Important Questions and Answers: Immunopharmacology

B.Pharm 6th Semester - Pharmacology III

Instructions: The following questions are categorized into 10-mark (long answer/essay), 5-mark (short answer), and 2-mark (brief answer) formats, covering immunopharmacology as per the Pharmacology III syllabus.

10-Mark Questions (Long Answer/Essay)

1. **Classify immunosuppressive drugs used in organ transplantation. Discuss the pharmacology of cyclosporine, including its mechanism of action, therapeutic uses, and adverse effects.**

   Answer Key:

   Classification of Immunosuppressive Drugs:

   - Calcineurin Inhibitors: Cyclosporine, tacrolimus.
   - mTOR Inhibitors: Sirolimus, everolimus.
   - Antiproliferative Agents: Azathioprine, mycophenolate mofetil.
   - Corticosteroids: Prednisolone, methylprednisolone.
   - Monoclonal Antibodies: Basiliximab, muromonab-CD3.
   - Polyclonal Antibodies: Antithymocyte globulin (ATG).

   Pharmacology of Cyclosporine:

   - **Mechanism of Action:** Cyclosporine binds to cyclophilin, forming a complex that inhibits calcineurin, a phosphatase required for T-cell activation. This prevents nuclear translocation of NFAT (nuclear factor of activated T-cells), reducing IL-2 production and T-cell proliferation, thus suppressing the immune response.
   - **Therapeutic Uses:**
     - Prevention of organ transplant rejection (kidney, liver, heart).
     - Autoimmune diseases: Rheumatoid arthritis, psoriasis, nephrotic syndrome.
     - Graft-versus-host disease (GVHD) in bone marrow transplantation.
   - **Pharmacokinetics:** Administered orally or IV; highly lipophilic, metabolized by hepatic CYP3A4; excreted in bile. Variable bioavailability requires therapeutic drug monitoring (TDM).
   - **Adverse Effects:**
     - Nephrotoxicity: Dose-dependent, reversible with dose adjustment.

- Hypertension, hepatotoxicity.
- Gingival hyperplasia, hirsutism.
- Neurotoxicity: Tremors, seizures (rare).
- Increased risk of infections and malignancies (e.g., lymphoma).

- **Note:** Drug interactions with CYP3A4 inhibitors (e.g., ketoconazole) or inducers (e.g., rifampicin) affect cyclosporine levels. Monitor blood levels (100–400 ng/mL for maintenance).

2. **Explain the role of immunostimulants in immunopharmacology, focusing on the pharmacology of recombinant cytokines (e.g., interferon-alpha) and their clinical applications.**

   Answer Key:

   Immunostimulants: These enhance immune responses, used in immunodeficiency, infections, or cancers. Include cytokines, vaccines, and levamisole.

   Pharmacology of Interferon-Alpha:

   - **Mechanism of Action:** Interferon-alpha (IFN-α), a recombinant cytokine, binds to specific cell surface receptors, activating JAK-STAT signaling pathways. This induces antiviral, antiproliferative, and immunomodulatory effects by upregulating MHC class I expression, enhancing cytotoxic T-cell and NK cell activity, and inhibiting viral replication.
   - **Clinical Uses:**
     - Chronic viral infections: Hepatitis B, hepatitis C.
     - Cancers: Chronic myeloid leukemia (CML), hairy cell leukemia, Kaposi's sarcoma.
     - Adjuvant therapy in melanoma.
   - **Pharmacokinetics:** Administered SC or IM; short half-life requires frequent dosing or pegylated forms (peginterferon). Cleared renally.
   - **Adverse Effects:**
     - Flu-like symptoms: Fever, chills, fatigue.
     - Myelosuppression: Neutropenia, thrombocytopenia.
     - Neuropsychiatric effects: Depression, anxiety.
     - Hepatotoxicity, thyroid dysfunction.
   - **Management:**
     - Gradual dose escalation to reduce flu-like symptoms.
     - Monitor complete blood counts and liver function tests.
     - Psychiatric evaluation for patients with depression history.

- **Note:** Pegylated interferon-alpha (e.g., peginterferon alfa-2a) improves efficacy with less frequent dosing. Resistance may occur due to viral mutations.

5-Mark Questions (Short Answer)

1. **Describe the mechanism of action and clinical uses of tacrolimus in immunopharmacology.**

   Answer Key:

   Mechanism of Action: Tacrolimus (FK506) binds to FK-binding protein (FKBP), forming a complex that inhibits calcineurin, preventing NFAT activation and IL-2 production. This suppresses T-cell activation and proliferation, reducing immune responses.

   Clinical Uses:

   - Prevention of organ transplant rejection (liver, kidney, heart).
   - Autoimmune diseases: Atopic dermatitis (topical), rheumatoid arthritis.
   - Prophylaxis of graft-versus-host disease in bone marrow transplantation.

   Pharmacokinetics: Administered orally or IV; metabolized by CYP3A4; excreted in bile. Requires TDM (target trough levels: 5–15 ng/mL).

   Adverse Effects:

   - Nephrotoxicity, neurotoxicity (tremors, headache).
   - Hypertension, hyperglycemia (diabetes risk).
   - Increased infection risk.

   Note: More potent than cyclosporine but similar toxicity profile. Avoid grapefruit juice (CYP3A4 inhibitor).

2. **Explain the role of mycophenolate mofetil in immunosuppression, including its mechanism and adverse effects.**

   Answer Key:

   Mechanism of Action: Mycophenolate mofetil (MMF) is a prodrug converted to mycophenolic acid, which inhibits inosine monophosphate dehydrogenase (IMPDH). This blocks purine synthesis, selectively inhibiting T- and B-cell proliferation, as lymphocytes rely on de novo purine synthesis.

   Clinical Uses:

   - Prevention of organ transplant rejection (kidney, liver, heart), often with cyclosporine or tacrolimus.
   - Autoimmune diseases: Lupus nephritis, vasculitis.

Pharmacokinetics: Oral or IV; metabolized to active mycophenolic acid; excreted renally. Enterohepatic recirculation prolongs action.

Adverse Effects:

- Gastrointestinal: Diarrhea, nausea, vomiting.
- Myelosuppression: Leukopenia, anemia.
- Increased risk of infections (e.g., CMV).

Note: Monitor for GI toxicity; enteric-coated formulations (mycophenolate sodium) may reduce GI side effects.

2-Mark Questions (Brief Answer)

1. **Name two calcineurin inhibitors used in immunosuppression.**

   Answer Key: Cyclosporine and tacrolimus.

2. **What is the primary therapeutic use of interferon-alpha?**

   Answer Key: Treatment of chronic hepatitis C and certain cancers (e.g., CML).

3. **Name one adverse effect of cyclosporine.**

   Answer Key: Nephrotoxicity.

4. **What is the role of IL-2 in immunosuppression?**

   Answer Key: Promotes T-cell proliferation; inhibited by cyclosporine/tacrolimus.

5. **Name one immunostimulant used in cancer therapy.**

   Answer Key: Interferon-alpha.