SLACPT NEWS

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SLACPT THEME 2025-2026

Personalized Medicine : Shaping the Future of Prescribing

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President's Message

Dear Colleagues and Friends,

As we approach the end of the first year of the current Council's term, I am pleased to reflect on the milestones we have achieved together over the past months at SLACPT.

One of our key highlights was the SLACPT Inter-Faculty Quiz for Medical Students, held virtually in June. It was a closely contested event with enthusiastic participation from all faculties. The quiz was expertly conducted by Dr. Chiranthi Liyanage, our dedicated Quiz Master. We extend our warm congratulations to the winning team from the Faculty of Medicine, University of Colombo. The teams from the Universities of Sabaragamuwa and Kelaniya were placed first and second runners-up, respectively.

In our continued efforts to strengthen members' competencies in drug evaluation, we conducted a session on Health Technology Assessment, led by Dr. Dhanushi Gunasekera, Senior Lecturer in Pharmacology at the Sir John Kotelawala Defence University. The session was very well received, and in response to strong interest from non-members, we plan to open future sessions to other professionals engaged in medicine evaluation.

We also hosted two successful webinars in collaboration with the Sri Lanka College of Endocrinologists and the Sri Lanka College of Pulmonologists, focusing on the rational use of medicines in commonly encountered clinical scenarios. These webinars aligned with our theme for the year, "Personalised Medicine: Shaping the Future of Prescribing," and explored emerging developments in this evolving field. Our final webinar for the year is scheduled for December, and we hope you will join us for this concluding event.

Looking ahead, we have initiated preparations for our Biennial Scientific Sessions, scheduled for August 2026. We will keep you informed as plans take shape, and I warmly encourage you to contribute your research and participate in what promises to be another exciting and enriching gathering.
Thank you for your continued engagement and support.
With best wishes,

Professor Chandanie Wanigatunge
President, SLACPT

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Cover Story

The roots of modern medicine lie in the use of plants for healing. Ancient systems such as Ayurveda, Traditional Chinese Medicine, and Egyptian practices relied on herbs, with knowledge passed through generations. Substances like willow bark, foxglove, and opium were early remedies, forming the foundation of later scientific discoveries.

A major turning point came in the 18th century when William Withering studied foxglove (Digitalis purpurea) for dropsy (heart failure). His careful documentation in An Account of the Foxglove (1785) marked one of the first examples of evidence-based pharmacology, leading to the isolation of digoxin, a heart medicine still in use.

In the early 19th century, Friedrich Sertürner isolated morphine from the opium poppy (Papaver somniferum). This was the first time a natural product was purified into a single compound, allowing accurate dosing and revolutionizing pain management, though it also revealed risks of addiction.

Later, research on the French lilac (Galega officinalis) led to the development of metformin, now the first-line treatment for type 2 diabetes. The plant's guanidine derivatives inspired one of the most widely used and effective modern medicines.

Other plant-derived breakthroughs include aspirin (willow bark), quinine (cinchona bark), and paclitaxel (yew tree), all of which have saved countless lives.

The evolution of plants into pharmaceuticals demonstrates the journey from traditional remedies to scientifically validated treatments. Pioneers like Withering, Sertürner, and later researchers bridged ancient wisdom and modern science. Even today, nature remains a vital source of inspiration for drug discovery, highlighting the enduring connection between plants and healing.

SLACPT Inter Medical Faculty Pharmacology Quiz

SLACPT Inter-Medical Faculty Pharmacology Quiz was held online on 28th June 2025 with the participation of all twelve medical faculties in Sri Lanka.
Dr Chiranthi Liyanage was the Quiz master.

1st Place
Colombo
2nd Place
Sabaragamuwa
3rd Place
Kelaniya

Winners

University of Colombo

Visal Perera
Dinal De Silva
S. Tharsikan
Sachini Wijewardena
Hirusha Fernando

Team Coordinator:
Dr Leonard Wanninayake

There was an enthusiastic participaton of the students and the academic staff from all medical faculties. SLACPT extends sincere thanks to Dr Chiranthi Liyanage and Dr Ruwanthi Jayasekera for organsing the quiz.

From Plants to Pharmaceuticals: A Pharmacological Journey

Mendis SA
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For thousands of years, human beings have turned to plants for healing. Ancient civilizations, from the Egyptians and Chinese to the Greeks and Indians, documented herbal remedies as part of their medical traditions. What began as empirical use of plants has, over the centuries, evolved into modern pharmacology, where active compounds are isolated, studied, and refined into effective pharmaceuticals. This transformation illustrates the remarkable journey from traditional herbal medicine to contemporary drug development.

The Roots of Modern Medicine

Plants contain complex chemical compounds that help them survive in nature, often as defense mechanisms against pests, fungi, or disease. Humans discovered that many of these compounds also interact with human physiology, producing therapeutic effects. Early healers may not have known the molecular mechanisms, but trial, error, and observation helped identify which herbs alleviated pain, reduced fever, or strengthened the heart.

Modern science has built on this knowledge by isolating these bioactive compounds, determining their structures, and synthesizing or modifying them to improve safety and efficacy. Several well-known drugs today can trace their lineage directly back to plants.

Metformin and French Lilac (*Galega officinalis*)

The plant French lilac, also known as goat's rue, was used in traditional European medicine to relieve symptoms of frequent urination and wasting, now recognized as signs of diabetes. In the late 19th century, scientists identified guanidine compounds within the plant that lowered blood sugar. These discoveries paved the way for the development of metformin, a biguanide that remains one of the most widely prescribed first-line treatments for type 2 diabetes today. Its herbal origins highlight how a centuries-old remedy shaped modern diabetes care.

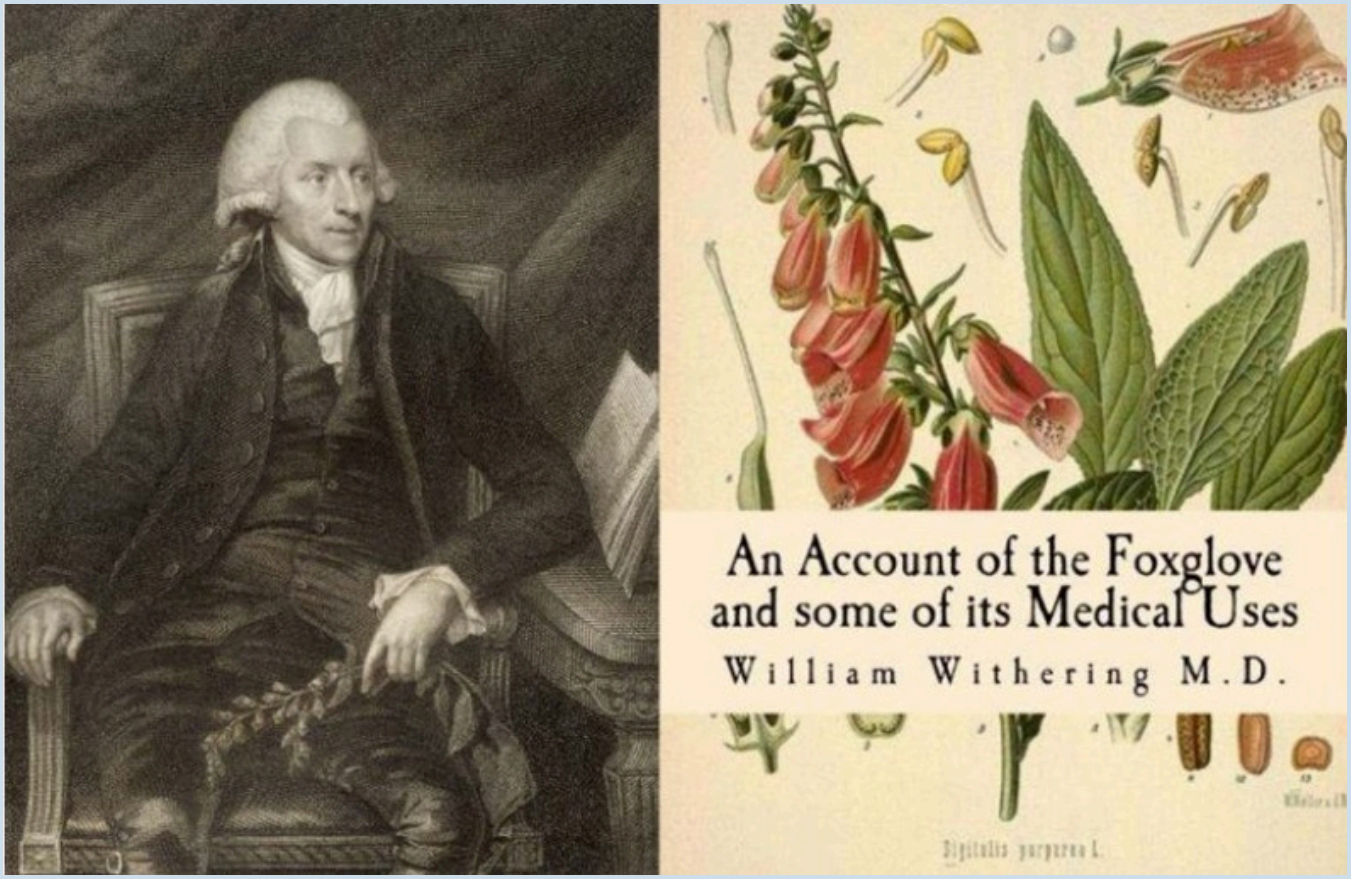
Morphine from the Opium Poppy (*Papaver somniferum)*

The opium poppy has been cultivated for thousands of years for its powerful pain-relieving effects. In 1804, **Friedrich Sertürner**, a German pharmacist, became the first to isolate morphine from **opium**.

Named after **Morpheus,** the Greek god of dreams, morphine was revolutionary in providing reliable and potent analgesia. Although opioid misuse and addiction present ongoing challenges, derivatives of the poppy remain essential in pain management, surgery, and palliative care. This case exemplifies both the promise and peril of plant-derived medicines.

Foxglove (*Digitalis purpurea)* and Dropsy

In the late 18th century, English physician William Withering famously described the use of foxglove leaves in treating dropsy, an old term for edema associated with heart failure. The active compounds—cardiac glycosides—were later identified as digoxin and related substances. By increasing the force of heart contractions, digoxin became a cornerstone in managing certain heart conditions. Though newer treatments have emerged, it remains in use today, bridging folk remedies and evidence-based cardiology.



The Legacy of Herbal Medicine in Modern Pharmacology

These examples underscore how herbal traditions provided the raw material for some of medicine's most important drugs. The process of observing therapeutic effects, isolating active compounds, and refining them into standardised treatments laid the foundation for pharmacology as a scientific discipline.

Today, pharmaceutical research continues to explore plants for new drug leads. The rainforest, for example, holds untapped botanical diversity that may yield future therapies. While modern medicine emphasizes rigorous testing and regulation, its roots remain deeply intertwined with the healing power of plants.

Future of Drug Discovery

The evolution of pharmaceuticals from herbs like French lilac, opium poppy, and foxglove demonstrates the enduring value of traditional plant knowledge. What began as folk remedies guided by observation has blossomed into a sophisticated science that continues to transform global health. As researchers seek new drugs, they stand on the shoulders of centuries of herbal wisdom—proof that the ancient bond between humans and plants remains a vital source of healing.

Reference

Parker, S. (2013). Kill or cure: An illustrated history of medicine. DK Publishing

Capacity Building Workshop Series

The SLACPT Capacity Building Workshop aims to enhance the knowledge and practice of clinical pharmacologists regarding their professional responsibilities. As part of this initiative, an online session on **Health Technology Assessment (HTA)** was conducted. The session was led by **Dr. Danushi Gunasekera**, Senior Lecturer in Pharmacology at the Faculty of Medicine, General Sir John Kothalawala Defence University. Participants found the workshop highly informative, gaining valuable insights to improve their ability to evaluate and apply health technology assessments in clinical pharmacology practice.

Blunting the Response???
Beta blockers And Adrenaline Resistance in Anaphylaxis

Mithunika AWK
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Anaphylaxis represents the most severe clinical presentation of acute systemic allergic reactions.

The World Allergy Organisation Anaphylaxis Committee defines anaphylaxis as:
"A serious systemic hypersensitivity reaction that is usually rapid in onset and may cause death. Severe anaphylaxis is characterized by potentially life-threatening compromise in airway, breathing and/or the circulation, and may occur without typical skin features or circulatory shock being present"(1).

Adrenaline or epinephrine is the most important and lifesaving medication in anaphylaxis. Intramuscular (IM) administration is the recommended route for anaphylaxis even if intravenous access is available. Its prompt use is vital, so much so that current guidelines advise administering epinephrine if there is any uncertainty about whether an allergic reaction is anaphylaxis.

As an alpha-receptor agonist, adrenaline reverses peripheral vasodilation and reduces tissue oedema. Its beta-receptor activity dilates the bronchial airways, increases the force of myocardial contraction, and suppresses histamine and leukotriene release. Adrenaline also acts directly on beta-2 adrenergic receptors on mast cells to inhibit activation, so early adrenaline may attenuate the severity of IgE-mediated allergic reactions. (2)

Refractory anaphylaxis is defined as anaphylaxis requiring ongoing treatment due to persisting respiratory or cardiovascular symptoms despite two appropriate doses of IM adrenaline. (2)

The effect of beta blockers on action of adrenaline in anaphylaxis has been controversial. However, adrenaline may be less effective in patients treated with a beta blocker. (2) In these cases, it is recommended to consider giving glucagon when symptoms remain refractory to adrenaline and adequate fluid resuscitation. (1,2)

Beta blockers are primarily used in patients with cardiovascular comorbidities like angina pectoris, heart failure, myocardial infarction, cardiac tachyarrhythmias and other conditions like hyperthyroidism and migraine. With the rise in cardiovascular diseases,

Beta blockers have become a widely used class of medication.

There are two types of beta blockers; cardio selective and non-cardioselective. Beta blockers selectively block the beta-adrenoreceptor effects of adrenaline and noradrenaline. Non-cardioselective beta blockers, in particular, can antagonize the bronchodilating effects of epinephrine by blocking beta-2 adrenergic receptors in smooth muscles of the bronchial tree.

All beta blockers can antagonize the cardiostimulatory effects of epinephrine by blocking beta-1 adrenergic receptors in the heart. Some investigators have suggested that the use of beta blockers itself is associated with an increased incidence and severity of anaphylaxis due to modulation of adenylate cyclase, which can influence release of anaphylactogenic mediator. (3)

The efficacy of glucagon for adrenaline resistant refractory anaphylaxis in patients on beta blockers is controversial. However, understanding the efficacy of glucagon is crucial because adrenaline-resistant anaphylactic shock is fatal. Moreover, beta blockers are used widely today. Glucagon exerts positive inotropic and chronotropic effects by directly activating adenylyl cyclase and bypassing β-adrenergic receptor blockade.
Several case reports have documented significant clinical improvement following glucagon administration in patients on beta blockers experiencing refractory anaphylaxis. (4,5)

The recommended dose of Glucagon in refractory anaphylaxis is an initial bolus of 1-5mg. Later an infusion of glucagon can be given at a rate of 5-15 micrograms per minute. (4) Patient should be monitored for adverse events, including hyperglycaemia, vomiting, hypokalaemia and hypocalcaemia following administration of glucagon. (2)

Despite very limited evidence, most clinical guidelines for management of anaphylaxis including Resucitation Council UK guideline for emergency treatment of anaphylaxis and World Allergy Organization Anaphylaxis Guidance recommend to consider glucagon in refractory anaphylaxis for patients who are on beta blockers.(1,2,6)

In a world with increasing prevalence of cardiovascular disease, more patients are being prescribed beta blockers. Recognizing the potential for epinephrine resistance in these individuals is crucial. In cases of refractory anaphylaxis, a thorough review of the patient's medication history can be lifesaving. When beta blockers are involved, consideration of glucagon as a rescue therapy is not just reasonable—it may be vital.

References

1. Cardona V, Ansotegui IJ, Ebisawa M, El-Gamal Y, Fernandez Rivas M, Fineman S, et al. World Allergy Organization Anaphylaxis Guidance 2020. World Allergy Organization Journal. 2020;13(10).

2. UK RC. Emergency treatment of anaphylaxis, Guidelines for healthcare providers. 2021

3. American Academy of Allergy, Asthma & Immunology. Epinephrine therapy in patients receiving beta-blocker treatment [Internet]. Milwaukee (WI): AAAAI; Available from: https://www.aaaai.org/tools-for-the-public/conditions-library/anaphylaxis/epinephrine-therapy-and-beta-blockers

4. Rukma P. Glucagon for Refractory Anaphylaxis. American Journal of Therapeutics. 2019;26(6):e755-e6.

5. M. Mansour, S. Merten, K. Gifford, M. Hammoud, P. Buhi, A. Garg, and E.R. Shehada. The Utilization of Glucagon in Refractory Anaphylactic Shock in a Patient on β-blockers [abstract]. Am J Respir Crit Care Med 2025;211:A5520. https://doi.org/10.1164/ajrccm.2025.211.Abstracts.A5520

6. Australasian Society of Clinical Immunology and Allergy (ASCIA). ASCIA guidelines—Acute management of anaphylaxis. [Internet]. 2024 Jul. Available from: Australasian Society of Clinical Immunology and Allergy website.

Finasteride - Will it make the patient suicidal?

In April, 2025, FDA issued a safety alert highlighting serious risks associated with unapproved compounded topical finasteride, based on 32 adverse event reports (2019–2024). Reported adverse effects included sexual dysfunction, mood changes, insomnia, and suicidal ideation, many persisting after drug discontinuation (1).

EMA concluded that finasteride and dutasteride "can cause depressed mood, depression or suicidal thoughts." Their review, published in May 2025, identified 313 cases linked to finasteride and 13 to dutasteride. While the EMA retained the benefit–risk balance as favourable, warnings were reinforced (2).

Nine international observational studies, including a recent analysis of the FDA Adverse Event Reporting System (FAERS), which found significant safety signals for suicidal ideation, particularly in patients on 1 mg finasteride for androgenetic alopecia. Signals for suicidal ideation were detected from 2013 onwards, with reporting odds ratios (RORs) as high as 9.9 for finasteride 1 mg, suggesting a markedly increased risk compared to other medicines (3).

Implications for Clinical Practice

For clinicians, this development underscores the importance of balancing cosmetic indications with safety concerns. While finasteride remains widely prescribed for androgenic alopecia and benign prostatic hyperplasia, healthcare providers should:

- Conduct baseline mental health assessments before initiating therapy.
- Provide clear counselling on potential psychiatric and sexual side effects.
- Encourage open communication so patients feel comfortable reporting mood changes.
- Document counselling and follow-up closely, particularly in younger male patients treated for alopecia.

Recommendations for Prescribers

- Inform patients about the risk of mood changes, depression, and suicidal ideation.
- Instruct patients to discontinue therapy and seek medical help immediately if such symptoms occur.
- Counsel patients on the impact of sexual dysfunction on mental health, with consideration for treatment discontinuation.
- Implement a risk-management plan for oral finasteride used in androgenic alopecia, including provision of a patient information card.

References

1. U.S. Food and Drug Administration. (2025, April 22). FDA alerts health care providers, compounders and consumers of potential risks associated with compounded topical finasteride products. https://www.fda.gov/drugs/human-drug-compounding/fda-alerts-health-care-providers-compounders-and-consumers-potential-risks-associated-compounded
2. European Medicines Agency. (2025, May 8). Measures to minimise risk of suicidal thoughts with finasteride and dutasteride medicines. https://www.ema.europa.eu/en/news/measures-minimise-risk-suicidal-thoughts-finasteride-dutasteride-medicines
3. Gorelik, A., et al. (2021). Investigation of suicidality and psychological adverse events in patients treated with finasteride. Journal of Clinical Psychopharmacology, 41(6), 635–641. European Medicines Agency. (2025, May 8). Meeting highlights from the Pharmacovigilance Risk Assessment Committee (PRAC) 5–8 May 2025. https://www.ema.europa.eu/en/news/meeting-highlights-pharmacovigilance-risk-assessment-committee-prac-5-8-may-2025

PRECISION MEDICINE MEETS RESPIRATORY CARE

Sri Lanka Association of Clinical Pharmacology and Therapeutics and Sri Lanka College of Pulmonology jointly organised a Continuous Professional Development Webinar on Precision Medicine in the therapeutics of Respiratory Diseases.

There were sixty five particpants joined online. Participants and Reosurce Persons were offered Ministry of Health accredited CPD points.

Drug Information Summary

Apixaban

Apixaban is a selective, reversible, direct factor Xa inhibitor that reduces thrombin generation and subsequent thrombus formation. It is indicated for the prevention of stroke and systemic embolism in non-valvular atrial fibrillation, as well as for the treatment and secondary prevention of venous thromboembolism (DVT and PE) and postoperative thromboprophylaxis following major orthopedic surgery. Its predictable pharmacokinetic profile, minimal food–drug interactions, and lack of requirement for routine anticoagulation monitoring distinguish it from vitamin K antagonists.

Mechanism of Action

Potent, oral, reversible, and selective direct Factor Xa inhibitor.
Inhibits both free and clot-bound Factor Xa and prothrombinase activity.
Prevents thrombin generation and thrombus formation.
No direct effect on platelet aggregation, but indirectly reduces thrombin-induced aggregation.
Preclinical studies: effective in preventing arterial/venous thrombosis while preserving haemostasis.

Pharmacodynamic Effects

Prolongs clotting tests (PT, INR, aPTT), but effects are variable and not reliable for monitoring.
Thrombin generation assays: reduce endogenous thrombin potential.
Shows anti-Factor Xa activity (AXA) that is:
Linearly related to plasma concentration.
Peaks at the same time as apixaban's peak plasma concentration.
Consistent across adults and paediatric patients.

Pharmakokinetic properties

Absorption

Oral bioavailability in adults: 50% for doses up to 10 mg.
Rapid absorption: Cmax reached 3–4 hours post-dose in adults; ~2 hours in pediatric patients.
Food does not significantly affect Cmax or AUC at standard doses.
Dose-proportional pharmacokinetics up to 10 mg; doses ≥25 mg show reduced bioavailability due to dissolution-limited absorption.
Crushing tablets or administering via nasogastric tube does not significantly alter exposure; minor reductions with apple puree are not clinically relevant.

Distribution

Plasma protein binding: 87% in adults.
Volume of distribution (Vss): 21 L.
No pediatric-specific protein binding data available.

Metabolism and Elimination

Multiple elimination routes: 25% metabolized, mostly excreted in feces.
Renal clearance: 27% of total elimination in adults. Additional biliary and intestinal excretion observed. Total clearance: 3.3 L/h in adults; 3.0 L/h in pediatric patients. Half-life: 12 hours in adults. Metabolism primarily via CYP3A4/5, minor contributions from CYP1A2, 2C8, 2C9, 2C19, 2J2.
Major metabolite: unchanged apixaban; no active circulating metabolites.
Substrate for transport proteins: P-gp and BCRP.

Therapeutic Indications

Adults

- Treatment of DVT/PE and prevention of recurrence.
- Venous Thromboembolic Events (VTE) prevention after elective hip or knee replacement.
- Stroke/systemic embolism prevention in non-valvular atrial fibrillation (NVAF) with ≥1 risk factor (e.g., prior stroke/TIA, age ≥75, hypertension, diabetes, symptomatic HF).

Paediatrics (≥28 days to <18 years)

- Treatment and prevention of recurrent VTE.

Posology and Method of Administration

Adults

VTE prophylaxis (post-surgery): 2.5 mg BID, start 12–24 h after surgery.
Hip: 32–38 days
Knee: 10–14 days
Non-Valvular Atrial Fibrillation (NVAF): 5 mg BID
Reduce to 2.5 mg BID if ≥2 of: age ≥80, weight ≤60 kg, serum creatinine ≥1.5 mg/dL.
DVT/PE treatment:
10 mg BID × 7 days → 5 mg BID
For extended prevention: 2.5 mg BID (after 6 months of full-dose treatment).

Paediatrics (≥35 kg):

- Days 1–7: 10 mg BID
- Day 8 onward: 5 mg BID

Paediatrics <35 kg → weight-tier dosing (granule formulations).

- Renal impairment:
  - Mild/moderate: no adjustment (except NVAF if criteria met).
  - Severe (CrCl 15–29): use with caution; NVAF → 2.5 mg BID.
  - <15 mL/min or dialysis: not recommended.
- Hepatic impairment:
  - Contraindicated in hepatic disease with coagulopathy.
  - Not recommended in severe impairment; use caution in mild/moderate (Child-Pugh A/B).
- Missed dose: Take as soon as possible (same day only), continue regular schedule.
- Switching:
  - From VKA: start when INR <2.
  - To VKA: overlap ≥2 days, continue until INR ≥2.
  - From/to parenteral anticoagulants: switch at next scheduled dose.
- Administration: Oral, with/without food. Tablets may be crushed, suspended (water, juice, puree) or given via NG tube.

Contraindications

- Hypersensitivity.
- Active clinically significant bleeding.
- Hepatic disease with coagulopathy/bleeding risk.
- High-risk bleeding lesions (e.g., GI ulcers, intracranial hemorrhage, varices, vascular abnormalities).
- Concomitant anticoagulant therapy (except in specific switching/UFH catheter situations).

Special Warnings and Precautions
Bleeding risk: monitor for hemorrhage, discontinue if severe bleeding.
Reversal agent: Andexanet alfa (adults only). PCCs/recombinant factor VIIa may be considered.
Drug interactions:
Contraindicated with other anticoagulants (unless switching).
Caution with antiplatelets, SSRIs/SNRIs, NSAIDs (↑ bleeding risk).
Specific cautions: Not recommended in prosthetic heart valves, antiphospholipid syndrome, hip fracture surgery.
Hold ≥48 h before high-risk procedures; ≥24 h before low-risk procedures.
Increased risk with neuraxial anesthesia/epidural puncture → strict timing protocols.
Not for use in hemodynamically unstable PE patients requiring thrombolysis/embolectomy.
Caution in cancer patients due to dual thrombotic/bleeding risk.
Patient factors:
↑ bleeding risk in elderly, low body weight, renal/hepatic impairment.

Drug Interactions
- Strong CYP3A4 + P-gp inhibitors (ketoconazole, itraconazole, ritonavir): contraindicated (↑ apixaban levels 2-fold).
- Strong CYP3A4 + P-gp inducers (rifampin, carbamazepine, phenytoin, St John's Wort): ↓ apixaban exposure (50%); avoid in DVT/PE treatment.
- Antiplatelets/SSRIs/SNRIs/NSAIDs: ↑ bleeding risk; use with caution.
- Other agents: minimal interactions with atenolol, digoxin, naproxen, famotidine.
- Activated charcoal reduces apixaban exposure (useful in overdose).

Fertility, Pregnancy and Lactation
- Pregnancy: Not recommended; no human data, precautionary avoidance.
- Breastfeeding: Unknown if excreted in milk; animal studies show excretion.
  Decision: discontinue breastfeeding or apixaban.
- Fertility: No adverse effects seen in animal studies.

Adverse Effects
Common Adverse Effects
- Blood and Lymphatic System: Anaemia, Thrombocytopenia (some indications)
- Vascular: Haemorrhage, Haematoma
- Gastrointestinal: Nausea, GI haemorrhage (some indications), Rectal/gingival bleeding (some indications)
- Renal & Urinary: Haematuria (some indications)
- General & Procedural: Contusion, Post-procedural haemorrhage (some indications)
- Skin & Subcutaneous Tissue: Skin rash (some indications), Alopecia (pediatric)
- Reproductive System (Pediatric): Abnormal vaginal/urogenital haemorrhage (very common)
- Respiratory (Pediatric): Epistaxis (very common)
- Immune System (Pediatric): Hypersensitivity, Anaphylaxis (common)
- Other (Pediatric): Pruritus, Hypotension, Haematochezia, AST elevation, Post-procedural haemorrhage

Uncommon Adverse Effects
Blood and Lymphatic System: Thrombocytopenia (some indications)
Immune System: Pruritus, Hypersensitivity reactions, Allergic oedema
Vascular: Hypotension (some indications)
Respiratory: Epistaxis (adults), Haemoptysis
Gastrointestinal: GI haemorrhage (some indications), Haematochezia, Mouth haemorrhage, Haemorrhoidal haemorrhage
Hepatobiliary: Abnormal liver function tests, AST/ALT/ALP/bilirubin elevations
Skin & Subcutaneous Tissue: Alopecia (some indications)
Musculoskeletal & Connective Tissue: Muscle haemorrhage
Renal & Urinary: Haematuria
General & Procedural: Application site bleeding, Post-procedural haemorrhage

In paediatric patients, epistaxis (very common), abnormal vaginal haemorrhage (very common), hypersensitivity and anaphylaxis (common), pruritus (common), hypotension (common), haematochezia (common), aspartate aminotransferase increased (common), alopecia (common), and post procedural haemorrhage (common) were reported more frequently as compared to adults treated with apixaban, but in the same frequency category as the paediatric patients in the standard of care (SOC) arm; the only exception was abnormal vaginal haemorrhage, which was reported as common in the SOC In all but one case, hepatic transaminase elevations were reported in paediatric patients receiving concomitant chemotherapy for an underlying malignancy.

Apixaban Overdose: Key Points
- Risk: Overdose increases bleeding risk. Discontinue apixaban and investigate bleeding sources.
- Supportive Measures: Consider surgical hemostasis, transfusion of fresh frozen plasma (FFP), or use of a reversal agent for factor Xa inhibitors.
- Activated Charcoal: Effective if administered within 2–6 hours of ingestion; reduces apixaban exposure and half-life.
- Haemodialysis: Minimal effect on apixaban clearance; not an effective treatment.

Reversal Agents:
- Andexanet alfa is available for adults with life-threatening or uncontrolled bleeding.
- Prothrombin complex concentrates (PCCs) or recombinant factor VIIa may be considered; clinical experience is limited.
- PCCs can reverse apixaban effects within 4 hours in healthy subjects.
- Paediatric Use: Andexanet alfa is not established in children.
- Expert Consultation: Seek coagulation expert guidance for major bleeding, considering local availability of treatments.

Source:
Summary of Product Characteristics of Apixaban, European Medicines Agency (EMA)
Detailed information of this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu/.

Drug Information Summary

Finerenone

Finerenone is a novel non-steroidal mineralocorticoid receptor antagonist used in patients with chronic kidney disease and type 2 diabetes. It helps reduce renal disease progression and lowers the risk of cardiovascular events, with fewer hormonal side effects compared to older MRAs like spironolactone.

Mechanism of Action

Blocks MR activated by aldosterone and cortisol.
Inhibits transcription of pro-inflammatory and pro-fibrotic mediators.

Pharmacodynamic Effects

FIDELIO-DKD & FIGARO-DKD (Phase III, CKD + T2D patients): Finerenone reduced urinary albumin-to-creatinine ratio (UACR) by 31–32% at month 4, sustained throughout the studies.
ARTS-DN (Phase IIb): UACR reduction of 25–38% at Day 90 for 10 mg and 20 mg doses.
Cardiac Safety: No QT/QTc prolongation observed in healthy volunteers.

Clinical Efficacy

FIDELIO-DKD: 5,674 patients; median follow-up 2.6 years. Primary composite endpoint: kidney failure, sustained ≥40% eGFR decline, or renal death. Key secondary endpoint: CV death, non-fatal MI, stroke, or heart failure hospitalization. Statistically significant benefits observed for both endpoints across subgroups.
FIGARO-DKD: 7,352 patients; median follow-up 3.4 years. Primary endpoint: CV death, non-fatal MI, stroke, or heart failure hospitalization. Significant benefit in CV outcomes; renal secondary endpoint showed lower event rates but did not reach statistical significance overall, with greater benefit in patients with UACR ≥ 300 mg/g.

Dosing and Adjustment

Finerenone administered 10–20 mg once daily. Dose adjustments primarily based on serum potassium levels.
Patient Population:
Adults with CKD and type 2 diabetes, mostly on ACE inhibitors or ARBs.
Excluded patients with heart failure with reduced ejection fraction (NYHA II–IV).

Finerenone provides renal and cardiovascular protection in adults with CKD and T2D, demonstrating a favorable efficacy profile, sustained UACR reduction, and no significant QT prolongation. Treatment benefits were consistent across multiple patient subgroups.

Pharmacokinetic properties

Absorption:

Rapid and almost complete after oral administration.
Peak plasma concentration (C_{max}) occurs 0.5–1.25 hours post-dose in the fasted state.
Absolute bioavailability is ~43.5% due to first-pass metabolism.
Food slightly increases overall exposure (AUC +21%) and delays C_{max} but is not clinically significant; can be taken with or without food.

Distribution:
Volume of distribution (V_{ss}) is 52.6 L.
Plasma protein binding is high (91.7%), mainly to albumin.

Metabolism:
Primarily metabolized by CYP3A4 (90%) and CYP2C8 (10%).
Four major metabolites detected, all pharmacologically inactive.

Elimination:
Rapid plasma clearance with half-life of 2–3 hours.
Systemic clearance 25 L/h.
Excretion mostly via urine (80%) and faeces (20%), mainly as metabolites; unchanged drug excretion is minimal (<1% urine, <0.2% faeces).

Linearity:
Finerenone pharmacokinetics are linear across the investigated dose range from 1.25 to 80 mg given as single dose tablets.

Pharmacokinetic/pharmacodynamic relationships
The concentration-effect relationship over time for UACR was characterised by a maximum effect model indicating saturation at high exposures. The model-predicted time to reach the full (99%) steady-state drug effect on UACR was 138 days. The pharmacokinetic (PK) half-life was 2-3 hours and PK steady state was achieved after 2 days, indicating an indirect and delayed effect on pharmacodynamic responses.

Therapeutic Indications
Finerenone is indicated for the treatment of chronic kidney disease (CKD) with albuminuria in adults with type 2 diabetes.

Posology and Administration
- Recommended dose: 20 mg once daily. Maximum dose: 20 mg once daily.
- Initiation: Assess serum potassium and eGFR before starting.

Serum potassium ≤4.8 mmol/L: treatment can be started.
Serum potassium 4.8–5.0 mmol/L: treatment may be started with close monitoring.
Serum potassium >5.0 mmol/L: treatment should not be initiated.

- eGFR-based dosing:

≥60 mL/min/1.73 m²: 20 mg
25–<60 mL/min/1.73 m²: 10 mg starting dose
<25 mL/min/1.73 m²: not recommended

Continuation and dose adjustment: Monitor serum potassium 4 weeks after initiation, restart or dose increase; adjust according to Table 2 guidelines.
Missed dose: Take the same day; do not double dose.

Special Populations

- Elderly: No dose adjustment needed.
- Renal impairment: Avoid initiation if eGFR <25 mL/min/1.73 m²; discontinue if eGFR <15 mL/min/1.73 m².
- Hepatic impairment: Avoid in severe hepatic impairment; monitor potassium in moderate impairment.
- Paediatric population: Safety and efficacy not established.

Method: Oral tablets, with or without food; do not take with grapefruit. Tablets may be crushed for administration with water or soft food.

Contraindications

Hypersensitivity to finerenone or excipients.
Concomitant use with strong CYP3A4 inhibitors.
Addison's disease.

Warnings and Precautions

- Hyperkalaemia: Most common adverse effect. Monitor potassium and eGFR regularly. Discontinue temporarily if potassium >5.5 mmol/L.
- Concomitant medications: Avoid potassium-sparing diuretics, other MRAs, strong/moderate CYP3A4 inducers; monitor potassium with moderate/weak CYP3A4 inhibitors, potassium supplements, trimethoprim.
- Heart failure: Not studied in NYHA II–IV with reduced ejection fraction.
- Pregnancy and lactation: Avoid use unless benefits outweigh risks; women of childbearing potential should use contraception; breastfeeding not recommended.
- Grapefruit: Avoid due to CYP3A4 interactions.

Adverse Reactions

- Very common: Hyperkalaemia (14%).
- Common: Hyponatraemia, hypotension, pruritus.
- Uncommon: Hyperuricaemia, decreased GFR, decreased haemoglobin.
- Most adverse events are mild to moderate; serious hyperkalaemia reported in 1.1% of patients; hyperkalaemia may lead to discontinuation in 1.7%.
- Initial eGFR decline is mild (~2 mL/min/1.73 m²) and reversible.

Overdose

- Most likely effect: hyperkalaemia. Treat according to standard protocols.
- Haemodialysis is unlikely to remove finerenone effectively due to high plasma protein binding (~90%).

Source:

Summary of Product Characteristics of Finerenone, European Medicines Agency (EMA)
Detailed information of this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu/.

SLACPT Pharmacology MCQ course

SLACPT MCQ course targeting the MD selection examinations was meticulously organised by Dr Asanka Eriyawa and Dr Supun Wedasinghe, for the second time for the year 2025 . This course is conducted for two days, 23rd August 2025 and 6th September 2025 as an online programme.

MCQ Course Targeting MD Selection Exams Organized by the

SRI LANKA ASSOCIATION OF CLINICAL PHARMACOLOGY & THERAPEUTICS (SLACPT)

23rd August &
6th September 2025

23rd August 2025		
09.00 – 10.30 am	Basic Pharmacology	Prof Pradeepa Jayawardane
10.45 AM – 12.15 PM	Respiratory and Autonomic Nervous System Pharmacology	Dr Ruwanthi Jayasekara
01.00 PM – 02.30 PM	Cardiovascular Pharmacology	Dr Solith Senanayake
02.45 PM - 04.15 PM	Pharmacology of Gastrointestinal and Liver Disease	Prof Anuradha Dassanayake
6th September 2025		
09.00 AM – 10.30 AM	Prescribing in Rheumatology	Dr Sujeevani Kurukulasuriya
10.45 AM – 12.15 PM	Pharmacology in Special Population	Prof Shalini Sri Ranganathan
01.00 PM – 02.30 PM	Antidiabetic Agents and other Drugs in Endocrine Disorders	Dr Gayana Amiyangoda
02.45 PM - 04.15 PM	Pharmacology of Anti-infectives	Dr Sahan Mendis

(Reserve your place by paying the fee since only a limited number will be registered)

HOW TO REGISTER?
By filling the google form. https://forms.gle/R5eDpDm7AGr33dnw6
Please upload payment slip to the google form.
Payments to be made to the following account.
Conducted on a zoom platform

A/C Name - SRI LANKA ASSOCIATION OF CLINICAL PHARMACOLOGY AND THERAPEUTICS
A/C Number – 167200180013901
Bank - Peoples' Bank
Branch - 00167 Colombo Town Hall

FOR MORE INFORMATION (office@slacpt.lk)
Ms. Jayani Dasanayake (0704008070)
Ms.L. D. Dulakshi Chathurika (0719795121)

Following SLACPT members contributed as resource persons in MCQ discussions:

Senior Professor
Shalini Sri Ranganathan

Professor
Pradeepa Jayawardena

Professor
Anuradha Dassanayake

Dr Sujeevani Kurukulasuriya

Dr Solith Senanayake

Dr Ruwanthi Jayasekera

Dr Gayana Amiyangoda

Dr Sahan Mendis

Wall of Fame

Professor Chamila Mettananda
Professor in Pharmacology, Faculty of Medicine, University of Kelaniya was awarded the “Pramod Ranathunga Research Award” at the Annual Academic Sessions 2025 of Sri Lanka College of Cardiology.

SLACPT upcoming events

SLACPT/SLCIM Joint CME Webinar – December 2025

Next SLACPT joint CME webinar will be conducted in collaboration with Sri Lanka College of Internal Medicine in December 2025 on Clinical Toxicology

SLACPT NEWS

The Official Newsletter of
the Sri Lanka Association of
Clinical Pharmacology and Therapeutics

Compiled by
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Write to Us!

SLACPT welcomes suggestions from readers towards improving the image of the Association and the newsletter.

Please send your suggestions to:
Email: office@slacpt.lk