Tabba Heart Institute

PHARMA CONNECT | 2025

VOLUME 5

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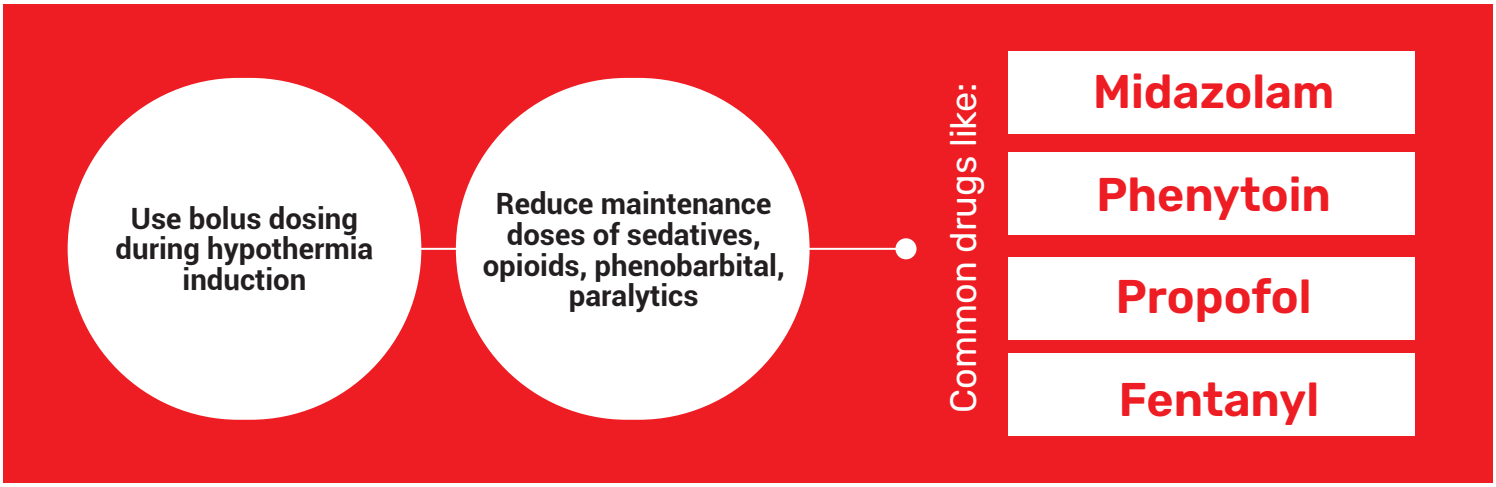
1. Reduced Drug clearance during Hypothermia

Submitted by: Areeba Nayab (Clinical Pharmacist)

Drug clearance is typically reduced during hypothermia, including a depressed activity of cytochrome P450 (CYP) 3A4 and 3A5 hepatic enzymes. Hypothermia can also affect the distribution of drugs to their site of action (e.g., propofol). These effects become more pronounced at cooler temperatures.

Twenty-one studies were included in the review paper of critical care medicine. The effects of therapeutic hypothermia on drug disposition include both the effects during cooling and the effects after rewarming on drug metabolism and response. The studies cited in this review demonstrate that the addition of mild to moderate hypothermia decreases the systemic clearance of cytochrome P450 metabolized drugs between 7% and 22% per degree Celsius below 37°C during cooling. The addition of hypothermia decreases the potency and efficacy of certain drugs.

Based on impaired clearance, dosages should be decreased considerably, especially for drugs with a low therapeutic index.



Clinicians should understand and anticipate potential drug-therapy interactions of targeted temperature management and mitigate adverse outcomes by appropriate medication selection, dosing, and monitoring.

Reference:

Crombez T, Hachimi-Idrissi S. The influence of targeted temperature management on the pharmacokinetics of drugs administered during and after cardiac arrest: a systematic review. Acta Clin Belg [Internet]. 2017;72(2):116–22.

2. Role of oral anti-diabetic drugs in mitigating non-alcoholic fatty liver disease in type 2 diabetics

Submitted by: Museera Zahid (Pharmacist-Inpatient Pharmacy)

Abstract

Objective:
To determine the outcome of oral anti-diabetic drugs and lifestyle modifications in non-alcoholic fatty liver disease (NAFLD) and type 2 diabetic mellitus patients.

Table 1. sub-groups of drug therapy showing N (no. Of patients) in each group

Sub-groups	Therapy	Number of patients N=200	Ultrasound improvement (Grade-I,II) n (%)
A	Empagliflozin/metformin	30	20(10)
B	Empagliflozin/linagliptin	30	10(5)
C	Metformin	30	8(4)
D	Sitagliptin and metformin	30	5(3)
E	Sitagliptin	30	2(1)
F	Lifestyle modification	50	3(2)
		200	48(24)

Methodology

This observational study was performed in the Primary care Hospital to estimate the effectiveness of oral anti-diabetic drugs through ultrasound, CBC, HbA1c, LFTs in NAFLD and diabetic patients from 1st January 2023 to 31st December 2023. 200 patients were divided into sub-groups based on anti-diabetic drugs, Empagliflozin + Metformin in sub-group 'A' (n=30), Empagliflozin + Linagliptin in sub-group 'B' (n=30), Metformin in sub-group 'C' (n=30). Sitagliptin + Metformin in sub-group 'D' (n=30), Sitagliptin in sub-group 'E' (n=30). The lifestyle modifications were suggested only in sub-group 'F' (n=50) for 6 months.

Results

Approximately 20 (10%) patients in sub-group 'A', 10(5%) in 'B', 8(4%) in 'C', 5(3%) in 'D', 2(1%) in 'E', 3(2%) in 'F' showed improvements in HbA1c (<5.7%), blood sugar level (70-100 mg/dL), mean BMI (18.5-24.9) and lipid profile (cholesterol <200 mg/dL, triglycerides <150 mg/dL), liver enzymes (SGPT/SGOT = 1:1), better ultrasound results of liver after 6 months therapy.

Conclusion

Empagliflozin/Metformin showed better improvements in maintaining HbA1c, ultrasound changes, liver enzymes, reducing BMI, total cholesterol and triglycerides in NAFLD among type-2 diabetics.

Table 2. Pre and Post Treatment Comparison

Parameters	Pre-Treatment	Post-Treatmen	Improvement
HbA1c (%)	>6.4 (Diabetic)	<5.7 (Normal)	Significant reduction
Blood Sugar (mg/dL)	>126 (Diabetic)	70-100 (Normal)	Normalized
BMI (kg/m²)	>29 (Obese)	18.5-24.9 (Normal)	Reduced to normal range
Cholesterol (mg/dL)	200-239 (High)	<200 (Normal)	Reduced
Triglycerides (mg/dL)	200-499 (Very High)	<150 (Normal)	Reduced
SGPT/SGOT Ratio	<1 (Imbalance)	1:1 (Normalized)	Improved liver function
Ultrasound Grade	Grade-II or III Fatty Liver	Grade-I Fatty Liver / Normal Parenchyma	Liver fat reduced
Liver Size (cm)	17-18 cm (Enlarged)	15-16 cm (Reduced to normal)	Improved liver size

Reference:

Seetlani, N. K., Memon, A. R., Tanveer, S., Ali, A., Ali, P., Imran, K., & Haroon, H. (2016). Frequency of non-alcoholic steatohepatitis on histopathology in patients of type 2 diabetes mellitus with duration of more than 5 years. J Coll Physicians Surg Pak, 26(8), 643.

Magkos, F., Su, X., Bradley, D., Fabbrini, E., Conte, C., Eagon, J. C., ... & Klein, S. (2012). Intrahepatic diacylglycerol content is associated with hepatic insulin resistance in obese subjects. Gastroenterology, 142(7), 1444-1446.

Galicia-Garcia, U., Benito-Vicente, A., Jebari, S., Larrea-Sebal, A., Siddiqi, H., Uribe, K. B., ... & Martín, C. (2020). Pathophysiology of type 2 diabetes mellitus. International journal of molecular sciences, 21(17), 6275.

3. Vericiguat: A New Horizon in Heart Failure Management

Submitted by: Muhammad Nehal Nadir (Clinical Pharmacist)

Mechanism and Clinical Benefits

Vericiguat is a novel oral soluble guanylate cyclase (sGC) stimulator that enhances the nitric oxide (NO)-sGC-cGMP pathway, often impaired in heart failure with reduced ejection fraction (HFrEF). By directly stimulating sGC, vericiguat increases intracellular cGMP, leading to vasodilation, reduced myocardial fibrosis, inflammation, and hypertrophy, and improved cardiac and vascular function. This unique action helps counteract heart failure progression even when NO levels are low.

The pivotal VICTORIA trial showed vericiguat reduced the combined risk of cardiovascular death or first heart failure hospitalization by 10% in over 5,000 patients with recent worsening HFrEF, with greatest benefits in patients under 75 years, those with moderate kidney dysfunction, and NYHA class III-IV.

Pharmacist's Role

Pharmacists optimize vericiguat therapy by educating patients on adherence and side effects, monitoring drug interactions, and collaborating with healthcare teams to integrate vericiguat into guideline-directed therapy. Monitoring includes N-terminal pro-BNP (NT-proBNP) and blood pressure due to its potential to cause symptomatic hypotension.

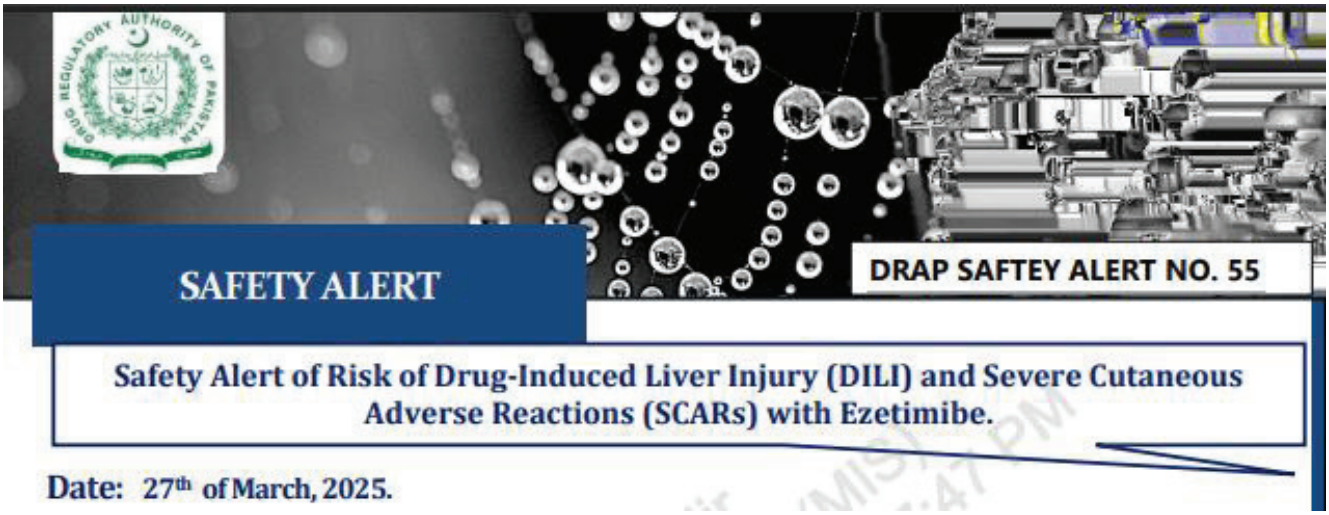
Future Directions

Vericiguat's once-daily dosing and novel mechanism complement existing treatments, offering hope for reducing hospitalizations and mortality in high-risk HFrEF patients. Future research should explore long-term safety, use in heart failure with preserved ejection fraction (HFpEF), and combination therapies to enhance outcomes

References:

DrugBank Online. Vericiguat: Uses, Interactions, Mechanism of Action. 2023.
StatPearls. Vericiguat in Heart Failure with Reduced Ejection Fraction. 2023.
U.S. Pharmacist. Vericiguat in the Treatment of Heart Failure. 2023.

DRAP SAFTEY ALERT—March 2025

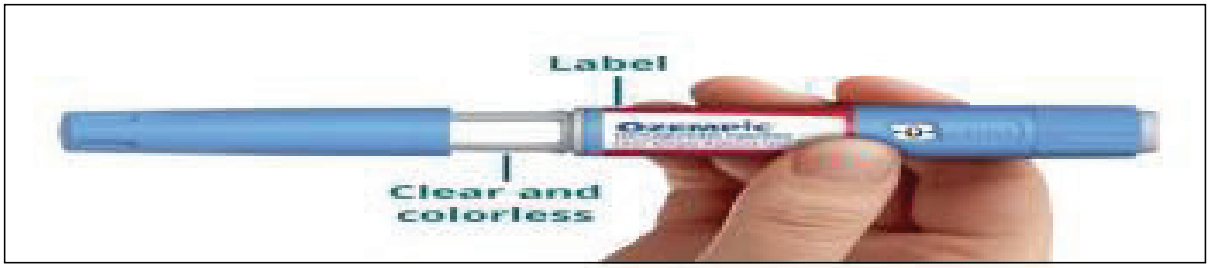


The Drug Regulatory Authority of Pakistan (DRAP) issued Safety Alert No. 55 on March 27, 2025, regarding the risk of drug-induced liver injury (DILI) and severe cutaneous adverse reactions (SCARS) associated with ezetimibe, a cholesterol absorption inhibitor. This alert follows Health Canada's March 2024 update, which added warnings about serious adverse reactions, including DILI and SCARs such as Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and drug reaction with eosinophilia and systemic symptoms (DRESS)

The recommendation now includes performing liver function tests at initiation and during treatment with ezetimibe, whether used alone or in combination Advise patients to seek immediate medical attention if they experience symptoms of liver injury (e.g., severe abdominal pain, dark urine, yellowing of skin/eyes) or serious skin reactions (e.g., blistering, swelling, fever, flu-like symptoms). Instruct patients to discontinue ezetimibe and seek urgent care if symptoms of SCARs develop.

4. Semaglutide: A Breakthrough in Diabetes and Weight Management

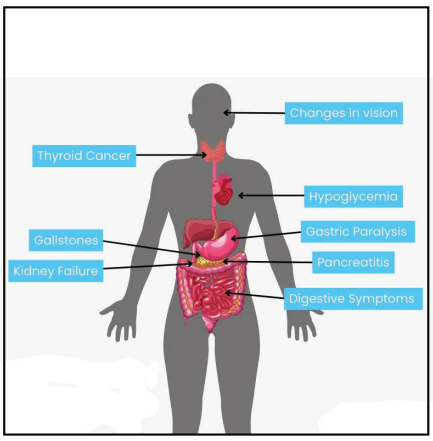
Submitted by: Rimsha Ismail (Senior inpatient Pharmacist)



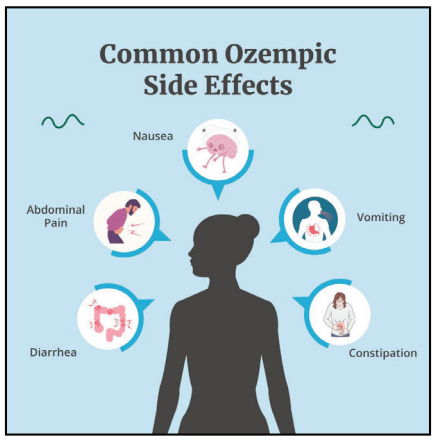
Semaglutide, a GLP-1 receptor agonist (glucagon-like peptide-1). It mimics the effects of the natural GLP-1 hormone, which plays a key role in glucose regulation. Here's how it works:

1. **Stimulates Insulin Secretion:** When blood sugar is high, semaglutide prompts the pancreas to release more insulin-helping lower glucose levels.
2. **Suppresses Glucagon Release:** It reduces the amount of glucagon (a hormone that raises blood sugar) produced by the liver, especially after meals.
3. **Slows Gastric Emptying:** Semaglutide delays how quickly food leaves the stomach, which reduces the speed of glucose entering the bloodstream and helps with satiety.
4. **Reduces Appetite:** It acts on appetite centers in the brain (hypothalamus), leading to decreased hunger and lower calorie intake contributing to weight loss.

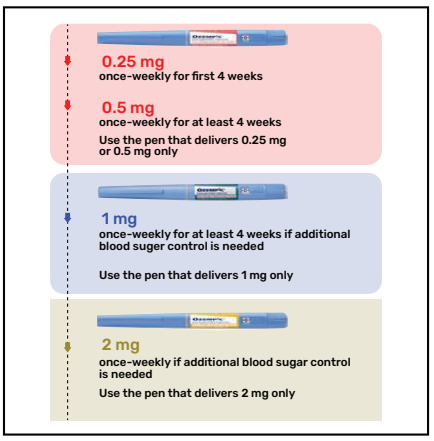
RISK FACTOR



SIDE EFFECTS



DOSING



OZEMPIC PREVENTS CANCER

Submitted by: Aleena Khan (Ambulatory care Pharmacist)

Yes, you read that right! Ozempic, the famous weight reducing pill, also helps in preventing various types of cancer.

Ozempic (Semaglutide) belongs to the class of GLP-1 receptor agonists. Primarily used in managing type 2 Diabetes by mimicing the action of naturally occurring hormones GLP-1. It promotes production of insulin hormone, suppresses and inhibits the release of glucagon and delays gastric emptying. As a result, we have decreased blood sugar, decreased hunger and weight loss.

Type 2 diabetic patients are at a high risk of developing different types of liver, pancreatic and colorectal cancers. It could be due to insulin resistance, unmanaged diabetes or chronic inflammation. Scientists through recent studies have found that Ozempic has potential to reduce these risks of cancer in diabetic patients.

The GLP-1 receptors are also found in some types of cancer cells. Scientists have found that Semaglutide has anti proliferative, suggesting that it may hinder the production and spreading of cancer cells. However, we are still in the early stages of trial and are hopeful that this study will improve the lives of diabetic patients at risk of cancer.

Whilst these studies are positive, additional clinical research is required to verify the link of Semaglutide with reducing cancers. Ozempic not only provides metabolic control for diabetic patients but also offers the promising added benefit of reducing the likelihood of cancer.

References:

- https://www.ozempic.com/why-ozempic/what-is-ozempic.html
- https://www.ema.europa.eu/en/documents/product-information/ozempic-epar-product-information_en.pdf
- https://www.cancer.org/research/acs-research-highlights/colon-and-rectal-cancer-research-highlights/risk-factors... prevention-colorectal-studies/can-ozempic-and-mounjaro-reduce-the-risk-of-colorectal-cancer.html

5. Propofol Causing Zinc Losses

Submitted by: Palwashay Iqbal (Supervisor Inpatient Pharmacist)

Propofol, especially in formulations containing edetate disodium, can increased urinary zinc loss. This is due to lead to the chelation properties of edetate disodium, which binds to zinc and other trace metals, potentially increasing their excretion in the urine. Studies have shown that patients receiving propofol EDTA-containing formulations experience higher urinary excretion of zinc and iron compared to those receiving sedatives without EDTA. While critical illness itself is also associated with increased urinary losses of these trace metals, the combination of propofol EDTA and critical illness can exacerbate the problem.

Propofol and EDTA

Propofol is a common anesthetic and sedative used in various medical settings. Some formulations of propofol, like Diprivan, contain edetate disodium (EDTA), a chelating agent.

Zinc Chelation and Excretion

EDTA can bind to zinc, reducing its bioavailability and increasing its excretion in the urine. This means the body loses zinc through urine at a higher rate when propofol containing EDTA is used

Clinical Implications

Prolonged propofol infusions, especially in critically ill patients who may be predisposed to zinc deficiency, can lead to significant zinc depletion

Renal Function

While propofol itself doesn't typically cause renal impairment, high doses of EDTA can be associated with renal toxicity

Monitoring and supplementation

Practitioners should monitor patients receiving prolonged propofol therapy for signs of zinc deficiency, especially in those at risk, such as those with burns, diarrhea, or major sepsis. Supplementation with zinc may be necessary in these cases

Common Signs of Zinc Deficiency

Submitted by: Palwashay Iqbal (Supervisor Inpatient Pharmacist)

Clinical symptoms include irritability, withdrawn disposition, growth impairment, anorexia, night blindness, pica, and photophobia. Cutaneous involvement includes the periorificial, gluteal, perineal, and acral predominant burn-like psoriasiform lesions. Nail dystrophy and paronychia occur, and alopecia may develop. Delayed wound healing, conjunctivitis, and increased susceptibility to infection may also be clues.

References:

- Higgins TL, Murray M, Kett DH, Fulda G, Kramer KM, Gelmont D, Dedhia HV, Levy H, Teres D, Zaloga GP, Ko H, Thompson KA. Trace element homeostasis during continuous sedation with propofol containing EDTA versus other sedatives in critically ill patients. Intensive Care Med. 2000;26 Suppl 4:S413-21. doi: 10.1007/pl00003785. PMID: 11310904.
- George AA, Mishra AK, Sahu KK, Sargent J. Acquired Acrodermatitis Enteropathica. Am J Med. 2021 Jan;134(1):e2-e3.

6. Pharmacotherapy in MINOCA: A Focused Review for Clinical Pharmacists

Submitted by: Ayesha Mehdi (In-patient Pharmacist)

Myocardial Infarction with Nonobstructive Coronary Arteries (MINOCA) accounts for approximately 5-10% of all acute myocardial infarctions and encompasses a heterogeneous group of pathophysiological mechanisms. Management requires cause-directed therapy, supported by pharmacist-led medication optimization.

MINOCA Etiologies at a Glance

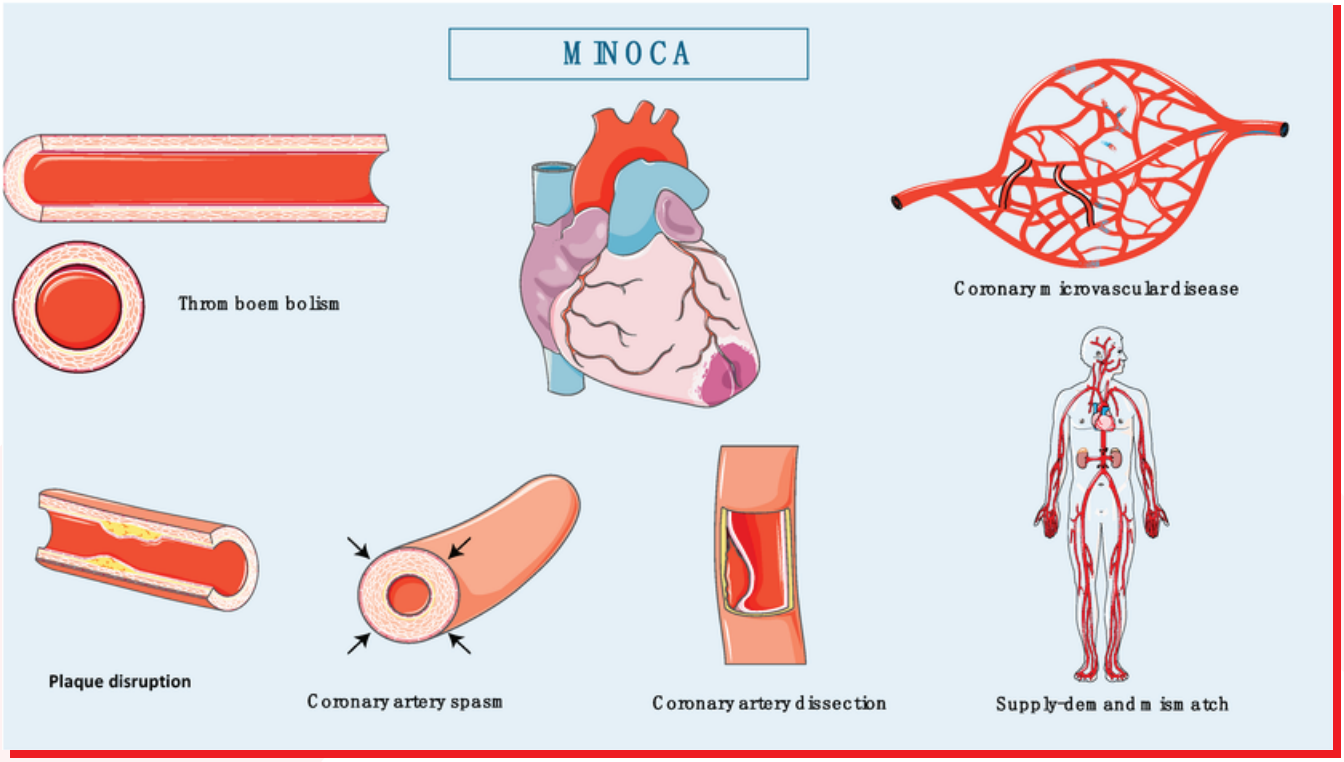


Figure 1: Common causes of MINOCA: plaque disruption, coronary artery spasm, thromboembolism, coronary dissection, coronary microvascular disease, and supply-demand mismatch.

Table: Management by Cause

Cause	Pharmacotherapy
Plaque Disruption	Dual antiplatelet therapy (DAPT), high-intensity statin, ACEI/ARB, selective beta-blockers.
Coronary Artery Spasm	High-dose calcium channel blockers (dihydropyridine or non-dihydropyridine), nitrates, low-dose aspirin.
Coronary Micro vascular Disease	Beta-blockers, calcium channel blockers, ranolazine, L-arginine, ACEI/ARB, lifestyle modification.
Thromboembolism	Anticoagulation, antiplatelet therapy as indicated, management of underlying thrombotic conditions
SCAD	Conservative management, single antiplatelet (aspirin), beta-blockers, selective PCI if unstable.
Supply-Demand Mismatch	Treat precipitating condition (anemia, sepsis, arrhythmia), secondary prevention tailored individually.

The Pharmacist's Role

- Therapeutic optimization based on identified etiology.
- Monitoring adverse drug reactions, interactions, and adherence.
- Patient education on medication use, lifestyle, and symptom recognition.
- Active participation in diagnostic clarification and therapeutic decision-making.

References:

- Tognola, C.; Maloberti, A.; Varrenti, M.; Mazzone, P., Giannattasio, C.; Guarracini, F. Myocardial Infarction with
- Nonobstructive Coronary Arteries (MINOCA): Current Insights into Pathophysiology. Dioonosis, and Management.
- Diagnostics 2025, 15, 942

7. Pharmacists at the Frontline: Safeguarding Patients through Medication Reconciliation

Submitted by: Arooba Salman (Ambulatory care Pharmacist)

globally. Medication reconciliation is a key strategy to minimize medication-related harm and improve care quality. Pharmacist involvement has been shown to enhance the accuracy and efficiency of this process, reducing discrepancies and improving patient outcomes.

Medication discrepancies occur when inconsistencies arise between a patient's current and previous medication lists, especially during transitions of care such as admission, discharge, or transfer. These discrepancies may include omitted medications, therapeutic substitutions, and changes in dose, frequency, or administration route. While some discrepancies are intentional, unintentional ones require timely clarification and correction to avoid adverse outcomes. Left unresolved, they can lead to extended hospital stays, readmissions, emergency visits, and increased healthcare costs.

At Tabba Heart Hospital, pharmacist-led reconciliation has effectively addressed such issues. Following examples highlight the vital role pharmacists play in ensuring safe and accurate medication use.

Omission of drug

A patient's insulin therapy was unintentionally omitted during admission, resulting in elevated blood glucose levels, which was corrected upon pharmacist review Drug

Drug Wrong entry

A patient discharged on fluoxetine instead of levofloxacin had their prescription corrected before harm occurred

Incorrect Dosing

A patient reported gastric pain due to incorrect aspirin dosing, which was promptly identified and resolved by the pharmacist.

References:

Patel E, Pevnick JM, Kennelty KA. Pharmacists and medication reconciliation: a review of recent literature. Integrated pharmacy research and practice. 2019 Apr 30:39-45. Bakr OM. Medication Reconciliation and Review Among Pharmacists in Kirkuk Province Iraq a Kap Study.

Ahmadi H. Houshmand Y. Raees-Jalali GA. Karimzadeh L. Medication Reconcillation of Patients by Pharmacist at the Time of Admission and Discharge from Adult Nephrology Wards. Pharmacy. 2024 Nov 18:12(6):170.

8. Guardians of Safe Disposal: Elevating the Pharmacist's Role in Drug Take-Back

Submitted by: Umme Haani (Ambulatory care Pharmacist)

The rise in prescription and OTC medication use means more unused or expired drugs piling up at home. This build up, caused by factors like therapy changes and noncompliance, wastes billions of dollars and poses serious risks accidental poisoning, misuse, and environmental damage. Improper disposal-flushing meds or tossing them in the trash-contaminates water, harms ecosystems, and threatens soil health, especially where wastewater treatment is weak. Plus, throwing away meds with labels intact risks identity theft and drug diversion. Enter drug take-back programs, championed by the FDA and WHO, which let people safely return unused meds to pharmacies for eco-friendly disposal.

Pharmacists are the frontline heroes here: educating the public, managing secure collection points, and ensuring safe handling and disposal. They also break down barriers like privacy concerns or lack of awareness by engaging directly with patients and communities. Through workshops, counselling, and clear guidance, pharmacists promote responsible disposal habits and protect both health and the environment. By leading these efforts, pharmacists help reduce medication waste, prevent misuse, and build a safer, greener future-one returned pill at a time.

References:

Ehrhart Al., Granek EF, Nielsen-Pincus M. Horn DA. Leftover drug disposal: Customer behavior, pharmacist recommendations, and obstacles to drug take-back box implementation. Waste Management 2020 Dec 1:118:416-25

9. ALZHEIMER'S TREATMENT BY MONOCLONAL ANTIBODIES FOR AMYLOID LOWERING THERAPY

Submitted by: Sarwat Jabeen (Ambulatory care Pharmacist)

Myocardial Infarction with Nonobstructive Coronary Arteries (MINOCA) accounts for approximately 5-10% of all acute myocardial infarctions and encompasses a heterogeneous group of pathophysiological mechanisms. Management requires cause-directed therapy, supported by pharmacist-led medication optimization.

Abstract

Alzheimer is the most prevalent of the dementias.
Cholinesterase Inhibitors and memantine only approved drug therapies for Alzheimer disease for over 20 years, it provides only systematic relief.

In recent trials, amyloid lowering therapies are treatments designed to reduce the amount of amyloid protein in the brain, in order to slowing the progression of disease and improving symptoms. Lecanemab have been approved

Introduction

Monoclonal Antibodies i.e Lecanemab and Donanemab binds to amyloid-beta plaques in the brain, marking them for removal by the immune system and slowing the disease progression.

CLINICAL TRIAL RESULTS
The Clarity AD trial showed that lecanemab slowed cognitive decline by 27% compared to placebo over 18 months.
The TRAILBLAZER-ALZ 2 trial demonstrated that donanemab slowed cognitive decline by 35% compared to placebo in patients with early stage Alzheimer's.

Potential side effects

- Amyloid-Related Imaging Abnormalities i.e two subtypes:
- ARIA-E (vasogenic oedema) and ARIA-H (microhaemorrhage)
- Infusion-Related Reactions

Conclusion

It is unlikely to be sufficient for treating Alzheimer's disease, multimodal therapies may be required. Until that disease-modifying therapies are effective and broadly available.

References:

- https://pmc.ncbi.nlm.nih.gov/articles/PMC11216914/

Case Study:

Shared by: Iqra Yaseen (Trainee Pharmacist 2025)

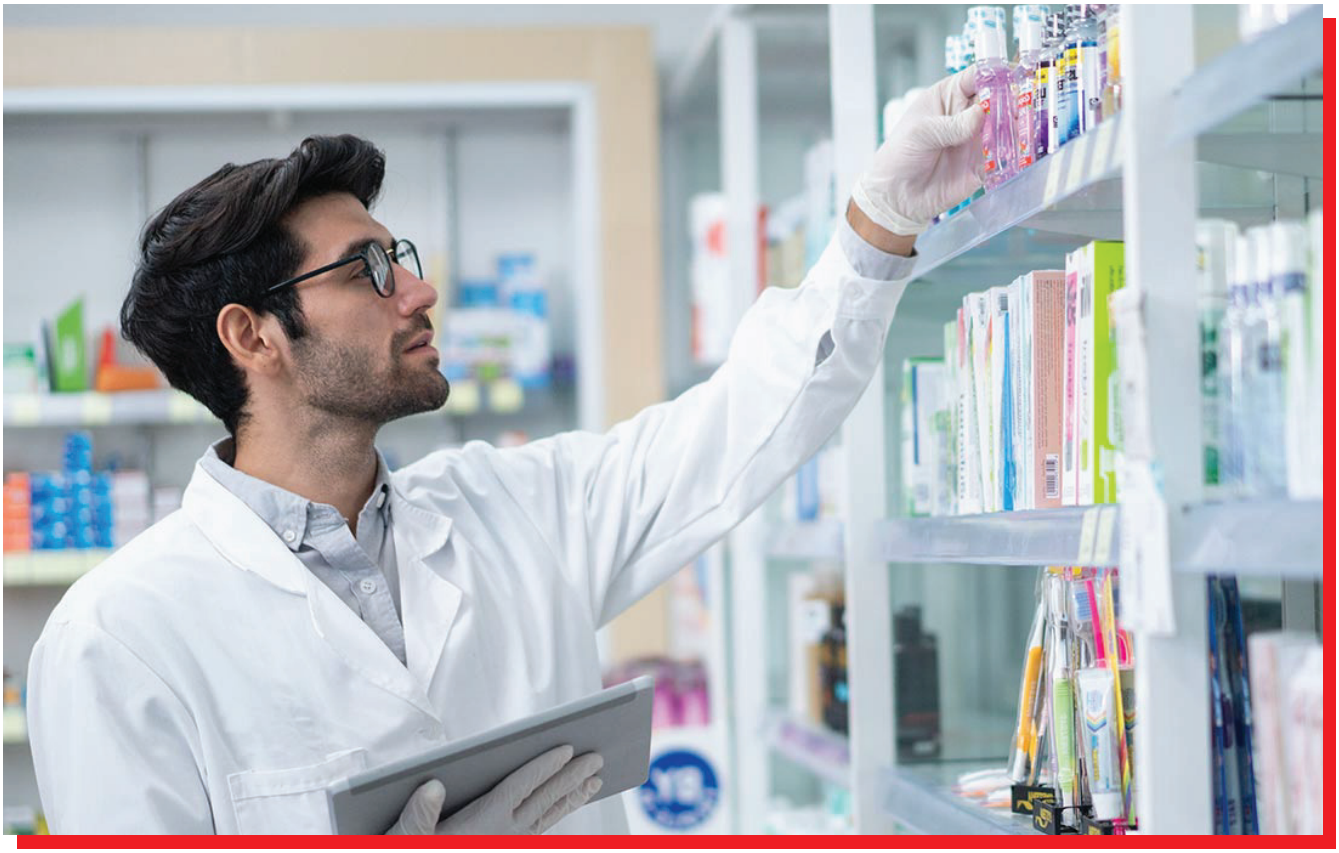
Drug-drug Interaction Linezolid and Digoxin

An 82-year-old man was admitted to the ICU with severe pneumonia and heart failure. His condition demanded swift intervention. Linezolid (600 mg every 12 hours) was started for infection (when the rapid sputum smear showed 80% gram-positive cocci), while oral digoxin (0.25 mg daily) was introduced for cardiac support.

By day four, things took an unexpected turn. Blood work revealed alarmingly high levels of both linezolid (26.9 mg/L trough) and digoxin (2.6 ng/mL trough), despite normal kidney and liver function. Platelet counts had already dropped by 30%. There were no overt signs of digoxin toxicity, but silent danger loomed.

The clinical team halved both doses. Yet, by day eight, digoxin levels remained high (1.6 ng/mL), and thrombocytopenia worsened. Eventually, digoxin was reduced further to alternate-day dosing, and linezolid was discontinued after day 18. The digoxin level finally normalized by day 24 (0.8 ng/mL), and platelet counts recovered.

This rare interaction-possibly via P-glycoprotein inhibition or altered intestinal flora-calls for therapeutic drug monitoring (TDM) when using these agents together. The case emphasizes proactive dosing and lab vigilance to prevent adverse outcomes.



References:

Yulin Z, Lingti K, Shan G, Yong Z. A possible interaction between linezolid and digoxin: a case report of therapeutic drug monitoring. Saudi Pharmaceutical Journal. 2020 Nov 1;28(11):1408-10.

10. Unlocking the Alzheimer's-Cholesterol Connection

Submitted by: SANA KHALID (Trainee Pharmacist 2025)

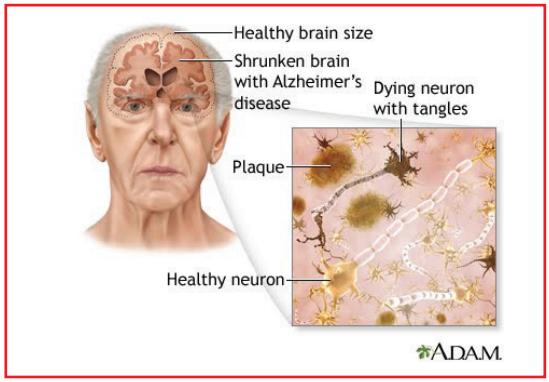


FIGURE 01:
Brain presentation in Alzheimer

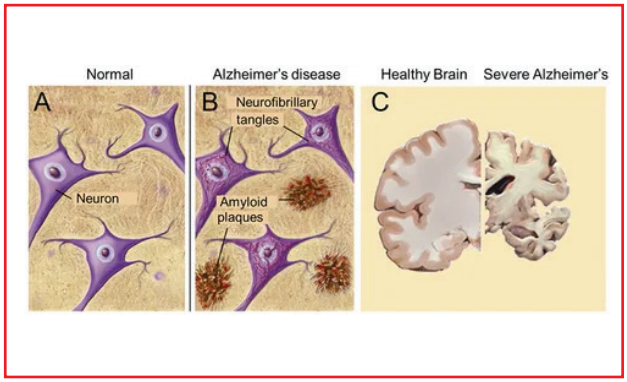


Figure 02:
Comparing Healthy brain and Alzheimer Brain

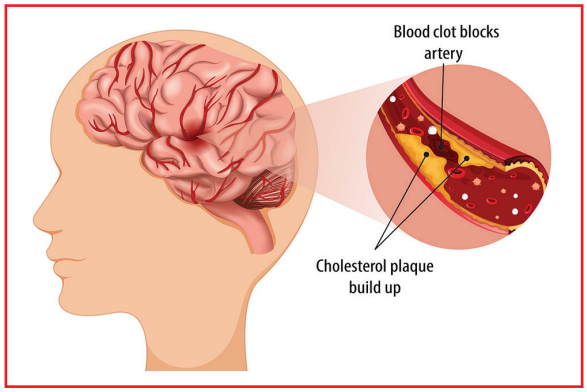


Figure 03:
Deposition of cholesterol in blood vessels

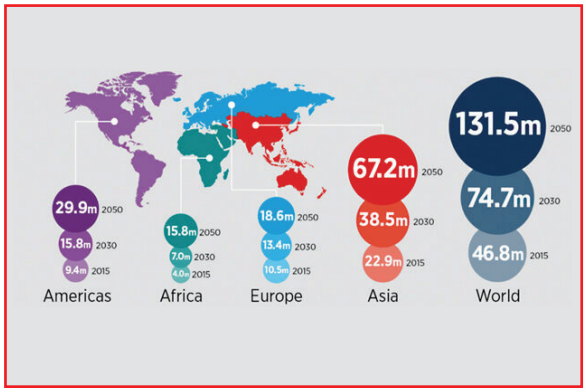


Figure 04:
People living with dementia around the world

Abstract

memory impairment and cognitive decline. It is mainly linked to the accumulation of beta-amyloid plaques and neurofibrillary tangles in the brain. Recent studies indicate that cholesterol, an essential lipid, may play a role in the onset and advancement of Alzheimer's disease. While cholesterol is crucial for cell membrane integrity and hormone production, abnormal cholesterol levels, particularly during midlife, might lead to neurodegenerative transformations.

Cholesterol is vital for synaptic function and the metabolism of amyloid proteins in the brain. Elevated cholesterol levels have been associated with increased production of amyloid beta, a key feature of Alzheimer's pathology. Additionally, certain genetic factors, such as the ApoE4 allele, which is involved in lipid transport, are linked to both higher cholesterol levels and an elevated risk of developing Alzheimer's.

Research suggests that cholesterol imbalances may trigger inflammation, oxidative stress, and compromise the blood-brain barrier, all of which could hasten neurodegeneration. Gaining insight into this intricate relationship paves the way for potential preventive measures aimed at cholesterol management to promote cognitive health and lower the risk of Alzheimer's disease.

Keywords:
Cholesterol, Alzheimer's disease, Cognitive health

PHARMA GALLERY