WELCOME

TO

This is an Education Platform

We Provide PDF Notes for Pharmacy Students

Web Site http://www.fdspharmacy.in/

You tube https://www.youtube.com/c/FDSpharmacy

Telegram https://t.me/Fdspharmacy

App https://play.google.com/store/apps/details?id=com.FDSPharmacyMedia.FDSPharmacy

E-mail fdspharmacyinfo@gmail.com

MEDICINAL CHEMISTRY - II

UNIT 4

TOPIC :

- **Corticosteroids :** Cortisone, Hydrocortisone, Prednisolone, Betamethasone, Dexamethasone

Corticosteroids

- Corticosteroids are steroid hormones produced by the adrenal cortex.
- They are classified into:
    1. Glucocorticoids – regulate carbohydrate metabolism and immune response
    2. Mineralocorticoids – regulate electrolyte and water balance
- Synthetic corticosteroids are widely used in inflammation, autoimmune disorders, allergies, and adrenal insufficiency.

Classification

Class	Examples	Primary Action
Glucocorticoids	Hydrocortisone, Prednisone, Dexamethasone	Anti-inflammatory, immunosuppressive
Mineralocorticoids	Aldosterone, Fludrocortisone	Sodium retention, potassium excretion
Mixed Action	Cortisone	Moderate glucocorticoid + mineralocorticoid effects

Mechanism of Action

1. Glucocorticoids:
    - Bind cytoplasmic glucocorticoid receptors → translocate to nucleus
    - Regulate transcription of anti-inflammatory proteins (e.g., lipocortin)
    - Suppress pro-inflammatory cytokines and immune cell activation
2. Mineralocorticoids:
    - Bind mineralocorticoid receptors in renal distal tubules
    - Increase Na^+ reabsorption and K^+ excretion → water retention

Pharmacological Effects

A. Glucocorticoids

- Metabolic: ↑ gluconeogenesis, ↑ protein catabolism, ↑ lipolysis
- Anti-inflammatory: Inhibit phospholipase A2 → ↓ prostaglandins & leukotrienes
- Immunosuppressive: Reduce T-cell proliferation and cytokine production
- CNS: Mood elevation or euphoria
- CVS: Maintain vascular tone

B. Mineralocorticoids

- ↑ Na^+ reabsorption → ↑ water retention → ↑ blood pressure
- ↑ K^+ and H^+ excretion → electrolyte balance

Therapeutic Uses

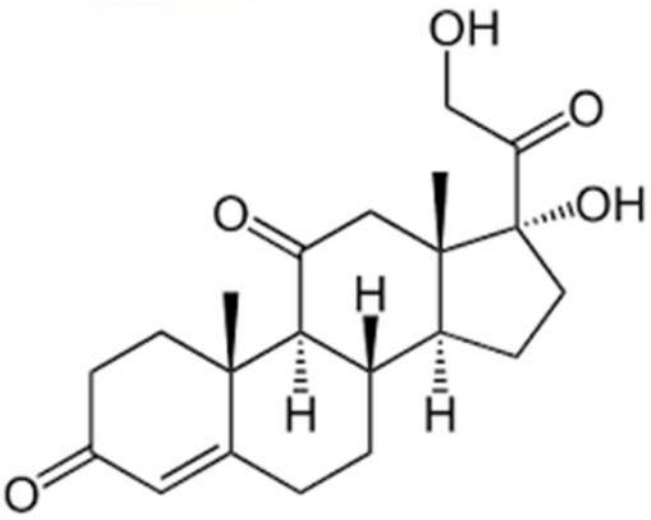
Class	Clinical Use
Glucocorticoids	Asthma, rheumatoid arthritis, lupus, inflammatory bowel disease, organ transplantation, adrenal insufficiency
Mineralocorticoids	Addison's disease, salt-wasting conditions
Short-term use	Acute allergic reactions, shock, cerebral edema
Chronic use	Hormone replacement, autoimmune diseases

Cortisone

- Cortisone is a glucocorticoid steroid hormone naturally produced by the adrenal cortex.
- It is a prodrug, converted in the liver to cortisol (hydrocortisone), which exerts the anti-inflammatory and immunosuppressive effects.
- Synthetic cortisone is used in treating adrenal insufficiency, inflammatory disorders, and autoimmune diseases.
- Administered orally, intramuscularly, or intravenously.

Chemical Structure

- Chemical name: 17α,21-Dihydroxy-3,11-dioxopregn-4-ene- corticoid
- Molecular formula: $C_{21}H_{28}O_5$
- Molecular weight: 360.44 g/mol
- Chemical class: Glucocorticoid; corticosteroid
- Structural



Mechanism of Action

- Target: Glucocorticoid receptors (GR) in cytoplasm of target cells

Stepwise Mechanism:

1. Cortisone is converted to cortisol by 11β-hydroxysteroid dehydrogenase in the liver.

2. Cortisol binds to cytoplasmic glucocorticoid receptors, forming a hormone-receptor complex.
3. The complex translocates into the nucleus → binds glucocorticoid response elements (GREs) on DNA.
4. Modulates transcription of target genes → anti-inflammatory and immunosuppressive effects:
    - Suppresses pro-inflammatory cytokines
    - Inhibits leukocyte migration and function
    - Reduces vascular permeability
    - Alters carbohydrate, protein, and fat metabolism

Synthesis

1. Starting material: Corticosterone or similar steroid intermediates
2. Step 1: Oxidation at C11 to form ketone
3. Step 2: Oxidation at C3, introduction of C4–C5 double bond
4. Step 3: Purification and crystallization → pharmaceutical-grade cortisone

Uses

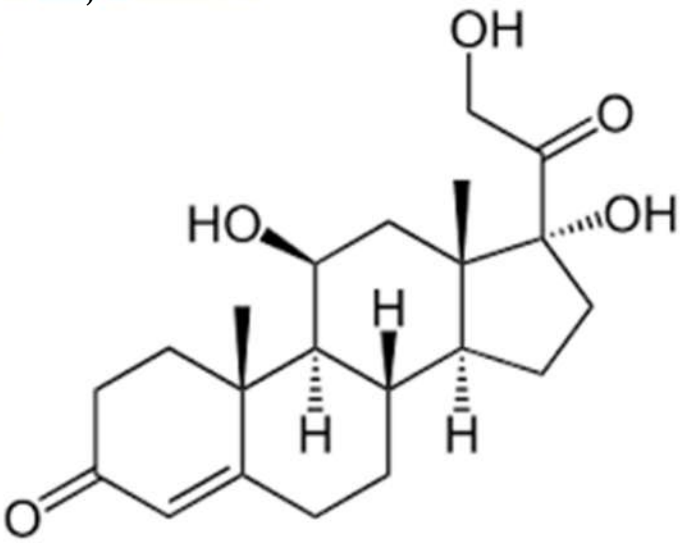
- **Therapeutic Uses:**
    1. **Adrenal insufficiency (Addison's disease)**
    2. **Anti-inflammatory therapy** (arthritis, bursitis, asthma)
    3. **Allergic conditions** (anaphylaxis, severe dermatitis)
    4. **Autoimmune disorders** (lupus, multiple sclerosis)
    5. **Adjunct therapy in certain cancers** (lymphomas)

Hydrocortisone

- Hydrocortisone (also known as cortisol) is a natural glucocorticoid steroid hormone produced by the adrenal cortex.
- It exhibits anti-inflammatory, immunosuppressive, and metabolic effects.
- Clinically used for adrenal insufficiency, inflammatory disorders, and allergic reactions.
- Available in oral, topical, and parenteral formulations.

Chemical Structure

- Chemical name: 11β,17α,21-Trihydroxypregn-4-ene-3,20-dione
- Molecular formula: $C_{21}H_{30}O_5$
- Molecular weight: 362.46 g/mol
- Chemical class: Glucocorticoid; corticosteroid
- Structural



Mechanism of Action

- Target: Glucocorticoid receptors (GR) in cytoplasm of target cells

Stepwise Mechanism:

1. Hydrocortisone binds to cytoplasmic glucocorticoid receptors → forms hormone-receptor complex.

2. Complex translocates into the nucleus → binds glucocorticoid response elements (GREs) on DNA.
3. Modulates transcription of target genes → physiological effects:
    - Anti-inflammatory: Suppresses cytokines, chemokines, leukocyte migration
    - Immunosuppressive: Reduces immune responses
    - Metabolic: Increases gluconeogenesis, protein catabolism, fat redistribution
    - Cardiovascular: Maintains vascular tone and responsiveness

Synthesis

1. Starting material: Pregnenolone or related steroid precursors
2. Step 1: Hydroxylation at C11, C17, and C21
3. Step 2: Ketone formation at C3 and C20, double bond at C4–C5
4. Step 3: Purification → pharmaceutical-grade hydrocortisone

Uses

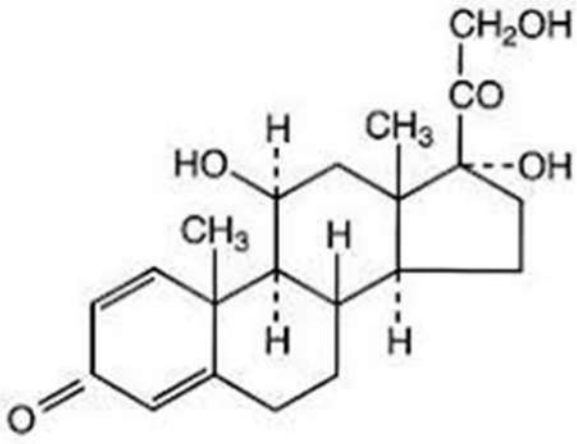
- **Therapeutic Uses:**
    1. **Adrenal insufficiency** (Addison's disease, adrenal crisis)
    2. **Anti-inflammatory therapy** (arthritis, asthma, dermatitis)
    3. **Allergic conditions** (anaphylaxis, severe eczema)
    4. **Autoimmune diseases** (lupus, multiple sclerosis)
    5. **Shock or severe inflammation** in ICU settings

Prednisolone

- Prednisolone is a synthetic glucocorticoid corticosteroid derived from cortisol (hydrocortisone).
- It exhibits potent anti-inflammatory, immunosuppressive, and metabolic effects.
- Prednisolone is more potent than hydrocortisone (≈4–5 times) with less mineralocorticoid activity, reducing fluid retention.
- Administered orally, intravenously, intramuscularly, and topically for various inflammatory and autoimmune conditions.

Chemical Structure

- Chemical name: 11β,17α,21-Trihydroxypregna-1,4-diene-3,20-dione
- Molecular formula: $C_{21}H_{28}O_5$
- Molecular weight: 360.44 g/mol
- Chemical class: Synthetic glucocorticoid; corticosteroid
- Structural



Mechanism of Action

- Target: Glucocorticoid receptors (GR) in cytoplasm of target cells

Stepwise Mechanism:

1. Prednisolone binds to cytoplasmic glucocorticoid receptors → forms hormone-receptor complex.

2. Complex translocates into the nucleus → binds glucocorticoid response elements (GREs) on DNA.
3. Modulates transcription of target genes → physiological effects:
    - Anti-inflammatory: Suppresses cytokine and prostaglandin synthesis, inhibits leukocyte migration
    - Immunosuppressive: Reduces T-cell and B-cell activity
    - Metabolic: Increases gluconeogenesis, protein catabolism, and lipolysis
    - Other: Maintains vascular tone, stabilizes lysosomal membranes

Synthesis

1. Starting material: Cortisone or hydrocortisone
2. Step 1: Introduction of C1–C2 double bond (dehydrogenation) → increases glucocorticoid potency
3. Step 2: Purification → Prednisolone in pharmaceutical grade

Uses

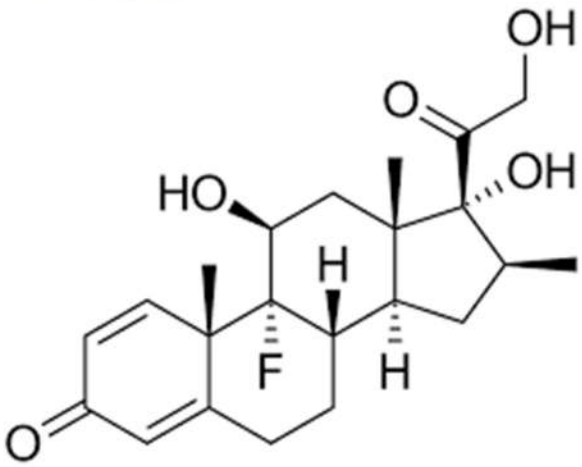
- **Therapeutic Uses:**
    1. **Inflammatory disorders** (arthritis, asthma, dermatitis)
    2. **Autoimmune diseases** (lupus, multiple sclerosis)
    3. **Allergic conditions** (anaphylaxis, severe urticaria)
    4. **Adrenal insufficiency** (alternative to hydrocortisone)
    5. **Certain cancers** (lymphoma, leukemia, as part of chemotherapy protocols)

Betamethasone

- Betamethasone is a synthetic glucocorticoid corticosteroid with potent anti-inflammatory and immunosuppressive activity.
- It is more potent than hydrocortisone and prednisolone and has minimal mineralocorticoid activity, reducing fluid retention.
- Clinically used for inflammatory, allergic, dermatologic, and autoimmune disorders, as well as adrenal insufficiency.
- Available in oral, parenteral, topical, and inhalation formulations.

Chemical Structure

- Chemical name: 9-fluoro-11β,17,21-trihydroxy-16β-methylpregna-1,4-diene-3,20-dione
- Molecular formula: $C_{22}H_{29}FO_5$
- Molecular weight: 392.47 g/mol
- Chemical class: Synthetic glucocorticoid; fluorinated corticosteroid
- Structural



Mechanism of Action

- Target: Glucocorticoid receptors (GR) in cytoplasm of target cells

Stepwise Mechanism:

1. Betamethasone binds to cytoplasmic glucocorticoid receptors → forms hormone-receptor complex.

2. Complex translocates into the nucleus → binds glucocorticoid response elements (GREs) on DNA.
3. Modulates transcription of target genes → physiological effects:
    - Anti-inflammatory: Suppresses cytokine, prostaglandin, and leukotriene synthesis, inhibits leukocyte migration
    - Immunosuppressive: Reduces T-cell and B-cell activity
    - Metabolic: Increases gluconeogenesis, protein catabolism, lipolysis
    - Other: Maintains vascular tone, stabilizes lysosomal membranes

Synthesis

1. Starting material: Cortisone, hydrocortisone, or other suitable steroid precursors
2. Step 1: Introduction of fluoro group at C9 → increases anti-inflammatory activity
3. Step 2: Introduction of 16β-methyl group → reduces mineralocorticoid effects
4. Step 3: Formation of C1–C2 double bond → enhances glucocorticoid potency
5. Purification: Crystallization → pharmaceutical-grade betamethasone

Uses

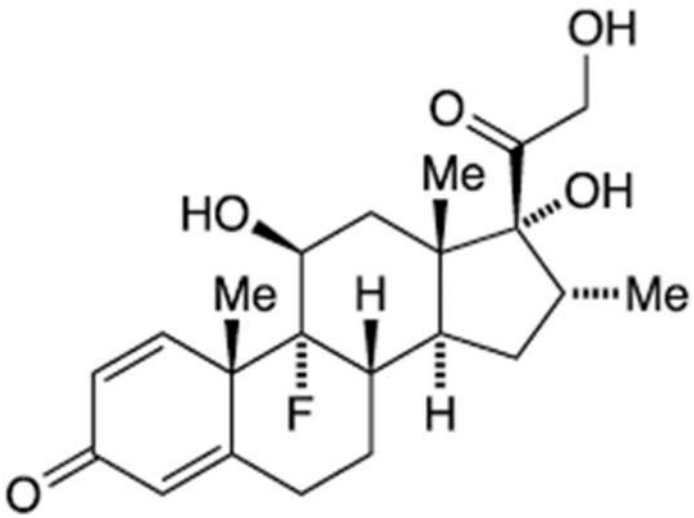
- **Therapeutic Uses:**
    1. **Inflammatory disorders** (arthritis, asthma, dermatitis)
    2. **Allergic conditions** (severe urticaria, anaphylaxis)
    3. **Autoimmune diseases** (lupus, multiple sclerosis)
    4. **Adrenal insufficiency** (replacement therapy)
    5. **Dermatologic and ocular disorders** (eczema, keratitis)
    6. **Prenatal use** to accelerate **fetal lung maturation** in preterm labor

Dexamethasone

- Dexamethasone is a synthetic fluorinated glucocorticoid corticosteroid with very potent anti-inflammatory and immunosuppressive activity.
- It has minimal mineralocorticoid activity, reducing fluid retention and hypertension risk.
- Widely used in inflammatory, allergic, autoimmune, and oncologic conditions, and in cerebral edema management.
- Available in oral, injectable, topical, and inhalation formulations.

Chemical Structure

- Chemical name: 9-fluoro-11β,17α,21-trihydroxy-16α-methylpregna-1,4-diene-3,20-dione
- Molecular formula: $C_{22}H_{29}FO_5$
- Molecular weight: 392.47 g/mol
- Chemical class: Synthetic glucocorticoid; fluorinated corticosteroid
- Structural



Mechanism of Action

- Target: Glucocorticoid receptors (GR) in cytoplasm of target cells

Stepwise Mechanism:

1. Dexamethasone binds to cytoplasmic glucocorticoid receptors, forming a hormone-receptor complex.

2. The complex translocates to the nucleus → binds glucocorticoid response elements (GREs) on DNA.
3. Modulates transcription of target genes → physiological effects:
    - Anti-inflammatory: Inhibits cytokine, prostaglandin, and leukotriene synthesis; reduces leukocyte migration
    - Immunosuppressive: Suppresses T-cell and B-cell function
    - Metabolic: Stimulates gluconeogenesis, protein catabolism, lipolysis
    - Other: Maintains vascular tone, stabilizes lysosomal membranes

Synthesis

1. Starting material: Cortisone, hydrocortisone, or other suitable steroid precursors
2. Step 1: Introduction of 9-fluoro group → enhances anti-inflammatory activity
3. Step 2: Introduction of 16α-methyl group → reduces mineralocorticoid effects
4. Step 3: Formation of C1–C2 double bond → increases glucocorticoid potency
5. Purification: Crystallization → pharmaceutical-grade dexamethasone

Uses

- **Therapeutic Uses:**
    1. **Inflammatory disorders** (arthritis, asthma, dermatitis)
    2. **Allergic conditions** (anaphylaxis, severe urticaria)
    3. **Autoimmune diseases** (lupus, multiple sclerosis)
    4. **Cerebral edema** (brain tumors, trauma)
    5. **Oncologic uses** (lymphoma, leukemia, as part of chemotherapy regimens)
    6. **Adrenal insufficiency** (replacement therapy)
    7. **Severe COVID-19 or systemic inflammatory conditions**