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R_x FACTOR

Newsletter by

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**National Association of
Pharmacology & Therapeutics**

Promoting Pharmacology & Therapeutics for a better tomorrow

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EDITORIAL

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Warm greetings to all.

Welcome to the Volume 8 of 'RxFactor', from the NATIONAL ASSOCIATION OF PHARMACOLOGY AND THERAPEUTICS (NPT). RxFactor has been designed to encompass the range and breadth of Pharmacology and therapeutics ranging from Medical Education, Pharmaco-vigilance, Research and Therapeutics. Previous editions of Rxfactor have been well received and we thank you all for the words of encouragement and appreciation.

This edition of Rxfactor newsletter includes many informative articles. We have an article on Pleotropic effects of SGLT-2 Inhibitors, the essay explores the diverse physiological impacts of SGLT-2 inhibitors, highlighting their potential implications for cardiovascular health, renal function, and metabolic parameters.

In the medical education corner we have article on Authentic Learning. This article will give insight on requirements of and expectations from Authentic Learning. Case reports on Amoxicillin-Clavulanate Induced Anaphylactic Shock and Levetiracetam induced severe allergic reaction highlight the

importance of ADR Reporting. Novel drug molecules discussed are Mirikizumab, a monoclonal antibody and a new Anticancer drug Fadraciclib. An interesting incorporation is the article on Artificial intelligence (AI)- Potential applications in the field of MD Pharmacology program.

Other notable inclusions are Amazing Drug Molecules and Extract from NMDP WhatsApp Group. The cool corner includes a crossword puzzle and an interesting Quiz for brain storming .

We would like to thank all the contributors of RxFactor for their efforts and support in making this issue of Rxfactor a grand success. We are especially happy to see the PG students who are the future of our speciality contributing to Rxfactor.

We look forward to a happy education and mutual learning with all our readers.

Jai Hind.

Pleiotropic Effects of SGLT-2 Inhibitors: Beyond Glycemic Control



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Introduction:

Sodium-glucose co-transporter 2 (SGLT-2) inhibitors have emerged as a transformative class of medications in the management of type 2 diabetes mellitus. Initially recognised for their ability to lower blood glucose levels by inhibiting renal glucose reabsorption, SGLT-2 inhibitors have demonstrated an array of pleiotropic effects that extend beyond glycemic control. This essay explores the diverse physiological impacts of SGLT-2 inhibitors, highlighting their potential implications for cardiovascular health, renal function, and metabolic parameters.

Cardiovascular Benefits:

One of the most significant pleiotropic effects of SGLT-2 inhibitors is their favourable impact on cardiovascular outcomes. Clinical trials, such as the EMPA-REG OUTCOME and DECLARE-TIMI 58 studies, have shown that SGLT-2 inhibitors like empagliflozin and dapagliflozin can reduce the risk of major adverse cardiovascular events, including cardiovascular death, nonfatal myocardial infarction, and stroke. The mechanisms underlying these cardiovascular benefits are complex and may involve improved arterial compliance, reduced arterial stiffness, and favourable effects on cardiac remodelling.

Reno-protective Effects:

SGLT-2 inhibitors have demonstrated remarkable reno-protective effects, particularly in patients with diabetes and chronic kidney disease. The CREDENCE trial highlighted the efficacy of canagliflozin in reducing the risk of renal failure and cardiovascular events in individuals with type 2 diabetes mellitus and chronic kidney disease. These agents lower intraglomerular pressure, decrease albuminuria, and mitigate the progression of diabetic nephropathy, making them a valuable therapeutic option for preserving renal function.

Metabolic and Weight Benefits:

Beyond glucose regulation, SGLT-2 inhibitors influence various metabolic parameters. They promote weight loss by increasing urinary excretion of glucose and calories, contributing to reductions in body weight and visceral adiposity. Additionally, these agents have been associated with improved insulin sensitivity and decreased blood pressure, further addressing key components of the metabolic syndrome.

Anti-inflammatory and Anti-fibrotic Effects:

Recent research suggests that SGLT-2 inhibitors possess anti-inflammatory and anti-fibrotic properties. These medications may exert protective effects on the cardiovascular system and other organs by attenuating oxidative stress and inflammation. The reduction in markers of systemic inflammation and fibrosis seen in some studies underscores the potential broader impact of SGLT-2 inhibitors on mitigating the chronic inflammatory processes associated with diabetes and its complications.

Safety and Tolerability:

SGLT-2 inhibitors exhibit a generally favourable safety profile. While adverse events such as genital mycotic infections and an increased risk of diabetic ketoacidosis have been noted, the overall cardiovascular and renal benefits often outweigh these concerns. Their tolerability, coupled with their pleiotropic effects, positions SGLT-2 inhibitors as versatile agents in the management of type 2 diabetes, especially in individuals with a high cardiovascular or renal risk.

Conclusion:

The pleiotropic effects of SGLT-2 inhibitors have elevated these medications beyond their primary role in glycemic control. As cardiovascular and renal protective agents with metabolic, anti-inflammatory, and anti-fibrotic benefits, SGLT-2 inhibitors represent a paradigm shift in the management of type 2 diabetes mellitus. The comprehensive impact on multiple physiological systems positions these medications not only as glucose-lowering agents but also as valuable contributors to overall cardiometabolic health. Ongoing research continues to unravel the full spectrum of their pleiotropic effects, promising further insights into the multifaceted benefits of this innovative class of medications.

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2. Kaneto H, Obata A, Kimura T, Shimoda M, Kinoshita T, Matsuoka TA, Kaku K. Unexpected pleiotropic effects of SGLT2 inhibitors.



Authentic Learning : An Overview



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The primary focus of medical education is to provide necessary care to the student's patients. With the start of the student's professional lives, they should be able to provide safe and effective patient care. While traditional methods of education are effective in providing the knowledge required for successful patient care, the need for a more practical approach for medical education should always be preferred. This is what authentic learning is designed to address.

Authenticity in a philosophical sense is about those things that genuinely define people as who they are, and what being human means to them. Authentic learning refers to an educational approach that allows students to build concepts and the ability to apply knowledge in contexts that involve real world problems that are relevant to the learner while accurately representing the modern expectations of the patients.

Research has shown that there are four requirements and expectations from authentic learning:

- Ability to reason and discern
- Autonomy in managing the patient and follow-up processes
- Creating relationships
- Experiencing responsibility

Ability to reason and discern

While providing authentic contexts for learning, developing the student's ability for elevated levels of thinking is significant. Investigational and hypothetical inquiries in which they engage in asking questions, conducting studies, drawing conclusions, and communicating results to others provides a major experience boost. Similarly, metacognition provides an effective self-assessment in which they determine the limits of their own knowledge and assess their own personal responsibilities.

Autonomy in managing the patient and follow-up processes

Autonomy does not mean working on their own but working according to their own choices. Providing them with opportunities to handle the patients their own. Having a structure for autonomy is important for self-regulated learning. Autonomy does not mean independent, but rather acting by their own choice. Autonomy in learning should be supported by the educational structure by not being distant, vague or leaving them to manage on their own, but rather to set standards and give feedback in a way that provides choice and lets them find solutions and answers on their own.

Creating Relationships

A learning relationship with the professors can be formed by gaining useful feedback and the opportunity for open discussions to test the student's thought processes and knowledge with.

The relationship with the patient is the basis of clinical learning efficiency. With these relationships they feel like the patient's doctor which is the cornerstone for authentic learning. The sense of being a doctor was the feeling of belonging which played a real part in the clinical work. This is especially evident when they succeeded in helping the patient and gain their trust.

Experiencing responsibility

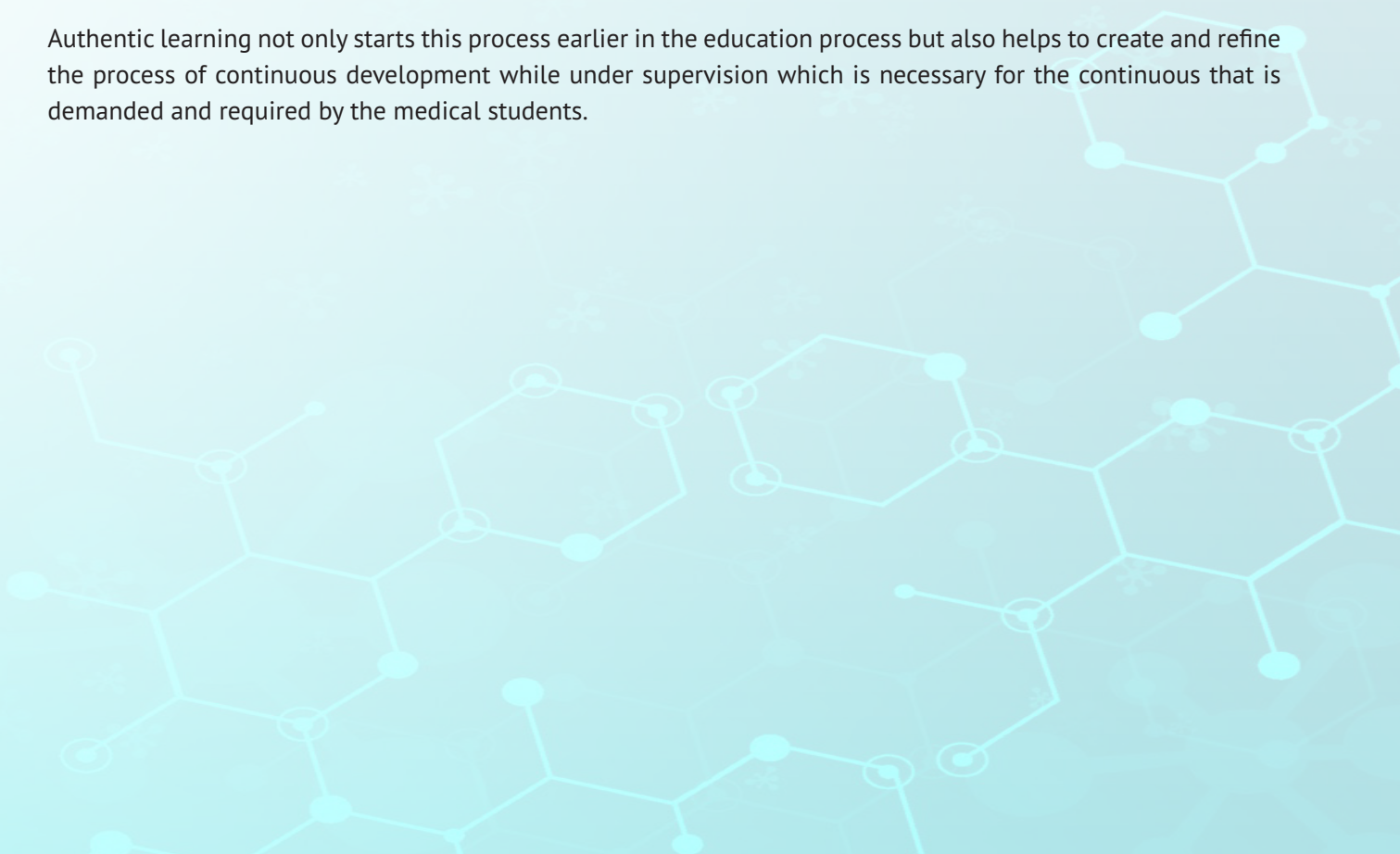
They feel like doctors when provided with the opportunity to interact with patients it leads to sense of increased responsibility when they could handle a patient case on their own. It is important for them to complete the consultation alone even if the doctor in charge visits the patient later. The most important step of handling a patient case is to decide on the course of action and make choices before checking with the doctor in charge. If the doctor approves the steps recommended by them, a strong feeling of being a doctor emerged.

Another important factor in feeling like a doctor is being able to perform practical tasks without support.

Conclusion

The process of becoming a medical professional is never ending adventure. This process involves developing and refining an exemplified understanding of professional practices. This process does not have any fixed stages or paths but is unique to every individual.

Authentic learning not only starts this process earlier in the education process but also helps to create and refine the process of continuous development while under supervision which is necessary for the continuous that is demanded and required by the medical students.



Amoxicillin-Clavulanate Induced Anaphylactic Shock : A Case Report



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Abstract

In an emergency room setting, Anaphylactic Shock is often an avoidable disaster with unavoidable consequences, that throws the entire medical team on their toes. It demands quick diagnosis and treatment.

In this article, we present a case report of a 52 years old male patient who developed breathlessness and low Oxygen saturation, following administration of intravenous Amoxicillin – Clavulanate. The hallmark of the case was anaphylaxis that occurred before the setting in of sepsis, which could possibly have caused a detrimental impact on an already worsening prognosis.

Keywords: Anaphylactic Shock, Amoxicillin, Clavulanic Acid, Anaphylaxis

Introduction

Anaphylaxis is a potentially life – threatening systemic allergic reaction involving one or more organ systems that typically occurs within seconds to minutes of exposure to the anaphylactic trigger¹ which may be food, allergen, or insect bite.

According to Turner et al, true global scale of anaphylaxis remains elusive, because many episodes occur in the community without presentation to health care facilities, and most regions have not yet developed reliable systems with which to monitor severe allergic events.²

According to Patel et al, majority reactions developed in perioperative conditions (53.70%), ward (20.37%) and home (11.11%).³ Common causative drugs were diclofenac (11.11%), atracurium (7.41%) and β -lactams (5.96%).³

Case Report

We present the case of a 52 years old male patient who was brought into the emergency department of our tertiary care hospital with history of fall and complaint of black necrotic patch on Right Leg – he was diagnosed as a case of Necrotising Fasciitis of Right Knee and Leg with spreading cellulitis.

On admission patient's pulse was 96 beats per minute and oxygen saturation (spO₂) was 99%.

Patient developed breathlessness 5-6 minutes after administration of Inj. Amoxicillin Clavulanate 1.2 g intravenous, & saturation suddenly dropped to 80%, even while on 15L Oxygen supplementation.

Injection Amoxicillin Clavulanate was stopped after the reaction, and patient was started on Noradrenaline support. The saturation had improved to 98% on room air.



Patient had history of fall and developed black necrotic patch on Right leg with necrotising fasciitis and spreading cellulitis

Inj. Meropenem and Clindamycin, were initiated after test doses and he was taken for Surgical Debridement on NRBM support.

Investigations revealed deranged KFT, CBC, and worsening acidosis, possibly due to sepsis and acute kidney injury following multiple organ dysfunction syndrome (MODS).

Patient was intubated and succumbed to Cardio Respiratory Arrest, four days later.

Discussion

Anaphylactic Shock is explained under the purview of Anaphylaxis. Anaphylaxis shows rapid development and is predominantly mediated by IgE. A profound distributive pattern of shock is seen, mediated by histamine release. There is evidence of both venous and arterial vasodilatation and studies have demonstrated extravasation of up to 35% of the circulating blood volume within 10 minutes.¹

Anaphylactic reactions are dangerous when hypotension or hypoxia occur, leading potentially to cardiovascular collapse and respiratory failure.¹

Penicillin group of antibiotics are amongst the most commonly implicated cause of drug allergy and hypersensitivity reactions.

Amoxicillin is an aminopenicillin whose antimicrobial activity is similar to Penicillin G. Penicillin like drugs are known to form covalent bonds with host proteins which serve as haptens that trigger an immune response.

In more than 90% of patients¹, cutaneous manifestations occur in the form of urticarial eruptions, flushing, erythema and hives. There may be airway obstruction due to laryngeal oedema or bronchial obstruction, which can have fatal outcomes.

Anaphylaxis is a clinical diagnosis and the temporal relationship between onset of symptoms and administration of offending drug is most important in establishing causality, which according to the defined clinical criteria – is few minutes to hours.⁴

In the present case, based on the WHO-UMC causality assessment scale, it is probable/likely that the event occurred due to the drug, owing to the reasonable time relationship and response following withdrawal of the drug. The presence of fasciitis and spreading cellulitis, which led to sepsis and eventually the development of septic shock, led to the death of the patient. Whether or not, anaphylaxis caused a detrimental impact on an already worsening prognosis, is cause for concern and speculation.

Conclusion

Based on the time relationship, and response following withdrawal of drug, it is probable that Inj. Amoxicillin Clavulanate caused anaphylactic shock in the patient. Performing allergy testing with a test dose prior to administration of intravenous antibiotics maybe advisable, to prevent anaphylaxis in hospital settings, in situations where history of drug allergy cannot be elicited.

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FDA Warns of Potentially Lethal Reaction to Seizure Medications

The antiseizure drugs levetiracetam (Keppra, Keppra XR, Elepsia XR, Spritam, generic) and clobazam (Onfi, Sympazan, generic) can cause a rare but serious drug hypersensitivity reaction that can be life threatening if not detected and treated promptly, the US Food and Drug Administration (FDA) warns.

Known as drug reaction with eosinophilia and systemic symptoms (DRESS), it may start as a rash but can quickly progress and cause injury to internal organs, the need for hospitalization, and death, the FDA notes.

A search of the FDA Adverse Event Reporting System (FAERS) and the medical literature through March 2023 identified 32 serious cases of DRESS worldwide that were associated with levetiracetam.

Three cases occurred in the US, and 29 occurred abroad. In all 32 cases, the patients were hospitalized and received medical treatment; in two cases, the patients died.

The median time to onset of DRESS in the levetiracetam cases was 24 days; times ranged from 7 to 170 days. The reported signs and symptoms included skin rash (n = 22), fever (n = 20), eosinophilia (n = 17), lymph node swelling (n = 9), and atypical lymphocytes (n = 4).

Twenty-two levetiracetam-associated cases of DRESS involved injury to one or more organs, including the liver, lungs, kidneys, and gallbladder.

In 25 of the 29 cases for which information on treatment discontinuation was available, DRESS symptoms resolved when levetiracetam was discontinued.

As for clobazam, a search of FAERS and the medical literature through July 2023 identified 10 serious cases of DRESS worldwide — one in the US, and nine abroad. All 10 patients were hospitalized and received medical treatment. No deaths were reported.

The median time to onset of clobazam-associated DRESS was 21.5 days (range, 7 to 103 days). The reported signs and symptoms included skin rash (n = 10), fever (n = 8), eosinophilia (n = 7), facial swelling (n = 7), leukocytosis (n = 4), lymph node swelling (n = 4), and leukopenia/thrombocytopenia (n = 1). In nine cases, there was injury to one or more organs, including the liver, kidneys, and gastrointestinal tract.

DRESS symptoms resolved in all 10 cases when



treatment with clobazam was stopped. DRESS and other serious skin reactions reported with clobazam, a benzodiazepine, have not generally been associated with other benzodiazepines, the FDA notes.

Label Updates

As a result of these cases, warnings about the risk of DRESS will be added to the prescribing information and patient medication guides for these medicines, the FDA announced.

"Health care professionals should be aware that prompt recognition and early treatment is important for improving DRESS outcomes and decreasing mortality," the FDA said.

They note that diagnosis is often difficult because early signs and symptoms, such as fever and swollen lymph nodes, may be present without evidence of a rash.

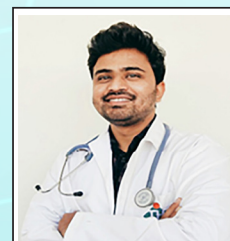
DRESS may develop 2 to 8 weeks after starting levetiracetam or clobazam. Symptoms and intensity can vary widely.

DRESS can also be confused with other serious skin reactions, such as Stevens-Johnson syndrome and toxic epidermal necrolysis.

The FDA says patients should be advised of the signs and symptoms of DRESS and be told to stop taking the medicine and seek immediate medical attention if DRESS is suspected during treatment with levetiracetam or clobazam.

The FDA says patients should be advised of the signs and symptoms of DRESS and be told to stop taking the medicine and seek immediate medical attention if DRESS is suspected during treatment with levetiracetam or clobazam.

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Mirikizumab: A Novel Therapeutic Breakthrough in the Treatment of Inflammatory Disorders



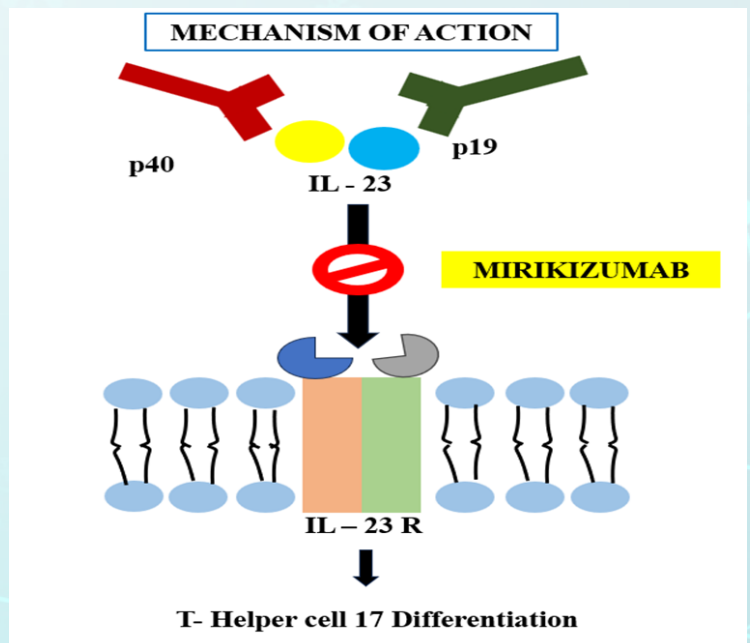
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Introduction:

Mirikizumab, a monoclonal antibody, has emerged as a promising therapeutic agent in the realm of inflammatory disorders, particularly in the treatment of autoimmune conditions such as psoriasis and Crohn's disease. Developed to target specific components of the immune system, mirikizumab represents a significant advancement in precision medicine. This essay explores the key features, mechanisms of action, and therapeutic potential of mirikizumab in managing inflammatory disorders.

Biological Basis and Mechanism of Action:

Mirikizumab is a humanized immunoglobulin G4 (IgG4) monoclonal antibody designed to selectively target and inhibit the p19 subunit of interleukin-23 (IL-23). IL-23 is a cytokine involved in immune system regulation, particularly in the activation and differentiation of T-helper 17 (Th17) cells. By blocking the p19 subunit, mirikizumab interferes with the IL-23 signalling pathway, thus modulating the immune response implicated in various inflammatory diseases.



Therapeutic Applications Psoriasis:

Psoriasis, a chronic inflammatory skin disorder, is characterized by the abnormal proliferation of skin cells and the presence of red, scaly patches. Mirikizumab has shown remarkable efficacy in the treatment of moderate to severe plaque psoriasis. Clinical trials, such as the OASIS-1 and OASIS-2 studies, demonstrated that mirikizumab-treated patients experienced significant improvements in psoriasis severity scores compared to placebo, highlighting its potential as a transformative therapy for this dermatological condition.

Inflammatory Bowel Disease:

Beyond dermatological applications, mirikizumab has shown promise in the management of inflammatory bowel disease (IBD), particularly Ulcerative colitis. By targeting the IL-23 pathway, mirikizumab helps regulate the aberrant immune response associated with Crohn's disease, reducing inflammation in the gastrointestinal tract. Clinical trials like the VISION study have reported positive outcomes, with mirikizumab demonstrating efficacy in inducing and maintaining clinical remission in patients with moderate to severe Crohn's disease.

Safety Profile and Tolerability:

Mirikizumab's safety profile appears favourable in clinical trials, with adverse events generally mild to moderate in severity. Common side effects include upper respiratory tract infections, injection site reactions, and headaches.

The Role of Mirikizumab in Precision Medicine:

Mirikizumab exemplifies the principles of precision medicine, tailoring therapeutic interventions to specific molecular targets within the immune system. Its precise targeting of the IL-23 pathway minimizes non-specific effects, offering a more focused and effective treatment strategy. This approach aligns with the evolving paradigm of individualized patient care, aiming to optimize treatment outcomes while minimizing adverse effects.

Future Directions and Challenges:

Ongoing studies are exploring its effectiveness in conditions such as ankylosing spondylitis, further expanding its therapeutic scope. As research progresses and its applications expand, it provides new avenues for personalized and effective patient care in the realm of autoimmune disorders. Challenges include the need for long-term safety assessments, cost considerations, and addressing the variability in individual patient responses.

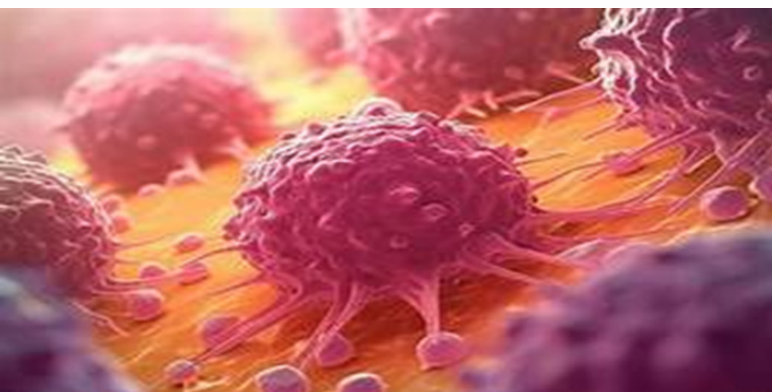
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New Anti-cancer drug: Fadraciclib



Researchers have shared information about a novel medication that may be used to treat a variety of cancers, including some solid tumors and blood cancers.

The drug, called fadraciclib, was jointly discovered by scientists at The Institute of Cancer Research, London, in collaboration with the company Cyclacel.

It is already being tested in early clinical trials targeting select hematological malignancies and solid tumors.

Scientists from Cyclacel and the Cancer Research UK Cancer Therapeutics Unit at The Institute of Cancer Research (ICR) have discovered fadraciclib, formerly known as CYC065. Fadraciclib is a leading dual inhibitor of two cancer-driving proteins from the cyclin-dependent kinase (CDK) family, CDK2 and CDK9.

CDK2/9 inhibitor

It was designed by improving the chemical properties of a previous CDK inhibitor drug from Cyclacel, called seliciclib. These structural design modifications led to a 20-fold more potent activity against the CDK2 and CDK9 targets and an equivalent 30-fold increase in therapeutic potency against a panel of human cancer cells, as well as a high degree of selectivity versus a wide range of 256 other protein kinases.

The researchers also provide clear evidence that CDK2 and CDK9 are inhibited in fadraciclib-treated cancer cells, leading to altered gene expression and cell death by apoptosis.

The researchers also explain trials in cells and animals that show fadraciclib's potential as a leukemia

treatment in the published paper, which was mostly supported by Cyclacel. The researchers discovered that fadraciclib could completely stop human acute myeloid leukemia tumors from developing in immune-deficient mice.

A significant and long-lasting reduction in the levels of MCL1, a protein implicated in cancer cell survival and treatment resistance, was one of the most significant effects the researchers observed in cancer cells treated with fadraciclib. They tested fadraciclib in combination with medications that target additional drug-resistant and cancer-survival proteins in the BCL2 family in an effort to build on this effect, and they discovered synergistic anticancer action.

Early-stage clinical trials

Fadraciclib is currently undergoing Phase I clinical studies as a single agent in patients with advanced solid tumors, and also in combination with the approved BCL2 inhibitor venetoclax in relapsed or refractory chronic lymphocytic leukemia and relapsed refractory acute myeloid leukemia or myelodysplastic syndrome

Fadraciclib is one of 20 drug candidates discovered by scientists at the ICR since 2005, of which 10 have entered clinical trials—making the ICR the most successful academic center in cancer drug discovery in the world.

More information: Sheelagh Frame et al. Fadraciclib (CYC065), a novel CDK inhibitor, targets key pro-survival and oncogenic pathways in cancer, PLOS ONE (2020). DOI: 10.1371/journal.pone.0234103

Journal information: PLoS ONE



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Artificial intelligence (AI)- Potential applications in the field of MD Pharmacology program

1	Drug Discovery:	AI can help analyze vast datasets to identify potential drug candidates, predict their efficacy, and optimize their chemical structures.
2	Personalized Medicine:	AI can assist in tailoring drug regimens to individual patient profiles, taking into account genetics, lifestyle, and other factors.
3	Disease Diagnosis:	AI algorithms can aid in the early and accurate diagnosis of diseases by analyzing medical images, patient data, and genetic information.
4	Drug Interaction Analysis:	AI can assist in identifying potential drug interactions and adverse effects to enhance medication safety.
5	Pharmacovigilance:	AI can automate the monitoring of adverse drug reactions and safety profiles of medications in real time
6	Predictive Analytics:	AI can help forecast disease trends, drug usage, and patient outcomes, aiding in resource allocation and healthcare planning.
7	Drug Formulation and Delivery:	AI can optimize drug formulations and delivery methods to enhance efficacy and reduce side effects.
8	Literature Review:	AI-powered tools can rapidly search, summarize, and extract relevant information from a vast amount of medical literature
9	Clinical Trials:	AI can streamline patient recruitment, monitor trial data, and identify potential candidates for clinical trials.
10	Education and Training:	AI can be used to develop interactive educational tools and simulations for pharmacology students.

These applications can help improve the effectiveness, efficiency, and safety of pharmacological research and practice in MD Pharmacology programs.

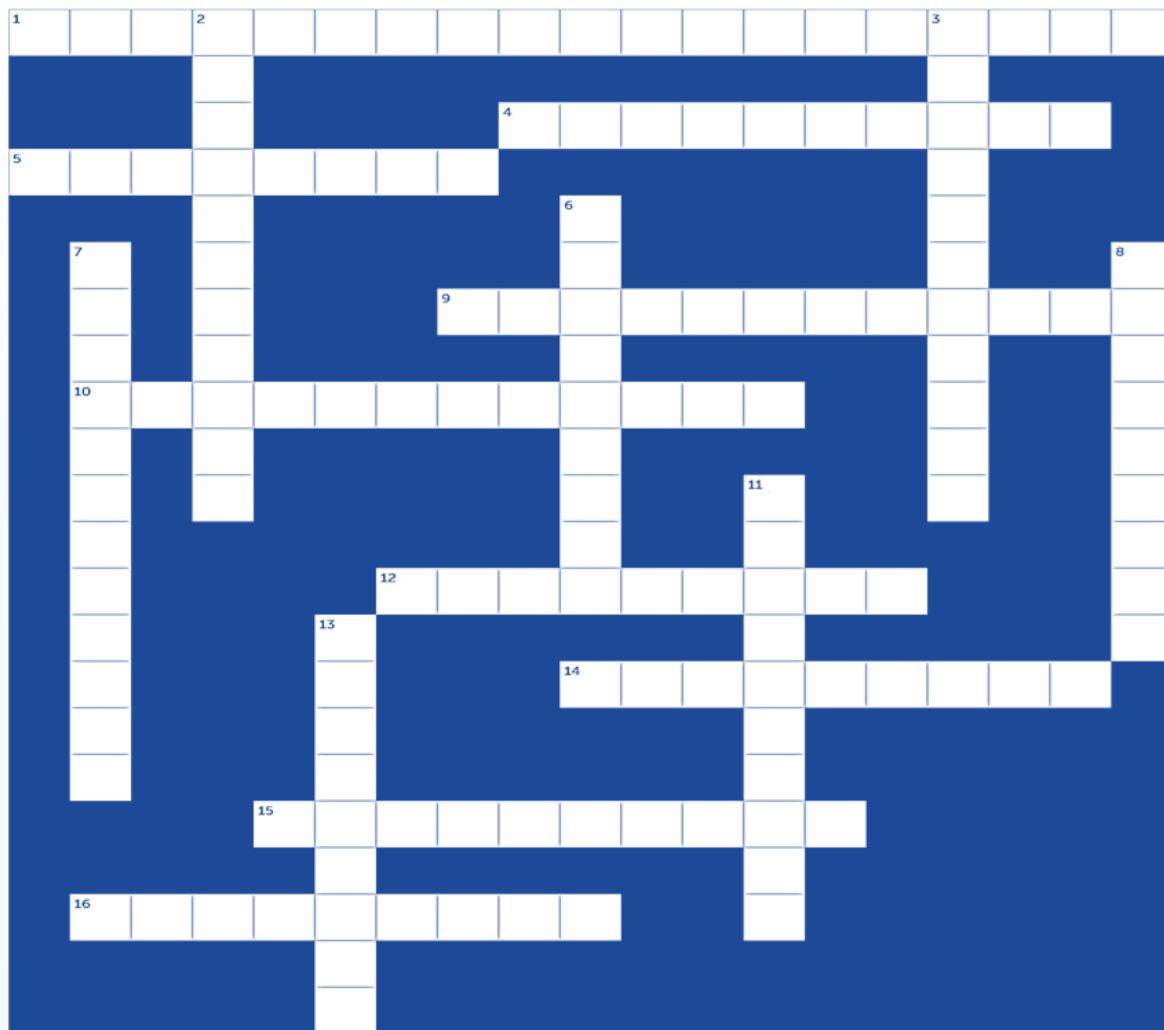
ROLE OF A PHARMACOLOGIST

ROLE IN AN ACADEMIC INSTITUTION	1. Medical Education 2. Research 3. Patient care
ROLE IN PHARMACEUTICAL INDUSTRY	1. Research and development 2. Handling Regulatory Affairs for an Industry 3. Prelaunch activities 4. Marketing 5. Patient safety
SOCIAL RESPONSIBILITIES	1. Community Education 2. Social Pharmacist
ROLE IN REGULATORY AFFAIRS	1. Essential drug concept-Formulation and implementation 2. Formulation of national drug Policy 3. Monitoring and audit of clinical trials 4. Pharmacovigilance 5. To Participate in National Drug Authority Functions
ROLE IN INDIAN ACCREDITED HOSPITALS	1. Medication Management System 2. Medication safety 3. Clinical research
ROLE IN COMMUNITY PHARMACOLOGY	1. Pharmacogenetics 2. Pharmacoeconomics 3. Pharmacovigilance 4. Toxicologist 5. Physician Education 5. Physician

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Crossword Puzzle on therapeutics



Across

1. A synthetic progestin for long-acting contraception
4. A novel monoclonal antibody for treating various cancers
5. An N-methyl-D-aspartate (NMDA) receptor antagonist anaesthetic for treating depression
9. Atypical antipsychotic for treating various psychiatric disorders
10. HIV integrase inhibitor employed to treat HIV infection
12. A melatonin receptor agonist in insomnia
14. You will need in BHP treatment
15. A drug that blocks the funny channel, used to treat heart rhythm disorders
16. Neuromuscular blocking agent reversal agent

Down

2. A pleuromutilin for bacterial skin infections
3. Monoclonal antibody for osteoporosis
6. A catechol-O-methyltransferase (COMT) inhibitor utilized for Parkinson's disease treatment
7. An anticoagulant with slick design
8. Synthetic opioid used for addiction treatment
11. Novel drug for MDR tuberculosis
13. A monoclonal antibody for COVID-19 treatment, with a unique structure



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Quiz

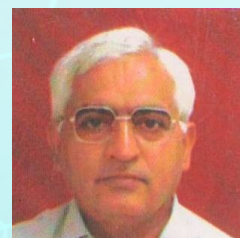


S No	Question
1	Which two drugs show "Robin Hood effect"?
2	Which two Drugs require DRUG HOLIDAYS on prolonged therapy?
3	Examples of drugs which are almost always given as prolonged/slow release SR (CR) formulations to avoid ADRs....
4	Why does glycyrrhizic acid cause hypertension?
5	Omeprazole-Clopidogrel interaction is well known. If a patient on clopidogrel requires a PPI which one can be suggested?
6	What is Cardio IQ® Genotype test and how is it relevant in therapeutics?
7	Which two currently used antidiabetic drugs have ketogenic effect?
8	Metoclopramide like many antipsychotic agents is a central D2 antagonist and, shares antiemetic and extrapyramidal symptoms (ADRs) with them. Then, why is metoclopramide not used as antipsychotic agent?
9	A potential biomarker that may help curb empiric Antimicrobial overuse in suspected serious bacterial infections (Under Antibiotic Stewardship program), is-...
10	Compared to GRADED dose response curve (DRC), a QUANTAL DRC does NOT assess- a: Maximum Efficacy b: Potency c: Selectivity d: Variability

Answers of Quiz on Page No. 20

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Extract



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What is EXTRACT

Extract are the collections of some important points taken from the discussion in National MD Pharmacology group. NMDP is a group of eminent pharmacologists from all over the country. The head of departments of pharmacology, deans, directors of institutions and people with significant contribution in the field of pharmacology are members of NMDP family. National association of Pharmacology and Therapeutics is promoted by NMDP group.

Drug Alert on Mefenamic acid, a commonly used NSAID: IPC has issued a drug safety alert about the NSAID, Mefenamic acid that it triggers severe allergic reactions like the DRESS syndrome.

Significant amount of money was paid by Indian researchers: Indian researchers paid a whopping \$17 million in 2020 to publish their research articles in Open Access formats. Mostly it was paid with funding agencies and not by individual researcher.

CDSCO flagged 61 different medicine batches: CDSCO has flagged 61 medicine batches to qualify for a random drug sample test for the month of October. These samples were declared not to be off standard quality and includes many antimicrobials formulations.

FDA approved Protein kinase Inhibitors: Owing to the dysregulation of protein kinase activity in many diseases including cancer this new enzyme family has become one of the most important drug targets in the 21st century. There are 72 FDA approved therapeutic agents that target about two dozen different protein kinases and three of these drugs were approved in 2022. 62 of these drugs are prescribed for the treatment of neoplasms.

NPPA caps prizes of 49 drug formulations: National pharmaceutical pricing authority Has set the ceiling prices 49 drug formulation, including tacrolimus and cotrimoxazole.

#World's second malaria vaccine gets WHO approval: The highly effective malaria vaccine developed by Pune's serum institute of India and University of Oxford R21/Matrix M malaria vaccine gets WHO approval.

#NMC has clarified faculty leave: All faculties are allowed 25% leave in addition to vacation that means minimum 75% attendance is required.

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Eligibility Criterias to appear in examination after student is detained: If a student is detained for internal assessment he/she has to clear his internal assessment before supplementary exam. If he/she is detained for attendance then he/she must attend extra/remedial classes after regular exam and complete the attendance. Then he/she will be eligible for supplementary exam. If his/her attendance has short deficit he/she can make up loss with extra classes before supplementary exam if his/her attendance is too short he/she will not become eligible for supplementary exam.

Prescribing branded medicines Vs generic drugs: Supreme court's notice seeking action and guidelines against the doctors prescribing branded medicines to patients instead of generic drugs which have the same active ingredients has sparked a debate among medical fraternity. There is opinion that prescribing generic medicines could create a liability of professional negligence on the doctor when a better formulated branded product is available. So, we need database of results of bioequivalence studies to see the evidence that generic drugs will be as effective as their branded counterparts.

#NMC orders separate faculties in MEU and Curriculum Committee: NMC has issued new order directing all the colleges to have separate faculties in MEU and CC except Dean/Principal and MEU Coordinator.

Patient safety programme from 17th to 25th September and NMC Foundation day on 25th September: NMC requested all the medical colleges to participate in celebration of patient safety programme from 17th to 25th September 2023 and national medical Commission foundation day on 25th September 2023.



Answers of Quiz

	Question	Answer	Ref
1	Which two drugs show "Robin Hood effect"	1: Propranolol (BBs), BBs improve coronary microcirculation in ischaemic zone by "reverse steal phenomenon" 2: Empagliflozin**	*GG: p- 617 ** Kalra et al: The Robin Hood effect. Indian J Endocr Metab 2016;20:725-9.
2	Which two Drugs require DRUG HOLIDAYS on prolonged therapy	Levodopa and Bisphosphonates (BSPs) [When used for prolonged period BSPs may cause atypical femur fracture and osteonecrosis of Jaw. The antiresorptive effect persists even after discontinuation. So DRUG HOLIDAY is suggested as It reduces risk of atypical femur fracture]	GG: P-147
3	Examples of drugs which are almost always given as SR (CR) formulations to avoid ADRs	Nifedipine - to avoid sympathetic stimulation and tachycardia.	
		Carbamazepine SR - avoids high peaks in plasma concentration and the resultant neurologic symptoms (ataxia, diplopia)	Cochrane Database Syst Rev PMC6463840
		Micronized progesterone : micronized progesterone apart from longer t _{1/2} , better oral bioavailability and less food impact it also causes less mood changes It does not significantly alter beneficial estrogen effects on either HDL or LDL profiles	GG: p-971 J Clin Diagn Res. 2016 Feb; 10(2): QE01–QE04
		Venlafaxine CR : The Immediate release formulation of venlafaxine can induce sustained diastolic hypertension (diastolic blood pressure >90 mmHg...this risk is reduced with the extended-release form	GG:p-351
		Metformin SR : Less GIT effects	GG:p-1036
4	Why does glycyrrhizic acid cause hypertension?	It inhibits 11β-HSD2 enzyme which normally inactivates cortisol to cortisone in kidney. This allows high conc of cortisol to stimulate Mineralocorticoid Receptors (Cortisol and aldosterone have equal affinity at MR) to raise BP by salt retention	GG: p- 1009
5	Omeprazole-Clopidogrel interaction is well known. If a patient on clopidogrel requires a PPI which one can be suggested?	Pantoprazole is less likely to result in this interaction; concurrent use of clopidogrel and PPIs (mainly pantoprazole) significantly reduces GI bleeding without increasing adverse cardiac events	GG:p-1076
6	What is Cardio IQ® Genotype test and how is it relevant in therapeutics?	It detects CYP2C19 genotypes. Asians (25-30%) and Oceanians (60%) have CYP2C10 genotype that correlates with reduced inactivation of omeprazole. With a single 20 mg omeprazole dose, the AUC of omeprazole in Asian subjects was approximately four-fold of that in Caucasians: -Dose reduction is needed on chronic use	GG: p-1075
7	Which two currently used antidiabetic drugs have ketogenic effect	Metformin and Empagliflozin : ---The SGLT2 inhibitors mediate a metabolic switch from glucose to lipid utilization as the predominant substrate resulting in formation of ketone bodies	J Endocr Metab 2016;20:725-9.
8	Metoclopramide is a D ₂ antagonist like many antipsychotic agents and, shares antiemetic and extrapyramidal symptoms-ADRs) with them. Then why is metoclopramide not used as antipsychotic agent?	1-The extent of D ₂ receptor blockade in dopaminergic neurons determines beneficial v/s adverse effects. -Occupancy of greater than 78% of D ₂ receptors in the basal ganglia is associated with greater risk of EPSs across all DA antagonist antipsychotic agents, while occupancies in the range of 60% to 75% are associated with antipsychotic efficacy and lower EPS risk 2-Moreover, the therapeutic efficacy of antipsychotic drugs in humans correlates with their ability to induce depolarization block of mesolimbic dopamine neurons , whereas their potential to produce extrapyramidal side effects correlates with their propensity for inducing depolarization block in the nigrostriatal dopamine system	GG pp 364-66 White, F.J. and Wang, R.Y. (1983) Science 221, 1054–1057.
9	A potential biomarker that may help curb empiric Antimicrobial overuse in suspected serious bacterial infections (Under Antibiotic Stewardship program)	Procalcitonin (PCT): It is a rapid-reacting biomarker which indicates the host response specifically to a bacterial infection. PCT provides information about the likelihood of a clinically relevant bacterial infection and the risk of progression to sepsis and septic shock and aids in antibiotic therapy decisions.	1: World Health Organization (2021). (WHO Technical Report Series, No. 1031) 2: Harrison's Int Med: P-944
10	Compared to GRADED dose response curve (DRC), a QUANTAL DRC does NOT assess- a: maximum efficacy b: Potency c: selectivity d: Variability	A : In a graded DRC, the magnitude of an individual's response usually increases as the dose of the drug is increased. In a quantal DRC, the percentage of the population (that responds) increases as the dose of the drug increases, but the response is only judged to be either present or absent in a given individual.	GG: p-156 Rang: p-109 Katzung: p-37

AMAZING DRUG MOLECULES: Drugs with Multiple Mechanisms of Action

Some drug molecules exert their pharmacodynamic therapeutic actions by multiple mechanisms which is important to have broad spectrum of activity against pathophysiological clinical conditions.

Drug	Class	MECHANISM OF ACTION		Remark(s)
		Target		
Propranolol Metoprolol Atenolol etc	Antihypertensive [β Blockers]	Smooth Muscle	(\square) PVR; On long term use;	Major MOA of Class Effect of All β blockers
		β Receptor	Antagonism	Class Effect of β blockers
		CNS: Sympathetic Outflow	Inhibition	Class Effect of β blockers
		PGI ₂	Inhibition	Vasodilatation & Natriuresis
Carvedilol Labetalol Bucindolol Bevantolol Nipradilol	Antihypertensive [β Blockers]	α Receptor	Antagonism	Additional α Receptor Blocking Property
Celiprolol	Antihypertensive [β Blockers]	Smooth Muscle	Direct Vasodilatation	Vasodilatation
Carvedilol Betaxolol Bevantolol	Antihypertensive [β Blockers]	Ca ²⁺ Channel	Blockade	Hyperpolarization
Tilisolol	Antihypertensive [β Blockers]	K ⁺ Channel	Opener	Hyperpolarization
Celiprolol Nebivolol Carteolol Bopindolol Nipradilol	Antihypertensive [β Blockers]	Nitric Oxide	Synthesis	Vasodilatation
Carvedilol	Antihypertensive [β Blockers]	Oxidative Stress	Inhibition	Favourable for Reduction of BP
Celiprolol Carteolol Bopindolol Pindolol	Antihypertensive [β Blockers]	β_2 Receptor	Agonism	Vasodilatation
OCPs	Contraceptive(s)	LH	Inhibition	
		FSH	Inhibition	
		Ovulation	Inhibition	
Atorvastatin Rosuvastatin Lovastatin Simvastatin etc	Hypolipidaemic	HMG-CoA reductase	Inhibition	Broad Spectrum Hypolipidaemic(s) with 'Pleiotropic Actions'
		Nitric Oxide	Production	
		LDL Oxidation	Reduction	
		Athermanous Plaque	Stabilization	

*ACE: Angiotensin Converting Enzyme;;

NE: Norepinephrine;

REFERENCES: Goodman and Gilman's The Pharmacological Basis of Therapeutics. 13th ed. New York: McGraw-Hill Education; 2018



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NATIONAL ASSOCIATION OF PHARMACOLOGY AND THERAPEUTICS

Promoting Pharmacology and Therapeutics for a better tomorrow

About the organization

A national organization of medical doctors specialized in pharmacology/clinical pharmacology and therapeutics. Envisaged to provide strong leadership to promote pharmacology and therapeutics for a better tomorrow. The association is fostered by NMDP (National MD Pharmacology), a prestigious group of eminent pharmacologists.

Aims and objectives

Empowering medical doctors specialized in Pharmacology/Clinical Pharmacology and Therapeutics.
Promoting academic and clinical research in Pharmacology/Clinical Pharmacology and Therapeutics.
Enhancing the standard of teaching/training in Pharmacology/Clinical Pharmacology and Therapeutics
Promoting Pharmacology/Clinical Pharmacology and Therapeutics for the benefit of patients and society.



BENEFITS OF LIFE MEMBERS

- Receive notifications on of the organization
- Keep yourself updated in the world of pharmacology and therapeutics .
- Get connected with fellow pharmacologists of the country.
- Contest for various posts in the organization.
- Receive of the permanent membership e-certificate through email, enhance your profile by writing MNPT
- Participate in general body meetings (GBM) to speak and to vote.
- Participate in conferences/seminars/workshops/symposiums/training sessions at subscribed charges.
- Receive an e-copy of the official publications (i.e. News letter, Journal, academics, research material etc.

Glimpses of NAPTICON 2023

NAPTICON 2023, the 2nd Annual National conference of **National association of Pharmacology & Therapeutics (NPT)** was held in **Lucknow**, the capital city of Uttar Pradesh on **30th November, 1st & 2nd December, 2023**. The conference brought together over 700 Medical Pharmacologists from academia and industry all over the country to discuss the latest advances in field of Pharmacology & Therapeutics.

As promised, the conference was a great mixture of obtaining scientific knowledge, knowing recent advances, learning from experts of the field and of course all were done in an enjoyable way altogether. It had various scientific sessions by keynote speakers, E-poster and Oral paper presentations by young and energetic pharmacology residents and faculty, NAPTQUIZ by the great quiz masters and what not.

On 30th November, the Pre-conference workshop on ACLS/BLS and AI had a great start with lectures and hands-on training been given to the delegates by the respective resource faculty.

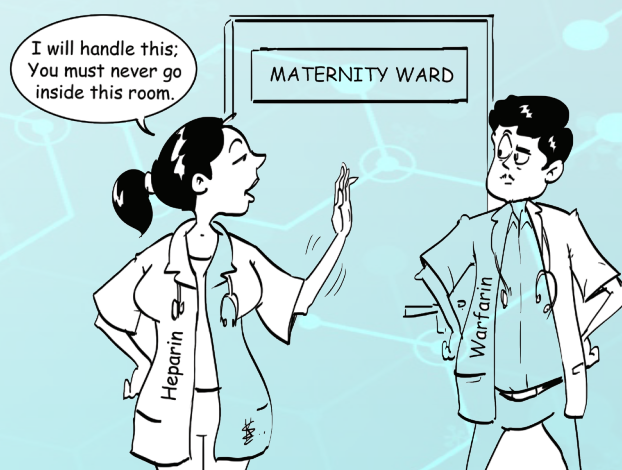
December 1, the main event started with a grandeur inauguration ceremony where all the chief guests, faculty and delegates graced the occasion with their esteemed presence. The scientific and plenary sessions followed covering a multitude of topics. Around three hundred of the E-poster and Oral paper presentations were simultaneously happening in the respective halls and being judged by the expert judges. The E-poster and Oral paper presentation sessions featured presentations on the latest research in Pharmacology & Therapeutics.

The highlight of the day was Dr. Nilima Arun Kshirsagar ma'am being awarded the lifetime achievement award from the NPT. She's really an achiever and deserved one. The day came to an end with the last event being the Young Pharmacologists Session (YPS).

Even the day was over, the night was still alive. Gala Night, as the name suggests, it had all. Food, fun, laughter, music, dance, etc. The participants, young and not so young let their hair down to indulge in fun and frolic making it a memorable night indeed.

December 2, the last day of the conference started with short scientific sessions and YPS sessions. The panel discussion on 'off-label use of prescription drugs' saw the stage coming alive with the insightful comments by the esteemed panellists covering the topic in a comprehensive and holistic manner. Then came the NAPTQUIZ, the much awaited event of the day. It was indeed a scientific and an academic feast to all the participants as well as audience, thanks to our quiz masters, Dr. Dinesh K Badyal and Dr. Prithpal Singh Matreja. The day ended with the General Body Meeting (GBM) of NPT and the Valedictory Session for congratulating all the winners of various events.

Yes, NAPTICON 2023 will be remembered by everyone for many more years for creating the best memories of lifetime. The conference was a great success, and it provided a valuable forum for Medical Pharmacologists from academia and industry to share their work and discuss on many important topics. Thanking everyone who was involved in making this event a grand success.





GLIMPSES OF NAPTICON 2023 LUCKNOW

2nd National Conference of National Association of Pharmacology & Therapeutics

1st-2nd December 2023: Organized by Department of Pharmacology & Therapeutics KGMU, Lucknow





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NATIONAL ASSOCIATION OF PHARMACOLOGY AND THERAPEUTICS

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