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CIMETIDINE: AN OVERVIEW AND DEVELOPMENT OF IT'S DOSAGE FORM

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ABSTRACT

Cimetidine is a histamine H_2-receptor antagonist widely used in the treatment of peptic ulcer disease, gastroesophageal reflux disease (GERD), heartburn, and other acid-related gastrointestinal disorders. This article reviews the causes, pathophysiology, symptoms, and management of peptic ulcers, with a particular focus on the pharmaceutical formulation of cimetidine tablets. The study discusses the drug's mechanism of action, pharmacokinetic properties, therapeutic uses, adverse effects, contraindications, and drug interactions. Preformulation studies, including organoleptic, physicochemical, and micromeritic evaluations, were conducted to assess the suitability of cimetidine for tablet formulation. The manufacturing processes of wet granulation and direct compression, along with coating methods, are described. Quality control parameters such as weight variation, hardness, friability, disintegration, dissolution, and content uniformity tests were reviewed to ensure product quality, safety, and efficacy. Packaging, labeling, and storage requirements were also examined to maintain tablet stability and patient compliance. Overall, the study highlights the importance of proper formulation development, evaluation, and packaging in producing safe, stable, and effective cimetidine tablets for the management of acid-related disorders.

INTRODUCTION

An ulcer is defined as a break or erosion in the protective lining of an organ or tissue. Ulcers are a common medical condition that affects millions of people worldwide. These painful sores can occur in various parts of the body , including the stomach, small intestine, and mouth .Peptic ulcer occurs in that part of the gastrointestinal tract which is exposed to gastric acid and pepsin, i.e. the stomach and duodenum. The etiology of peptic ulcer is not clearly

known. It results probably due to an imbalance between the aggressive (acid, pepsin, bile and H. pylori) and the defensive (gastric mucus and bicarbonate secretion, prostaglandins, nitric oxide, high mucosal blood flow, innate resistance of the mucosal cells) factors.An understanding of the mechanism and control of gastric acid secretion will elucidate the targets of anti-secretory drug action.

CAUSES OF ULCER

- Helicobacter pylori infection
- Long term use of painkillers (NSAIDs)

Examples : Aspirin, Ibuprofen, Diclofenac

- Excess stomach acid
- Smoking
- Alcohol
- Severe physical stress
- Certain medications

Example :- Corticosteroids(especially with NSAIDs)

- Anticoagulants
- Genetic factors(family history increases risk)

SIGNS AND SYMPTOMS

- Feeling full too soon while eating a meal.
- Pain or discomfort in the upper part of your abdomen, anywhere between your belly button and breastbone.
- Feeling uncomfortably full after eating a meal.
- Nausea and vomiting.
- Bloating&Belching

You should call or see your doctor right away if you have symptoms that could be caused by a complication. These symptoms include

- Black or tarry stool, or red or maroon blood mixed with your stool.
- Red blood in your vomit or vomit that looks like coffee grounds.
- Sudden, sharp, or severe abdominal pain
- Feeling dizzy or fainting.
- A rapid pulse or other symptoms of shock.

PATHOPHYSIOLOGY

The peptic ulcer disease (PUD) mechanism results from an imbalance between gastric mucosal protective and destructive factors. Risk factors predisposing to the development of PUD:

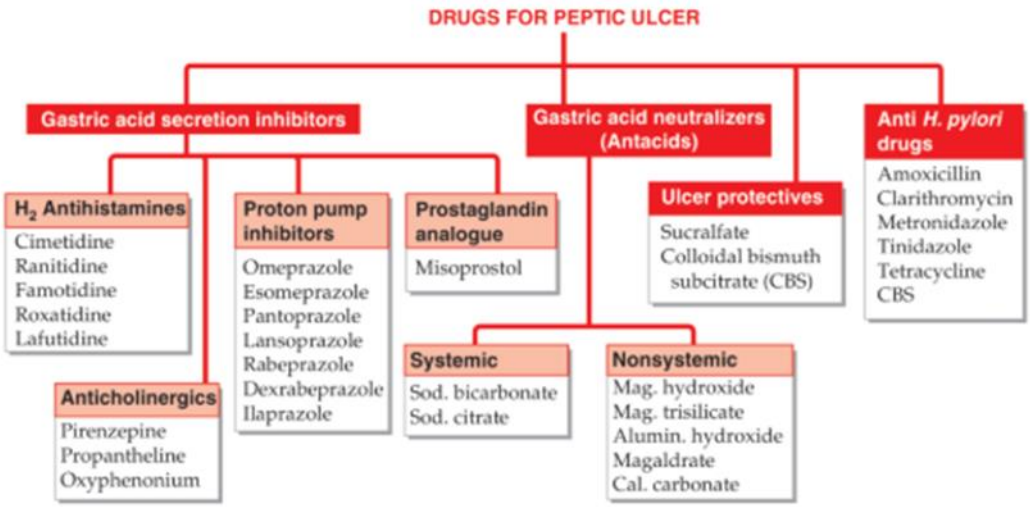
- H. pylori infection
- NSAID
- First-degree relative with PUD
- Emigrant from a developed nation
- African American/Hispanic ethnicity

With peptic ulcers, there is usually a defect in the mucosa that extends to the muscularis mucosa. Once the protective superficial mucosal layer is damaged, the inner layers are susceptible to acidity H. pylori is known to colonize the gastric mucosa and cause inflammation. H. pylori also impair the secretion of bicarbonate, promoting the development of acidity and gastric metaplasia.

COMMON SIDE EFFECT OF ANTI ULCER DRUGS

- Headache
- Dizziness
- Constipation
- Diarrhea
- Nausea
- Vomiting

CLASSIFICATION OF ANTI-ULCER DRUGS

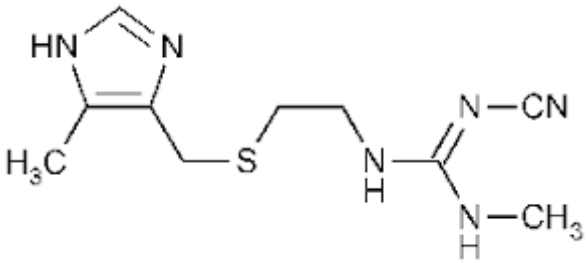


H2 ANTI HISTAMINES

These are the first class of highly effective drugs for acid-peptic disease, but have been surpassed by proton pump inhibitors (PPIs). Four H2 antagonists cimetidine, ranitidine, famotidine and roxatidine are available in India. Their interaction with H2 receptors has been found to be competitive in case of cimetidine, ranitidine and roxatidine.

OVERVIEW OF CIMETIDINE

It is a H2 receptor antagonist. It competitively inhibits histamine binding to histamine receptors. It inhibits gastric acid secretion.



MECHANISM OF ACTION

Cimetidine

↓

Blocks H_2 receptors

↓

cAMP production

↓

Proton pump activity

↓

Gastric acid secretion

PHARMACOKINETICS

- Rapidly absorbed
- Widely distributed
- About 20% bound to plasma proteins
- It undergoes first pass metabolism
- It is excreted unchanged in urine

ADVERSE DRUG REACTIONS

- Headache
- Dizziness
- Drowsiness
- Diarrhea
- Confusion
- Restlessness
- Convulsion

DRUG INTERACTION

- Cimetidine with warfarin ,leading to higher bleeding risk.
- Cimetidine increase serum level of phenytoin ,causes toxicity.
- Cimetidine enhances sedative effect of benzodiazepines (diazepam,chlordiazepoxide)
- Respiratory Drugs: May raise theophylline levels, leading to toxicity.
- Pain & Antidepressants: Increases toxicity risks for tricyclic antidepressants and certain opioids.

CONTRAINDICATIONS

- Hypersensitivity
- Renal impairment: Dosage adjustments are usually required because cimetidine is excreted by the kidneys.
- Pregnancy
- Lactation
- Gastric Cancer
- Liver disease: Use with caution, as cimetidine is processed by the liver

USES

- It is used for the treatment and the management of acid-reflux disorders(GERD)
- Peptic ulcer disease
- Heart burn
- Acid indigestion
- To treat active benign gastric ulcer in adults.
- To treat active duodenal ulcer in adults

MARKETED FORMULATION

Some marketed formulations of cimetidine;

BRAND NAME	DOSE	DOSAGE FORM
Tagamet	200mg,300mg,400mg,800mg	Tablet
Tagamet HB	200mg	Tablet
Tagamet	300mg/2ml,300mg/50ml	Injection
Tagamet	300mg/5ml	Oral solution

PREFORMULATION STUDIES

Pre-formulation studies were evolved in 1950 and early 1960s. Pre-formulation testing is the first step in the rational development of dosage form of a drug substance. It can be defined as an investigation of physical and chemical properties of a drug substance alone and when combined with excipients.

OBJECTIVES OF PREFORMULATION STUDIES

- To generate useful data needed in developing stable and safe dosage forms that can be manufactured on a commercial scale.
- To provide on a depth knowledge and physical characters of a drug molecule prior to dosage form development.
- To generate useful information on how to design a drug delivery system with good bioavailability.

1) ORGANOLEPTIC PROPERTIES

Property	Observation
Color	White to pale yellow color crystalline powder
Odor	Odorless
Taste	Bitter

2) PHYSICOCHEMICAL PROPERTIES

A. Melting point

The compound melts at temperature 140ºC-143ºC

B. Molecular Formula & Molecular Weight

- $C_{10}H_{16}N_6S$
- 252.34g/mol

C. Physical State

Cimetidine appears as white crystals with a slight sulfur-mercaptan odor.

D. pH

A gastric pH >4.0 correlated directly with a therapeutic serum cimetidine level.

E. Solubility

Soluble in water at 37°C and soluble in ethanol very slightly soluble in chloroform insoluble in diethyl ether. The hydrochloride is freely soluble in water soluble in ethanol; very slightly soluble in chloroform; and practically insoluble in diethyl ether.

F. Solution Stability:

Cimetidine hydrochloride is stable in most common intravenous fluids at room temperature for at least one week.

3) MICROMERITIC PROPERTIES

A) Bulk Density

$$Bulk\ density = \frac{Mass\ of\ powder}{Bulk\ volume}$$

B)Tapped Density

$$Tapped\ density = \frac{Mass\ of pwder}{Tapped\ voume}$$

C) Carr's Index

$$.Carr's\ index = \frac{Tapped\ density - Bulk\ density}{Tapped\ density} \times 100$$

SI.NO	CARR'S INDEX%	TYPE OF FLOW
1	5-10	Excellent
2	12-16	Good
3	18-21	Fair to Passable
4	23-35	Poor
5	33-38	Very Poor

D)Angle of Repose

tan θ = h/rwhere, h = height of pile

SI.NO	FLOW ABILITY	ANGLE OF REPOSE
1	Excellent	<25
2	Good	25-30
3	Moderate flow	30-40
4	Poor flow	>40

r = radius of the base of the pile

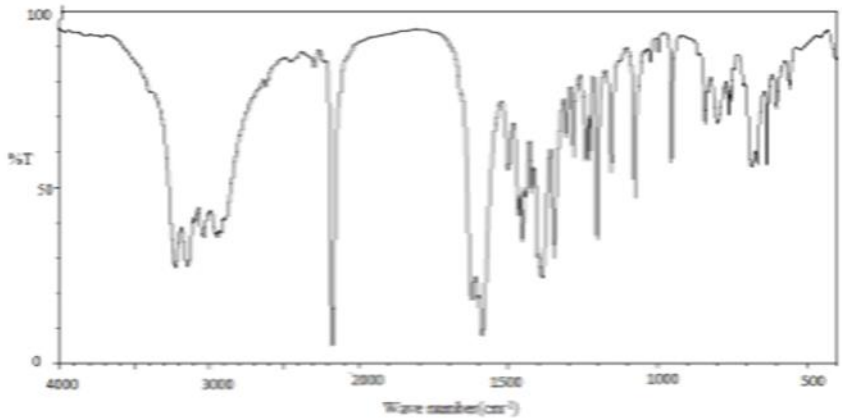
E)Hausner's Ratio

The Hausner's ratio is a number that indicates flow ability of a powder. Hausner's ratio is calculated by given equation -

Hausner's ratio = Tapped density / Bulk density

HAUSNER RATIO	TYPE OF FLOW
<1.25	Good flow
>1.25	Poor flow

3) COMPATIBILITY STUDY WITH



4) EXCIPIENTS

FORMULATION OF CIMETIDINE TABLE

The formulation of cimetidine tablets involves combining the active pharmaceutical ingredient (API) with suitable excipients to produce a stable, effective, and patient-friendly dosage form. Since cimetidine is administered in relatively high doses and has a bitter taste, careful selection of excipients is necessary to ensure adequate tablet size, palatability, and mechanical strength.

Category	Ingredients	Quantity per tablet	Function
Active ingredient	Cimetidine USP	400.0mg	Reduces gastric acid secretion
Diluent	Lactose Monohydrate	18.5mg-30.0mg	Adds bulk, improves compressibility
Binder	Povidone	10.0mg-15.0mg	Provides cohesion
Disintegrant	Sodium Starch Glycolate	8.0mg-12.0mg	Helps tablet break apart
Lubricant	Magnesium Stearate	2.0mg-5.0mg	Prevents sticking during compression
Glidant	Colloidal Silicon Dioxide,Talc	1.0mg-2.0mg	Improves powder flow
Coating agent	Hypromellose/PEG	10.0mg(approx.)	Masks taste, improves stability
Colorant	Titanium Dioxide	Trace amounts(<1mg)	improve product identification, enhance brand recognition, and increase patient compliance

WET GRANULATION

1.Weighing and Dispensing

All raw materials are accurately weighed according to the formulation:

- Cimetidine (active pharmaceutical ingredient)
- Excipients such as diluents (lactose, microcrystalline cellulose), binders,

2. Mixing (Blending)

- The API is mixed with diluents and disintegrants in a suitable mixer to ensure uniform distribution.

3. Granulation (Wet Granulation)

- A binder solution (e.g., starch paste or PVP solution) is prepared.
- The binder is added to the powder blend to form a wet mass.
- The wet mass is passed through a sieve to form granules.

4. Drying

- The wet granules are dried using a tray dryer or fluidized bed dryer.
- Drying is done at controlled temperature to remove moisture.

5.Sizing (Milling)

- Dried granules are passed through a sieve or mill to achieve uniform size.

5.Final Blending

- Lubricants (e.g., magnesium stearate) and glidants (e.g., talc) are added.
- The mixture is blended gently to avoid over-lubrication.

7. Compression

- The granules are compressed into tablets using a tablet compression machine.
- Parameters like hardness, weight, and thickness are controlled.

8. Coating

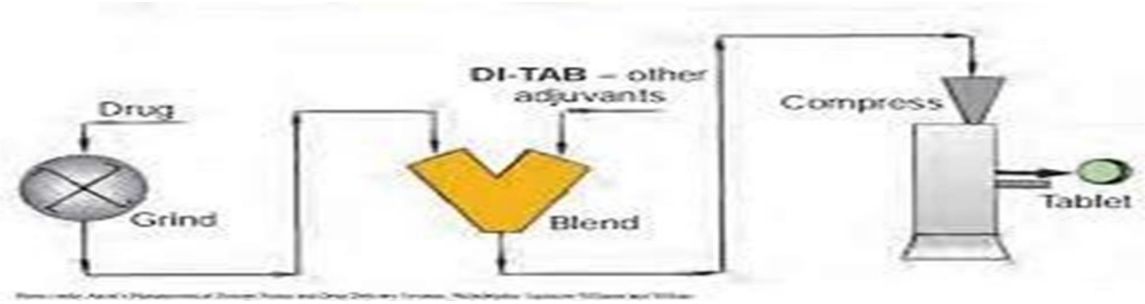
1. Tablets may be film-coated to improve:

- Stability
- Taste masking
- Appearance

Direct Compression

➢ Direct compression involves compressing the powder mixture directly into tablets without any prior granulation.This method is suitable for drugs and excipients that posses good flow and compressibility properties.

This method ensures uniform dosage, stability, and effectiveness of Cimetidine tablets.



Steps

1. **Weighing and Mixing:** Accurately measure and blend the API with excipients to achieve a homogeneous powder mixture.
2. **Blending with Lubricants:** Add lubricants and other excipients to the blend and mix thoroughly.
3. **Compression**: Compress the final blend into tablets using a tablet press.

Coating method for cimetidine tablet

I. Film coating(mostly preferred)

II. Dry coating

1.**Film coating**

Principle:

applying a uniform, thin layer of material (liquid, gas, or powder) onto a substrate—such as tablets, metal, or polymers—to protect, modify, or enhance its surface properties.

Steps:

1.Tablet Preparation (Core Preparation):

Tablets are pre-warmed to the required coating temperature (typically 30-70°C) and cleared of dust to ensure good adhesion.

2.Coating Solution Preparation:

Polymers, plasticizers, colorants, and solvents (aqueous or organic) are prepared. A precise dispersion or solution is formulated to ensure consistent, high-quality application.

3.Equipment Setup:

Tablets are placed in a coating pan (e.g., perforated drum) and set to rotate, creating a cascading motion.

4.Spraying (Coating Application):

The coating solution is atomized through spray guns onto the cascading tablet bed, building up a uniform thin film.

5.Drying and Evaporation:

Simultaneously, heated, dry process air is passed through the tablet bed to evaporate the solvent immediately upon contact, fixing the coating and preventing tablet adhesion (sticking).

6.Cooling and Discharge:

Once the desired thickness is achieved, the tablets are cooled and unloaded.

EVALUATION OF CIMETIDINE TABLET

The evaluation of cimetidine tablets is crucial step in ensuring their quality,safety,and efficacy. Tablets must meet specific pharmacopoeial standards and quality control parameters before they can be approved for use.These evaluations are essential to confirming stability,&acid resistance which are essential for cimetidine's therapeutic efficacy.

1)WEIGHT VARIATION TEST

The average weight of 20 tablet individually weighed tablets on an analytical balance and compared with permissible limits.

Average tablet weight	Permitted percentage deviation
130mg or less	±10%
130mg to 324mg	±7.5%
More than 324	±5%

Friability: Randomly twenty selected tablets of each brand and trial formulation batches which were cleared from any loose dust with help of soft brush and weighed accurately for their initial weight .Each set of tablets were placed separately in Friability Tester and run for 4minutes(25rpm).After removing from tester, were cleared from any loose dust and their final weight was determined to calculate loss.

2) HARDNESS

Tablet requires a certain amount of strength or hardness and resistance to friability to withstand mechanical shakes during handling in the manufacture, packaging , and shipping.Hardness generally measures the tablet crushing strength. It was determining by using Monsanto hardness tester

3)DISINTEGRATION TEST

Use disintegration apparatus, place one tablet in each tube. Operate the apparatus for 2 hours without the discs in 0.1 M hydrochloric acid. No tablet shows signs of disintegration or of 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 30 minutes. Remove the apparatus from the medium and examine the tablet. They pass the test if no residue remains on the No. 10 mesh screen

4)DISSOLUTION TEST

The dissolution test is carried out using the dissolution apparatus as per U.S.P.most commonly used USP Apparatus 2 (Paddle Apparatus) .The tablet is placed in a basket, and the basket is immersed in the dissolution medium and caused to rotate at a specified speed(50-100 rpm). The dissolution medium is held in a covered 1000ml glass vessel and maintained at 370 c +-0.50c by means of a constant temperature suitable water bath. Samples withdrawn at intervals for analysis via UV or HPLC.

5)CONTENT UNIFORMITY TEST

Content uniformity test checks whether every tablet contains an equal amount of drug. Individual tablets are analyzed separately, and the drug content should fall within official limits (usually 85–115% of label claim). It ensures uniform dosing and quality of tablets.

PACKAGING

Tablet packaging is an important part of pharmaceutical manufacturing. It protects tablets from environmental factors such as moisture, light, air, and contamination, thereby maintaining their stability, safety, and effectiveness throughout their shelf life.

PRIMARY PACKAGING

1.Blisterpackaging

Blister packs consist of pre-formed plastic cavities (“blisters”) that hold individual tablet, sealed with a backing (foil or plastic). This primary packaging offer unit-dose protection.

Blisters provide excellent barrier properties: they can be made with materials like PVC/PVDC or foil (Alu-PVC, Alu-Alu) to block moisture, oxygen and light.

2.Strip packaging

Strip packs are another form of unit-dose primary pack. Strip packs often use aluminum foil which is impermeable to moisture and oxygen. This makes them ideal for moisture-sensitive tablet or pediatric meds where long shelf life is needed. They are lighter and flatter than blisters, saving space.

3.Bottle packaging

Bottles are the classic multi-dose container. Tablets are filled into bottles (plastic or glass). They are usually made from HDPE or PET plastic, or glass (for strong chemical inertness).

SECONDARY PACKAGING

After choosing a primary pack, capsules are usually placed into secondary packaging like carton boxes or shrink-wrapped cases. Cartons provide extra protection during shipping.

1)Cartons& Inserts: Medical cartons must include product inserts (Leaflets with dosage instructions, batch number, expiry, manufacturer info, etc.). These are often paper leaflets inserted into the box

LABELLING REQUIREMENTS OF CIMETIDINE TABLET:

- Labeling is an important part of pharmaceutical packaging.
- It provides essential information about the medicine to ensure safe and effective use.
- A tablet label usually includes;

drug name, strength, dosage instructions, manufacturing and expiry dates, storage the manufacturer's details.

- Proper labeling helps patients and healthcare professionals identify the medicine and avoid errors.
- It also ensures that the product meets legal and regulatory requirements.

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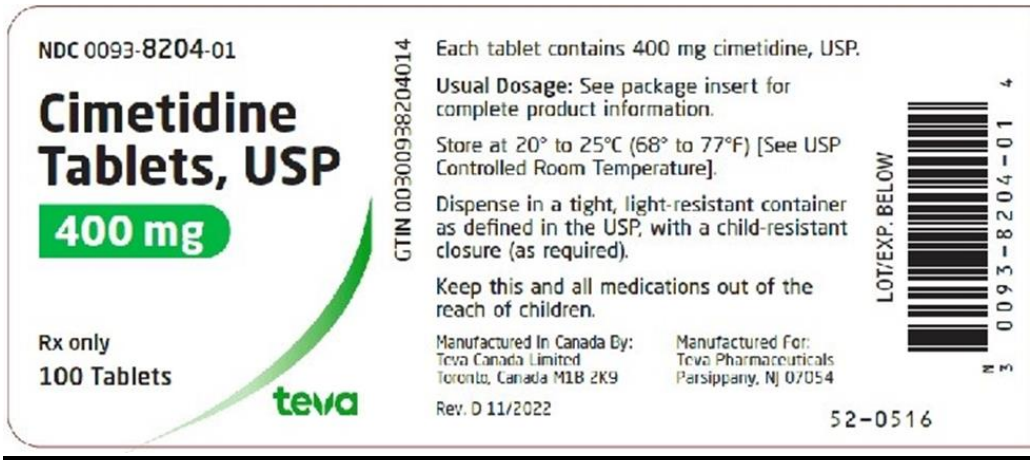

STORAGE

- Store at 15°C to 30°C (room temperature)
- Keep the tablets away from direct sunlight
- Store in a tight, light-resistant container with proper closure
- Keep in a dry place (avoid humidity)

- Keep out of reach of children

CONCLUSION

This study explained the formulation, manufacturing, evaluation, and packaging of Cimetidine tablets used in the treatment of peptic ulcer and acid-related disorders. Preformulation studies and evaluation tests confirmed the stability, quality, and effectiveness of the formulation. Overall, the report highlights the importance of proper pharmaceutical formulation and quality control in developing safe, stable, and effective cimetidine tablets for patient use.

REFERENCE

1. Hall JE. *Guyton and Hall textbook of medical physiology*. 14th ed. Philadelphia Elsevier; 2021.
2. Kasper DL, Fauci AS, Hauser SL, Longo DL, Jameson JL, Loscalzo J. *Harrison's principles of internal medicine*. 21st ed. New York: McGraw-Hill; 2022.
3. Brunton LL, Hilal-Dandan R, Knollmann BC. Goodman & Gilman's the pharmacological basis of therapeutics. 14th ed. New York: McGraw-Hill; 2023
4. Gibson M. Pharmaceutical Preformulation and Formulation: A Practical Guide from Candidate Drug Selection to Commercial Dosage Form. 2nd ed. Boca Raton: CRC Press;2016.
5. Brunton LL, Hilal-Dandan R, Knollmann BC. *Goodman & Gilman's the pharmacological basis of therapeutics*. 14th ed. New York: McGraw-Hill; 2023
6. Aulton ME, Taylor KMG. Aulton's Pharmaceutics: The Design and Manufacture of Medicines. 5th ed. Edinburgh: Elsevier; 2018
7. Aulton's Pharmaceutics: The Design and Manufacture of Medicines Aulton ME, Taylor KMG. *Aulton's pharmaceutics: the design and manufacture of medicines*. 5th ed. Edinburgh: Elsevier; 2018.
8. Lachman L, Lieberman HA, Kanig JL. The Theory and Practice of Industrial Pharmacy. 3rd ed. Mumbai: Varghese Publishing House; 2009.
9. Banker GS, Rhodes CT. Modern Pharmaceutics. 4th ed. New York: Marcel Dekker; 2002.
10. Indian Pharmacopoeia Commission. *Indian Pharmacopoeia*. Ghaziabad: IPC; 2022.
11. United States Pharmacopeial. *United States Pharmacopeia–National Formulary (USP–NF)*. Rockville: USP; 2023.
12. Dean DA, Evans ER, Hall IH. Pharmaceutical Packaging Technology. London: Taylor & Francis; 2000
13. Katzung BG, Trevor AJ. *Basic and Clinical Pharmacology*. 15th ed. New York: McGraw-Hill Education; 2021.

14. Tripathi KD. *Essentials of Medical Pharmacology*. 9th ed. New Delhi: Jaypee Brothers Medical Publishers; 2020.
15. Aulton ME, Taylor K. *Aulton'sPharmaceutics: The Design and Manufacture of Medicines*. 6th ed. London: Elsevier; 2022.
16. United States Pharmacopeia and National Formulary (USP 43–NF 38). Rockville, MD: United States Pharmacopeial Convention; 2020.
17. British Pharmacopoeia Commission. *British Pharmacopoeia 2023*. London: The Stationery Office; 2023.
18. Sinko PJ. *Martin's Physical Pharmacy and Pharmaceutical Sciences*. 7th ed. Philadelphia: Wolters Kluwer; 2017.
19. Allen LV, Ansel HC. *Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems*. 11th ed. Philadelphia: Wolters Kluwer; 2020.
20. Tripathi KD. Essentials of Medical Pharmacology. 8th ed. New Delhi: Jaypee Brothers Medical Publishers; 2019.
21. Brunton LL, Hilal-Dandan R, Knollmann BC, editors. Goodman & Gilman's: The Pharmacological Basis of Therapeutics. 13th ed. New York: McGraw-Hill Education; 2017.
22. Allen LV, Ansel HC. Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems. 10th ed. Philadelphia: Lippincott Williams & Wilkins; 2014.
23. Sinko PJ, Singh Y. Martin's Physical Pharmacy and Pharmaceutical Sciences. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2011.
24. Rowe RC, Sheskey PJ, Quinn ME, editors. Handbook of Pharmaceutical Excipients. 6th ed. London: Pharmaceutical Press; 2009.
25. Aulton ME, Taylor KM, editors. Aulton's Pharmaceutics: The Design and Manufacture of Medicines. 5th ed. Edinburgh: Elsevier; 2017.
26. Indian Pharmacopoeia Commission. Indian Pharmacopoeia 2022. Vol. 2. Ghaziabad: Ministry of Health and Family Welfare, Government of India; 2022.
27. United States Pharmacopeial Convention. United States Pharmacopeia and National Formulary (USP 43-NF 38). Rockville: United States Pharmacopeial Convention; 2020.
28. Lockhart H, Paine FA. Packaging of Pharmaceuticals and Healthcare Products. London: Blackie Academic & Professional; 1996.