Review Article

Self-medication: A Mechanistic Review of Common Drugs

Shiksha Kaushal[1], Vivek Kumar Sharma[2], Raneev Thakur[2], Harish Kumar[2]

1. Project Scholar (B. Pharm.), Department of Pharmacology, Govt. College of Pharmacy, Rohru, Distt. Shimla-171207, Himachal Pradesh, India.
2. Govt. College of Pharmacy, Rohru, Distt. Shimla-171207, Himachal Pradesh, India.

***Corresponding author's E-mail:** v4vksharma@gmail.com

Received: 18-03-2023; **Revised:** 22-05-2023; **Accepted:** 30-05-2023; **Published on:** 15-06-2023.

ABSTRACT

Self-medication, the practice of diagnosing and treating one's own health conditions without professional guidance, has become increasingly prevalent in society. This article aims to explore the ill effects of self-medication. The first section examines the causes of self-medication and potential physical harm caused by it. It highlights the dangers of misdiagnosis, inadequate dosage, and adverse drug reactions, drug-drug and food-drug interactions, which can lead to severe health complications or even fatalities. Moreover, self-medication often fails to address the underlying causes of symptoms, resulting in temporary relief rather than long-term solutions. The second section discusses about some common drugs that are being self-medicated, some among which are from the category of OTC drugs like Ibuprofen and Paracetamol. The article also discusses the development of superbugs and antibiotic resistance because of such irrational use. This paper urges a balanced approach to self-medication that acknowledges the hazards it entails. It puts forward the idea of public awareness regarding the rational use of the drugs and also talks about the necessity of regulatory frameworks that safeguard consumers and provide access to accurate and trustworthy health information. This study contributes to a better understanding of self-medication by addressing its intricacies, opening the door for evidence-based interventions and regulatory reforms that will improve healthcare outcomes.

Keywords: Adverse Drug Reactions, Drug-drug/food interactions, OTC, Superbugs, Antibiotic Resistance.

QUICK RESPONSE CODE →

DOI: 10.47583/ijpsrr.2023.v80i02.020

DOI link: http://dx.doi.org/10.47583/ijpsrr.2023.v80i02.020

1. INTRODUCTION

Self-medication is the use of medications, herbs, or home remedies at one's own initiative or on the suggestion of a friend or family member without first seeking medical recommendations.[1] Which means consuming, buying, or suggesting a medicine without consulting any physician or without any prescription.

1.1 Why Do We Self-Medicate?

Jam-packed government hospitals and the heavy cost of consultation in a private hospital are a common challenge faced by the general public in our country, which makes it difficult for people to have an appointment with the physicians. When coupled with our unhealthy lifestyle the problem broadens. The unhealthy lifestyle is associated with chronic stress, and a variety of health issues, including hypertension, weakened immune function, digestive disorders, and mental health problems such as anxiety and depression. When faced with such health difficulties, people turn to self-medication to treat their conditions or manage their symptoms without consulting a doctor.

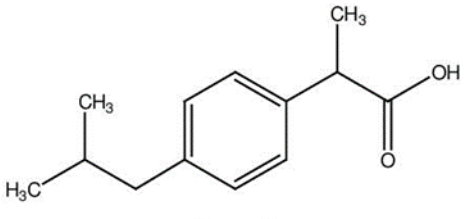
1.2 Hazards of Self-Medication

Self-medication practices carry a number of potential risks, such as incorrect self-diagnosis, delays in seeking medical help, when necessary, rare but severe adverse reactions, unsafe drug interactions, incorrect administration, incorrect dosage, incorrect therapy selection, masking of a severe disease, drug abuse and drug dependence risks.[2]

Painkillers, antibiotics, antihistaminics, antipyretics, laxatives, cough syrups, antacids, and other medications are frequently used as self-medication. The majority of these are OTC or non-prescription medications, making them accessible to patients without a prescription. These OTC drugs may help us get rid of symptoms, but they may as well potentially mask the original cause of the symptoms. Thereby leading to misdiagnoses and delayed treatment of problems. The administration of the wrong medicine or a medicine at wrong dose would certainly cause side effects.

2.COMMONLY USED DRUGS FOR SELF MEDICATION

2.1 Ibuprofen



Ibuprofen

Ibuprofen is NSAID (non-steroidal anti-inflammatory drug) which possesses antipyretic and analgesic character. It is an over-the-counter drug.

2.1.1. Structure and IUPAC

- **IUPAC Name:** 2-[4-(2-methylpropyl) phenyl] propionic acid
- **Molecular weight:** 208.68gmol^-1
- Ibuprofen is a stable, colourless-crystalline solid with a characteristic odour and melting point 75-77°C.[3] [4]

2.1.2 History

Ibuprofen was developed by Dr. Stewart Adams OBE as he was searching for other non-steroidal anti-inflammatory drug which possesses activity as that of aspirin, which could be used for the treatment of pain in rheumatoid arthritis. In the year 1961, he was granted the patent on the molecule 2-(4-isobutylphenyl) propionic acid, the most widely used anti-inflammatory drug, today.[5] Dr. Adams was the first person, who used Ibuprofen, he used the drug to overcome his hangover.[4] 1969 Ibuprofen was launched into the market of England with a recommended dose of 600mg-800mg per day, for the treatment of rheumatoid arthritis. Ibuprofen was validated as an OTC drug in England in the year 1983 with a dose limit of 1200mg per day. It was the first NSAID other than Aspirin that was being sold as OTC.[5] [6] The United States was the first country to approve the injectable formulation of the drug in year 2003.[7]

2.1.3. Commonly prescribed for:

- Acute and long-term management of rheumatoid arthritis [8]
- Osteoarthritis and psoriatic arthritis [8]
- Analgesic and anti-inflammatory [3]
- OTC painkiller [9]
- Antipyretic [3]
- Painful mensuration
- Headache

2.1.4. Mechanism Of Action

Ibuprofen is a non-selective; non-steroidal anti-inflammatory drug, which means it inhibits both of Cyclooxygenase isoforms namely COX-1 and COX-2.[10] Arachidonic Acid which an unsaturated fatty acid molecule, made up of 20 Carbons undergoes consecutive reactions in the presence of Cyclooxygenase enzymes and results in the formation of prostanoids which are responsible for inflammation and pain.

Ibuprofen reversibly inhibits the COX-1 and COX-2.[10] And production of Prostaglandins which was causing inflammation and pain is also inhibited. PGE2 and PGI2 reduce the threshold of pain receptors, known as nociceptors which are intensely present on skin, respiratory tract, joints and GIT, these prostaglandins are also responsible behind the high vascular permeability, formation of edema and increased leucocyte infiltration.[11] Ibuprofen increases the pain threshold and decreases signs of inflammation by inhibiting the synthesis of prostanoids. Increased level of PGE2 in the hypothalamus causes fever or pyrosis. Pyrogens like endotoxins and cytokines are responsible behind the increased level of PGE2 in the hypothalamus.[6] Antipyretic property of Ibuprofen is because of its ability to block the syntheses of PGE2.

2.1.5. Current Status of Ibuprofen in India and Abroad

India is the second largest supplier of Ibuprofen, as it holds 30% share of production market of Ibuprofen, whereas China enjoys the privilege of being number one supplier of Ibuprofen with a production market share of 48%. Whereas North America is the largest sales place of this drug holding sales share of 29%.

2.1.7. MOA of Nephrotoxicity

Ibuprofen also possesses nephrotoxic properties which means the drug can cause harm to kidney, as the biosynthesis of Prostaglandins is inhibited by the use of NSAIDs. The renal prostaglandins are inhibited which are responsible for maintaining renal hemodynamic.[12]

The glomerular filtration rate along with the renal blood flow is regulated by the prostacyclin, whereas PGI2 is responsible for renin release.[13] [14] This PGI2 is basically not functional in healthy individuals as it does not play very significant role in regulation renal hemodynamics.

Prostaglandins PGE2 and PGEI2 play a crucial role in the maintenance of renal perfusion. One of major side effects of NASIDs is sodium retention which causes hypertension and edema, as well as hyperkalemia and disturb acid-base balance.[15] [16]

2.1.8. MOA of GI Disturbances

Gastrointestinal Disturbances caused by NSAIDs like Ibuprofen is due to inhibition of enzyme COX, which results in the decreased production of Prostaglandins.[17] As Ibuprofen, is the blocker of both isoforms of COX therefore a decrease in the level of Prostaglandins is observed, as by limiting the availability of COX, the synthesis of PGs is limited. PGE2, a prostaglandin which is responsible for the secretion of gastro-protective mucus is also affected by the use of Ibuprofen. The lack of PGE2 causes lack of gastro-protective mucus secretions, which may cause ulceration, gastritis, or perforation. Some studies have also suggested the blockade of COX-2, may also result in the production of free radicals in the gut.[18] [19]

2.1.9. MOA of Asthma

Andrzej Szczeklik first described that, the inhibition of COX pathway by the NSAIDs, leads towards an increased availability of arachidonic acid for the LOX pathway which results in the hyperactivity of the LOX i.e., Lipoxygenase pathway. This activation of LOX account for the elevated synthesis of Leukotrienes. These Leukotrienes are

responsible for bronchoconstriction thereby worsening Asthma [20] [21]. Studies have suggested that, expect aspirin other NSAIDs like: Ibuprofen, diclofenac and naproxen show cross-sensitivity reaction.[22] [23]

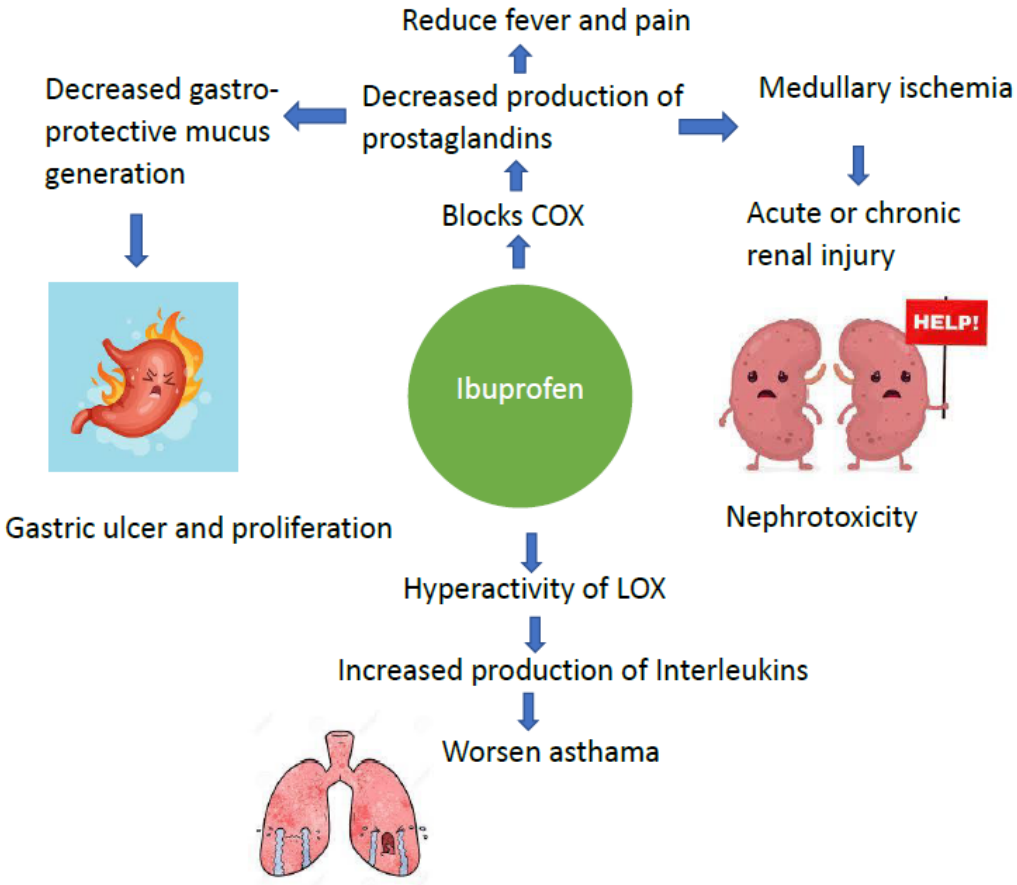
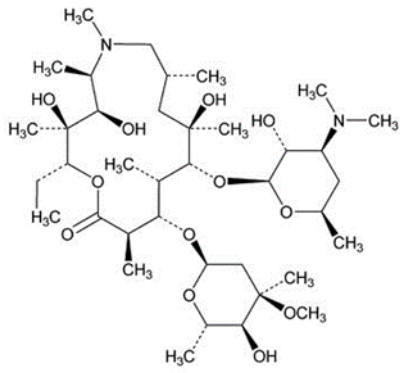


Figure 1: Proposed mechanism of action of Ibuprofen (physiological effects and side effects)

2.2 Azithromycin

Azithromycin is abroad spectrum; bacteriostatic agent, coming from the class of macrolide antibiotics. It's effective against several gram-positive and gram-negative bacteria, along with this it shows potency against mycoplasma pneumoniae, Treponema pallidum, Chlamydia species and Mycobacterium avium complex.[24]

2.2.1. Structure of Azithromycin



- **IUPAC:** (2R,3S,4R,5R,8R,10R,11R,13S,14R)-11-[(2S,3R,4S,6R)-4-(dimethylamino)-3-hydroxy-6-methyloxan-2-yl]oxy-2-ethyl-3,4,10-trihydroxy-13-[(2R,4R,5S,6S)-5-hydroxy-4-methoxy-4,6-dimethyloxan-2-yl]oxy-3,5,6,8,10,12,14-heptamethyl-1-oxa-6-azacyclopentadecan-15-one.
- **Molecular weight:** 749.0 gmol^-1.l
- It is an amorphous solid with a melting point of 113-116°C.[25]

2.2.2 History

Croatian pharmaceutical company Pliva in 1980 discovered the drug and in 1988 it was approved for medicinal use.[26] [27] It's a generic medication and sold under various brand names worldwide.[28]

2.2.3. Commonly prescribed for

- Respiratory bacterial infections
- Dermal bacterial infections
- Immunomodulatory effect in chronic inflammatory disorder.[24]

2.2.4 Mechanism of Action

Azithromycin binds to bacterial ribosome thereby inhibiting the synthesis of bacterial protein it also gets accumulated in the phagocytes hereby ensuring higher availability in the site of infection.[24] Azithromycin's antileishmanial activity is also reported, in a cell-free culture Azithromycin showed a

50-fold decrease in count of leishmania major promastigote during log phase, as well as it also showed a significant decrease of parasite level in cell-culture infected with Leishmania major amastigote.[29]

2.2.3 Current Status in India

The irrational use of antibiotics is the principal reason behind antibiotic resistance in India, India is the largest consumers of antibiotics and Azithromycin tops the list, as India consumed 640 million tablets Azithromycin in one year.[30]

2.2.4. Fatal Heart Rhythms

According to FDA Azithromycin can cause a problem in the normal electrical functioning of heart and can cause irregular heartbeat. It can cause fatal heart rhythms especially in the patients who are already suffering from or are at risk of cardiovascular problems.

2.2.5. Antibacterial Resistance

The long term and inappropriate use of azithromycin causes the developer of resistant bacterias. The risk of antibacterial resistant was increased by 2.7-fold in patients receiving long-term treatment with Azithromycin.[31]

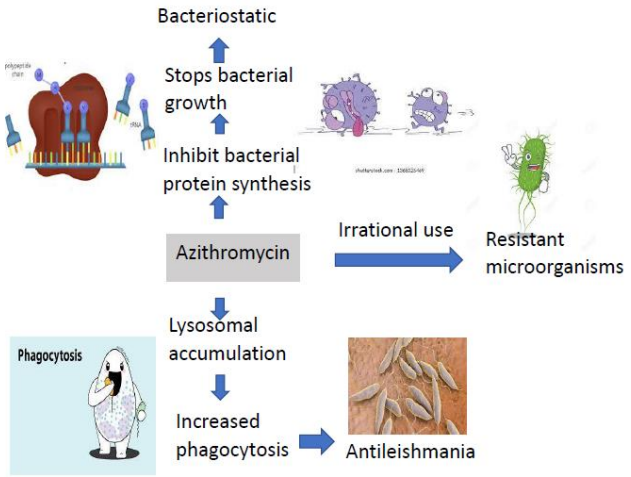
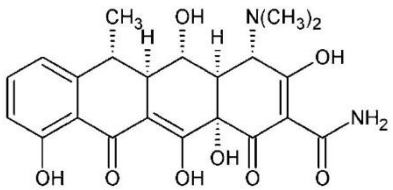


Figure 2: Azithromycin Mechanism of Action and development of superbugs

2.3. Doxycycline

Doxycycline belongs to tetracycline class of medicine. Which is the first class of broad-spectrum antibiotic drug to be discovered.

2.3.1 Structure and IUPAC



- **IUPAC:** (4S,4aR,5S,5aR,6R,12aR)-4-(dimethylamino)-1,5,10,11,12a-pentahydroxy-6-methyl-3,12-dioxo-4a,5,5a,6-tetrahydro-4H-tetracene-2-carboxamide.
- Doxycycline is a yellow crystalline powder, which is very slightly soluble in water, freely soluble in alcohol practically insoluble in chloroform and ethanol.[32]

2.3.2. History

Doxycycline is semi-synthetic, broad-spectrum antibiotic developed from the naturally occurring tetracyclines. Pfizer Inc. in the 1960s firstly developed it and marketed it under the brand name Vibramycin. In 1967, Vibramycin was approved by FDA.[33]

2.3.3. Commonly prescribed for

- Bacterial Pneumonia
- Lyme disease
- Cholera
- Typhus and syphilis
- Prevention of malaria along with quinine[34]

2.3.4. MOA

Doxycycline like other Tetracycline shows the bacteriostatic function by inhibiting with the bacterial protein synthesis, by binding with 30S subunit of bacterial ribosome.[35]

2.3.5. Gastrointestinal Disturbances

Gastrointestinal problems and photosensitivity are common side-effects of the drug. The gastrointestinal issues consist of nausea (4–33%), abdominal pain (12–33%), vomiting (4–8%), and diarrhea (6–7.5%).[33]

2.3.6. Esophageal Ulcer and Erythematous Rash

Those patients who consume Doxycycline, empty stomach esophageal ulcer has been commonly reported, where as in some individuals exposing skin to sunlight after consuming Doxycycline erythematous rash was reported.[36 37]

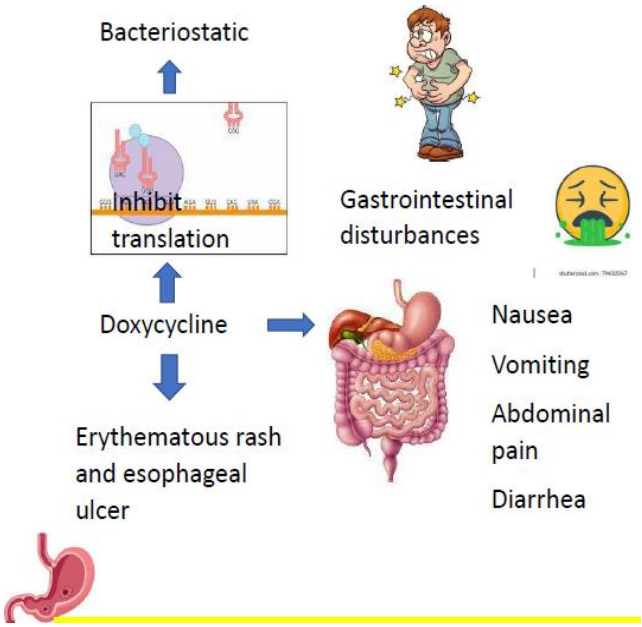
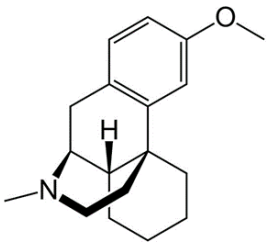


Figure 3: Doxycycline's Bacteriostatic Action and GI Disturbances

2.4. Dextromethorphan

Dextromethorphan is an antitussive agent used in various over the counter drugs to prevent cough and cold. It is used in the form of lozenges, oral stripes and liquid filled capsules.[38]

2.4.1 Structure and IUPAC



- **IUPAC**:6-methoxy-11-methyl-1,3,4,9,10,10a-hexahydro-2H-10,4a(epiminoethano)phenanthrene
- **Molecular weight :** 271.4g/mol.

2.4.2. History

Dextromethorphan is a synthetic derivative of codeine, which received FDA approval in the year 1958 and is one the most common compound to be found in the OTC antitussive. Soon after this, the drug Abuse of the drug begun. In 2010 it was approved for pseudobulbar affect with quinidine.[39]

2.4.3.MOA

The synthetic derivative of codeine, it acts on nucleus tractus solitarius, the site of pulmonary vagal afferent fibers synapse in the central nervous system, which operates a door for the cough reflex in the CNS, dextromethorphan is a non-competitive antagonist for N-methyl-D-aspartate (NMDA) receptors and it may have other site of action:[39]

- Sigma-1 receptors agonist
- Nicotinic receptors (a3b4, a4b2, a7) antagonist
- Serotonin transporters inhibitor
- Norepinephrine transporters inhibitor
- Voltage-gated calcium channels inhibitor

2.4.4. Commonly prescribed for:

1. Antitussive
2. Methotrexate Neurotoxicity
3. Pseudobulbar affect (PBA)

2.4.5. Drug Abuse

At higher doses >4mg/kg patients it affects CNS , in various ways where hallucinations , euphoria and persecutory delusions has been reported.[39]

2.4.6. Serotonin Syndrome

In those patients who are already consuming antidepressant drugs (MAOI) the life threatening toxicity like Serotonin syndrome has been reported with Dextromethorphen, as it inhibits the serotonin reuptake mechanism, thereby increasing the amount of serotonin in the body and leading towards Serotonin Syndrome. Which consists of agitation, confusion, dilated pupils, headache, tachycardia, hypotension, high fevers, seizures, irregular heartbeat, and can lead to unconsciousness.[39]

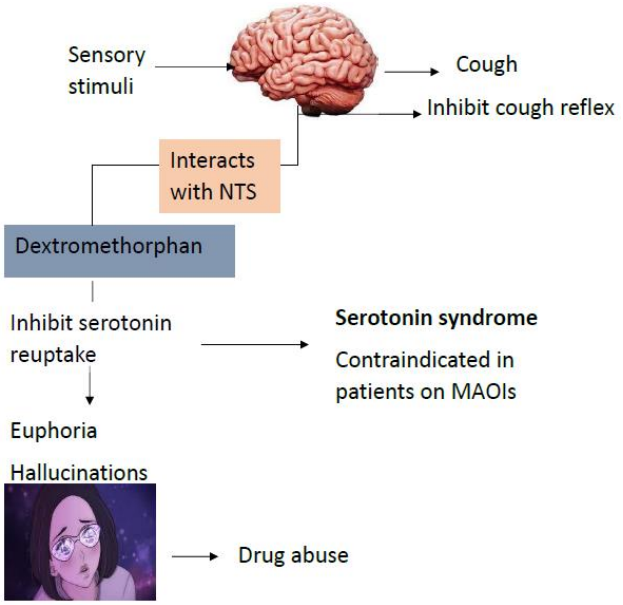


Figure 4: The proposed mechanisms of physiological actions and side effects of Dextromethorphan

2.5. Pentoprazole

Pantoprazole is an irreversible blocker of the proton pump,belonging to the class of benzimidazole proton pump inhibitor and is widely used as an antiulcer agent.

2.5.1. Structure and IUPAC

IUPAC :6-(difluoromethoxy)-2-[(3,4-dimethoxypyridin-2-yl)methylsulfinyl]-1H-benzimidazole.

Molecular weight : 383.371 g/mol.

2.5.2. History

The drug was discovered in the year 1985 by the scientists at Byk Gulden, a subsidiary of Altana; Germany became the first country to market the drug in the year 1994 , Wyeth licensed the US patent from Altana and the drug was approved by US FDA in the year 2000 under the brand name protonix.

2.5.3. Commonly prescribed for

1. Gastric Ulcer
2. Erosive Esophagitis
3. Zolinger Elison Syndrome

2.5.4. MOA

Pantoprazole is an FDA approved drug used for the treatment of erosive esophagitis, Zolinger-Elison Syndrome. Pantoprazole is a benzimidazole proton pump inhibitor which means it do have a shorter plasma presence.

Pantoprazole show irreversible blockade of the H/K pump which are present in the gastric parietal cells.by binding with the proton pump they inhibit the efflux of H to the gastric lumen, and hence prohibit gastric acid secretion upto 24 hours as after that new proton pumps can be synthesized by the body hence other dose of the drug is required for further prohibition.[40]

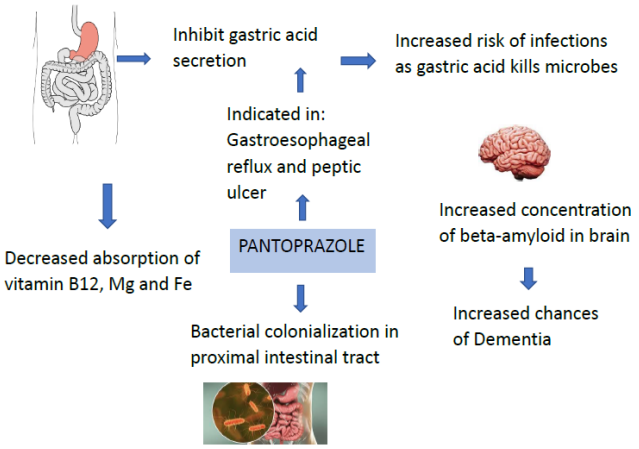


Figure 5: Pantoprazole: Mechanism of Action

2.5.5. Deficiency of magnesium, vitamin B12 and iron

Hypomagnesemia means the deficiency of magnium in 2006 several cases were reported where patients suffer from the magnesium deficiency, after a use of the drug continuous 12 months. As the production of HCl is inhibited by the PIPs , this acid is crucial for the absorption of vitamin B12 and iron salt, hence the inhibiton of the production of HCl can also lead towards the decreased absorption of these nutrients.[41]

2.5.6. Dementia

The effect of the proton pumps inhibitors on the amyloid metabolism has been studied using the animal models and the hypothesis states that PIPs effects both the synthesis and degradation of the beta-amyloid,where it is responsible for triggered synthesis and changes in the degradation in microglia by the lysosomes, which is a reason behind increased levels of the beta-amyloid in the brain of mice.although the evidences and studies on this subject regarding human is limitedbut according to Harnisch and his colleagues there is an increased threat for demnitia along with Alzheimer disease in patients who are consuming PIPs.[41 42]

2.5.7 kidney related issues

The proton pump inhibitors are observed to cause renal damage especially acute kidney damage in older patients. Three large population-based studies conducted in Canada, New Zealand and USA states that patients consuming PIPs are at higher risk level of developing acute kidney injury or acute interstitial nephritis.[41 42]

The mechanism of action of renal injury is stil not known , but these drugs are under continuous suspicion for inducing renal disease.

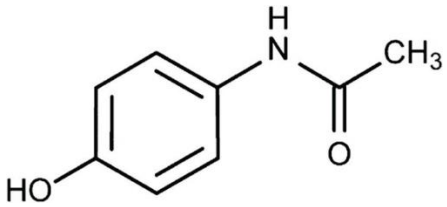
2.5.8. Altered Microbiota and increased chances of infection

The PIPs blockds the production of gastric acid there by weakening the defensive system of the gut against the ingested pathogen as the gastric acid plays a crucial part in protecting the body from them,the absence of this acid may lead to bacterial colonization in proximal intestinal tract. The PPIs decrease the intraluminal gastric acidity, making the altered GI environment more favourable for the survival of the spores the gastric environment.[41]

2.6 Paracetamol

Paracetamol also known as acetaminophen is an OTC drug and widely used for its antipyretic and analgesic activity.

2.6. IUPAC and structure



IUPAC : N-(4-hydroxyphenyl)acetamide

Molecular weight : 151.173g/mol

It is a white crystalline solid odorless and slightly bitter in taste with a melting point of 169-170.5°C.[43 44]

2.6.2 History

Von Mering used Paracetamol for the first time in the year 1893, and aperaed in the markets of United states in the year 1950 and in Australia in the year 1956. Until 1966 it was believed that Acetaminophen was one of the safest NASID but in 1966 the complications regarding the hepatotoxicity was discover.[45]

2.6.3Commonly prescribed for

- Fever
- Pain

2.6.4. Mechanism of action

Paracetamol being NSAID functions by inhibiting the synthesis of prostaglandins by inhibiting cyclooxygenase isoforms, it also exhibits blockade of T-type Ca channels and interacts with L-arginine in the synthesis of nitric oxide as well show involvement in endocannabinoid system and serotonergic pathways, which is responsible for it's antipyretic and analgesic effect respectively.[46]

2.6.5. Current status in India

According to a report from WION three and a half billion DOLO-650 tablets were sold in India since the beginning of 2019, DOLO-650 is an OTC drug in the country used for mild pain and fever. The DOLO-650 is paracetamol 650mg tablet. Three and a half billion of tablets means tablets that build up 6000 times taller tower than Mount Everest itself.

2.6.7. hepatotoxicity

The first case of paracetamol induced liver toxicity was reported in 1960s the drug causes serious irreversible damage to the hepatocytes especially at overdoses, studies shows that for acute liver failure, paracetamol induced hepatotoxicity is a major cause in United Kingdom,Canada, Australia and Scandinavia.[47 48]

the induction of P450 cytochrome isoenzymes CYP2E1 and CYP3A4 leads towards the higher production of toxic metabolite N-acetyl-benzoquinoneimine, followed by reduction in the liver glutathione stores, thereby causing liver toxicity.[48]

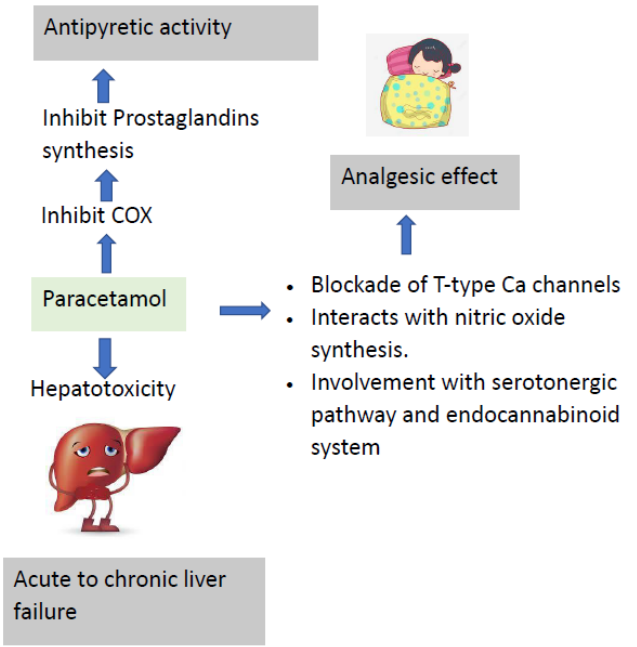
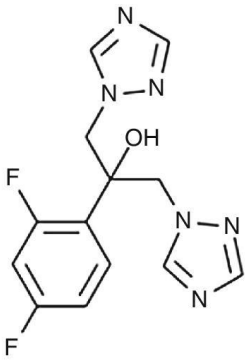


Figure 6: Paracetamol: Mechanism of Action and hepatotoxicity

2.7. Fluconazole

Fluconazole is a triazole antifungal drug with fungistatic properties and is one of the most prescribed drugs for infections caused by *candida.*

2.7.1. IUPAC and Structure



IUPAC: 2-(2,4-difluorophenyl)-1,3-bis(1,2,4-triazol-1-yl)propan-2-ol

Molecular weight: 306.27 g/mol

2.7.2. History

Fluconazole is the second drug from the category of triazole antifungals to be developed after ketoconazole. This drug was developed by Pfizer in the year 1990. Fluconazole belongs to the category of broad-spectrum antifungals. [49]

2.7.3. Commonly prescribed for

1. Vaginal candidiasis
2. Oropharyngeal candidiasis
3. Esophageal candidiasis
4. As well used for the treatment of fungal infections in immunocompromised patients. [50]

2.7.4. Mechanism of Action

The compound being a azole consists of N atom which binds with the iron atom from heme group in the enzyme cytochrome P450, which results in demethylation of lanosterol and hence thereby inhibiting the synthesis of ergosterol. Ergosterol is important for cell membrane of the fungi, the inhibition of ergosterol synthesis is responsible for inhibition of fungal cell growth.[51]

2.7.5. Resistance

Fluconazole is a fungistatic which means it only arrest the growth of fungal cell rather than killing the fungi, this favors the fungal cell as it gives it the opportunity to mutate and develop resistance against the drug. There are various mechanisms which are responsible behind the resistant micro-organism, like a change in the ergosterol biosynthesis pathway, loss of heterozygosity , changes in ploidy complimented with drug transporters.[51]

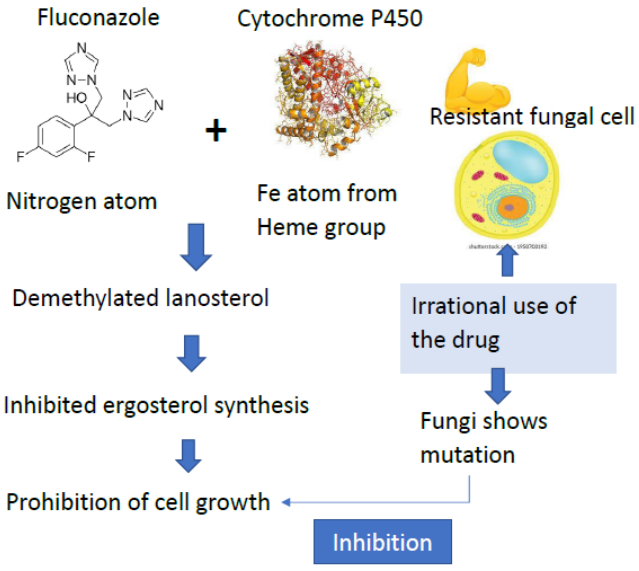


Figure 7: Fluconazole and resistant fungal cell

2.8. Hyoscine butylbromide

Hyoscine butylbromide is a quaternary ammonium anticholinergic agent derived from Belladonna from Solanaceae family, which is used as an agent for smooth muscles of gastro-intestinal and urinary tract.

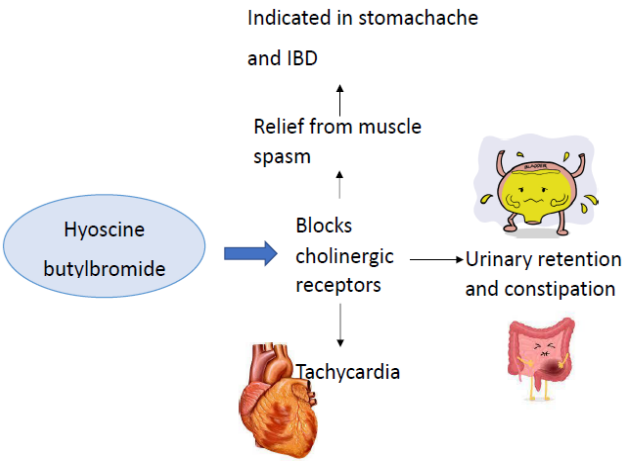
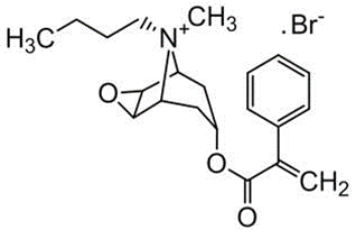


Figure 8: Hyoscine butylbromide: indications and side effects

2.8.1. Structure and IUPAC

IUPAC: 1-bromobutane;[(1S,2S,4R,5R)-9-methyl-3-oxa-9-azatricyclo[3.3.1.02,4]nonan-7-yl] (2S)-3-hydroxy-2-phenylpropanoate

Molecular weight: 440.4 g/mol.



2.8.2.History

Germany was first country to register and market Hyoscine butylbromide in the year 1951 followed by Australia in 1952.[52]

2.8.3. Commonly prescribed for

- Irritable bowl syndrome
- Stomach cramp
- Period pain

2.8.4 Mechanism of action

Hyoscine butylbromide is an anticholinergic drug which acts by blocking the transmission at parasympathetic ganglion. The inhibition of the cholinergic transmission leads towards the relief from the smooth muscle spasm in biliary tract, urinary and gastrointestinal tract, moreover it's not able to cross the Blood Brain Barrier because of attachment of the butylbromide moiety and hence don't affect the Brain.[53]

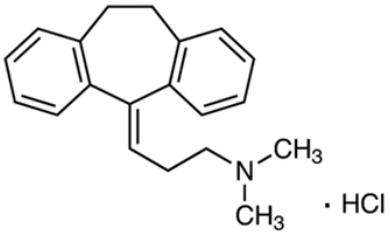
2.8.5. Urinary Retention, Constipation, and Tachycardia

The blockade of cholinergic Muscarinic receptors can cause urinary retention, constipation and Tachycardia.[54] As the parasympathetic system is responsible for the contraction of smooth muscles and the inhibition of its receptor can lead towards the Tachycardia which means increased heartbeat, urinary retention and constipation.

2.9 Amitriptyline

Amitriptyline is a tricyclic antidepressant indicated in many psychiatric manifestations like anxiety, depression, migraine, and severe pains.

2.9.1 Structure and IUPAC



IUPAC N,N-dimethyl-3-(2-tricyclo[9.4.0.03,8]pentadeca-1(15),3,5,7,11,13-hexaenylidene)propan-1-amine;hydrochloride.

Molecular weight: 277.4g/mol

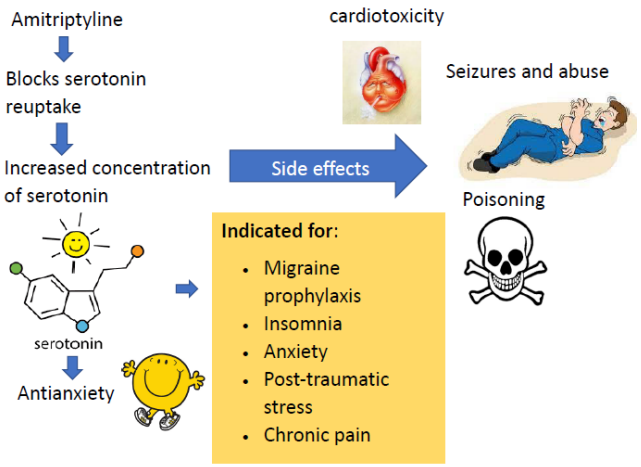


Figure 9: Amitriptyline: Mechanism of Action, Indications and Side-effects

2.9.2.History

In 1961, under the brand name Elavil, amitriptyline appeared in the market for the first time. It is a tricyclic antidepressant and was the second drug from this class to appear in the market.[55] Today it is a FDA approved drug used for the treatment of major depressive disorder i.e. MDD in adults. It's also indicated for management of anxiety, migraine prophylaxis, post therapeutic neuraglia, sialorrhea, chronic pain, insomnia, post-traumatic stress and chronic pain like diabetic neuropathy, irritable bowel syndrome.[56]

2.9.3. Commonly prescribed for :

1. anxiety
2. posttraumatic stress disorder
3. prevention of migraine
4. Insomnia
5. chronic pain (diabetic neuropathy, irritable bowel syndrome etc.)

2.9.4. Mechanism of Action

Amitriptyline on comparison to other tricyclic antidepressants possesses much more potent anticholinergic activity, it blocks the noradrenaline /serotonin transporter at for presynaptic terminals thereby blocking the reuptake of noradrenaline and serotonin. It is an antagonist to Muscranic (M1) receptors, alpha-adrenergic and histamine (H1) receptors. Long term treatment with amitriptyline produces long lasting changes in the monoaminergic neurotransmission as it is responsible for desensitization of presynaptic autoreceptors and heteroreceptors. The TCAs a large number of side effects due to its narrow therapeutic window.[55 56]

2.9.5. Suicidal Ideation and Behavior

The US FDA has issued a black box warning for the drug,according to which teenagers and young adults upto the age of 24yrs are at higher risk of developing suicidal behaviour.[56]

2.9.6. Cardiotoxicity

Amitriptyline being a tricyclic antidepressant produces quinidine like effect on the heart at high doses. They cause abnormalities in repolarization, by blocking mayocardial sodium channel. According to Kassim Thamer, H.M.Toufik et.al. a reduction in the level of consciousness, followed by sinus tachycardia, prolongation of QRS complex in ECG was observed in a 21-year-old who consumed amitriptyline in overdose in order to commit suicide, the overdose of this drug manifested mayocarditis with pericardial involvement.[57]

2.9.7. Poisoning

Tricyclic antidepressants continues to be the most common reason behind the fatal and non-fatal poisoning worldwide. They have a prominent effect on the parasympathetic system, brain and the heart. The common symptoms of poisoning are dry mouth, blurred vision, dilated pupil, drowsiness, and sinus tachycardia. Convulsions, respiratory depression, hypotension, ECG abnormalities like prolongation of QT and PR intervals or even coma could be observed.[58]

2.9.8. Seizures and Abuse

Amitriptyline is responsible for decreasing the human body's threshold to seizures and it can itself be a reason behind causing seizure itself at higher doses. Although its believed that the drug don't cause addiction or is not abused, but there are cases that showcased it's addictive properties especially in case of patients who had a history of psychotropic substance abuse.[59]

CONCLUSION

Self-medication can have negative effects on an individual's health and wellbeing. Even though it could seem practical or economical, self-medicating without the right medical counsel might have negative effects.

Self-medication can overlook underlying health issues and delay proper diagnosis and treatment. It can result in incorrect medication choices, inappropriate dosages, and harmful interactions with other medications. Moreover, self-medication may mask symptoms of serious conditions, leading to a false sense of security and potential worsening of the underlying problem.

To ensure safe and effective healthcare, it is crucial to consult healthcare professionals for proper diagnosis, guidance, and prescription of medications. They have the expertise to assess medical conditions, identify potential risks, and recommend the most suitable treatment options. Seeking professional help also allows for regular monitoring and adjustment of treatment plans as necessary.

In addition, promoting health literacy and educating individuals about the potential dangers of self-medication is essential. Encouraging individuals to be proactive in understanding their health and empowering them to seek appropriate medical advice fosters responsible healthcare practices.

Ultimately, the goal should be to prioritize individual health and well-being by making informed decisions regarding medication usage. By avoiding self-medication and seeking professional healthcare, individuals can better safeguard their health, minimize risks, and receive the most appropriate and effective treatment for their specific needs.

REFERENCES

1.Bennadi D, Self-medication: A current challenge, Journal of basic and clinical pharmacy, 2013;5(1):19. DOI:10.413/0976-0105.128253; PMID:24808684.

2.Ruiz ME, Risks of self-medication practices, Current drug safety,2010; 5(4):315-323. DOI: https://doi.org/10.2174/157488610792245966

3.O'Neil MJ, editor. The Merck Index – An Encyclopedia of Chemicals, Drugs, and Biologicals. 13th Edition, Whitehouse Station, NJ: Merck and Co., Inc., 2001;876

4. Lambert V. Dr. Stewart Adams: 'I tested ibuprofen on my hangover'. The Daily Telegraph. UK.2007.

5.Halford GM, Lordkipanidzé M, Watson SP. 50th anniversary of the discovery of ibuprofen: an interview with Dr Stewart Adams. Platelets. 2012 Sep 1;23(6):415-22. DOI: https://doi.org /10.3109/09537104.H.632032

6.Rainsford KD. Discovery, mechanisms of action and safety of ibuprofen. International journal of clinical practice. Supplement. 2003;(135):3-8. PMID: 12723739

7.FDA Approves Injectable Form of Ibuprofen" (Press release). U.S. Food and Drug Administration (FDA). 11 June 2009

8. Graf E. Ullmann's Encyclopedia of Industrial Chemistry; Fifth Compl. Revis. Edit. Vol.'s A 3 and A 4 Ed's W. Gerhartz (executive), Y. St. Yamamoto (Senior Ed.), FT Campbell, R. Pfefferkorn und JF Rounsaville. VCH Verlagsges. Weinheim 1985, A 3= 578 S., A 4= 584 S., geb., je Band DM 430. DOI: https://doi.org/10.1002/pauz.19870160207

9. Gessner G, Larrañaga MD, Lewis Sr RJ, Lewis RA.Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997; 603.

10.Davies NM. Clinical pharmacokinetics of ibuprofen: the first 30 years. Clinical pharmacokinetics. 1998 Feb;34:101-54. DOI:

https://doi.org/10.2165/00003088-199834020-00002 [PubMed: 9515184]

11. Smyth EM, Grosser T, Wang M, Yu Y, FitzGerald GA. Prostanoids in health and disease. Journal of lipid research. 2009 Apr 1;50:S423-8. DOI:https://doi.org/10.1194/jlr.R800094-JLR200

12. Navar LG, Inscho EW, Majid SA, Imig JD, Harrison-Bernard LM, Mitchell KD. Paracrine regulation of the renal microcirculation. Physiological reviews. 1996 Apr 1;76(2):425-536. DOI: https://doi.org/10.1152/physrev.1996.76.2.425

13. Whelton A, Hamilton CW. Nonsteroidal anti-inflammatory drugs: effects on kidney function. The Journal of Clinical Pharmacology. 1991 Jul;31(7):588-98. DOI: https://doi.org/10.1002/j.1552-4604.1991.tb03743.x

14. Carmichael J, Shankel SW. Effects of nonsteroidal anti-inflammatry drugs on prostaglandins and renal function. Am J Med. 1985;78:992–1000. DOI: https://doi.org/10.1016/0002-9343(85)90223

15.Harirforoosh S, Asghar W, Jamali F. Adverse effects of nonsteroidal antiinflammatory drugs: an update of gastrointestinal, Cardiovascular and renal complications. J Pharm Pharm Sci 2013;16:821-47. DOI: https://doi.org/10.18433/J3VW2F

16. Kim S, Joo KW. Electrolyte and acid-base disturbances associated with non-steroidal anti-inflammatory drugs. Electrolytes & Blood Pressure: E & BP. 2007 Dec 1;5(2):116-25. DOI: https://doi.org/10.5049/EBP.2007.5.2.116

17. Warner TD, Giuliano F, Vojnovic I, Bukasa A, Mitchell JA, Vane JR. Nonsteroid drug selectivities for cyclo-oxygenase-1 rather than cyclo-oxygenase-2 are associated with human gastrointestinal toxicity: a full in vitro analysis. Proc Natl Acad Sci U S A. 1999;96(13):7563–7568. DOI: https://doi.org/10.1073/pnas.96.13.7563

18. Wallace JL. Prostaglandins, NSAIDs, and gastric mucosal protection: why doesn't the stomach digest itself?. Physiological reviews. 2008 Oct;88(4):1547-65. DOI: https://doi.org/10.1152/physrev.00004.2008 [PubMed]

19. Lanas A, Scarpignato C. Microbial flora in NSAID-induced intestinal damage: a role for antibiotics? Digestion. 2006;73(1):136–150. DOI: https://doi.org/10.1159/000089789 [PubMed]

20.Szczeklik A. Mechanism of aspirin-induced asthma. Allergy 1997; 52:613–619. DOI: https://doi.org/10.1111/j.1398-9995.1997.tb01039.x [PubMed]

21.Szczeklik A. The cyclooxygenase theory of aspirin-induced asthma. European Respiratory Journal. 1990; 3:588–593. DOI: 10.1183/09031936.93.03050588 [PubMed]

22. Jenkins C, Costello J, Hodge L. Systematic review of prevalence of aspirin induced asthma and its implications for clinical practice. Bmj. 2004 Feb 19;328(7437):434. DOI: https://doi.org/10.1136/bmj.328.7437.434

23. Hamad AM, Sutcliffe AM, Knox AJ. Aspirin-induced asthma: clinical aspects, pathogenesis and management. Drugs. 2004 Nov;64:2417-32. DOI: https://doi.org/10.2165/00003495-200464210-00004

24. Parnham MJ, Haber VE, Giamarellos-Bourboulis EJ, Perletti G, Verleden GM, Vos R. Azithromycin: mechanisms of action and their relevance for clinical applications. Pharmacology & therapeutics. 2014 Aug 1;143(2):225-45. DOI: https://doi.org/10.1016/j.pharmthera.2014.03.003

25. O'Neill MJ. The Merck Index. An Encyclopedia of Chemicals, Drugs and Biologicals. Whitehouse Station, New Jersey: Merck Research Laboratories, Division of Merck and Co.,2006;154.

26. Greenwood D. Antimicrobial drugs: chronicle of a twentieth century medical triumph. OUP Oxford; 2008 Feb 21.

27. Alapi EM, Fischer J. Table of selected analogue classes. Analogue-based Drug Discovery. 2006 Jan 20:441-552.

28. Hamilton RJ. Tarascon Pocket Pharmacopoeia 2017 deluxe lab-coat edition. Jones & Bartlett Learning; 2016 Dec 9.

29. Krolewiecki A, Leon S, Scott P, Abraham D. Activity of azithromycin against Leishmania major in vitro and in vivo. The American journal of tropical medicine and hygiene. 2002 Sep 1;67(3):273-7. DOI: 10.4269/ajtmh.2002.67.273 PMID: 12408666

30. Koya SF, Ganesh S, Selvaraj S, Wirtz VJ, Galea S, Rockers PC. Consumption of systemic antibiotics in India in 2019. The Lancet Regional Health-Southeast Asia. 2022 Sep 1;4:100025. DOI: https://doi.org/10.1016/j.lansea.2022.100025

31.Hui Li, Ding-Hui Liu et al.Meta-Analysis of the Adverse Effects of Long-Term Azithromycin Use in Patients with Chronic Lung Diseases. Antimicrob Agents Chemother. 2014 Jan; 58(1): 511–517.

32.Osol A., Hoover JE, et al. (eds.). Remington's Pharmaceutical Sciences. 15th ed. Easton, Pennsylvania: Mack Publishing Co., 1975;1140doi.org/10.1016/j.lansea.2022.100025.

33. Tan KR, Magill AJ, Parise ME, Arguin PM. Doxycycline for malaria chemoprophylaxis and treatment: report from the CDC expert meeting on malaria chemoprophylaxis. The American journal of tropical medicine and hygiene. 2011 Apr 4;84(4):517. DOI: 10.4269/ajtmh.2011.10-0285. PMID: 21460003.

34. Ejaz A, Haqnawaz K, Hussain Z, Butt R, Awan ZI, Bux H. Treatment of uncomplicated plasmodium falciparum malaria with quinine-doxycycline combination therapy. JPMA. The Journal of the Pakistan Medical Association. 2007 Oct 1;57(10):502.

35. Nelson ML, Levy SB. The history of the tetracyclines. Annals of the New York Academy of Sciences. 2011 Dec;1241(1):17-32. DOI: https://doi.org/10.1111/j.1749-6632.2011.06354.x

36. Rieckmann KH, Yeo AE, Davis DR, Hutton DC, Wheatley PF, Simpson R. Recent military experience with malaria chemoprophylaxis. Medical journal of Australia. 1993 Apr 5;158:446-.

37. Bott S, Prakash C, McCallum RW. Medication-induced esophageal injury: Survey of the literature. American Journal of Gastroenterology (Springer Nature). 1987;82(8):758–763. [PubMed]

38.Journey JD, Agrawal S, Stern E. Dextromethorphan Toxicity.2022, StatPearls Publishing, Treasure Island (FL). PMID: 30860737

39. Oh S, Agrawal S, Sabir S, Taylor A. Dextromethorphan. StatPearls. StatPearls Publishing, Treasure Island (FL); 2022. PMID: 30855804.

40.Bernshteyn MA, Umair M. Pantoprazole. Treasure Island (FL) StatPearls Publishing.2022. PMID: 29763120.

41. Novotny M, Klimova B, Valis M. PPI long term use: risk of neurological adverse events?. Frontiers in Neurology. 2019 Jan 8;9:1142. DOI:| https://doi.org/10.3389/fneur.2018.01142

42. Eusebi LH, Rabitti S, Artesiani ML, Gelli D, Montagnani M, Zagari RM, Bazzoli F. Proton pump inhibitors: risks of long-term use. Journal of gastroenterology and hepatology. 2017 Jul;32(7):1295-302. DOI: https:/ /doi.org /10.1111/jgh.13737.

43.O'Neil MJ, editor. The Merck index: an encyclopedia of chemicals, drugs, and biologicals. RSC Publishing; 2013;10.

44.National Toxicology Program, Institute of Environmental Health Sciences, National Institutes of Health (NTP). 1992. National Toxicology Program Chemical Repository Database. Research Triangle Park, North Carolina

45.Prescot LF. Paracetamol: past,present,and future.American Journal of Therapeutics,01 mar 2000,7(2):143-147.

46. Przybyła GW, Szychowski KA, Gmiński J. Paracetamol–An old drug with new mechanisms of action. Clinical and Experimental Pharmacology and Physiology. 2021 Jan;48(1):3-19. DOI: https://doi.org/10.1111/1440-1681.13392.

47. Craig DG, Bates CM, Davidson JS, Martin KG, Hayes PC, Simpson KJ. Overdose pattern and outcome in paracetamol-induced acute severe hepatotoxicity. British journal of clinical pharmacology. 2011;71(2):273-82.DOI:https://doi.org/10.1111/j.1365-2125.2010.03819.x

48. Kalsi SS, Dargan PI, Waring WS, Wood DM. A review of the evidence concerning hepatic glutathione depletion and susceptibility to hepatotoxicity after paracetamol overdose. Open Access Emergency Medicine: OAEM. 2011;3:87. DOI: 10.2147/OAEM.S24963. PMID: 27147856

49.Maertens JA. History of the development of azole derivatives. Clinical Microbiology and Infection. 2004;10(1):1-10. https://do.org /10.1111/j.1470-9465.2004.00841.x

50. Tavallaee M, Rad MM. Fixed drug eruption resulting from fluconazole use: a case report. Journal of Medical Case Reports. 2009 Dec;3(1):1-4. DOI: https://doi.org/10.4076/1752-1947-3-7368

51. Berkow EL, Lockhart SR. Fluconazole resistance in Candida species: a current perspective. Infection and drug resistance. 2017 Jul 31:237-45. DOI: https://doi.org /10.2147/IDR.S118892

52. Tytgat GN. Hyoscine butylbromide: a review of its use in the treatment of abdominal cramping and pain. Drugs. 2007;67:1343-57. DOI: https://doi.org/10.2165/00003495-200767090-00007

53. Imaralu JO, Kuti O, Badejoko OO, Loto OM, Olaleye A. Effect of hyoscine butyl-bromide on the duration of active phase of labor: A randomized-controlled trial. Taiwanese Journal of Obstetrics and Gynecology. 2017 Dec 1;56(6):725-30. DOI: https://doi.org/10.1016/j.tjog.2017.10.003

54. Chen GL, Hsu WH. Hyoscine-N-butyl-bromide-induced hypotension and myocardial ischemia. Case Reports in Critical Care. 2013 Jan 28;2013. DOI: https://doi.org/10.1155/2013/414856

55. McClure EW, Daniels RN. Classics in chemical neuroscience: Amitriptyline. ACS chemical neuroscience. 2021 Jan 13;12(3):354-62. DOI: https://doi.org /10.1021/acschemneuro.0c00467

56.Thour A, Marwaha R. Amitriptyline. StatPearls Publishing LLC.Feb 2019; Bookshelf id: NBK537225. PMID:30725910.

57. Kassim T, Haddad TM, Rakhra A, Kabach A, Qurie A, Selim M, Nayfeh AS, Aly A, Holmberg MJ. A case of amitriptyline-induced myocarditis. Cureus. 2018 Jun 19;10(6). DOI: https://doi.org/10.7759/cureus.2840

58. Crome P. Poisoning due to tricyclic antidepressant overdosage: clinical presentation and treatment. Medical toxicology. 1986 Aug;1(4):261-85. DOI: https://doi.org/10.1007/BF03259843

59. Umaharan T, Sivayokan S, Sivansuthan S. Amitriptyline dependence and its associations: a case report and literature review. Case Reports in Psychiatry. 2021 Jan29. DOI: https://doi.org /10.1155/2021/6647952

Source of Support: The author(s) received no financial support for the research, authorship, and/or publication of this article.

Conflict of Interest: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.