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DRUG-DRUG INTERACTIONS

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ABSTRACT

Drug-drug interactions, dietary interactions, and other factors may cause a drug's effect on a person to differ from what is anticipated. Beverages and dietary supplements that person consumes (drug-nutrient/food Interaction) or a different illness the person is suffering from (drug-disease interaction). A when a substance impacts a drug's activity, it is said to be a drug interaction. i.e., the effects change or produce a new impact that neither generates on its own. These interactions could happen by cchanceabuse or a lack of understanding of the relevant substances' active components. Physicians and pharmacists are aware that various meals and medications can interact when consumed together in terms of food-drug interactions might affect the body's capacity to utilize a specific diet or medication, or can result in significant adverse consequences. Interactions between clinically significant drugs that could be harmful alterations in pharmacokinetic, pharmacological, or other factors may affect the patient.or their Pharmacodynamic qualities. Some people might be exploited to the adverse drug events are sometimes caused by drug interactions, however this is less common. As a result, it is recommended that patients adhere to their doctor's and physician's orders.

To achieve the most advantages with the fewest food-drug interactions. The literature survey was carried out by obtaining information from various reviews. And innovative works on general or particular medication and food interactions. This review provides details on the various ways that meals interact with one another.Indrug-drug provide patients with the greatest possible benefit, doctors and pharmacists must carefully choose which medications to prescribe.

KEYWORDS: *Absorption, adverse drug reaction, distribution, drug-drug metabolism, interactions, and excretion.*

INTRODUCTION

Drug-drug interactions (DDIs) are common, expensive, and a major factor in morbidity. Worldwide mortality [1] as well. Only in the United States, DDIs account for 20% of all Unwanted medication effects [2]Many health issues can be treated and resolved with medicines. They must, however, be Taken. Properly to guarantee their effectiveness and safety. Medications need to be very careful. Specific in their effects, predictable in their outcomes for all patients, and never be completely affected by concomitant food or medication, have linear potency, and Contains no hazardous ingredients at any dosage and just needs one dose to provide a long-lasting cure. However, this optimal medication has yet to be found [3].

Numerous medications contain ingredients that interact with the body In various ways. Drug use can occasionally be significantly impacted by diet and lifestyle choices. An instance when substance influences a drug's activity is known as a drug interaction. i.e., the effects are boosted, lowered, or they create a brand-new impact that neither of the previous two produces independently. Usually, drug interactions spring to mind (drug substance interaction). However, interactions between medications and meals are also possible drug-food interactions. In addition to prescription medications and other remedies (drug-herb interactions).these can happen as a result of careless usage or ignorance of the active components In the relevant substances. Inadvertent drug effect reduction or enhancement may result from diet and drug interactions. Some frequently alcohol, used herbs, and fruits can all contribute to the therapy's failure. to significant changes in the patient's health. 90% of clinically significant food-induced variations in the bioavailability of drugs are what lead to food drug Interactions. about the medicine. Some diet (food) medications' significant adverse effects include changes in absorption by fiber-rich, high-protein diets.[4] biological availability is an essential pharmacokinetic factor that is related to the therapeutic impact of most Drugs. However, the impact of food intake on the therapeutic effect of the drug must also be quantified in order to assess the clinical relevance of a food-drug Interaction.

Interactions connected with are the most crucial a high chance of treatment failure brought on by a markedly decreased bioavailability federated state.Chelation frequently results in such interactions. Have food-related components. Moreover, the body's reaction

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to food consumption, Particularly, The bioavailability may be increased or decreased by gastric acid secretion. of particular medications. [5,6] pharmacokinetics can be changed by drug interactions. and/or pharmacodynamics of a drug.

The effects of a drug's Pharmacodynamic interaction may be antagonistic, synergistic, or additive. Drug interactions (Dis) are a significant but underappreciated cause of medication mistakes. The concurrent use of additional medications that,[3] have a wide surface area upon which the drug might be absorbed,[4] bind or chelate,[5] alter stomach pH,[6] alter gastrointestinal motility, or[7] impact transport proteins such as P-glycoprotein, may affect the gastrointestinal absorption of pharmaceuticals. Clinically rarely is a drug's absorption rate reduced alone.whereas a decrease in the amount of absorption will be clinically significant if it causes serum levels that are below therapeutic levels. [7] Extrapolating data from in vitro to the human situation can be challenging since factors such nonspecific binding, atypical kinetics, low effector solubility, as well as varied accessory protein ratios, may affect an enzyme's kinetic activity. [8] Coenzyme Q-10 (CoQ10) is widely taken as a nutritional supplement.

Selection of doctors: We selected participants from a list of more than 25,000 PCPs that was nationally representative. Medical association workforce databases and list serves, hospital organization physician rosters, and participants of national medical conferences were some of the resources used to construct the recruitment lists. We invited randomly chosen physicians from the assembled list between may and July 2018. A physician questionnaire of 20 questions was used to assess the participants' eligibility. Up till 330 doctors were included in the study sample, doctors who met the eligibility requirements were invited to take part.because it is acknowledged by the general people as a crucial component for sustaining human health. P-glycoprotein (P-gap), an intestinal efflux transporter, is hampered by it as a result, drug-food interactions occur.[9] drug and natural product interactions is a typical concealed issue seen in clinical practices. The exchanges the same pharmacokinetic principle underlie both natural compounds and pharmaceutical. principles of pharmacodynamics as they relate to medication Interaction agents that have recently been discovered to alter drug-metabolizing enzymes.[10]
The most well-known example is grapefruit, but other fruits like star fruit, pomelo, and civilian oranges all contain substances that inhibit CYP3A4, the most significant enzyme in drug metabolism[11].

EVALUATION AND IDENTIFICATION OF DRUG-DRUG INTERACTION

Material and procedures

From May to July 2018, we conducted a prospective, cross-sectional research of DDI preventive care practices among PCPs working in the US. Board-certified family and internal medicine doctors treated identical simulated patients known as Clinical Performance and Value (CPV®) vignettes as we assessed their DDI screening, workup,and care recommendations.

Ethics

This research complied with ethical guidelines, was authorized by theAdjaraInstitutional Review Board in Columbia, Maryland, and was registeredwith clinicaltrials.gov (NCT03581994). All participants gave their informed consent.

Selection of doctors

We selected participants from a list of more than 25,000 PCPs that was nationally representative. Medical association workforce databases and list serves, hospital organization physician rosters, and participants of national medical conferences were some of the resources used to construct the recruitment lists. We invited randomly chosen physicians from the assembled list between may and July 2018. A physician questionnaire of 20 questions was used to assess the participants' eligibility. Up till 330 doctors were included in the study sample, doctors who met the eligibility requirements were invited to take part.

Physicians must treat patients

They would in an office environment in order to provide for their needs in Clinical Performance and Value vignettes: simulated patients [12] By using the technology, doctors can simulate a real patient visit by asking questions, reviewing medical records, and ordering tests and procedures in the lab. the five domains of care for open-ended questions in the CPVs are as follows: Taking a history, having a physical exam, ordering a diagnostic test, and 4) Establishing a diagnosis, followed by 5) a treatment strategy and follow-up. Between 49 and 72 evidence-based criteria are reviewed for each instance. Two doctors separately scored each case using clear, predetermined criteria, with a third doctor making decisions in the event of a tie on any one of the particular criteria. Thus, a score between 0% and 100% is assigned to each domain as well as the overall performance. a clear measurement of clinical practice variance is provided by CPV vignettes, whichaccount for case-mix variation because all doctors are treating the same patients.

Evaluation of current DDI

Evaluationprocedures and identification of challenges and potential for DDI prevention in the primary care environment were the main outcomes of the analysis. In more detail, we sought to: 1) ascertain the frequency with which PCPs were able to recognize, classify, and treat DDIs in simulated CPV patients; and 2) assess the influence of provider characteristics (e.g., age, gender, practice setting) and clinical practice characteristics (e.g., inquiring about medication history, ordering a presumptive or definitive

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drug test) on the likelihood of DDI diagnosis and treatment. For studies involving binary outcome variables (such as diagnosing a DDI), chi-squared tests and logistic regression modelling were employed; for analyses involving continuous outcomes, t-tests and linear regression modelling were utilized (e.g., diagnosis-treatment score).

MECHANISM OF DRUG-DRUG INTERACTION

Two part of mechanism of action

- Pharmacokinetics interaction
- Pharmacodynamicsinteraction

Pharmacokinetic Interaction

In this interaction, drug affect the absorption, distribution, metabolism and elimination of drug.

IN thisinteraction, one agent altering the absorption, distribution. If there is delaying in the absorption of drug then there is decrease in plasma concentration level, reducing effect or sometime prolonged the onset of action variables involved in alteration of absorption are follows[**13**]

- **ABSORPTION**

1. Alteration gastrointestinal absorption
    - Complexation.
    - Altered gastric PH.
    - Food.
    - GIT flora.
    - Inhibition of GI enzyme.
    - Complexation/chelation/Adsorption:
      Example of alteration in absorption process by Complexation formation are chelation between antacids and tetracycline, tetracycline with metals.
    - Altered GT Transit/emptying:

Absorption of drugs also affected by alteration in GI Transit or emptying rate. the drugs which affecting the GI Transit time administered with other influences the absorption process.Ex. Administration of acetaminophen with anticholinergics delay in absorption process of acetaminophen.

- Altered Gastric PH

Non-ionized drugs get more readily absorbed than ionized drug.in acidic environment of stomach, acidic drugs are available in the form of non-ionized state so, it rapidly absorbed while in alkaline environment (intestine) acidic drug become ionized and the further absorption get reduced basic drugs in contrast and these are readily absorbed from the gastrointestinal tract than from the stomach.the drugs that alter the PH of DIT may modify the absorption of subsequently administered drugs.

Ex. Administration of H2 blocker along with ketoconazole'sdecrease the dissolution rate of ketoconazole resulting in reduced absorption.

- Food

In stomach, presence of food influence the absorption of number of drugs.

The food also reduces the absorption of drug by binding with it or by changing the PH of GI content or changing dissolution rate of drugs.

Presence of food in stomach reduces the absorption of penicillin, erythromycin, rifampicin.

So, it recommended that antibiotics should be given at least two hours after or one hour before the meal to achieve optimum absorption.

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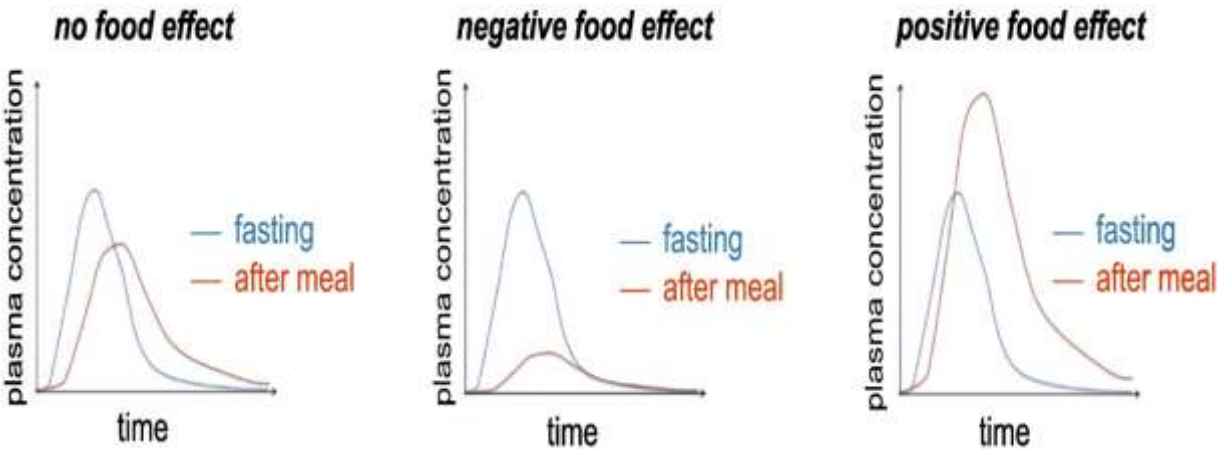

- Gastrointestinal flora

Certain antibiotics may enhance the response of anticoagulants by altering thegastrointestinal flora and thus interfering with vitamin k synthesis and results to alter in the efficiency of anticoagulant.

Inhibition of GI Enzyme:

The absorption of certain drugs depends on their metabolism by the enzyme.If these enzymes are inhibited then the absorption of drugs also decreases.Ex. Administration of folic acid along with phenytoin decrease the absorption of folic acid In the diet folic acid is present in the formula of polyglutamate which is poorly soluble.

1. Alteration in distribution:

Interactionsin plasma protein binding:

These types of interactions are more significant when the two drugs are capable of binding to similar site on the protein. The drug which has greater affinity for binding positions will dislocate the other from plasma protein.

Ex. In administration of phenytoin along with valproic acid protein binding of valproic acid is reduced and total steady state concentration.

2. Alteration in hepatic metabolism:

(A)Induction of metabolism

One drug enhances the metabolism of other drug usually by stimulating the production of the hepatic enzyme involved in drug metabolism. Due to enzyme induction may cause rapid metabolism of drug resulted to decrease in pharmacological action of a subsequent drug.Ex. When phenobarbital administered with warfarin there is increase in the metabolism of warfarin resulting in reduced anticoagulant.

(B)Inhibition of metabolism:

A drug that inhabits the microsomal enzyme production may raise the blood level of drug resulted to increase drug effect and longer duration of action .

Ex. When cimetidine administered with theophylline cimetidine increases the plasmaconcentration of theophylline results in increased in adverse effect.

3. Alteration in renal clearance of dioxin:

A)Increased in renal blood flow:

Drug which increases the rate of clearance increases the excretion of another drug.

Ex. When hydralazine administered with dioxin, there is increase the renal clearance of dioxin.

B) Decreased renal blood flow:

Drug which decreases the rate of renal clearance decreases the excretion of other drug results in risk of toxic effects.

Ex. When NSAIDS Administered with lithium ,NSAIDS decrease clearance of lithium results in increased in risk of toxicity.

C) Inhibition of active tubular secretion:

When penicillin/Nalidixic acid/methotrexate/Dispone administered with preboned, probenecid prolonged the half-life of penicillin and other drugs by increasing the plasma concentration thus allowing single dose therapy for preventing toxic reaction.

D) Alteration in tubular reabsorption affected the renal clearance process.

Ex. When antacids administered with aspirin there is reduction in the reabsorption of salicylate from tubules through increased in PH urine.

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Drug Distribution

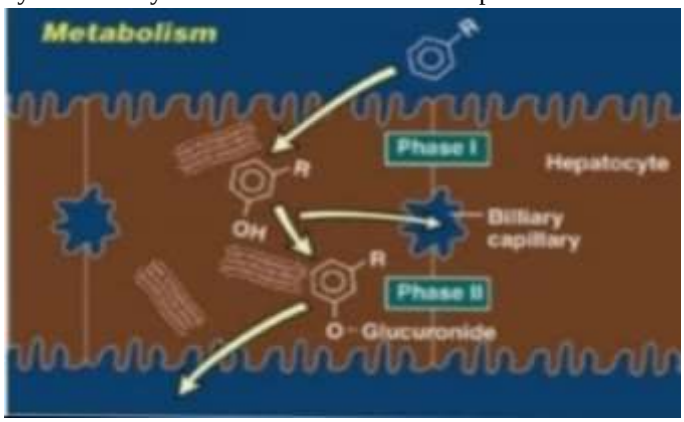
Drugs are delivered to a location for use or disposal. Serum proteins-bound. Basic medicines are bound to a-acid Glycoprotein, while acidic drugs are linked to plasma albumin [14]. The medication is pharmacologically inert while attached to a plasma protein because it cannot be filtered by the kidney and does not affect the concentration gradient. the medication is pharmacologically active when it is unbound or "free. The pharmacokinetics of bound medicines may be affected if albumin levels in the serum are reduced. A drug with a high affinity for binding may displace a molecule with a lower affinity, raising the free concentration of the drug with the lower affinity. However, the unbound portion of the drug is more readily available for both removal and the site of action. Using this rule has frequently been applied to medications with a narrow therapeutic index (490%) and high protein binding (490%) levels, where modest changes in free drug concentration could have a big impact on pharmacological effects.

Generally speaking, protein-binding displacement interactions do not result in clinically significant modifications of drug response [15,16] with the exception of situations where the displacing medication may also lessen the substrate drug's rate of elimination.Interactions between methotrexate and non-steroidal anti-inflammatory medicines (NSAIDs) are a good illustration of this idea. Different NSAIDs have an impact on the pharmacokinetics of methotrexate. Ibuprofen, for instance, may reduce the clearance of methotrexate by 40–50% [17], perhaps by lowering renal perfusion as a result of a reduction in renal prostaglandin synthesis (18).

Break Down Of Medication

Research in the field of biotransformation, sometimes referred to as metabolism, is expanding. Recent research suggests that metabolic pathways are involved in the majority of clinically significant medication interactions. The majority of medications leave the body via being chemically changed into a less lipid-soluble substance, at least in part. They are expelled by the kidney or in bile and are not reabsorbed across a lipid membrane. The majority of metabolism happens in the smooth endoplasmic reticulum of the hepatocyte, while it also takes place in the plasma, intestines, lungs, and skin.

Briefly, there are two phases to metabolism. The oxidation, hydrolysis, or reduction of a medication are all part of phase I metabolism. These processes make the drugs more water soluble and make it easier for the body to get rid of them. Stage Il Metabolism necessitates the joining of an additional adding a chemical to the medication to produce an inactive chemical and a medication that is more water soluble. Stage II Glutathione conjugation, sulfation, acetylation, and methylation are among the processes. The hepatic CYP is the enzyme responsible for this reaction's catalysis. Iron, heme, and a protein complex make up CYP. NADPH and molecular oxygen are used.Using (a reduced version of NADP) as an electron source, this a number of oxidations are catalyzed by the cytochrome system.Oxidised medication is produced as a result of reduction processes. the item



[19]. Even

Phase 1 and 2 metabolism

if there are over 50 differentJust three families of enzymes have been found. the CYP1, CYP2, and CYP3 enzymes are in charge of the most substances, including steroid metabolism, prostaglandins, vitamins, other Drugs form endogenous substances, and numerous medications.

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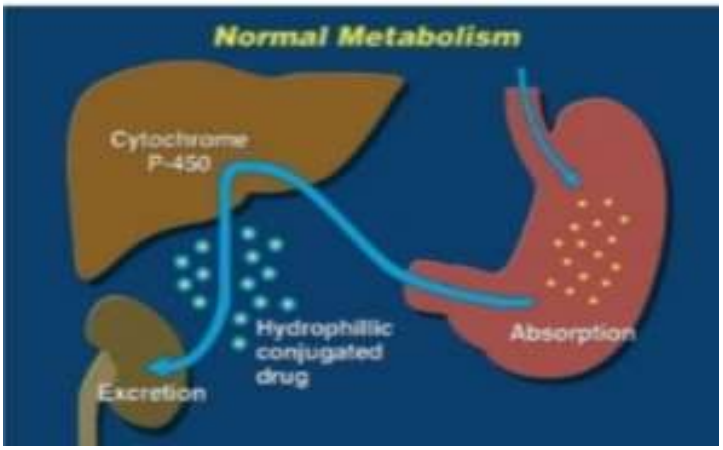


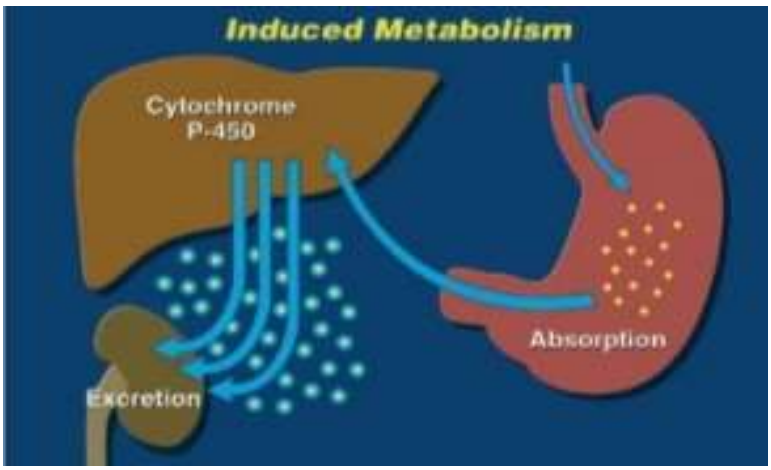
Normal metabolism

Used in dentistry: Depending on whether an enzyme is induced or inhibited, the rate of drug metabolism may be increased or decreased. Following prolonged exposure to an inducing substance, enhanced gene transcription typically results in the induction of drug metabolism As a result, the effects of enzyme induction might not manifest completely right away. An accelerated rate of metabolism, improved oral first-pass metabolism, and a decreased bioavailability are the results of enzyme induction. As a result of everything, the drug's plasma concentration falls. Contrarily, medications that are digested into an active or harmful Increased impact or increased toxicity may be linked to metabolite induction. An established and well-known case of enzyme induction involves the use of oral contraceptives with the medication rifampin (OCs). A powerful metabolic inducer of CYP, rifampin is an antibiotic used to treat tuberculosis. Due to the OC's altered metabolism, contraception may fail [20]. The barbiturates, phenytoin, and carbamazepine are further common CYP inducers. Drug-metabolizing inhibition results in a decrease in the drug's metabolite and an increase in the plasma concentration of the parent drug, which has a more pronounced, lasting pharmacological impacts.

Drug Excretion

Kidney is the main organ involved in removing substances from the body, just as the liver is the main organ involved in drug metabolism. The liver, lungs, digestive tract, saliva, sweat, tears, and breast milk are additional locations where drugs can be excreted. Changes in urine pH, which can affect a drug's passive reabsorption, competition for the same transport route, variations in active tubular secretion, or changes in renal blood flow are just a few of the mechanisms that might cause changes in renal excretion. The rate of urinary excretion of weak bases increases as a result of acidification of the urine.

Induced metabolism



Pharmacodynamics Interaction

A)Combinations of drugs are frequently used as therapeutic advantages because of their additive or synergistic beneficial effects. These combinations are categorized as either beneficial or harmful interactions based on their effects. a drug with comparable or connected biological effects synergistic effects are produced by drugs that operate at the same place or that affect the same

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physiological system. due to the usage of drugs with identical pharmacological effects, there are excessive pharmacological effects. drug with adverse pharmacological effects.

(B)The usage of two medications with pharmacologically distinct effects results in the interaction. These results are a result of a certain drug's side effects. For instance, an anti-diuretic drug.

C) Interaction at receptor site: When drugs are administered, they bind to specific regions of the receptor site and produce the effects that are observed. These interactions can occur at the same receptors or at different receptors that are located at physiologically related sites. both the opioid morphine and the medicine naltrexone work on the same receptor location when administered, but naltrexone blocks some of the effects of morphine, namely respiratory desorption.

D) Electrolyte level changes:

When adding a drug to a therapy regimen and changing the electrolyte level, it's critical to monitor the results.For instance, thiazide diuretics can lead to severe potassium loss.

The origins of unintended medication interactions [21]

- Mistaken medication selection.
- Not accounting for renal function.
- Inadequate dose.
- The incorrect administration method.
- Incorrect medication administration.
- Transmission mistakes

Managing Drug Interactions

Avoiding Concomitant Therapy; Changing the Main Drug's Dose

- Altering the timing of two drug intakes.
- Observation of combined therapies when employed.
- It's crucial to inform the patient about possible interactions.
- To find interactions, advanced screening procedures must be applied.[22]

TYPES OF INTERACTIONS

Drug interactions can take many different forms, so be cautious. Let's investigate each of them in more detail.

- **Drug-drug**

When two or more prescription drugs interact, it is known as a drug-drug response. One illustration is the interaction between fluconazole (Dipluran), an antifungal drug, and warfarin (Coumadin), an anticoagulant (blood thinner). Combining these two medications can increase bleeding to potentially severe levels.

- **Non-prescription medication:**

Treatment this is an interaction between a drug and one or more over-the-counter medications. These include herbal remedies, vitamins, supplements, and over-the-counter (OTC) drugs. Ibuprofen and a diuretic, a medication used to help the body get rid of excess water and salt, can interact in this way (Advil). Because ibuprofen frequently causes the body to retain salt and fluid, it may lessen the effectiveness of the diuretic. Both prescription and over-the-counter diuretics are available.

- **Drug food introduction:**

This occurs when consuming food or beverages changes how a medicine behaves. For instance, there may be an interaction between different statins and grapefruit juice. You run the risk of overdosing and developing liver or kidney failure if you drink a lot of grapefruit juice while taking one of these statins. Rhabdomyolysis is a potential adverse reaction to the statin-grapefruit juice combo. A protein known as myoglobin is released into the blood as skeletal muscle degrades. Myoglobin may potentially harm the kidneys.

- **Drug-alcohol:**

Some medicines should not be taken with alcohol, according to a reliable source. Combining these substances with alcohol frequently results in fatigue and slower reflexes. Additionally, it may raise your risk of unpleasant side effects. For instance, taking metronidazole and drinking alcohol at the same time can result in stomach pain, vomiting, and Trusted Source flushing. Antibiotic metronidazole is widely used.

- **Drug-disease interaction:**

This occurs when the usage of a drug changes or exacerbates an ailment or disease. Additionally, various medical conditions can raise the possibility of adverse medication reactions. For illustration, several decongestants that individuals use to treat colds might raise bloodHigh blood pressure sufferers should avoid using these products (hypertension). metformin, a medication used to treat diabetes, and renal problems are another example. Those who metformin dosages should be reduced or avoided in people with renal disease. ThisIs as a result of metformin's ability to build up in the kidneys of those who have this condition, the likelihood of serious adverse effects increasing.

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- **Drug-laboratory:**

Some drugs can affect the results of certain lab tests. Test findings may be inaccurate as a result of this. Tricyclic antidepressants, for instance, have been demonstrated toInterfere with skin prick tests needed to identify some diseasesallergies

DRUG INTERACTIONS EXAMPLES

1. Fluconazole with Simvastatin

Some CYP450 enzymes are prevented from operating normally by the fluconazole (Dipluran) medication. due to this modification, interactions with fluconazole are frequent. Fluconazole is one instance. simvastatin (Zocor), a cholesterol-lowering drug, induces an increase in blood levels of the drug. Because of simvastatin side effects more probable.

2. Dofetilide and Ondansetron

Zofran, a medication that contains ondansetron, is used to treat nausea and vomiting. However, it has a variety of possible interactions. The heart's beat is one illustration. dofetilide medicine (Tikosyn). Both drugs have the potential to prolong the period of time among heartbeats. This time can become excessive when used collectively. This could lead to fainting, dizziness, and in severe cases, even death. This conversation typically involves more severe when ondansetron is administered intravenously.

3.Digoxin (Lanoxin) and amiodarone

Digoxin is a heart medication. It is regarded as a limited therapeutic medicine for an index (NTI). This implies that even a small variation in its dosage could result in major issues Digoxin may be susceptible to medication interactions as a result.another heart drug called amiodarone (Pacerone) may interact with how much digoxin is absorbed into the circulation. This may result in effects that require more digoxin than usual.

4.WarfarinandBactrim

Some antibiotics, like Bactrim (sulfamethoxazole/trimethoprim), can make bleeding more likely. Interactions with blood thinners like warfarin may result from this.(Jantoven, Coumadin). when coupled with Bactrim, there is an increased risk of severe bleeding.

5.Omeprazole and levothyroxine

Levothyroxine (Synthroid), a medication for the thyroid, is another example of an NTI drug. Consequently, you must be cautious of any drugs that can have an impact on howit operates. Omeprazole (Prilosec) treats heartburn by reducing stomach acid production. heartburn. however, it may decrease levothyroxine's absorption, which would reduce its effectiveness.

6.Quinolones with Theophylline

Patients with asthma and other respiratory diseases often find relief using theophylline. nowadays, less people utilize it because there are better alternatives available. medications. antibiotics called quinolones are used to treat urinary tract infections.(UTIs) and other infections. Ciprofloxacin and ofloxacin are a few examples. sparfloxacin as well as norfloxacin.Quinolones interfere with theophylline's metabolism, which raises the drug's blood levels and raises the risk of the drug's toxicity as well as seizures.

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7. Sulfa drugs and warfarin

Warfarin: It's an oral anticoagulant that's used to stop blood clots from forming.Antibiotics with the sulfa class: These drugs are used to treat bacterial infections. I examplesInclude sulfisoxazole and sulfamethoxazoleSulfa medications and warfarin interact enhancing the effects of the former.

8. Phenytoin and Warfarin

Warfarin: It's an oral anticoagulant that's used to stop blood clots from forming. phenytoin: used to treat seizures and as an anti-convulsant. Warfarin's effects may be intensified by phenytoin, and vice versa. can raise phenytoin levels in the blood.

9. Macrolides and Warfarin

To stop blood clots from forming, people take warfarin, an oral anticoagulant. antibiotics called macrolides are commonly used to treat bacterial infections. examples azithromycin, clarithromycin, and erythromycin are some examples. warfarin's metabolism and clearance are reduced by macrolides, which has the effectOfthe effects of warfarin, such as bleeding, are increased.

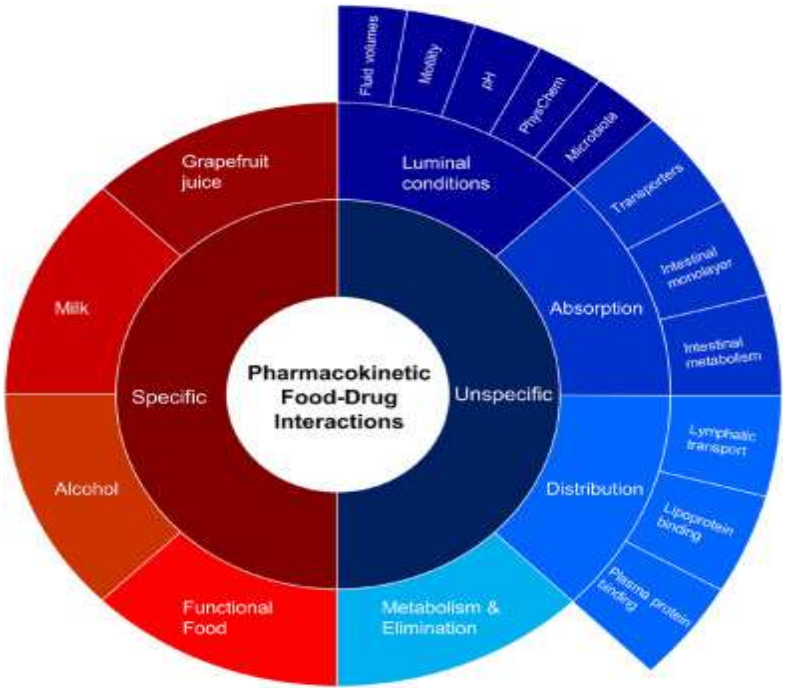
10. Verapamil and digoxin

Digoxin: When there is a disturbance in cardiac rhythm, it is used to treat congestive
heart failure and to reduce the heart rate. high blood pressure is treated with verapamil. the heart rate is slowed by it. verapamil may reduce the clearance of digoxin, resulting in higher levels. and possible toxicity of digoxin in the body. Digoxin with verapamil consumption may cause the heart to beat more slowly than necessary.

MECHANISM OF ACTION OF DRUG-FOOD INTERACTION

1.Interaction involving Absorption:

Due to changes in gastric pH and gastric acid production, many commonly used drugs may not be absorbed as well when food is



present in the stomach. motility, secretion, and of course GITtransit time. As an illustration, azithromycin taking it with food reduces absorption, which has a considerablenegative impact on the body's metabolic rate. a decrease in bioavailability of the food's nutrients, including calcium. the medicine and the anison may combine to generate complexes that are less readily absorbed. On the on the other hand, meals may improve the bioavailability of several medications (Fehr, 1998).

PHARMACOKINETIC INTERACTION

1.Interaction involving Absorption

Presence of food in the stomach may affect the absorption of many commonly used drugs, due to alteration of gastric pH, gastricsecretion, and motility and of course transit time of the GIT. For instance, azithromycin absorption is Decreased when it is taken with food, resulting in significant reduction in bioavailability. [**23**], the components of the food, such as calciumorison, may form complexes with the drug that are less easily absorbed. On the other hand, the bioavailability of some drugs may be enhanced by food (Fehr, 1998).

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2.Interactions With regard to distributions

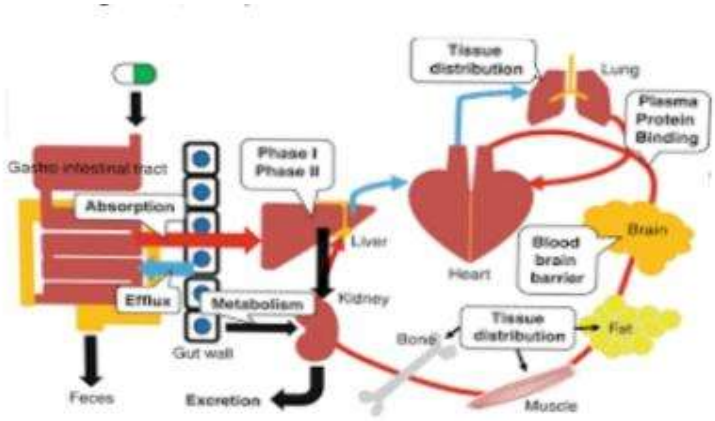
The blood or plasma concentrations of a medicine once it is in the systemic circulation depend on how widely it is transported to extravascular locations. The amount of drugs in the overall drug concentrations in the blood are represented by whole blood. the amount of drug molecules in the plasma is unaffected by their sequestration in red or white blood cells. Red blood cells. In general, unless the drug is preferentially sequestered by red blood cells, the quantities in the blood and plasma are believed to be equal. Whether a medicine can passively spread across tissue or organs will depend on the flow of blood through those areas. the amount to which cell membranes serve as a substrate for active uptake or efflux transporters binding to tissue and plasma protein sites.

3.Interaction involving Metabolism

Many drugs undergo hepatic metabolism, which can occasionally interact with food. For instance, when provided along with the hypertension medications felodipine and nifedipine, concentrated grape fruit juice increases the bioavailability of both. It is hypothesized that flavonoid components in grapefruit juice concentrate prevent felodipine nifedipine from being metabolised by cytochrome P-450. This interaction might make a substance more hazardous and effective.nifedipine felodipine. This interaction might make these medications more harmful and effective at the same time. Citrus fruit or its juice is frequently used in morning foods, therefore it has enormous clinical significance. Patients need to be made aware of this potential interaction (Fehr, 1998).

4.Excretion-related interactions

A number of food ingredients may change the pH of urine, which ultimately results in a decrease or increase in the patient's drug intake. Due to diets like these, acidic urine will have a longer half-life of acidic medications. meats, fish, cheese, and eggs), as long as the medication is still in its unionised form in an acidic medium. form and half-life of an acidic medication in an alkaline environment.



DIAGRAMMATIC SUMMARY OF DRUG -FOOD INTERACTION (ABSORPTION DISTRIBUTION, METABOLISM, EXCRETION).

Pharmacodynamic Interactions

Foods and medicines may change the pharmacologic effects of each other. Vitamin K-rich diets may impair the therapeutic efficacy of warfarin and produce antagonism. of the clotting agent. Among the foods high in vitamin K are green leafy vegetables.(Brussels sprouts, broccoli, spinach, kale, and turnip greens), cauliflower, chickpeas, liver, liver, and green tea.

Alcohol may enhance the effects of medications that slow the central nervous system, such as benzodiazepines, antihistamines, and Modes: o Narcotics, muscle relaxants, antipsychotics, antidepressants, or any medication with sedative properties (Booth, et al 1997). Coffee is an illustration of a meal that can enhance the effects of a drug because caffeine interacts with theophylline in a variety of ways. Caffeine has reportedly enhanced theophylline levels in the blood. Levels by 20% to 30% and lengthened theophylline's half-life by reducing clearance. Patients may express anxiety, trembling, or sleeplessness.

Caffeine has some bronchodilator effects, which may enhance.drugs with sedative effects include opioids, muscle relaxants, antidepressants, antipsychotics, and antipsychotics (Booth, et al 1997). Coffee is an illustration of a meal that can enhance the effects of a drug because caffeine interacts with theophylline in a variety of ways. There have been reported that caffeine boosted theophylline levels in the blood by 20%–30%. and decreased elimination, which lengthened theophylline's half-life. Patients mightcomplain of trembling, anxiety, or insomnia. There are some bronchodilator effects of caffeine. Which could improve.

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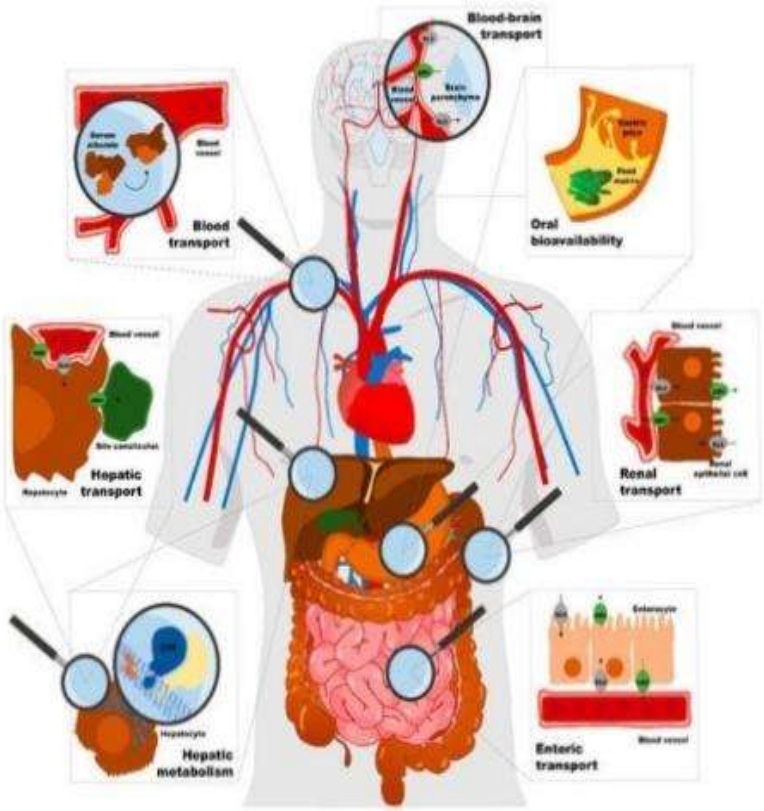

DIAGRAM DRUG-FOOD PHARMACODYNAMICS INTERACTION

EXAMPLES OF HOW FOOD AND DRUGS INTERACT.

1.Grapefruit and Atorvastatin

A cholesterol-lowering drug called atorvastatin (Lipitor) is broken down and eliminated from the by certain CYP450 enzymes in your body. Oranges and orange juice can prevent these the same CYP450 enzymes, which can increase your body's atorvastatin levels. This can make side effects more likely.

2.Leafy greens and warfarin

Warfarin functions by obstructing vitamin K's effects. Blood clots are influenced by vitamin K is abundant in leafy green vegetables, which can partially reverse the effects of warfarin. Finding a balance between the two is crucial. You must be constant in your approach. you consume a lot of leafy greens while taking warfarin.

3. Dairy and minocycline

Dairy products like milk and yoghurt can interact with certain antibiotics, including minocycline (Minocin). The amount of minocycline that is absorbed by your body can be decreased by dairy items. Minocycline should be taken either one hour before or two hours after consuming dairy products.

4.Alcohol and metformin

Alcohol and the diabetes drug metformin both increase the level of lactic acid in your blood.

Lactic acidosis is an uncommon but serious condition that can result from this. every now and then, having one or two drinks should be OK. But it's advisable to refrain from drinking.

5.Age-related meats and MAOIs

You can prevent your body from breaking down a protein called tyramine by taking a monoamine oxidase inhibitor (MAOI), such as selegiline (Emsam) or phenelzine (Nardil). aged meats, including tyramine levels are high in foods like salami and sausage. A body with too much tyramine can blood pressure to spike suddenly, which can be harmful. To keep away from this if you're taking an MAOI, you should consume a low-tyramine diet.

CONCLUSION

Elderly patients' prescriptions had more than five possible drug-drug interactions on average. By employing substitute drugs or congeners that are not linked to drug interactions, it would be simple to prevent the small percentage of drug interactions that belonged to risk category X (i.e., to be avoided drug combination). The two factors that were found to be predictive of probable drug interactions were increasing age and polypharmacy.

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