Planning Abilities:** Demonstrate effective planning abilities including time management, resource management, delegation skills and organizational skills. Develop and implement plans and organize work to meet deadlines.
3. **Problem analysis:** Utilize the principles of scientific enquiry, thinking analytically, clearly and critically, while solving problems and making decisions during daily practice. Find, analyze, evaluate and apply information systematically and shall make defensible decisions.
4. **Modern tool usage:** Learn, select, and apply appropriate methods and procedures, resources, and modern pharmacy-related computing tools with an understanding of thelimitations.
5. **Leadership skills:** Understand and consider the human reaction to change, motivationissues, leadership and team-building when planning changes required for fulfillment of practice, professional and societal responsibilities. Assume participatory roles as responsible citizens or leadership roles when appropriate to facilitate improvement in health and well- being.
6. **Professional Identity:** Understand, analyze and communicate the value of their professional roles in society (e.g. health care professionals, promoters of health, educators, managers, employers, employees).
7. **Pharmaceutical Ethics:** Honour personal values and apply ethical principles in professional and social contexts. Demonstrate behavior that recognizes cultural and personal variability in values, communication and lifestyles. Use ethical frameworks; apply ethical principles while making decisions and take responsibility for the outcomes associated with the decisions.
8. **Communication:** Communicate effectively with the pharmacy community and with society at large, such as, being able to comprehend and write effective reports, make effective presentations and documentation, and give and receive clear instructions.
9. **The Pharmacist and society:** Apply reasoning informed by the contextual knowledge to assess societal, health, safety and legal issues and the consequent responsibilities relevant to the professional pharmacy practice.
10. **Environment and sustainability:** Understand the impact of the professional pharmacy solutions in societal and environmental contexts, and demonstrate the knowledge of, and need for sustainable development.
11. **Life-long learning:** Recognize the need for, and have the preparation and ability to engage in independent and life-long learning in the broadest context of technological change. Self-assess and use feedback effectively from others to identify learning needs and to satisfy these needs on an ongoing basis.

PEOs

PEO 1: To inculcate quality pharmacy education and training through innovative Teaching Learning Process.

PEO 2: To promote professionalism, team spirit, social and ethical commitment with effective interpersonal communication skills to boost leadership role assisting improvement in healthcare sector.

PEO 3: To enhance Industry-Institute-Interaction for industry oriented education and research, which will overcome healthcare problems of the society.

PEO 4: To adapt and implement best practices in the profession by enrichment of knowledge and skills in research and critical thinking

PEO 5: To generate potential knowledge pools with interpersonal and collaborative skills to identify, assess and formulate problems and execute the solution in closely related pharmaceutical industries and to nurture striving desire in students for higher education and career growth.

Course Outcomes (COs):

Student will be able to:

- CO1: Explain how solubility, particle size, particle shape, crystallinity, amorphous structure of pure drug as preformulation parameters plays a major role in pharmaceutical.
- CO2: Determine the formulation and manufacturing procedures of different types of tablet dosage forms and capsule dosage forms.
- CO3: Develop different coating procedures to tablets and evaluate prepared coated tablets.
- CO4: Evaluate materials used for packaging such as glass, plastic and rubber containers.
- CO5: Formulate various types of cosmetics and perform evaluation of cosmetic preparations.

Index

Experiment No. 1

OBJECT:

To perform Preformulation studies for given drug and excipient sample.

Sample:

Sample No.	Particular	Ratio	Remark
1	Drug	1 (alone)	Use of excipients is depend on nature of active drug, dose of active drug and its feasibility on the bases of economy of finished dosage form
2	Drug + Excipient 1	1:1	
3	Drug + Excipient 2	1:1	
4	Excipient 1	1 (alone)	
5	Excipient 2	1 (alone)	
6	Excipient 1 + Excipient 2	1:1	
7	Drug + Excipient 1 + Excipient 2	1:1:1	

REFERENCES:

1. Indian Pharmacopoeia. The controlled publication, New Delhi. 2007, (3), pp 1514,1515,1814,1815.

2. Instruction manual pharmaspec. UV-1700 series. User's system guide. Shimadzu Corporation. Kyoto Japan.

3. Spectrum BX user's guide Perkin Elmer.

4. Beckett, A. H.; Stenlake, J. B. Practical Pharmaceutical Chemistry, 4th Ed (2), 2007, pp 282 – 288.

5. Lachman L., Liberman H.A., Kanig J.L.The Theory and Practice of Industrial Pharmacy, Varghese Publication, New Delhi, Third Edition, Page 171-196.

THEORY:

Delivery of any drug requires a suitable dosage form to get optimum therapeutic effects. The development of such dosage forms fundamental properties of the drug molecule either physical or chemical are required to be determined. Pre-formulation is to determination of physicochemical properties of drug molecule prior to the development of suitably designed drug delivery system. The classical preformulation studies require characterization in solid state as well as in solution state. A good pharmacological and toxicological profile of drug alone does not sufficient for product development. These studies for drug molecule and excipients are essential to reduce problems occur during product development. Hence, overall product development cost as well as manufacturing and distribution time to market also reduces. The ultimate goal of preformulation study is to select right physical form of drug molecule, determine physicochemical properties and evaluate stability of drug and excipients under different conditions. All of these results will contribute to develop suitable drug delivery system for effective therapeutic use. This

drug delivery system should deliver the molecules to its site of action with minimum side effects at a minimum cost. Preformulation studies are usually provides a tool to select suitable excipients compatible with selected drug and play a key role for development of new formulation. Important preformulation study includes identification of drug and excipients followed by particle size analysis, XRD analysis, DSC analysis, solubility analysis, partition coefficient, solution stability and compatibility studies. These all mentioned properties have their own significant effect on development process of formulation. For example, small size of liposome is very critical to avoid first pass effect. Hence, all excipients should be selected in such a manner that there should be minimum effect on liposomal size. Thus, measurement of particle size of excipients is important to design process for preparation of liposome. To reduce the size of liposome further sonication is performed till its particle size is reduced to a significant extent.

PROCEDURE:

Identification of drug and Compatibility Study:

All samples to be analysed are kept at room temperature in sample bag with label. Keep all samples separately in open and closed vial conditions. Finally analysed each samples using following parameters:

Physical Appearance: The physical appearance of the model drugs noted by visual observation as well as by microscopy.

Melting Point: The melting point of drug were determined in triplicate by placing the sample in sealed capillary which is heated using melting point apparatus till the melting of sample in the capillary and melting temperature was recorded using thermometer.

Solubility: Solubilise drug using water or using organic solvents and confirm the drug solubility shown as following category:

Table: Solubility Expressions

Term	Parts of solvent required for 1 part of solute
Very Soluble	Less than 1 part
Freely Soluble	1 to 10 parts
Soluble	10 to 30 parts
Sparingly Soluble	30 to 100 parts
Slightly Soluble	100 to 1000 parts
Very Slightly Soluble	1000 to 10000 parts
Practically Insoluble	More than 10000 parts

Ultraviolet (UV) Spectra of drug: An accurately weighed amount of drug was dissolved in suitable solvent (or phosphate buffer with pH 6.4, pH 6.8 etc.) and the resultant solution was filtered through 0.45 µ filter and scanned in the range of 200-800 nm using UV Spectrophotometer (UV 1800, Shimadzu, Tokyo, Japan). The absorption maxima for all the model drugs were similar to the reported absorption maxima which confirmed the identity of selected drugs.

OBSERVATION TABLE:

Paramter	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6	Sample 7
Physical Appearance							
Melting Point							
Solubility							
UV Spectra Reading (nm)							

RESULT & DISCUSSION:

VIVA QUESTIONS

Q.1. Define Preformulation study.

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Q.2. Write significance of Preformulation studies.

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Q.3. How you will perform compatibility study between drug(s) with excipient(s)?

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Q.4. Differentiate Dissolution and diffusion of drug.

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Q.5. Explain any two parameters of Preformulation studies with examples.

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Experiment No. 2

OBJECT:

To prepare and evaluate Paracetamol tablets.

Formula: Per unit tablet (given)

Ingredient	Quantity given (n)	Quantity taken (n x No. of tablets to be prepared)
Paracetamol	500 mg	
Starch	150 mg	
DCP	50 mg	
Starch (Paste)	10 % w/w	
Talc	2 % w/w	
Magnesium Stearate	2 % w/w	

REFERENCES:

1. Wang C. Application of In Vitro Models in Developmental Neurotoxicity and Pharmaceutics Research. J Mol Pharm Org Process Res.2015;3:e122.

2.http://www.rroij.com/open-access/tablets-manufacturing-methods-and-granulation-techniques-.php?aid=79986.

3. Lachman L., Liberman H.A., Kanig J.L.The Theory and Practice of Industrial Pharmacy, Varghese Publication, New Delhi, Third Edition, Page 293-345.

THEORY:

From past hundred years tablet manufacturers have developed materials and processes that can produce compressed tablets containing a precise amount of an active pharmaceutical ingredient (API) at high speed and at relatively low cost. Granulation may be defined as a size enlargement process which converts small particles into physically stronger & larger agglomerates. Granulation method can be broadly classified into two types: Wet granulation and Dry granulation.

Wet Granulation: The most widely used process of agglomeration in pharmaceutical industry is wet granulation. Wet granulation process simply involves wet massing of the powder blend with a granulating liquid, wet sizing and drying.

Important steps involved in the wet granulation

i) Mixing of the drug(s) and excipients.

ii) Preparation of binder solution.

iii) Mixing of binder solution with powder mixture to form wet mass.

iv) Drying of moist granules.

v) Mixing of screened granules with disintegrant, glidant, and lubricant.

Dry Granulation: In dry granulation process the powder mixture is compressed without the use of heat and solvent. It is the least desirable of all methods of granulation. The two basic procedures are to form a compact of material by compression and then to mill the compact to obtain a granules. Two methods are used for dry granulation. The more widely used method is slugging, where the powder is recompressed and the resulting tablet or slug are milled to yield the granules. The other method is to recompress the powder with pressure rolls using a machine such as Chilosonator.

Steam Granulation: It is modification of wet granulation. Here steam is used as a binder instead of water. Its several benefits includes higher distribution uniformity, higher diffusion rate into powders, more favourable thermal balance during drying step, steam granules are more spherical, have large surface area hence increased dissolution rate of the drug from granules, processing time is shorter therefore more number of tablets are produced per batch, compared to the use of organic solvent water vapour is environmentally friendly, no health hazards to operators, no restriction by ICH on traces left in the granules, freshly distilled steam is sterile and therefore the total count can be kept under control, lowers dissolution rate so can be used for preparation of taste masked granules without modifying availability of the drug.

Melt Granulation / Thermoplastic Granulation: Here granulation is achieved by the addition of moldable binder. That is binder is in solid state at room temperature but melts in the temperature range of 50 – 80˚C. Melted binder then acts like a binding liquid. There is no need of drying phase since dried granules are obtained by cooling it to room temperature.

Foam Granulation: Here liquid binders are added as aqueous foam. It has several benefits over spray(wet) granulation such as it requires less binder than Spray Granulation, requires less water to wet granulate, rate of addition of foam is greater than rate of addition of sprayed liquids, no detrimental effects on granulate, tablet, or in vitro drug dissolution properties, no plugging problems since use of spray nozzles is eliminated, no over wetting, useful for granulating water sensitive formulations, reduces drying time, uniform distribution of binder throughout the powder bed, reduce manufacturing time, less binder required for Immediate Release (IR) and Controlled Release (CR) formulations.

PROCEDURE:

Step 1. Wet granulation method of tablet manufacturing was employed with Starch paste (10 %) as a binding agent and as the granulating agent. Paracetamol tablets were formulated using compositions discussed in the table. Paracetamol, and lactose, weighed then mixed well, after mixing add starch paste and blended to form a damp coherent mass which was screened through a sieve No 10 and dried at 60°C for one hour using Tray Drier. After drying perform size reduction and then sieving using #16.

Step 2. Evaluation of granules:

Particle size distribution of the granules: Particle size distribution of the granules was determined by mesh analysis employing a stack of sieves after granules had been weighed (34 g) and the granules were shaken for 10 min. The quantities of granules on each sieve were obtained gravimetrically.

Evaluation of bulk and tapped densities of the granules: The volume of a known quantity of the

granules from each batch was obtained before and after tapping. The volume before tapping was used to determine the bulk density while the volume after tapping was employed to determine the tap density mathematically. Furthermore, Hausner's quotient and Carr's compressibility index used to determine the flow and compressibility properties of granules were obtained from the equations:

Hausner's quotient = Tapped density / Bulk

Carr's compressibility = Tapped density – Bulk density / Tapped density X 100

Assessment of rate of flow and angle of repose: A simple method whereby weighed quantity of granules from each batch was allowed to flow through an orifice (funnel) at a fixed height was used to determine flow rate. The time taken for the weighed granules to flow out completely from the orifice was recorded. This was performed in triplicate. Flow rate was obtained by the equation below:

Flow rate = Weight of granules / Time (sec)

Furthermore, the angle of repose was determined by calculating tan θ from the height and radius of the cone formed by the granules as they flowed out of the orifice and subsequently obtaining the inverse of tan θ.

$$\theta = \tan^{-1} 2h / d$$

Where: θ = Angle of repose. h = Height of the particles pile. d = Distance from the center of the pile to the edge.

Step 3. Compression of granules

The granules were blended with the glidant (talc) and lubricant (magnesium stearate) for 20 minutes. The blend was compressed using a single punch tableting machine with a punch diameter of 0.75 cm set at 933 Pa (N/m2) compression pressure. The die volume was to correspond to the weight of the tablet to ensure that 500 mg paracetamol is obtained.

Step 4. Evaluation of Tablets

Weight variation: All prepared tablets were evaluated for weight variation as per USP XXIV monograph. Twenty tablets of each batch were used to evaluate weight variation among tablets and mean and standard deviation was calculated.

Table: Weight variation as per USP XXIV monograph.

Weight of tablet	% weight variation allowed
130 mg or less	10 %
130 to 320 mg	7.5 %
320 or above	5 %

Drug content: The tablets were powdered, and 250 mg equivalent weight of Paracetamol in tablet powder was accurately weighted and transferred into a 100 ml volumetric flask. Initially, 10 ml of phosphate buffer (pH 7.4) was added and shaken for 10 min. Thereafter, the volume was made up to 100 ml with buffer. Subsequently, the solution in volumetric flask was filtered, and 1 ml of the filtrate was diluted and analyzed at 247nm using UV-Visible spectrophotometer (Shimadzu UV-1800, Japan). The drug content

of the each sample was estimated from their previously prepared standard curve.

Friability: Friability testing was done by Roche Friabilator with readings in triplicate. To evaluate the degree of friability of the tablets from each batch, ten tablets were randomly selected, dusted and weighed. The tablets were placed in a Roche friabilator (Erweka Gmbh, Germany) and subjected to its tumbling actions at 25 revolutions per minute for four minutes. Afterwards, the tablets were once again dusted and reweighed to determine the percentage loss of weight. Percentage weight loss does not exceed 1 %.

F = Initial Weight – Final Weight / Initial Weight x 100

Mechanical strength of tablets: Although, the crushing strength test is non-compendial, it is undertaken to determine the ability of the tablets to withstand pressure during handling, packaging and transportation. A Monsanto tablet hardness tester (Copley Scientific Ltd, Nottingham, United Kingdom) was employed to determine the mechanical strength of the tablets. The average force required to crush the tablets from each batch was obtained.

Thickness and diameter: The thickness of the matrix tablets was determined using Vernier caliper (Mitutoyo Dial Thickness Gauge, Mitutoyo, Japan) and the results were expressed as mean values of 10 determinations, with standard deviations.

Disintegration studies on the tablets: Six tablets from each batch were utilized for disintegration studies in distilled water at 37°C (plus / minus 2°C) using an Educational Sciences Disintegration Apparatus (Es Eagle Scientific Limited, Nottingham, United Kingdom). The disintegration time was taken to be the time no granule of any tablet was left on the mesh of the apparatus.

In vitro drug release studies: In vitro drug release studies were undertaken using USP apparatus I (basket method). The dissolution medium was 1000 mL of 0.1 N HCl at 37°C for 30 min to depict the gastric medium where the tablets will disintegrate. In all experiments, 5 mL of sample was withdrawn at 5 min interval and replaced with fresh medium to maintain sink condition. Samples were filtered and assayed spectrophotometrically at 230 nm.

Data analysis: Simple statistical analysis was utilized for content uniformity of weight, uniformity of diameter and uniformity of thickness while dissolution efficiency (DE) was used for the *in vitro* dissolution studies.

OBSERVATION TABLE:

S.No.	Parameter	Observation
1	General Appearance	
2	Weight variation	
3	Content Uniformity	
4	Disintegration time	
5	Friability	
6	Drug release % (Dissolution test)	
7	Hardness	
8	Thickness & Diameter	

RESULT & DISCUSSION:

VIVA QUESTIONS

Q.1. Define tablet.

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Q.2. Discuss methods of tablet manufacturing.

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Q.3. What are advantages and disadvantages of tablets ?

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Q.4. Explain role of Starch, Talc and Magnesium Stearate in tablet making.

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Q.5. Write *In Process* evaluation parameters for tablets.

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Experiment No. 3

OBJECT:

To prepare and evaluate Aspirin tablets.

Formula: Per unit tablet (given)

Ingredient	Quantity given (n)	Quantity taken (n x No. of tablets to be prepared)
Aspirin	300 mg	
Maize Starch	20 mg	
Microcrystalline Cellulose	20 mg	
Talc	2 % w/w	
Magnesium Stearate	2 % w/w	

REFERENCES:

1. Kalvimoorthi V., Narasimhan N., Formulation development and evaluation of aspirin delayed release tablets 2011 7(1); Article-004.

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3. Allen L. V and Ansel H. C. (2014). Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems. Philadelphia: Lipincott Williams and Wilkins.

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5. Lachman L., Liberman H.A., Kanig J.L.The Theory and Practice of Industrial Pharmacy, Varghese Publication, New Delhi, Third Edition, Page 293-345.

THEORY:

Direct Compression method: Direct Compression is the simplest form of oral dosage production as it contains the fewest process stages, leading to a shorter process cycle and faster production times.

The processes involved in the manufacture of tablets by direct compression method can be summarized in three steps.

Direct compression technique using induced die feeders: This involves the use of a special feeding device which prevents segregation and enhances the flow of powders from the hopper into the die cavity of a tablet press. The use of induced die feeder also reduces air entrapment, making the fill powder more dense and amenable to compaction. Direct compression technique using induced die feeder is used when formulation ingredients will compact but will not adequately fill the die cavity. Examples of dry binders used in the manufacture of tablet by direct compression method include microcrystalline cellulose, polyethylene glycol 400, polyethylene glycol 6000 etc.

Direct compression technique using dry binders: This technique will affect compression of drugs at relatively low filler to drug ratio, with little addition of preparatory techniques. Materials used as dry binders should possess adequate cohesive or compressibility properties in order to form satisfactory tablets of acceptable hardness and friability. They should possess adequate flowability and bulk density to ensure the die cavities are uniformly filled and hence tablets of uniform weight and drug content would be obtained. They should also have high capacity or low binder to drug ratio in order to make possible the manufacture of suitable sized tablets containing relatively high doses of drugs.

Direct compression technique using direct compression excipients: A direct compression excipient also referred to as direct compressible excipient or direct compression filler/binders are inert, non-medicinal substances which may be compacted with no difficulty and which may do so even when mixed with drug substances. Direct compressible excipients should exhibit satisfactory tableting characteristics. This is because they determine the overall characteristics of the tablet, particularly in regard to the fluidity of the component powders. Direct compressible excipients can also influence the hardness, disintegration and dissolution characteristics of the finished tablets.

PROCEDURE:

Preparation of tablets:

Ensure cleaning of all apparatus, and ensure atmospheric percentage RH below 40 %.

Weigh all the ingredient, sieve by using #20 and mix well in a mortar using pestle for 20 minutes.

Collect the mixed mass and transfer in hopper of compression machine then prepare tablets.

Perform evaluation as per given parameters.

Evaluation of Tablets

Weight variation: All prepared tablets were evaluated for weight variation as per USP XXIV monograph. Twenty tablets of each batch were used to evaluate weight variation among tablets and mean and standard deviation was calculated.

Table: Weight variation as per IP

Weight of tablet	% weight variation allowed
80 mg or less	10 %
80 to 250 mg	7.5 %
250 or above	5 %

Drug content: Dissolve 2 gm of sodium 1-heptanesulfonate in a mixture of 850 ml of water and 150 ml of acetonitrile and adjust with glacial acetic acid to a ph of 3.4 is used as a mobile phase. Mixture of acetonitrile and formic acid (99:1) is used as a diluting solution. Dissolve an accurately weighed quantity of Aspirin in diluting solution to obtain a solution having a known concentration of about 0.5mg per ml as a Standard 20 tablets were weighed and powdered. Powder equivalent to about 100 mg of aspirin dissolved in 20.0ml of diluting solution. Separately Inject equal volumes (20µl) of standard preparation

and sample solution, record the chromatograms and measure the responses for the major peaks. Using c18 column Ultra violet Detector wavelength set at 280 nm

Friability: Friability testing was done by Roche Friabilator with readings in triplicate. To evaluate the degree of friability of the tablets from each batch, ten tablets were randomly selected, dusted and weighed. The tablets were placed in a Roche friabilator (Erweka Gmbh, Germany) and subjected to its tumbling actions at 25 revolutions per minute for four minutes. Afterwards, the tablets were once again dusted and reweighed to determine the percentage loss of weight. Percentage weight loss does not exceed 1 %.

F = Initial Weight – Final Weight / Initial Weight x 100

Mechanical strength of tablets: Although, the crushing strength test is non-compendial, it is undertaken to determine the ability of the tablets to withstand pressure during handling, packaging and transportation. A monsanto tablet hardness tester (Copley Scientific Ltd, Nottingham, United Kingdom) was employed to determine the mechanical strength of the tablets. The average force required to crush the tablets from each batch was obtained.

Thickness and diameter: The thickness of the matrix tablets was determined using vernier caliper (Mitutoyo Dial Thickness Gauge, Mitutoyo, Japan) and the results were expressed as mean values of 10 determinations, with standard deviations

Disintegration studies on the tablets: Six tablets from each batch were utilized for disintegration studies in distilled water at 37°C (plus / minus 2°C) using an Educational Sciences Disintegration Apparatus (Es Eagle Scientific Limited, Nottingham, United Kingdom). The disintegration time was taken to be the time no granule of any tablet was left on the mesh of the apparatus.

In vitro drug release studies: In vitro drug release studies were undertaken using USP apparatus I (basket method). The dissolution medium was 1000 mL of 0.1 N HCl at 37°C for 30 min to depict the gastric medium where the tablets will disintegrate. In all experiments, 5 mL of sample was withdrawn at 5 min interval and replaced with fresh medium to maintain sink condition. Samples were filtered and assayed spectrophotometrically at 230 nm.

The in vitro dissolution studies were carried out using USP apparatus type II at 100 rpm. The dissolution medium consisted 0.1N HCl for 2 hours after 2 hours medium is replaced with phosphate buffer pH 6.8 for 45mins (900 mL), maintained at 37°C ±0.5°C. The drug release at different time intervals was measured by UV-visible spectrophotometer at 265 nm for 0.1N HCl and 280nm for 6.8 phosphate buffer.

Data analysis: Simple statistical analysis was utilized for content uniformity of weight, uniformity of diameter and uniformity of thickness while dissolution efficiency (DE) was used for the *in vitro* dissolution studies.

OBSERVATION TABLE:

S.No.	Parameter	Observation
1	General Appearance	
2	Weight variation	
3	Content Uniformity	
4	Disintegration time	
5	Friability	
6	Drug release % (Dissolution test)	
7	Hardness	
8	Thickness & Diameter	

RESULT & DISCUSSION:.....

VIVA QUESTION

Q.1. Explain Direct Compression process

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Q.2. Which types of drug we can easily be formulated by direct compression method?

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Q.3. Discuss physics of tablet compression in brief.

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Q.4. Write about significance of weight variation test.

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Q.5. How you will handle powder during manufacturing to avoid loss of powder for direct compression to increase productivity and to prevent cross contamination?

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Experiment No. 4

OBJECT:

To perform Enteric coating of tablets.

Formula: Per unit coated tablet: For preparation of Coating Solution

Ingredient	Quantity given (n) Mg/tablet	Quantity taken (n x No. Of tablets to be coated)
Drug coat N-100	10	
HPMC-phthalate	10	
Acetone	100	
Isopropyl alcohol	100	
Dibutyl phthalate	3	
Sunset yellow lake	3	
Titanium Di Oxide	3	

REFERENCES:

1. Kalvimoorthi V., Narasimhan N., Formulation development and evaluation of aspirin delayed release tablets 2011 7(1); Article-004.

2. Lachman L., Liberman H.A., Kanig J.L.The Theory and Practice of Industrial Pharmacy, Varghese Publication, New Delhi, Third Edition, Page 346-373.

THEORY:

Tablet coating is one of the oldest pharmaceutical processes still is existence. Coating is a process by which an essentially dry, outer layer of coating material is applied to the surface of a dosage form in order to confer specific benefits over uncoated variety. Tablet coating is the key step involved in the manufacturing of tablets having controlled release, delayed release profiles. The tablet coating have number of advantages like masking odor, taste, color of the drug, providing physical and chemical protection to drug, Protecting drug from the gastric environment. 3 primary components of tablet coating are tablet properties, coating process and coating composition. Tablets are usually coated in horizontal rotating pan with coating solution is either directly poured or sprayed on to them. The amount of coating on the surface of a tablet is critical to the effectiveness of the oral dosage form. Recent trends in tablet coating focuses on overcoming disadvantage of solvent based coating. This article concerns with the coating process, equipments involved, coated tablets evaluation and specialized coating techniques.

PROCEDURE:

Coating with enteric polymers: The coating suspension was prepared with Drug coat N100, Hydroxypropylmethylcellulose phthalate in different ratios, and Dibutyl phthalate as plasticizer and talc as anti adherent. 140 g core were coated using conventional pan Coating method with enteric polymers coating suspension.

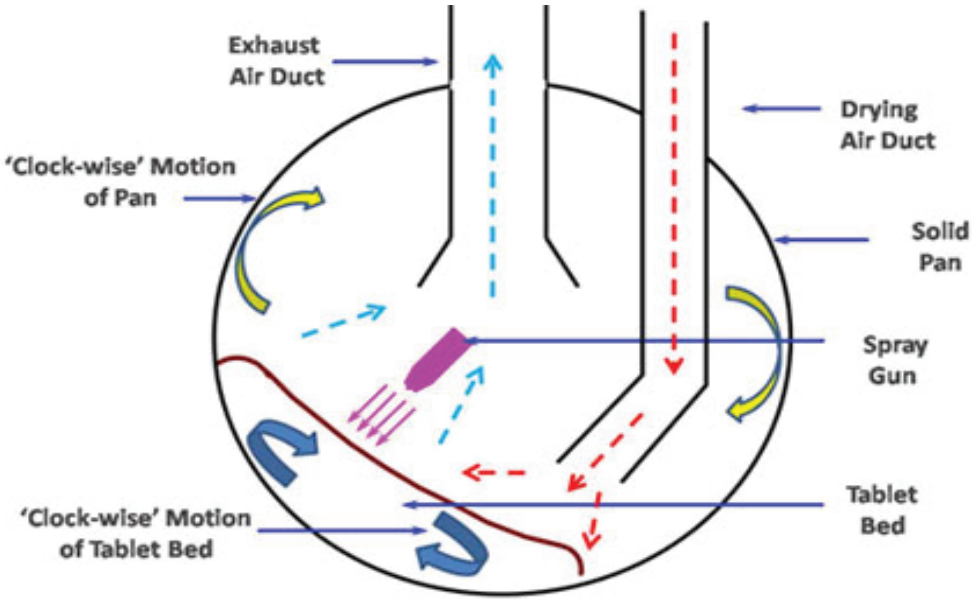

Fig. Coating process by Conventional Coating Pan.

Sprayer was filled with polymer suspension and then applied to the tablet bed with essentially by continuous application of hot air. After completion of coating allow to keep coated tablets cool to room temperature and perform evaluation.

Evaluation of coated tablets:

Percentage weight gain: % Weight gain defined by difference between weight of tablets after coating (Wta) and weight of tablets before coating (Wtb) divided by weight of tablets before coating. It was calculated by following equation.

$$\% \text{ Weight gain} = (Wta\text{-}\ Wtb) / Wtb \times 100$$

Disintegration Time: Disintegration testing of coated dosage forms was carried out in the six tablet basket rack USP disintegration apparatus. One tablet was introduced into each tube of the basket rack assembly of the disintegration apparatus without disc. The assembly was positioned in the beaker containing 0.1N HCl (pH 1.2) maintained at 37±2°C and operated the apparatus for 2 hours. After 2 hours 0.1N HCl was replaced with phosphate buffer 8.0 pH. A disc was added to each tube and operated for further 60 minutes. The disintegration time of each tablet was recorded.

In vitro drug release studies: *In vitro* drug release studies were undertaken using USP apparatus I (basket method). The dissolution medium was 1000 mL of 0.1 N HCl at 37°C for 30 min to depict the gastric medium where the tablets will disintegrate. In all experiments, 5 mL of sample was withdrawn at 5 min interval and replaced with fresh medium to maintain sink condition. Samples were filtered and assayed spectrophotometrically at 230 nm.

The in vitro dissolution studies were carried out using USP apparatus type II at 100 rpm. The dissolution medium consisted 0.1N HCl for 2 hours after 2 hours medium is replaced with phosphate buffer pH 6.8 for 45mins (900 mL), maintained at 37°C ±0.5°C. The drug release at different time intervals was measured by UV-visible spectrophotometer at 265 nm for 0.1N HCl and 280nm for 6.8 phosphate buffer.

Observation table:

S.No.	Parameter	Observation
1	General Appearance	
2	Weight Gain	
3	Disintegration time	
4	Drug release %	

RESULT & DISCUSSION

VIVA QUESTIONS

Q.1. Discuss types of coating of uncoated tablets

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Q.2. Why tablet coating is required?

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Q.3. What is enteric coating?

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Q.4. Write about coating process in brief.

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Q.5. How you will evaluate coated tablets?

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Experiment No. 5

OBJECT:

To fill and evaluate Tetracycline capsules

Formula: Per unit capsule

Ingredient	Quantity given (n)	Quantity taken (n x No. Of capsules to be prepared)
Tetracycline Hydrochoride	250 mg	
Strach	50 mg	
Talc	2 % w/w	
Empty Capsule	1 (No. 2 Size)	

REFERENCES:

1. Lachman L., Liberman H.A., Kanig J.L.The Theory and Practice of Industrial Pharmacy, Varghese Publication, New Delhi, Third Edition, Page 371-411.

2. Pujara N.D., Parmar R.B., Formulation and Evaluation of Hard Gelatin Capsule of Losartan PotassiumInventi Rapid: Pharm Tech Vol. 2013, Issue 2

THEORY:

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, colorless, 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 slower than tableting, generally more costly than tablets, but must judge on a case-by-case basis; concern over maintaining proper shell moisture content and cross-linking.

PROCEDURE:

Powder preparation and Filling of capsules: Weigh all the ingredients and pass through sieve no. #20 and mixed in a mortar using pestle. Ensure proper functioning of Hand Operated Capsules filling machine, as per standard Operating procedure. Empty capsules are to be filled by using manually operated capsules filling machine are subjected to upper plate then allow to unlock then spread mixed powder on the perforated plate followed by body part of hard gelatine empty shell, transfer mixed powder on unlocked body part and allow to re-lock caps and body to furnish two piece one unit hard capsule.

Evaluation of Hard Gelatin Capsule:

Disintegration Time: One capsule was placed in each of six tubes of assembly and assembly was suspended in water. Discs were added to each tube, temperature was maintained at 37±2°C and assembly was operated for 60 min.

Drug Content: Weigh an amount of the granules equivalent to 250 mg of Tetracycline was dissolved in 100 ml of phosphate buffer pH 6.8, filtered, diluted suitably and analyzed for the drug content at 360 nm using UV-visible spectrophotometer.

In-vitro Drug Release Study: The release rate of Tetracycline Hydrochloride from granules was determined using IP Dissolution Test Apparatus Type II (basket type). Granules were first incorporated in empty hard gelatin capsule of size #3 and then placed in a dry basket at the beginning of each test. Lower the basket in the dissolution medium and apparatus was run at 50 rpm, The dissolution test was performed using 900 ml of phosphate buffer pH 6.8, at 37±0.5ºC and 50 rpm. 5 ml were withdrawn at time intervals of five minute for 60 minutes. This was maintained at same temperature, was added to the bulk. The samples were filtered through Whatman filter paper no. 41. Absorbance of these solutions was measured at 360 nm using UV-Visible spectrophotometer. Cumulative percentage drug release was calculated using an equation obtained from a standard curve.

Stability Study as Per ICH Guideline, Stability study as per ICH guidelines were performed for one month under the conditions of 40°C±2°C 75 % RH ±5%. The formulation was evaluated for disintegration time, drug content and in-vitro drug release.

Observation table:

S.No.	Parameter	Observation
1	General Appearance	
2	Weight Variation	
3	Drug Content	
4	Disintegration time	
5	Drug release % (Dissolution test)	
6	Stability Studies	

RESULT & DISCUSSION:.....

VIVA QUESTIONS

Q.1. Define capsule.

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Q.2. Write about type of capsules.

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Q.3. Discuss difference between hard gelatin and soft gelatin capsules

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Q.4. Discuss contents of capsules with example.

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Q.5. Write a note on advantages of capsules over tablets.

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Q.6. Why capsules are formulated?

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Experiment No. 6

OBJECT:

To Prepare Calcium Gluconate 10% w/v Injection B.P

Formula: Per unit ampoule (10 ml)

Ingredient	Quantity given (n)	Quantity taken (n x No. of unit container)
Calcium Gluconate	940 mg	
Sod. Chloride	0.9 % w/v	
Water for injection	q.s. (10 ml)	

REFERENCES:

International Pharmacopoeia, Seventh Edition, 2017, Parenteral Preparations, Page 1-4.

https://www.old.health.gov.il/units/pharmacy/trufot/alonim/CALCIUM_GLUCONATE_10_INJECTION_B.P_dr_1433675212243.

Lachman L., Liberman H.A., Kanig J.L.The Theory and Practice of Industrial Pharmacy, Varghese Publication, New Delhi, Third Edition, Page 639-680.

THEORY:

Parenteral preparations are sterile preparations containing one or more active ingredients intended for administration by injection, infusion or implantation into the body. They are packaged in either single-dose or multidose containers. Parenteral preparations may require the use of excipients such as solvents, substances to enhance solubility, suspending agents, buffering agents, substances to make the preparation isotonic with blood, stabilizers or antimicrobial preservatives. The addition of excipients is kept to a minimum. When excipients are used they do not adversely affect the stability, bioavailability, safety or efficacy of the active ingredient(s), or cause toxicity or undue local irritation. There must be no incompatibility between any of the components of the dosage form. Water for injections is used as the vehicle for aqueous injections. Sterilization at this stage may be omitted, provided that the preparation is subject to terminal sterilization. For non-aqueous injections, fixed oils of vegetable origin are used as vehicles. Unless otherwise specified in the individual monograph, sodium chloride or other suitable substance(s) may be added to an aqueous solution for injection in order to render the preparation isotonic. When an individual monograph defines a particular parenteral preparation simply as a solution, emulsion or suspension in Water for injections, this does not preclude the inclusion of such substances, where necessary, for this purpose. The different categories of parenteral preparations include: - injections; - intravenous infusions; - powders for injections or intravenous infusions; - concentrates for injections or intravenous infusions; - implants.

Manufacture: The manufacturing process should meet the requirements of good manufacturing practices (GMP). The following information is intended to provide broad guidelines concerning the main steps to be followed during production. The quality and grade of starting materials, the design and maintenance

of the equipment and the method of manufacture must be such as to ensure the stability of the active substance and of the final product and that the final product is sterile and free of pyrogens and particulate matter. During development the effectiveness of any antimicrobial preservative present in the preparation shall be demonstrated to the satisfaction of the relevant regulatory authority. For the sterilization of parenteral preparations follow Methods of sterilization. Heating in an autoclave (steam sterilization) is the method of choice for aqueous preparations and should therefore be used whenever possible. When a parenteral preparation is liable to deterioration due to oxidation the operation of filling may be performed in an atmosphere of suitable sterile inert gas, such as nitrogen, whereby the air in the container is replaced by this gas. In the manufacture of preparations containing dispersed particles measures are taken to ensure a suitable and controlled particle size with regard to the intended use. In the manufacture of liquid preparations measures are taken to ensure that the volume of the preparation in the container is sufficient to permit withdrawal and administration of the nominal dose using a normal technique. Extractable volume for parenteral preparations. Throughout manufacturing certain procedures should be validated and monitored by carrying out appropriate in-process controls. These should be designed to guarantee the effectiveness of each stage of production. In-process controls during manufacture of parenteral preparations should include monitoring of environmental conditions (especially with respect to particulate and microbial contamination), bacterial endotoxins, pH and clarity of solution, freedom from particulate matter and integrity of the container closure system (absence of leakage, etc.). For powders for injections controls should also include uniformity of mass, moisture content and the ease of reconstitution of a solution or suspension. The validation of the manufacturing process and the in-process controls are documented.

PROCEDURE:

All steps of parenteral formulation must be done In aseptic conditions (Grade A or Class 100 aseptic area)

Primary washing: Ensure all Apparatus are cleaned and sterilized.

Compounding: All contents of the formulation are dissolved in Water for injection using volumetric flask and compounded under aseptic condition.

Terminal Sterilization: By ultra filtration technique

Packaging and Labeling: Formulated injection were packaged in ampoules, then sealed and labelled well under aseptic conditions.

OBSERVATION:

S.No.	Parameter	Observation
1	General Appearance	
2	Clarity Test	

RESULT & DISCUSSION:

VIVA QUESTION

Q.1. Why injections are required?

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Q.2. Which parenteral route of drug administration is showing highest bioavailability (in general) ?

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Q.3. Discuss significance of parenterals over other dosage form.

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Q.4. Why Aseptic area is required for formulation process of parenterals ?

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Q.5. Why parenterals are also known as sterile dosage forms?

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Q.6. What is basic difference between large volume and small volume parenterals?

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Experiment No. 7

OBJECT:

To Prepare Ascorbic acid injection

Formula:

Ingredient	Quantity given (n) Mg/ampoule	Quantity taken (n x No. of unit container)
Ascorbic Acid	250	
Sod. Chloride	0.9 % w/v	
Water for injection	q.s. (10 ml)	

REFERENCES:

1. Lachman L., Liberman H.A., Kanig J.L.The Theory and Practice of Industrial Pharmacy, Varghese Publication, New Delhi, Third Edition, Page 639-680.

THEORY:

Ascorbic Acid Injection is a clear, colorless to slightly yellow sterile solution of Ascorbic Acid in Water for Injection, for intravenous, intramuscular or subcutaneous use. Each mL contains: Ascorbic Acid 500 mg, Disodium Edetate 0.25 mg, Sodium Hydroxide 110 mg, in Water for Injection q.s. pH (range 5.5 to 7.0) adjusted with Sodium Bicarbonate and Sodium Hydroxide. Contains no preservatives. In humans, an exogenous source of ascorbic acid is required for collagen formulation and tissue repair. Ascorbic acid is reversibly oxidized to dehydroascorbic acid in the body. These two forms of the vitamin are believed to be important in oxidation-reduction reactions. The vitamin is involved in tyrosine metabolism, conversion of folic acid to folinic acid, carbohydrate metabolism, synthesis of lipids and proteins, iron metabolism, resistance to infections, and cellular respiration.

PROCEDURE:

All steps of parenteral formulation must be done In aseptic conditions (Grade A or Class 100 aseptic area)

Primary washing: Ensure all Apparatus are cleaned and sterilized.

Compounding: All contents of the formulation are dissolved in Water for injection using volumetric flask and compounded under aseptic condition.

Terminal Sterilization: By ultra filtration technique - assembled the apparatus well with mebrane filter, vacuum pump and soultion to be sterilized, then performed the strilization process.

Packaging and Labeling: Formulated injection were packaged in ampoules, then sealed and labelled well under aseptic conditions.

OBSERVATION:

S.No.	Parameter	Observation
1	General Appearance	
2	Clarity Test	

RESULT & DISCUSSION:.....

VIVA QUESTION

Q.1. Why Ascorbic acid injections are required?

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Q.2. Why IV route of drug administration is showing highest bioavailability (in general)

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Q.3. Discuss significance of drug administration by several parenteral routes.

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Q.4. Why Grade A or Class 100 Aseptic area is required for formulation process of parenterals

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Q.5. What is basic difference between sterile and non-sterile dosage forms?

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Experiment No. 8

OBJECT:

To perform Quality control tests (as per IP) of marketed tablets and capsules.

REFERENCES:

1. Balamuralidhara V, Vinay S, Sudeendra Bhat R and Pramod Kumar T M, Comparative study of in-process and finished products quality control tests of Indian Pharmacopoeia, British Pharmacopoeia & United States Pharmacopoeia for capsules and liquid orals, IRJP 2011, 2 (9), 65-69

2. Lachman L., Liberman H.A., Kanig J.L.The Theory and Practice of Industrial Pharmacy, Varghese Publication, New Delhi, Third Edition, Page 293-411.

THEORY:

The concept of total quality control test refers to the process of striving to produce a quality product by a series of measures, requiring an organized effort in order to eliminate errors at every stage in the production. In process product testing is done in order to check the conformance of the final product with the compendial standards as specified in the pharmacopoeias. As the final sample taken for the finished product testing is only a representative of a large batch, a significant difference still remains. The pharmacopoeias have laid down the specified limits within which the value should fall in order to be compliant as per the standards. The official pharmacopoeias in different parts of the world specify the quality requirements for pharmaceutical products. However the parameters and standards differ to some extent from each other. Hence an attempt is being made to compare and bring out the harmonized limits within which a product should fall in order to meet the pharmacopoeial specifications that satisfy quality requirements for many regions. The main aim is to study the quality control tests for capsules and liquid orals and to list down the similarities and differences as per various Pharmacopoeias. The parameters examined for capsules and liquid orals dosage forms as per the Pharmacopoeias were compared and certain similarities and differences were observed. It was noted that except for a few parameters, the quality control tests were broadly similar.

PROCEDURE:

Evaluation of Capsules

Uniformity of weight:

Weigh an intact capsule. Open the capsule without losing any part of the shell and remove the contents as completely as possible. To remove the contents of a soft capsule the shell may be washed with ether or other suitable solvent and the shell allowed to stand until the odour of the solvent is no longer detectable.

Weigh the shell. The weight of the contents is the difference between the weighing. Repeat the procedure with a further 19 capsules. Determine the average weight. Not more than 2 of the individual weights deviate from the average weight by more than the percentage deviation shown in the Table 1(B) and none deviates by more than twice that percentage.

Content of active ingredients:

Determine the amount of active ingredient by the method described in the assay and calculate the amount of active ingredient in each capsule.

The result lies within the range for the content of active ingredient stated in the monograph. This range is based on the requirement that 20 capsules, or

such other number as may be indicated in the monograph, are used in the Assay.

Where 20 capsules cannot be obtained, a smaller number, which must not be less than 5, may be used, but to allow for sampling errors the tolerances are

widened in accordance with the Table 2(A) below.

The requirements of the Table 2(A) apply when the stated limits are between 90 and 110 percent. For limits other than 90 to 110 percent, proportionately

smaller or larger allowances should be made.

Table 1(A): Limits for content of active ingredients

Weight of active ingredients in each tablet	Subtract from lower limit for samples of			Add to the upper limit for samples of		
	15	10	5	15	10	5
0.12g or less	0.2	0.7	1.6	0.3	0.8	1.8
More than 0.12g But less than 0.3g	0.2	0.5	1.2	0.3	0.6	1.5
0.3g or more	0.1	0.2	0.8	0.2	0.4	1.0

Uniformity of content :

This test is applicable to capsules that contain less than 10mg or less than 10 percent w/w of active ingredient. For capsules containing more than one active ingredient carry out the test for each active ingredient that corresponds to the before mentioned conditions. The test should be carried out only after the content of active ingredient in a pooled sample of the capsules has been shown to be within accepted limits of the stated content.

Determine the content of the active ingredient in each of 10 capsules taken at random using the method given in the monograph or by any other suitable analytical method of equivalent accuracy and precision. The capsules comply with the test if not more than one of the individual values thus obtained is outside the limits 85 to 115 percent of the average value and none is outside the limits 75 to 125 percent. If 2 or 3 individual values are outside the limits 85 to 115 percent of the average values, repeat the determination using another 20 capsules. The capsules comply with the test if in the total sample of 30 capsules not more than 3 individual values are outside the limits 85 to 115 percent and none is outside the limits 75 to 125 percent of the average value.

Uniformity of mass:

Weigh an intact capsule. Open the capsule without losing any part of the shell and remove the contents as completely as possible.

For soft shell capsules, wash the shell with a suitable solvent and allow standing until the odour of the solvent is no longer perceptible. Weigh the shell. The

mass of the contents is the difference between the weighing. Repeat the procedure with another 19 capsules.

Table 1(B): Limits for Uniformity of mass

Pharmaceutical form	Average mass(mg)	Percentage deviation (%)
Capsules, granules (uncoated, single dose), powders (single dose)	Less than 300mg	10
	300mg or more	7.5

Disintegration test:

Introduce one capsule into each tube and, if directed add a disc to each tube. Suspend the assembly in the beaker containing the specified liquid and operate the apparatus for the specified time. Remove the assembly from the liquid. The capsules pass the test if all of them have disintegrated. If 1 or 2 capsules fail to disintegrate, repeat the test on 12 additional capsules, not less than 16 of the total of 18 capsules tested disintegrate.

If the capsules adhere to the disc and the preparation under examination fails to comply, repeat the test omitting the disc. The preparation complies with the

test if all the capsules in the repeat test disintegrate.

Hard capsules: Disintegration test:

Use water as the dissolution medium. If the capsules float on the surface of the medium, a disc may be added. If the capsules adhere to the discs, attach a removable piece of stainless steel woven gauze with mesh aperture of 2.00 mm to the upper plate of the basket rack assembly and carry out the test omitting the discs.

Operate the apparatus for 30 minutes. Remove the assembly from the liquid. The capsules pass the test if all of them have disintegrated. If 1 or 2 capsules fail to disintegrate, repeat the test on 12 additional capsules, not less than 16 of the total of 18 capsules tested disintegrate.

Soft capsules: Disintegration test:

Use water as the medium and add a disc to each tube. Operate the apparatus for 60 minutes. Remove the assembly from the liquid. The capsules pass the test if all of them have disintegrated. If 1 or 2 capsules fail to disintegrate, repeat the test on 12 additional capsules, not less than 16 of the

total of 18 capsules tested disintegrate.

Enteric capsules: Disintegration test:

Place one capsule in each tube. Operate the apparatus for 2 hours without the discs in 0.1M hydrochloric acid. No capsule shows signs of disintegration or rupture permitting the escape of the contents. Replace the medium in the vessel with mixed phosphate buffer pH 6.8.

Add a disc to each tube and operate the apparatus for a further 60 minutes. Remove the apparatus from the medium and examine the capsules. They pass the test if no residue remains on the screen or on the underside of the discs, or if the residue remains, it consists of fragments of shell or of a soft mass with no palpable, unmoistened core.

Gastro-resistant capsules: Disintegration test:

Place one capsule in each tube. Operate the apparatus for 2 hours without the discs in 0.1M hydrochloric acid. Examine the state of the capsules and the time of resistance varies according to the formulation of the capsules to be examined. It is typically 2h to 3h but even with deviations it must not be less than 1h. No capsules show signs of disintegration or rupture permitting the escape of the content.

Replace the acid by phosphate buffer solution of pH 6.8. Add a disc to each tube; operate the apparatus for 60 min. If the capsules fail to comply because of adherence to the discs, the results are invalid. Repeat the tests on further 6 capsules omitting the discs.

Dissolution test:

Place the stated volume of the dissolution medium, free from dissolved air, into the vessel of the apparatus. Assemble the apparatus and warm the dissolution medium to 36.5 º to 37.5 º C. Unless otherwise stated, place one capsule in the apparatus, taking care to exclude air bubbles from the surface of the capsule.

When paddle is used, allow the capsule to sink to the bottom of the vessel prior to the rotation of the paddle. A suitable device such as a wire of glass helix may be used to keep horizontal at the bottom of the vessel capsules that would otherwise float. When basket type is used, place the capsule in a dry basket at the beginning of each test. Lower the basket into position before rotation. Operate the apparatus immediately at the speed of rotation specified in the individual monograph. Within the time interval specified, or at each of the times stated, withdraw a specimen from a zone midway between the surface of the dissolution medium and the top of the rotating blade or basket, not less than 10 mm from the wall of the vessel. Except in the case of single sampling, add a volume of dissolution medium equal to the volume of the samples withdrawn.

Perform the analysis as directed in the individual monograph. Repeat the whole operation 5 times. Where 2 or more capsules are directed to be placed together in the apparatus, carry out 6 replicate tests. For each of the capsule tested, calculate the amount of dissolved active ingredient in solution as a percentage of the stated amount where 2 or more capsules

are placed together, determine for each test the amount of active ingredient in solution per capsule and calculate as a percentage of the stated amount.

Evaluation of tablets: Given in previous experiments.

Observation table: Tablets:

S.No.	Parameter	Observation
1	General Appearance	
2	Weight variation	
3	Content Uniformity	
4	Disintegration time	
5	Friability	
6	Drug release %	
7	Hardness	
8	Thickness & Diameter	

Observation table: Capsules:

S.No.	Parameter	Observation
1	General Appearance	
2	Weight Variation	
3	Drug Content	
4	Disintegration time	
5	Drug release %	
6	Stability Studies	

RESULT & DISCUSSION:.....

VIVA QUESTION

Q.1. What is the difference between IPQC and IPQA Tests ?

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Q.2. Why QC Test is required for Finished products ?

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Q.3. What are the official parameters for testing of tablets?

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Q.4. What are the official parameters for testing of capsules?

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Q.5. Write difference between official and unofficial tests?

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Experiment No. 9

OBJECT:

To perform Preparation of eye drops.

Formula: Per unit 10 ml dropper container

Ingredient	Quantity given (n)	Quantity taken (n x No. of unit container)
Ciprofloxacin Hydrochloridel	0.3 % w/v	
Sod. Chloride	0.9 % w/v	
Water for injection	q.s. (10 ml)	

REFERENCES:

1. International Pharmacopoeia, Seventh Edition, 2017, Parenteral Preparations, Page 1-3.

2. http://apps.who.int/phint/pdf/b/6.2.1.3.Ophthalmic-preparations.pdf

3. Lachman L., Liberman H.A., Kanig J.L.The Theory and Practice of Industrial Pharmacy, Varghese Publication, New Delhi, Third Edition, Page 639-680.

THEORY:

Ophthalmic preparations (eye preparations) are sterile, liquid, semi-solid, or solid preparations that may contain one or more active pharmaceutical ingredient(s) intended for application to the conjunctiva, the conjunctival sac or the eyelids. The choice of base and any excipients used for the preparation of ophthalmic preparations must be proven through product development studies not to affect adversely either the stability of the final product or the availability of the active ingredients at the site of action. The addition of colouring agents is not recommended. Unless the active ingredient itself has antimicrobial activity, ophthalmic preparations supplied as multidose preparations may include a suitable antimicrobial agent. The antimicrobial activity should remain effective throughout the entire period of use. The different categories of ophthalmic preparations include drops consisting of emulsions, solutions or suspensions, and ointments.

The manufacturing processes should meet the requirements of Good Manufacturing Practices, especially with regard to cross contamination. The following information is intended to provide very broad guidelines concerning the main steps to be followed during production, indicating those that are the most important. Throughout manufacturing, certain procedures should be validated and monitored by carrying out appropriate in-process controls. These should be designed to guarantee the effectiveness of each stage of production. In-process controls during production of ophthalmic preparations should include monitoring environmental conditions (especially with respect to particulate and microbial contamination), pyrogens (use of a limulus amoebocyte lysate (LAL) test may be advantageous), pH and clarity of solution, and integrity of container (absence of leakage, etc.). Appropriate limits should be

set for the particle size of the active ingredient(s). It is essential that ophthalmic preparations are sterile. An aseptic manufacturing process is usually employed when the dosage form does not allow routine sterilization methods to be used.

Visual inspection Evidence of physical instability is demonstrated by the cloudiness of aqueous solutions, due to the formation of a precipitate. Containers Ophthalmic drops are normally supplied in suitable multidose containers that allow successive drops of the preparation to be administered. The container should be fitted with a tamper-evident device. The maximum volume of the preparation in such a container should be no more than 10 mL, unless otherwise specified and authorized. Multidose ophthalmic drop preparations may be used for up to 4 weeks after the container is initially opened.

Ophthalmic drops may also be provided in suitable single-dose containers that will maintain the sterility of the contents and the applicator up to the time of use. It is recommended that single-dose containers for surgical use should not include any antimicrobial agents.

PROCEDURE:

All steps of parenteral formulation must be done In aseptic conditions (Grade A or Class 100 aseptic area)

Primary washing: Ensure all Apparatus are cleaned and sterilized.

Compounding: All contents of the formulation are dissolved in Water for injection using volumetric flask and compounded under aseptic condition.

Terminal Sterilization: By ultra filtration technique

Packaging and Labeling: Formulated injection were packaged in ampoules, then sealed and labelled well under aseptic conditions.

OBSERVATION:

S.No.	Parameter	Observation
1	General Appearance	
2	Clarity Test	

RESULT & DISCUSSION:

VIVA QUESTION

Q.1. Why eye drops are required?

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Q.2. Discuss reqirement of isotonicity

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Q.3. Discuss complications associated with drug administration by ophthalmic route.

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Q.4. Why Grade A or Class 100 Aseptic area is required for formulation process of ophthalmics ?

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Q.5. What is basic difference between sterile and non-sterile dosage forms?

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Experiment No. 10

OBJECT:

To prepare and submit of cold cream

Formula: Ingredients % w/w

Ingredient	Quantity given (n) % w/w	Quantity taken (n x required qt.)
Liquid paraffin	45	
Bees wax	15	
Borax	1	
Preservative	0.1	
Perfume	q.s.	
Distilled water.	q.s. 100	

REFERENCES:

1. Lachman L., Liberman H.A., Kanig J.L.The Theory and Practice of Industrial Pharmacy, Varghese Publication, New Delhi, Third Edition, Page 534-565.

2. https://labmonk.com/preparation-of-cold-cream

THEORY:

Creams may be defined as the concerntration emulsion comes under o/w type or w/o type. The cold cream emulsion. The main principle of cold cream involves slow evaporation of water which leads to cooling sensati wax are used as an emulsifying agent. Cold creams are designed to smooth the skin and remove make up.

PROCEDURE:

Required quantity of bees wax and liquid paraffin were taken in a beaker and heated on a water bath upto 7 molter mask (Phase A or Qily phase).

In another beaker take borax, water and heated upto 75 c (Phase B or Aqueous phase).

Mix both the solution by adding are phase into another phase with contiuous stirring till a cream like consisten Add the preservative or methyl Paraber, Perfume and Pack it in a suitable container, label and submit it.

Observation table:

S.No.	Spreadability	Smoothness	Non sticky	Patch test
Group 1				
Group 2				

RESULT AND DISCUSSION:

VIVA QUESTIONS

Q.1. Define cold cream.

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Q.2. For which condition we will be applied cold creams on skin?

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Q.3. Discuss contents used in a typical cold cream.

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Q.4. How cold cream differs from other creams?

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Q.5. Discuss formulation complication and precautions in the formulation of cold cream.

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Experiment No. 11

OBJECT:

To perform Evaluation of glass containers.

REFERENCES:

1. Lachman L., Liberman H.A., Kanig J.L.The Theory and Practice of Industrial Pharmacy, Varghese Publication, New Delhi, Third Edition, Page 711-731.

2. https://www.pharmatutor.org/articles/quality-control-testing-packaging-materials?page=1

THEORY:

Packaging of materials is an integral part of any pharmaceutical industry. Packaging affects the quality stability and identification of drug product. Packaging provide an adequate degree of protection, minimize the loss of constituents and should not interact physically or chemically with the contents in a way that will alter their quality to an extent beyond the limits given in the individual monograph, or present a risk of toxicity. Pharmaceutical packaging is the means of providing protection, presentation, identification, information and convenience to encourage compliance with a course of therapy. The commonly used packaging materials are Container, Closure, Carton or Outer and Box. The containers may be made of glass, plastic, matel or paper. The material for closure may include Cork, Glass, Plastic, Metal or rubber. There are various tests for determination of quality, integrity and compatibility of packaging materials. The specification and requirement of quality testing depends on type of pharmaceutical materials used. Containers are tested by many methods of which commonly used test for glass are Crushed glass test, Whole-Container test, Chemical resistance of test, Water Attack Test etc. Similarly test. Closure materials are tested by Transparency test Penetrability Fragmentation test Self seal ability test, Extractive test etc. The requirement of packaging material testing is set according to specification of regulatory agencies like WHO GMP, USFDA and ICH guidelines.

A container for a pharmacopoeial article is intended to contain a drug substance or drug product with which it is, or may be in direct contact. The closure is a part of the container.

Containers must be chosen with care and after taking into consideration the nature of the articles and the likely effects of transportation and storage, even for short periods of time.

A container should be designed so that the contents may be removed in a manner suitable for the intended use of the article in it. It should also provide an adequate degree of protection, minimize the loss of constituents and should not interact physically or chemically with the contents in a way that will alter their quality to an extent beyond the limits given in the individual monograph, or present a risk of toxicity.

PROCEDURE:

Evaluation of Glass Containers:

Crushed – glass test:
This test is official in USP. The container is crushed and sieved to produce uniform particles of which a definite weight of taken. The control of the particle size and weight of powder ensures that a constant

surface area is exposed to the solution. Because all of the glass (not just the surface layer) is examined and extraction is enhanced by the rough surfaces of the particles, this is a severe test, and, if a glass passes, it is unlikely that containers made from it will give trouble while is use. Nevertheless, the technique is tedious and is not applicable to surface treated containers (sulphured or siliconed) because crushing would expose the alkaline glass below the surface. This test can be used for determining the nature of a glass or for distinguish between two types of glasses, such as neutral or surface – treated.

Whole-Container test:
This test is official in European, British and International Pharmacopoeias. it is used in the USP for treated soda-lime containers only. The containers are simply filled with the test solution and exposed to the test conditions. Glassware may pass the whole container test more easily because the surface layer of a container is smooth and less reactive.

In this test, surface area does not increase as much as volume with the increase in container size, consequently, the small sized containers are more attacked by the leaching of the alkali from the surface.

Container	Surface area which supplies alkali to each milliliter of the solution.
Ampoule (1 ml.)	5.9 cm2
Ampoule (10 ml.)	2.9 cm2
Bottle (1000 ml)	0.5 cm2

Chemical resistance of test
USP and IP provide two tests to determine the chemical resistance of glass containers.

Table shows limits of alkalinity for glass containers:-

Tests	Containers	Limits ml of 0.02 N H_2SO_4
1. Powdered Glass Test	Type I	1.0
	Type III	8.5
	Type NP	15.0
2. Water Attack Test	type II (100ml of less)	0.7
	type II (over 100ml)	0.2

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.

Water Attack Test

This test is used only with containers that have been exposed to sulphur dioxide fumes under controlled humidity conditions. Such a treatment neutralizes the surface alkali. Now the glass becomes 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.

OBSERVATION TABLE:

S.No.	Parameter	Observation
1	Crushed – glass test	
2	Whole-Container test	
3	Chemical resistance of test	
4	Powdered Glass Test	
5	Water Attack Test	
6	Minor/Major/Critical Defects	

RESULT & DISCUSSION:

VIVA QUESTIONS

Q.1. Write types of glasses used in Pharmaceutical Packaging.

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Q.2. Discuss composition of Type 1 glass.

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Q.3. Difference between Type 1 and type 2 glass.

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Q.4. Uses of type 1 and 2 glass

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Q.5. What are the defects found in glass containers ?

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