BP405T · B.PHARM THEORY

BP405T Systemic Pharmacology I

Unit V — Drugs Acting on Respiratory & Immune Systems

Pills & Python Notes

From-zero teaching standard: every technical term is defined before use.

Syllabus coverage: Unit V (6 hours).

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CHAPTER 4 (UNIT V): Pharmacology of Drugs Acting on the Respiratory System

4.1 Learning objectives

1. Define bronchial asthma and COPD and classify the drugs used in their treatment.
2. Explain the mechanism of action of bronchodilators, inhaled corticosteroids and leukotriene antagonists.
3. Define and classify nasal decongestants, mucolytics, expectorants and antitussives with therapeutic uses.
4. Describe respiratory stimulants.

4.2 Definitions

- **Bronchial asthma:** a disease where the airways become narrow (bronchospasm), swollen and full of mucus, causing wheezing and breathlessness. Attacks come and go (reversible).
- **COPD (chronic obstructive pulmonary disease):** long-term lung damage (chronic bronchitis + emphysema), mostly from smoking; airway narrowing is largely irreversible.
- **Bronchodilator:** a drug that widens (opens) the airways.
- **Nasal decongestant:** a drug that shrinks swollen nasal blood vessels, opening a blocked nose.
- **Mucolytic:** a drug that thins thick mucus so it can be coughed out easily.
- **Expectorant:** a drug that increases the volume of respiratory secretions, making coughing more productive.
- **Antitussive:** a cough suppressant — a drug that reduces the urge to cough (used for dry, irritating cough).
- **Respiratory stimulant:** a drug that stimulates the brain's breathing centre to increase the rate and depth of breathing.

4.3 Terminology table

Term	Simple meaning
Wheeze	Whistling sound when breathing out through narrowed airways
Status asthmaticus	A severe asthma attack that does not respond to usual drugs — a medical emergency
MDI	Metered-dose inhaler — the common "puff" device
DPI	Dry powder inhaler (e.g., Rotahaler)
Spacer	A chamber attached to an MDI that improves drug delivery to lungs
Productive cough	Cough with mucus/sputum
Non-productive (dry) cough	Cough without mucus — irritating

4.4 Drugs used in bronchial asthma and COPD

A. Bronchodilators

1. **β2-agonists (sympathomimetics):** relax airway smooth muscle.

- Short-acting (SABA): salbutamol, terbutaline — rescue inhalers for acute attacks.
- Long-acting (LABA): salmeterol, formoterol — used with inhaled steroids for maintenance (never alone in asthma).

1. **Anticholinergics:** block vagal bronchoconstriction.

- Short-acting: ipratropium bromide (used in acute severe asthma with salbutamol).
- Long-acting: tiotropium — mainstay in COPD.

1. **Methylxanthines:** theophylline, aminophylline — relax airways and stimulate breathing; narrow safety margin (monitor for toxicity: nausea, tremor, fits).

B. Anti-inflammatory / preventive drugs

1. **Inhaled corticosteroids (ICS):** beclomethasone, budesonide, fluticasone — reduce airway inflammation; backbone of asthma control.
2. **Leukotriene receptor antagonists:** montelukast, zafirlukast — oral, useful in mild asthma and allergic rhinitis.
3. **Mast cell stabilizers:** sodium cromoglycate (cromolyn) — prevents mediator release; mainly in children.
4. **Monoclonal antibodies (for severe asthma):** omalizumab (anti-IgE).

C. Combination: ICS + LABA in a single inhaler (e.g., budesonide + formoterol) — the standard controller therapy.

Asthma treatment ladder (draw as steps): Step 1: SABA as needed → Step 2: low-dose ICS → Step 3: ICS + LABA → Step 4: higher-dose ICS + LABA → Step 5: add tiotropium/omalizumab/oral steroids.

> **COPD specifics:** smoking cessation is the most important step; tiotropium (LAMA) and ICS + LABA combinations are mainstays; oxygen therapy in advanced disease. Unlike asthma, airway narrowing is not fully reversible.

4.5 Nasal decongestants, mucolytics, expectorants, antitussives — definitions, classification, uses

Class	Definition	Examples	Therapeutic uses
Nasal decongestants	α-agonists that constrict nasal blood vessels	Oxymetazoline, xylometazoline (nasal drops); pseudoephedrine, phenylephrine (oral)	Common cold, allergic rhinitis, sinusitis. Caution: topical use beyond 3–5 days causes rebound congestion ("rhinitis medicamentosa")
Mucolytics	Break disulphide bonds in mucus, thinning it	Acetylcysteine, bromhexine, ambroxol, carbocisteine	COPD, chronic bronchitis, bronchiectasis — thick sticky sputum
Expectorants	Increase bronchial secretions, making cough productive	Guaiphenesin (guaifenesin), ammonium chloride, potassium iodide	Productive cough with thick mucus
Antitussives	Suppress the cough reflex (central or peripheral)	Codeine, dextromethorphan (central, opioid-type); benzonatate (peripheral)	Dry, irritating, non-productive cough

> **Key rule:** Never suppress a productive cough with antitussives — the mucus must come out. Antitussives are only for dry cough.

4.6 Respiratory stimulants

- **Doxapram:** stimulates carotid body chemoreceptors and the medullary respiratory centre; used short-term for post-anaesthetic respiratory depression and in COPD with CO2 retention.
- Older agents (nikethamide, picrotoxin, bemegride) are now obsolete/toxic.
- **Caffeine/theophylline:** used in neonatal apnoea (premature babies who forget to breathe).

Pharmacy relevance: Teach correct inhaler technique — shake MDI, breathe out, puff while breathing in slowly, hold breath 10 seconds, rinse mouth after steroid inhalers (prevents oral thrush).

India context: Asthma affects millions of Indian children; low-cost DPIs and the government's free essential drug lists make budesonide/formoterol inhalers widely available. Biomass fuel smoke is a major COPD cause among rural Indian women.

4.7 Infographic concept box

"Open the Airways" — Asthma/COPD drugs do two jobs: OPEN (bronchodilators: salbutamol, tiotropium, theophylline) and CALM (anti-inflammatory: inhaled steroids, montelukast). Cough drugs: thin it (mucolytic), bring it out (expectorant), or stop it (antitussive — dry cough only).

4.8 Key points

- Asthma: reversible; COPD: largely irreversible (smoking-related).
- Salbutamol = rescue; budesonide/formoterol = controller; tiotropium = COPD mainstay.
- Nasal decongestant drops beyond 5 days → rebound congestion.
- Mucolytic thins mucus; expectorant increases secretions; antitussive suppresses dry cough only.
- Doxapram = respiratory stimulant for post-anaesthesia use.

4.9 Common confusions

- **Expectorant vs antitussive:** opposite jobs — expectorant helps you cough mucus out; antitussive stops coughing. Using an antitussive for a chesty cough traps infected mucus.
- **SABA vs LABA:** salbutamol (short, rescue) vs salmeterol/formoterol (long, maintenance — never alone in asthma).
- **Asthma vs COPD drugs:** both use bronchodilators + steroids, but COPD centres on tiotropium and smoking cessation.

4.10 Common mistakes

- Prescribing LABA alone for asthma (increases risk of severe attacks — always combine with ICS).
- Long-term oxymetazoline nasal drops (rebound congestion).
- Giving codeine-based cough syrups to young children.

4.11 Mnemonics

- **Asthma drugs "BALT-M":** Beta-2 agonists, Anticholinergics, Leukotriene blockers, Theophylline, Mast-cell stabilizers/Monoclonal antibodies — plus inhaled Corticosteroids as the controller.
- **Cough: "TEM"** — Thin it (mucolytic), Expel it (expectorant), Mute it (antitussive — dry only).

4.12 Exam summary (one-minute revision)

- Asthma: SABA (salbutamol) rescue; ICS (budesonide) + LABA (formoterol) controller; montelukast oral add-on; theophylline narrow margin.
- COPD: tiotropium mainstay; smoking cessation most important.
- Nasal decongestants: oxymetazoline/xylometazoline (≤5 days), pseudoephedrine oral.
- Mucolytics: acetylcysteine, ambroxol, bromhexine. Expectorant: guaiphenesin. Antitussives: dextromethorphan, codeine (dry cough only).
- Respiratory stimulant: doxapram.

4.13 Exam questions

Short answers: 1. Classify drugs used in bronchial asthma. 2. Differentiate expectorant, mucolytic and antitussive with one example each. 3. Why should topical nasal decongestants not be used beyond 5 days? 4. Write the mechanism and uses of doxapram. 5. Compare asthma and COPD drug therapy. **Long answer:** Classify and describe the drugs used in the treatment of bronchial asthma and COPD, including their mechanisms of action. **MCQs:**

1. Rescue inhaler in acute asthma: (a) Salmeterol (b) Salbutamol ✓ (c) Tiotropium (d) Montelukast
2. Mainstay bronchodilator in COPD: (a) Salbutamol (b) Tiotropium ✓ (c) Theophylline (d) Cromolyn
3. Which is a mucolytic? (a) Dextromethorphan (b) Ambroxol ✓ (c) Codeine (d) Pseudoephedrine
4. Rebound nasal congestion is caused by prolonged use of: (a) cetirizine (b) oxymetazoline ✓ (c) ambroxol (d) guaiphenesin
5. Doxapram is a: (a) bronchodilator (b) respiratory stimulant ✓ (c) antitussive (d) mucolytic

Viva: Q: Why rinse the mouth after a steroid inhaler? A: To prevent oral candidiasis (thrush). **Application:** A patient with productive cough and thick sputum asks for a "cough suppressant." What would you advise? (Avoid antitussives; recommend a mucolytic/expectorant so the mucus is cleared.)

CHAPTER 5 (UNIT V): Pharmacology of Drugs Acting on the Immune System — Immunostimulants and Immunosuppressants

5.1 Learning objectives

1. Define immunostimulant and immunosuppressant.
2. Classify immunosuppressants by mechanism of action.
3. Describe the mechanism, adverse effects and therapeutic uses of major classes.
4. List immunostimulants with their uses.

5.2 Definitions

- **Immune system:** the body's defence army (white blood cells, antibodies, lymph nodes) that fights infections and rejects foreign tissue.
- **Immunosuppressant:** a drug that weakens/suppresses the immune response — used to prevent organ-transplant rejection and to treat autoimmune diseases.
- **Immunostimulant:** a drug that boosts the immune response — used in immunodeficiency and some cancers/chronic infections.
- **Autoimmune disease:** a condition where the immune system wrongly attacks the body's own tissues (e.g., rheumatoid arthritis, psoriasis).

5.3 Terminology table

Term	Simple meaning
Calcineurin	An enzyme inside T-cells needed to switch them on; blocked by ciclosporin/tacrolimus
IL-2	Interleukin-2 — a growth signal that makes T-cells multiply
mTOR	A cell-growth pathway; blocked by sirolimus
Purine synthesis	Making DNA building blocks; blocked by azathioprine/mycophenolate (stops lymphocyte division)
Graft rejection	The body attacking a transplanted organ as "foreign"
Opportunistic infection	Infections that strike when immunity is low (fungal, viral, TB)

5.4 Immunosuppressants — classification with mechanism of action

> **Technical concept:** Most immunosuppressants target T-lymphocyte activation or proliferation. **Simple explanation:** Transplant rejection is the immune army attacking the new organ. These drugs either stop the army's orders (calcineurin blockers), stop its reinforcements (antiproliferatives), or calm its generals (steroids).

Class	Examples	Mechanism of action	Key adverse effects	Therapeutic uses
Calcineurin inhibitors	Ciclosporin, tacrolimus	Block calcineurin → no IL-2 → T-cells not activated	Kidney damage, high BP, tremor; ciclosporin: gum swelling, excess hair	Organ transplant (kidney, liver, heart), psoriasis, RA
mTOR inhibitor	Sirolimus (rapamycin)	Blocks mTOR → stops T-cell growth signals	High lipids, mouth ulcers, poor wound healing	Transplant (kidney), drug-eluting stents
Antiproliferative / antimetabolites	Azathioprine, mycophenolate mofetil	Block purine synthesis → lymphocytes cannot divide	Bone-marrow suppression, infections, liver toxicity	Transplant, autoimmune diseases (lupus, RA)
Alkylating agent	Cyclophosphamide	Damages DNA of dividing lymphocytes	Bladder bleeding (haemorrhagic cystitis — prevented with mesna), marrow suppression	Severe lupus, vasculitis, cancers
Corticosteroids	Prednisolone, methylprednisolone	Broad anti-inflammatory; suppress lymphocyte function	Weight gain, diabetes, osteoporosis, infections	Transplant rejection episodes, autoimmune flares
Monoclonal antibodies	Basiliximab (anti-IL-2 receptor), rituximab (anti-CD20 B cells), infliximab (anti-TNF)	Target specific immune molecules	Infusion reactions, infections	Transplant induction, RA, Crohn's disease, psoriasis
JAK inhibitors	Tofacitinib	Block Janus kinase signalling inside immune cells	Infections, clots, lipid rise	RA, psoriatic arthritis

Flowchart — T-cell activation (draw): Foreign antigen → T-cell receptor signal → Calcineurin activated → IL-2 produced → IL-2 binds its receptor → mTOR signal → T-cell multiplies. Ciclosporin/tacrolimus block step 3; basiliximab blocks step 4; sirolimus blocks step 5; azathioprine/mycophenolate block the final division.

5.5 Immunostimulants — classification with mechanism and uses

Agent	Mechanism	Therapeutic uses
BCG vaccine	Stimulates cell-mediated immunity	Bladder cancer (intravesical), TB prevention
Levamisole	Boosts T-cell function	Adjunct in some cancers, worm infections (older use)
Thalidomide / lenalidomide	Immunomodulatory (anti-TNF, anti-angiogenic)	Multiple myeloma, leprosy (erythema nodosum leprosum) — strictly avoided in pregnancy (birth defects)
Interferons (α, β, γ)	Boost antiviral and immune activity	Hepatitis B/C (α), multiple sclerosis (β), chronic granulomatous disease (γ)
Interleukin-2 (aldesleukin)	T-cell growth factor	Metastatic kidney cancer, melanoma
Colony-stimulating factors (G-CSF: filgrastim)	Boost neutrophil production	Neutropenia after chemotherapy
IV immunoglobulin	Pooled antibodies	Immune deficiency, Guillain–Barré syndrome, ITP

5.6 Adverse effects — the common thread

Immunosuppressants share three big risks: **infections** (especially opportunistic — fungal, CMV, TB), **malignancy** with long use (skin cancers, lymphoma), and **organ toxicity** specific to each drug (kidney for ciclosporin, marrow for azathioprine). Patients need lifelong monitoring.

Pharmacy relevance: Counsel transplant patients never to stop immunosuppressants on their own — missing doses risks organ rejection. Live vaccines are contraindicated in immunosuppressed patients.

India context: India performs thousands of kidney transplants yearly; tacrolimus-based regimens are standard. TB screening before starting biologics/immunosuppressants is essential given India's TB burden. Thalidomide is used in leprosy reactions under strict pregnancy-prevention controls.

5.7 Infographic concept box

"Brakes vs Accelerator" — Immunosuppressants = brakes on the immune system (ciclosporin, tacrolimus, azathioprine, steroids) → transplants survive, autoimmunity calms — but infections sneak in. Immunostimulants = accelerator (BCG, interferons, G-CSF, thalidomide) → fights cancer and immune deficiency.

5.8 Key points

- Calcineurin inhibitors (ciclosporin, tacrolimus) block IL-2 → T-cell activation stopped; main transplant drugs; nephrotoxic.
- Azathioprine/mycophenolate block lymphocyte division (purine synthesis).
- Steroids are broad immunosuppressants for rejection episodes and flares.
- Biologics target precisely: basiliximab (IL-2 receptor), rituximab (B cells), infliximab (TNF-α).
- Immunostimulants: BCG, interferons, G-CSF (filgrastim), thalidomide (never in pregnancy).

5.9 Common confusions

- **Ciclosporin vs tacrolimus:** both calcineurin inhibitors; tacrolimus is more potent, less gum/hair effects, but more diabetes risk.
- **Azathioprine vs ciclosporin:** azathioprine stops lymphocyte division (antimetabolite); ciclosporin stops T-cell activation (calcineurin) — different steps.
- **Immunostimulant vs vaccine:** vaccines train immunity against one disease; immunostimulants generally boost immune activity.

5.10 Common mistakes

- Giving live vaccines to patients on immunosuppressants.
- Stopping transplant immunosuppressants abruptly.
- Using thalidomide without pregnancy testing and contraception.

5.11 Mnemonics

- **Transplant triple therapy: "CAT"** — Calcineurin inhibitor + Antimetabolite + sTeroid (e.g., tacrolimus + mycophenolate + prednisolone).
- **Ciclosporin side effects: "GHT"** — Gums (hyperplasia), Hair (hirsutism), Tremor — plus kidney damage and hypertension.

5.12 Exam summary (one-minute revision)

- Immunosuppressants: ciclosporin/tacrolimus (calcineurin → ↓IL-2), sirolimus (mTOR), azathioprine/mycophenolate (purine synthesis), cyclophosphamide (DNA), steroids (broad), basiliximab/rituximab/infliximab (monoclonals), tofacitinib (JAK).
- Uses: organ transplant, autoimmune diseases (RA, lupus, psoriasis).
- Common adverse effects: infections (opportunistic), malignancy risk, drug-specific organ toxicity.
- Immunostimulants: BCG, levamisole, thalidomide (myeloma, leprosy — teratogenic), interferons, IL-2, G-CSF (filgrastim).

5.13 Exam questions

Short answers: 1. Classify immunosuppressants with one example each. 2. Explain the mechanism of action of ciclosporin. 3. List immunostimulants with two uses each. 4. What are the common adverse effects of immunosuppressants? 5. Why is TB screening needed before biologic therapy? **Long answer:** Classify immunosuppressants. Describe the mechanism of action, adverse effects and therapeutic uses of calcineurin inhibitors and antimetabolites. Add a note on immunostimulants. **MCQs:**

1. Ciclosporin acts by: (a) blocking purine synthesis (b) inhibiting calcineurin ✓ (c) blocking mTOR (d) depleting B cells
2. Which is an mTOR inhibitor? (a) Azathioprine (b) Sirolimus ✓ (c) Tacrolimus (d) Basiliximab
3. Thalidomide is contraindicated in: (a) elderly (b) pregnancy ✓ (c) hypertension (d) diabetes
4. Filgrastim (G-CSF) is used for: (a) transplant rejection (b) neutropenia after chemotherapy ✓ (c) asthma (d) gout
5. Basiliximab targets: (a) TNF-α (b) IL-2 receptor ✓ (c) CD20 (d) JAK

Viva: Q: Name the standard triple therapy after kidney transplant. A: Tacrolimus + mycophenolate mofetil + prednisolone. **Application:** A transplant patient on tacrolimus asks whether he can take the live nasal flu vaccine. What do you advise? (No — live vaccines are contraindicated in immunosuppressed patients; recommend inactivated flu vaccine instead.)

Combined references

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