

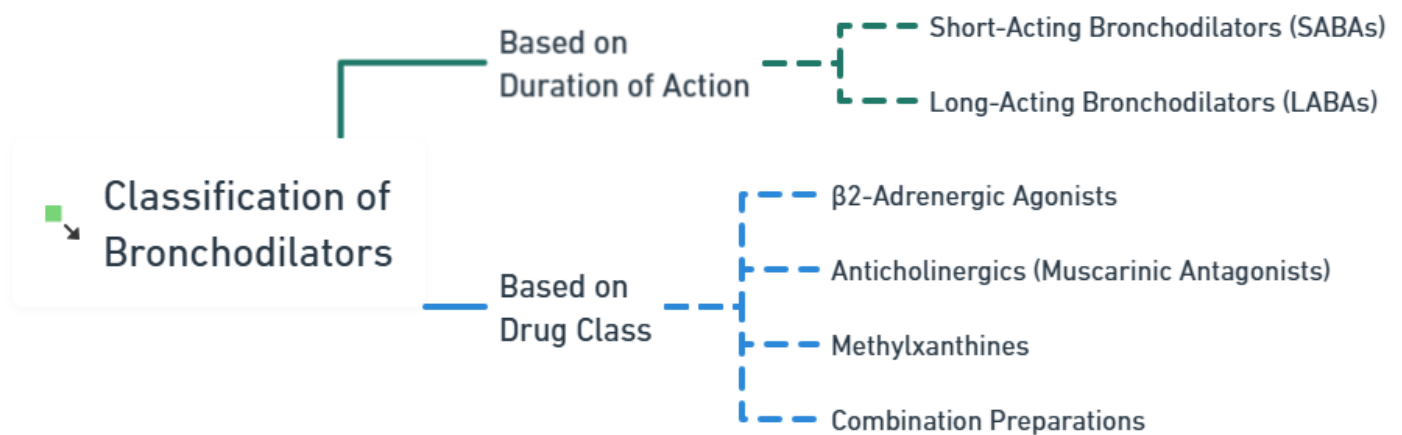
Drugs acting on Respiratory tract

Bronchodilators

Introduction

- Bronchodilators are a class of drugs that reduce resistance in the respiratory airway and increase airflow to the lungs.
- These drugs do not alter the underlying inflammation in airway diseases but help in symptom management by dilating constricted bronchi and bronchioles.
- There are three main types of bronchodilators based on their mechanism of action:
 - **β 2-adrenergic agonists**
 - **Anticholinergics (Muscarinic antagonists)**
 - **Methylxanthines**
- They may be used as short-acting for quick relief or long-acting for maintenance therapy.

Classification



A. Based on Duration of Action

1. Short-Acting Bronchodilators (SABAs)

- Provide quick relief
- Onset: Within minutes
- Duration: 4–6 hours
- Example: Salbutamol (Albuterol), Terbutaline

2. Long-Acting Bronchodilators (LABAs)

- Maintenance therapy
- Onset: Slower (variable)
- Duration: ≥ 12 hours
- Example: Salmeterol, Formoterol

B. Based on Drug Class

1. β 2-Adrenergic Agonists

- Mechanism: Stimulate β 2 receptors causing smooth muscle relaxation
- Examples:
 - Short-acting: Salbutamol, Terbutaline
 - Long-acting: Salmeterol, Formoterol
 - Ultra-long-acting: Indacaterol, Olodaterol

2. Anticholinergics (Muscarinic Antagonists)

- Mechanism: Block M3 muscarinic receptors, inhibit vagal-mediated bronchoconstriction
- Examples:
 - Short-acting: Ipratropium
 - Long-acting: Tiotropium, Aclidinium

3. Methylxanthines

- Mechanism: Non-selective phosphodiesterase inhibitors $\rightarrow$ $\uparrow$ cAMP $\rightarrow$ bronchodilation
- Example: Theophylline, Aminophylline

4. Combination Preparations

- β 2 agonist + anticholinergic (e.g., Salbutamol + Ipratropium)
- LABA + inhaled corticosteroid (e.g., Formoterol + Budesonide)

Mechanism of Action

A. β 2-Adrenergic Agonists

- These drugs bind to β 2-adrenergic receptors on bronchial smooth muscle.
- Activation of β 2 receptors $\rightarrow$ stimulation of adenylate cyclase $\rightarrow$ increased cyclic AMP (cAMP) $\rightarrow$ activation of protein kinase A $\rightarrow$ inhibition of myosin light chain kinase $\rightarrow$ smooth muscle relaxation $\rightarrow$ bronchodilation.

B. Anticholinergics

- Inhibit M3 muscarinic receptors on airway smooth muscle.
- M3 receptor stimulation normally causes bronchoconstriction via the parasympathetic nervous system.
- By blocking these receptors, these drugs prevent bronchoconstriction and reduce mucus secretion.

C. Methylxanthines

- Inhibit phosphodiesterase (PDE), especially PDE-3 and PDE-4.
- This prevents breakdown of cAMP → higher cAMP levels → smooth muscle relaxation.
- Also, have some anti-inflammatory and mild central stimulant effects.

Pharmacokinetics

Class	Absorption	Distribution	Metabolism	Elimination
β2-agonists	Inhaled forms act locally; oral absorbed well	Local for inhaled	Hepatic (CYP450 enzymes)	Urine (metabolites)
Anticholinergics	Poor systemic absorption (mainly local action)	Lungs	Minimal metabolism	Excreted in urine/feces
Methylxanthines	Well absorbed orally	Wide	Hepatic (CYP1A2, CYP3A4)	Renal (as metabolites)

Pharmacodynamics

- **Onset of action:**
 - SABAs: Within 5–15 minutes
 - LABAs: 30 minutes to few hours
 - Anticholinergics: 15–30 minutes
 - Methylxanthines: Oral onset within 1 hour
- **Duration of action:**
 - Varies widely (SABAs: 4–6 h, LABAs: ≥12 h)
- **Effectiveness:**
 - Most effective when inhaled due to direct action and fewer systemic effects.
- **Dose-response relationship:**
 - SABAs have a ceiling effect beyond which side effects increase without more benefit.

Adverse Effects

1. β2-Agonists

- Tremors
- Tachycardia
- Palpitations
- Hypokalemia
- Headache

- Tolerance with long-term use

2. Anticholinergics

- Dry mouth
- Metallic taste
- Urinary retention
- Glaucoma risk if aerosol contacts eyes (especially with nebulization)

3. Methylxanthines

- Nausea, vomiting
- CNS stimulation (tremor, insomnia, seizures at high doses)
- Cardiac arrhythmias
- Narrow therapeutic index → requires monitoring

Contraindications

A. β₂-agonists:

- Caution in patients with cardiac arrhythmias, hypertension, hyperthyroidism

B. Anticholinergics:

- Contraindicated in narrow-angle glaucoma, prostatic hypertrophy

C. Methylxanthines:

- Avoid in peptic ulcer, epilepsy, cardiac arrhythmias

Therapeutic Uses

1. Asthma:

- SABAs for acute attacks
- LABAs (with corticosteroids) for maintenance

2. COPD:

- Anticholinergics are especially useful
- LABAs and combination therapies preferred

3. Bronchospasm:

- Due to various triggers (exercise, allergens)
- **Apnea of prematurity** (methylxanthines like caffeine or theophylline)

Interactions

1. β₂-Agonists:

- May interact with non-selective beta-blockers (e.g., propranolol)
- Diuretics and corticosteroids may increase risk of hypokalemia

2. **Methylxanthines:**

- Interactions with CYP1A2 inhibitors (e.g., ciprofloxacin, erythromycin) → increased theophylline levels
- Smoking induces CYP1A2 → lowers levels

3. **Anticholinergics:**

- Additive anticholinergic effects with other anticholinergics (e.g., atropine)

Dose and Route of Administration

Drug/Class	Dose Example	Route
Salbutamol (SABA)	100–200 mcg every 4–6 h	Inhalation (MDI, nebulizer)
Salmeterol (LABA)	50 mcg BID	Inhalation (DPI)
Ipratropium (SAMA)	20–40 mcg every 6–8 h	Inhalation
Tiotropium (LAMA)	18 mcg once daily	Inhalation (DPI)
Theophylline	300–600 mg/day (divided)	Oral/IV
Aminophylline	Loading: 5–6 mg/kg IV, then infusion	Intravenous

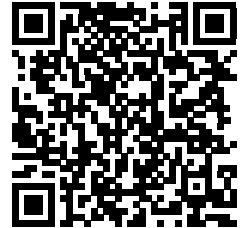


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