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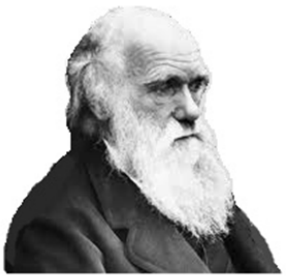

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A review on drug-diet interaction

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ABSTRACT

Food-drug interactions can have a significant impact on the efficacy of pharmacological treatment and the adverse effect profiles of many treatments. Interactions are not necessarily harmful to therapy, but they can be employed to promote drug absorption or reduce side effects in some circumstances. Drug interactions with grapefruit juice, in particular, have gotten a lot of attention recently. As new drugs are approved at a faster rate, there is less information accessible concerning their side effects and interactions once they hit the market. The use of herbal medicines and dietary supplements is a second source of worry. These items are not subjected to rigorous testing and may contain little or no of the ingredient listed on the label. Some of the herbs utilized have the potential to interact negatively with prescription medications. Mahuang (ephedra) and fever few are two noteworthy examples. Mahuang is a stimulant that can lead to hypertension in those who are on monoamine oxidase inhibitors. Fever fever has anticoagulant qualities that can help warfarin work better. The majority of food-drug interactions occur due to one of three mechanisms: decreased absorption rate or extent, enhanced absorption rate or extent, or chemical/pharmacologic effects. Acid-labile medicines, such as penicillin G, ampicillin, and dicloxacillin, are destroyed when there is an increase in stomach acid. In other circumstances, dietary components like calcium or iron may create compounds with the medicine that make it harder to absorb. Tetracycline, sodium fluoride, and ciprofloxacin are some examples. Food, calcium, and practically everything, including orange juice and coffee, interfere with lendronate absorption. The exact process through which food interferes with absorption is unknown in many circumstances. The area under the curve (AUC) may be comparable regardless of how the drug is administered; delayed absorption does not always diminish total overall exposure to the drug.

***Keywords*:** Drugs, Diet, Interaction, pharmaceuticals

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1. INTRODUCTION

Many health disorders can be treated and cured with the use of drugs. They must, however, be taken correctly to guarantee that they are both safe and effective. Patients may be unaware that otherwise healthful foods might have serious side effects when combined with certain medications. Prescriptions should have extremely specific effects, have the same predictable impact for all patients, never be altered by contemporaneous food or other medications, have linear potency, be completely non-toxic at whatever dosage, and only take a single dose to achieve a lasting cure. This ideal medicine, however, has yet to be discovered [1]. Many pharmaceuticals contain potent substances that interact with the human body in a variety of ways. Diet and lifestyle decisions can have a significant impact on the effectiveness of drugs. A drug interaction happens when a substance changes the activity of a drug, causing the effects to be heightened or diminished, or providing a new effect that neither of the medications would produce on their own. The first thing that springs to mind is generally drug interactions (drug-drug interaction). Drug-food interactions (drug-food interactions) and drug-herb interactions (drug-herb interactions) are also possible [2]. Depending on whether the drug interacts with another drug (drug-drug interaction), food, beverages, or dietary supplements (drug-food/drug-supplement interaction), or another ailment a person has, the effect of the medicine may differ (drug-disease interaction). Contrary to the ease with which information on drug-drug interactions is readily available, information on drug-food interactions is not always readily available [3].

Drug interactions include any changes in the pharmacokinetics or pharmacodynamics of drug substances caused by food, medications, dietary supplements, or beverages such as juices or alcohol. Polypharmacy and self-medication have led to inappropriate pharmaceutical use by increasing the risk of interactions with food and other medicines [4]. A nutrient is a chemical that is required for the growth and maintenance of cells in living beings [5]. It's worth noting that food and nutrition can have an impact on a patient's treatment response, with various degrees of significance. Though interactions can be beneficial in some situations, such as reducing side effects or increasing treatment efficacy, they can also lead to therapeutic failure [6]. Food-induced variations in medication bioavailability cause the bulk of clinically important food-drug interactions [7]. To better educate patients who self-medicate with OTC and prescription medications, health care practitioners must be aware of drug-food interactions. Health care providers must also devise techniques for detecting and preventing the negative consequences of these interactions. Those with a high probability of therapy failure due to low bioavailability are the most critical.

2. FOODS

Any material taken to give nutritional support for an organism is referred to as food. It mainly comes from a plant or animal and contains vital nutrients such carbohydrates, lipids, proteins, vitamins, and minerals. To supply energy, support life, or drive growth, the material is eaten by an organism and ingested by the organism's cell. Humans have traditionally obtained food through two methods: hunting and gathering and cultivation [7]. Food intake in conjunction to drug delivery could have a big impact on drug absorption and dissolution. The presence of food in the presence of a medicine increases stomach motility, changes

gastrointestinal pH, and provides components for chelation and absorption [5]. When there is food in the stomach, medications are often taken more slowly; nevertheless, there is a distinction to be made between slowed rate of absorption and decreased amount of drugs ingested. Reduced absorption rate allows for increased nutritional interaction, which may delay therapeutic efficacy without affecting the drug's overall bioavailability. Chelation with components in food, dairy products, or direct interaction with certain food components produce the majority of interactions resulting from drastically reduced bioavailability [7].

The interaction of aspirin with meals is an example of a nutrient delaying the commencement of activity without affecting bioavailability. When compared to placebo, it was revealed that nearly halved the serum salicylate level 10 and 20 minutes after a 650 mg dose in a trial of 25 participants [8]. The aspirin is absorbed into the meal, which causes a delay in gastric emptying, however this may be beneficial in some cases. Cimetidine, on the other hand, is frequently administered with food to help promote therapeutic blood contraction. With the presence of food, a portion of it is absorbed, allowing the remaining drug to be dissolved once the gut is cleansed. This ensures that therapeutic levels are maintained during the course of the dosage interval [9]. By binding with calcium in milk, dairy products including milk, yoghurt, and cheese can interfere with drugs like tetracycline, doxycycline, and ciproflaxin, generating an insoluble substance in the stomach and upper intestine that the body is unable to absorb. Other foods, such as pickled, cued, and fermented foods, may dangerously raise blood pressure in patients taking monoamine oxidase inhibitors and certain Parkinson's disease medications, while vitamin-rich foods may cause anticoagulant effects in patients taking warfarin who eat kale, spinach, and other leafy greens [10].

2. 1. Sources of food

Food comes from both plant and animal sources. Plants provide the majority of food, and some food is taken straight from plants; nevertheless, even animals employed as food sources are raised by feeding them plant-based food [11]. Many plants and plant parts are consumed as food, and over 2,000 plant species are cultivated for this purpose. There are various cultivars of several of these species. Plant seeds are a good source of nourishment for animals, including humans, because they contain the nutrients required for a plant's initial growth, as well as numerous beneficial fats like omega fats. In reality, seed-based foods account for the majority of human food consumption. Edible seeds include grains such as corn, wheat, rice, and others, as well as legumes such as beans, peas, lentils, and nuts [12]. Vegetables are a form of plant materials that is frequently consumed as food. This comprises root vegetables such as potatoes and carrots, bulbs such as onions, leaves such as spinach and lettuce, and stem vegetables such as bamboo shoots and asparagus. Animals are either directly or indirectly used as food via the items they produce. Meat is an example of a direct product that derives from an animal's systems or organs. Animal-derived foods include milk from the mammary gland, which is consumed or processed into dairy products such as cheese and butter in many cultures. Bees create honey, a reduced nectar from flower, which is a favorite sweetener in many cultures, and birds and other animals hatch eggs, which are widely consumed [13].

2. 2. Nutrients

A nutrient is a material that an organism needs in order to survive, grow, and reproduce. Animals, plants, fungi, and protists are all required to consume dietary nutrients. Nutrients can

either be incorporated into cells for metabolic reasons or expelled by cells to form non-cellular structures like hair, scales, feathers, or exoskeletons. Some nutrients, such as carbohydrates, lipids, proteins, and fermentation products (ethanol and vinegar), can be metabolically reduced to smaller molecules in the process of generating energy, resulting in a water and carbon dioxide end product. Water is essential for all living things. Energy sources, some amino acids that are combined to produce proteins, a subset of fatty acids, vitamins, and some minerals are all essential nutrients for mammals. Essential nutrients are vary for different sorts of organisms. Humans and certain other species require adequate levels of ascorbic acid (vitamin C), but not all animals and plants are able to manufacture it [14].

Organic and inorganic nutrients are both available. The majority of carbon-based molecules are organic, while all other chemicals are inorganic. Iron, selenium, and zinc are examples of inorganic nutrients, while energy-producing chemicals and vitamins are examples of organic nutrients [14]. Nutrients are divided into macronutrients and micronutrients in a classification system that is largely used to define animal nutrient requirements. Carbohydrates, lipids, protein, and water are examples of macronutrients that are ingested in relatively high amounts (grams or ounces). Vitamins, copper, and iron are examples of micronutrients that are required in small amounts (milligrams or micrograms) [14].

2. 3. Alcohol

Many medicines, especially those that impact the nervous system (antidepressants) or a prescription stimulant, may interact negatively with ethanol. Some medications lead the patient to be unconscious of their level of inebriation. In addition, when used with metronidazole, it causes headaches, palpitations, nausea, and vomiting [15]. The two primary sorts of interactions that can happen when you drink alcohol and take medicine at the same time are I CNS depression and (ii) flushing reaction [15]. Alcohol use enhances the effects of medications with CNS depressive activity, affecting ability and other skills. Amphetamines, analgesics, antiepileptics, antihistamines, antipsychotics, appetite suppressants, benzodiazepines, isoniazid, lithium, maproteline, metoclopramide, mianserin, selective serotonin reuptake inhibitors (SSRIs), and tricyclic antidepressants are among the drugs involved in this interaction [15].

Although unpleasant and potentially terrifying, the flushing reaction, also known as a disulfiram reaction, occurs when alcohol interacts with certain medicines, chemicals, and certain fungus. Disulfiram causes flushing, fullness of the face and neck, tachycardias, dyspnea, giddiness, hypotension, nausea, and vomiting by blocking the metabolism of alcohol and causing a buildup of acetaldehyde in the bloodstream. The effect might start within 10 minutes of consuming alcohol and last for several hours [5]. Azole antifungals, cephalosporins, furazolidone, griseofulvin, metronidazole, and topicaltacrolimus and pimecrolimus have all been linked to a similar response [15].

2. 4. Drugs

When ingested, a drug induces a change in the physiology or psychology of an organism. Food and substances that give nutritional assistance are usually distinguished from drugs. Drugs can be consumed by inhalation, injection, smoking, ingestion, absorption through a skin patch, or dissolving beneath the tongue. In pharmacology, a drug is a chemical substance with well-defined structures that has a biological impact when supplied to a living creature [15].

A pharmaceutical drug, often known as medication or medicine, is a medication or medicine that is used to treat, cure, prevent, or diagnose a condition or to improve one's health. Traditionally, medications were obtained by extracting them from medicinal plants, but more recently, organic synthesis has been used [17].

For chronic illnesses, pharmaceutical medications might be administered for a short time or on a regular basis. Medications are frequently categorized into drug classes, which are groups of drugs with comparable chemical structures, the same mechanism of action (binding to the same biological target), a similar mode of action, and are used to treat the same disease [16]. Caffeine, nicotine, and alcohol are the most extensively used drugs in the world, and they are also classified as recreational drugs because they are taken for enjoyment rather than medicinal objectives [6].

2. 5. Dietary supplements

Any vitamin, mineral, additional chemical substance, herbal product, botanicals, amino acids, or other ingestible preparation that is added to the diet to promote human health is referred to as a dietary supplement. Dietary supplements are a vast range of ingestible goods that are distinguishable from regular foods and pharmaceuticals that are utilized all over the world. A dietary supplement is a manufactured product that is taken by mouth as a pill, capsule, tablet, or liquid to complement the diet. To boost the number of nutrients consumed, a supplement can supply nutrients taken from dietary sources or synthetically synthesized nutrients, either individually or in combination. Dietary supplements may also contain compounds that have not been proven to be essential to life but are advertised as having a beneficial biological effect, such as plant pigments or polyphenols, but have not been proven to be essential to life. Supplement ingredients can also come from animals, such as collagen from chickens or fish. These can be used separately or in combination, and they can also be coupled with nutritious components [18].

Vitamins, nutritionally needed minerals, amino acids, essential fatty acids, and non-nutrient compounds taken from plants, animals, fungi, and bacteria are found in supplement products. Synthetic replicas of naturally occurring chemicals may also be found in dietary supplements (example; melatonin). All products containing these substances must be labeled as dietary supplements [19].

2. 6. Table

Table 1. Some significant food-drug interaction [19]

Drugs	Food	Drug-food Interaction
Warfarin	High protein diet Cooked onion	Raise serum albumin level Increase warfarin activity
Monoamine oxidase	Tyramine containing food	Hypertensive crisis
Antibiotics	With milk products	Decrease bioavailability and prevent absorption of some antibiotics

Theophyline	Hugh fat meal and grape fruit juice	Increase bioavailability Increase risk of toxicity
Acetaminophen	Pectin	Delay it's absorption and onset
NSAID	Alcohol beverages	Can increase risk of liver damage or stomach bleeding
Celiprolol	Orange juice	Intestinal absorption is inhibited
Isoniazide	Plants medicinal herbs, oleanolic acid	Exerts synergistic energy
Acarbose	At the start of each meal	Maximum effectiveness

2. 7. Therapy

A therapy is an attempt to treat a health problem after a diagnosis has been made. Each therapy, on the whole, includes indications and contraindications. There are numerous sorts of therapy available. Not all therapy are beneficial, and many of them have unpleasant side effects. Treatment and therapy are frequently used interchangeably. The word therapy is derived from the Latin word therapy, which literally means "curing" or "healing" (Online dictionary, therapy).

2. 8. Characteristics of Meal

Interactions are also influenced by the quantity and quality of the food. When lipophilic medications (albendazole) are taken with a high fat content, their absorption and bioavailability are improved. Certain cardiac medications, such as digoxin and lovastatin, have lower bioavailability when consumed with a high-fiber meal. When given with meals, several additional medications, such as labetalol, carbamazepine, and mebendazole, have a higher absorption rate [7].

The size and composition of a meal, as well as the precise timing of drug intake in relation to a meal, may influence the development of food-drug interactions. A high fat content, for example, increases the bioavailability of lipophilic medicines, either due to improved drug solubility (e.g. albendazole and isotretinoin) or stimulation of bile production (e.g. griseofulvin and halofantrine). A high fiber content, on the other hand, may lower the bioavailability of certain medications (e.g., digoxin and lovastatin) due to fiber binding. These situations, however, are frequently understudied, and many various definitions of fasting are utilized. Unless otherwise noted, fasting in this review refers to not eating for at least 1 hour before and after drug administration [20].

2. 9. Characteristics of Drugs

A drug is any chemical substance that, through its chemical effects, causes a change in biologic function. Drugs can be helpful or harmful, and when combined with another drug, food, or disease, they can be both [21]. The physical and chemical properties of a medicine play a crucial role in its potential for food interactions. Different medications in the same drug class, or different formulations of the same drug, can have very different chemical features, resulting

in completely different food-drug interactions. However, knowing the physicochemical features of a medication is insufficient to accurately anticipate food-drug interactions, and interaction studies of drug pharmacokinetics and effects with or without concomitant food intake are required [22].

Aspirin, ethanol, and nitrous oxide are examples of medicinal medications that can be solid, liquid, or gaseous [22]. The physical type of a medicine determines how it is taken, and drugs can be carbohydrates, lipids, or proteins, which impacts their mode of administration. Narcotics, depressants, stimulants, hallucinogens, and anabolic steroids are all types of drugs.

2. 10. Drug and Food Interaction

An modification in the kinetics or dynamics of a drug or a nutritional element, or a compromise in nutritional status as a result of the administration of a drug, is defined as a drug-nutrient interaction [23]. A physical, chemical, physiologic, or pathophysiologic relationship between a drug and a nutrient, multiple nutrients, food in general, or nutritional status is another complete description of a drug-nutrient interaction [23]. Drug interactions are more likely when medications are taken together, but no one knows what those interactions are for all of these drugs. However, research on drug-nutrient interactions is limited, and in certain circumstances, more research is required to confirm the findings.

Research studies sometimes provide contradictory results, and occasionally just one medicine in a group has been studied, leaving us to assume that others have the same impact. Some people are more vulnerable to nutrient loss than others, and thus are more likely to experience negative effects [24]. A food-drug interaction can hinder a medicine from working properly or cause a medicine's negative effects to worsen or improve. Furthermore, it may result in a new side effect [25].

2. 11. Classification of Food Drug Interaction

Pharmaceutical interactions, pharmacokinetic (PK) interactions, and pharmacodynamics (PD) interactions are the three main processes used to classify food-drug interactions [26]. Interactions between drugs. Pharmaceutical interactions can happen in delivery methods like enteral feeding tubes or in the gastrointestinal lumen (for example, phenytoin binding to the protein components of the enteral feeding product) [26].

2. 11. 1. Pharmacokinetic interactions

Foods influence processes associated to medicine absorption, distribution, metabolism, and excretion, resulting in PK interactions. The chelation of ciprofloxacin in the presence of divalent cations found in dairy products (altered absorption), grape fruit juice-induced inhibition of CYP3A4 metabolism of simvastatin (altered metabolism), and lithium and sodium competing for tubular reabsorption in the kidney are all examples of PK interactions (altered excretion).

2. 11. 2. Pharmacodynamics interactions

Foods can influence a drug's clinical effect on the body, which is known as pharmacodynamics interactions. A high-vitamin K diet that counteracts the therapeutic effects of warfarin is an example of a pharmacodynamics interaction. Green leafy vegetables (e.g. spinach, broccoli, turnip, etc.), cauliflower, chickpeas, green tea, hog liver, and beef liver are

high in Vitamin K, which causes antagonism with the anticoagulant medicine warfarin, resulting in decreased therapeutic efficacy. Alcoholic beverages boost the central nervous system depressing effects of benzodiazepines, antihistamines, antipsychotics, narcotics, or any other sedative substance. Caffeine in the diet, on the other hand, significantly increases the bioavailability and serum levels of theophylline [1].

2. 12. Fruits With Potential for Drug Interactions

Many fruits, including grapefruit, sevilla oranges, tangerines, grapes, mangos, apples, and papaya, have been linked to medication interactions. Grape fruit juice produces the most well-studied and clinically relevant food-drug interaction: over 85 drug-grape fruit juice interactions have been discovered. Ingestion of as little as one grapefruit or one cup of grapefruit juice can result in the inactivation of CYP3A4 enzymes in the stomach, which is clinically relevant and permanent. The body takes 48 to 72 hours on average to replenish the inactivated enzymes. As a result, isolating grapefruit consumption from daily medicine administration does not prevent this food-drug interaction [26]. Concurrent treatment of simvastatin and lovastatin in this scenario may result in increased exposure to these statins and consequent muscle damage, up to and including rhabdomyolysis, as a result of this suppression of CYP3A4 within the gut.

In patients who consume large amounts of grape fruit, rosuvastatin, pravastatin, and fluvastatin are therapeutic choices. Other fruits can cause food-drug interactions, but most patients will not consume enough of them to cause an interaction. Sevilla oranges can interact with atenolol, ciprofloxacin, cyclosporine, levofloxacin, and pravastatin by inhibiting CYP3A4 and P-glycoprotein (P-gp). Grapes inhibit the enzyme CYP3A4 and interact with the antibiotic cyclosporine. Tangerines interact with nifedipine and digoxin via stimulating CYP3A4 and inhibiting P-gp [26].

2. 13. Vegetables With Potential for Drug Interactions

Various vegetables, such as broccoli, spinach, tomatoes, carrots, and red peppers, have been linked to medication interactions. Broccoli, brussels sprouts, kale, and spinach are high in vitamin K; consuming large amounts or abrupt changes in the amount of the vegetable consumed can cause warfarin to lose its effectiveness and safety. With concurrent warfarin medication, patients should be counseled to maintain a consistent diet of vitamin K-containing vegetables [26].

2. 14. Other Foods With Potential for Drug Interactions

When combined with monoamine oxidase inhibitors, cured or smoked meats and seafood, aged dairy products, pickled or fermented foods, dried and overripe fruits, alcoholic beverages, broad (fava) beans, and damaged goods might produce a hypertensive crisis (MAOIs). Tyramine escapes breakdown in the presence of MAOIs and can build up in the systemic circulation to levels where it is taken up by adrenergic neurons, producing a hypertensive crisis [27]. Phenelzine, isocarboxazid, and tranylcypromine have all been linked to MAOI-induced hypertension. Linezolid and isoniazid are MAOI inhibitors that should not be taken with tyramine-rich meals [28].

High-fat meals improve theophylline absorption, resulting in "dose dumping" and higher serum levels. Grilled foods, on the other hand, can increase theophylline metabolism and lower serum levels. Because theobromine levels in caffeinated foods/drinks and chocolate vary,

consuming significant amounts of these products can raise the risk of theophylline poisoning [29]. Additionally, ciprofloxacin and cimetidine impede caffeine metabolism [29]. In the presence of dairy products (milk, cheese), the absorption of tetracyclines and quinolones (ciprofloxacin, levofloxacin) can be hampered [29]. A high-protein breakfast can boost propranolol bioavailability while limiting the absorption and efficacy of carbidopa/levodopa [30].

Dietary fiber can impair the absorption of digoxin, levothyroxine, and penicillin, resulting in subtherapeutic serum levels, thus it's important to keep an eye on it. Finally, dietary sodium is a pharmacotherapeutic factor to consider. Lithium can reduce salt absorption by the renal tubules, resulting in hyponatremia, particularly in patients who eat a low-salt diet. Furthermore, lithium reabsorption in the distal nephron is increased in hyponatremia, predisposing a patient to lithium toxicity. The efficacy of lithium has been demonstrated to be reduced when a high-salt diet is consumed on a regular basis. As a result, lithium patients should be advised to maintain a constant sodium intake to avoid potential toxicity [30].

2. 15. Taking drugs with alcohol

The alcohol can affect the work of medications in the basic conditions such as [25]:

- swallowing medicine with alcohol
- drinking alcohol after medicine has been taken
- taking medicine after alcohol.

Alcohol has an effect on the body's processes and interacts with a variety of medicines. It has an impact on a wide range of pharmaceuticals, including antidepressants and other treatments that affect both the brain and the neurological system. When metronidazole is used with alcohol, it might produce flushing, headaches, palpitations, nausea, and vomiting [31]. Patients should inform their doctor if they consume any alcohol or use any plants.

2. 16. Drug Interaction Risk Factors and Importance

The majority of people believe that because herbs and foods are natural, they are all safe. That can't be said to be true perspective. Herbs and foods frequently interact with commonly consumed drugs, causing dangerous side effects. According to experts, just because something is natural does not mean it is fully safe. Orally administered medication goes through the digestive system in the same manner that food and herbs do. When medications and certain meals are taken together, they may interact in such a way that the ingested drug's effectiveness is reduced or the absorption of food nutrients is reduced. Patients at high risk for drug-food interactions, such as the elderly who are taking three or more medications for chronic diseases, diabetics, hypertension, depression, high cholesterol, or congestive heart failure, should be closely watched [31].

Drug metabolism can be hampered by a lack of nourishment. Drug-nutrient interactions are more common in some people.

They are who:

- have impaired hepatic, renal or gastro-intestinal function
- are nutritionally compromised due to chronic disease
- have recent weight loss or dehydration
- are on multiple and prolonged drug therapy

- are at the extremes of age with changes in lean body mass, total body fluids and plasma protein concentration [32].

2. 17. Drug Food Interactions with Different Therapies Analgesics

Analgesics are commonly used pain relievers that might induce gastric discomfort [5]. Aspirin and other salicylates have long been known to cause stomach irritation. In individuals who take significant amounts over a long period of time, this can lead to anemia due to occult blood loss. When taken with food or milk, the risk of gastrointestinal upset is minimized [5]. An example of an analgesic is acetaminophen. If three or more drinks are consumed each day, doctors should be consulted to determine whether acetaminophen or other pain relievers/fever reducers should be used. Acetaminophen can harm the liverIf three or more alcoholic drinks are consumed on a daily basis, the risk of serious liver damage increases [25].

2. 17. 1. Antibiotics

Antibiotics are drugs that are used to treat infections caused by bacteria. Antibiotics are, without a question, the most routinely prescribed medications in the world. Antibiotics come in a variety of forms [5]. Folic acid, biotin, B complex vitamins, vitamin K, Lactobacillus acidophilus, and bifidobacteria are all depleted. These are beneficial bacteria that colonize the intestine and aid in digestion and immunological function. During and after treatment with this drug, the probiotic bacteria should be replaced with a supplement. Antibiotics, like other drugs, have a food-drug interaction. When ciprofloxacin is eaten with milk, its bioavailability and serum levels are reduced to a greater extent because the antibiotic is chelated with calcium and casein in the milk. When taken with meals, the oral bioavailability of azithromycin (a common antibiotic used to treat upper respiratory infections) is considerably lowered [33].

By chelation, a bivalent element present in food, such as calcium in milk, significantly lowers the oral bioavailability of medicines like tetracycline [34]. Caffeine metabolism is inhibited by Ciprofloxacin, whilst caffeine effects are amplified by the former. Because the activity of other fluoroquinolones is unaffected by caffeine consumption, they are the primary choice for patients who are addicted to caffeine or who consume it regularly throughout the day. Mineral supplements (such as magnesium, calcium, zinc, iron, selenium, and iodine) should be taken at least 2 hours before or after taking antibiotics, as they can bind to the medicine and decrease its absorption [35]. When taken with food, stomach acid destroys penicillin and erythromycin. As a result, it works best when taken on an empty stomach. Food, on the other hand, can help to lessen the likelihood of these medicines causing gastrointestinal distress [5]. If severe gastrointestinal distress develops, these medications can be given with food, albeit the pharmacokinetics of the dose will be altered. Furthermore, it should be carefully considered before consuming dairy products. Because milk products are one of the few high-quality sources of riboflavin, as well as a convenient and low-cost protein source [5].

2. 17. 2. Anticoagulants

Blood clotting is slowed by anticoagulants. This can reduce the risk of stroke in people whose blood clots too quickly. Warfarin (Coumadin) and other similar medications function by interfering with the usage of vitamin K in blood coagulation [5]. Vitamin K may reduce the effectiveness of the medication. Warfarin can be taken on an empty stomach or a full stomach. It is possible to consume a normal balanced diet with a consistent amount of leafy green

vegetables, but it is recommended that you see your doctor before making any dietary adjustments. Broccoli, cabbage, collard greens, spinach, kale, turnip greens, and brussel sprouts are all high in vitamin K. While taking anticoagulants, cranberry juice or products can alter the effects of warfarin. When taking warfarin, these products should be avoided. Furthermore, numerous dietary supplements and vitamins can interact with anticoagulants, reducing the benefit of warfarin or increasing the danger. Garlic, ginger, glucosamine, ginseng, and ginkgo can all induce bleeding and should be avoided. Furthermore, abstaining from alcohol is critical because it can impact the amount of warfarin [25].

2. 17. 3. Antitumor Drugs

A purine analog called mercaptopurine is used to treat acute lymphoblastic leukemia and chronic myelogenous leukemias. Because mercaptopurine is inactivated by xanthine oxidase (XO), taking it with other medicines that contain XO may impair its bioavailability. Cow's milk is reported to have a high concentration of XO. This connection could have clinical implications. As a result, most people should try to avoid taking mercaptopurine and drinking milk at the same time [36]. Tamoxifen is an effective anti-cancer drug. It interferes negatively with tamoxifen in promoting regression of established MCF-7 tumor size when administered with sesame seeds, but interacts positively with tamoxifen on bone in mice [25].

2. 17. 4. Antihypertensive drugs

When you eat a high-protein meal and take propranolol at the same time, the latter's bioavailability is increased. When propanolol was administered alongside protein-rich diets, there was a 53 percent increase in bioavailability [30]. The content of serum potassium is markedly increased, and a potassium excess of ten causes heart palpitation. Because several foods, such as bananas, oranges, and green leafy vegetables, are high in potassium, patients should avoid them. In terms of salt, it is well understood that a high intake of common salt is essential for the growth and maintenance of HT [37]. Despite this, felodipine (a calcium channel blocker with natriuretic characteristics) maintains its antihypertensive action, at least when administered at the maximum antihypertensive dose.

2. 18. Effects of Drug-diet Interaction

Changes in absorption caused by fatty, high protein, and fiber diets are major side effects of some diets on medications [38]. Bioavailability is an important pharmacokinetic parameter that is linked to a drug's clinical effect in the majority of cases. However, in order to assess the clinical significance of a food-drug interaction, the impact of food consumption on the drug's clinical effect must also be assessed [7].

The interactions that are most essential are those that are linked to a high probability of treatment failure due to markedly reduced bioavailability in the fed state. Chelation with dietary components is a common cause of such interactions. Furthermore, certain medications' bioavailability may be reduced or increased depending on the physical response to meal ingestion, particularly gastric acid secretion. A drug's pharmacokinetics and/or pharmacodynamics can be affected by a drug interaction. A drug's pharmacodynamic interaction could be addictive, synergistic, or antagonistic. Drug interactions are a significant and underappreciated source of medication [39].

2. 19. Effects of Nutritional Status on Drugs

Drugs may be affected by the existence of dietary disorders. For some medications, drug dosages may need to be adjusted based on real body weight. Other medicines may need to be dosed differently in obese, normal, and underweight individuals based on their actual, ideal, or adjusted body weight corrected for lean body mass. The dose of drugs that bind to somatic protein may be affected by somatic protein status [40].

Data on pharmacokinetics and pharmacodynamics in specific patient populations mainly focuses on people with renal impairment, hepatic dysfunction, or specific life stage characteristics. Despite the fact that dietary status has an impact on medication metabolism, drug disposition is rarely examined based on it (e.g., protein-calorie malnutrition, obesity, micronutrient deficits). Subjects' dietary state in clinical medication studies isn't often well described [26]. One of the five broad areas in the classification of drug-nutrient interactions is the impact of dietary status on drug disposition and effect. Nutrition status, as a triggering component in the interaction, may result in drug toxicity or drug treatment failure, depending on the severity of malnutrition. The field of drug-nutrient interactions is related to other domains of drug-nutrient interactions.

2. 20. Effects of Food Consumption on Oral Drug Absorption

Oral drug absorption can be influenced by changes in the gastric and intestinal systems, such as changes in gastrointestinal pH, increased gastrointestinal motility, delayed gastric emptying and prolonged intestinal transit, increased luminal fluids, bile salt release, and increased hepatic and splanchnic blood flow. In healthy people, the stomach environment ranges from pH 1 to pH 3 and stores 250 mL of luminal fluids when they are fasted. Chemically and physically, the ingested food is broken down into chyme, a viscous combination. The stomach pH rises from an average of 1.88 to 4.98 after meal eating and remains raised for up to 4.5 hours. There is also a 500 mL or greater increase in stomach fluid volume, with fluid dynamics dependant on the calorie intake (low or high fat) of the meal. Ionizable chemicals' solubility and dissolution can be affected by a more basic pH. To welcome food, the proximal stomach relaxes and produces a continuous tonic contraction, while the distal stomach produces phasic contractions that mix and breakdown the food. The chyme can travel from the stomach, through the duodenum, and into the small intestine thanks to the mechanism involving the migrating motor complex.

The pH of the duodenum and small intestine does not fluctuate as much as the pH of the stomach, remaining about pH 6 to pH 8. The volume of the small intestine increases from 200 to 12, 672 4 of 181000 mL in Pharmaceutics 2020. Under fed settings, the pH profile along the intestinal tract is dynamic and is influenced by a number of factors, including the type of food consumed, gastric output, and bile salt concentrations. The gall bladder's production of bile salts improves the solubility of medicines with low water solubility. Furthermore, depending on the intraluminal solubility and viscosity, intestinal motility in the post-prandial stage exhibits distinct patterns [26].

Medication metabolism enzymes or euxtransporters in the gastrointestinal system can be inhibited, allowing for a higher percentage of drug absorption. Grape fruit juice, for example, is a well-known cytochrome P450 (CYP)3A4 inhibitor, and co-administration with medications metabolized by CYP3A4 can have major bioavailability consequences [41]. Furthermore, lymphatic uptake aids in the absorption of large-molecular-weight medicines or lipophilic

chemicals, and this process is accelerated after consuming high-fat meals [42]. As a result, medication absorption into the plasma compartment is boosted.

2. 21. Effects of Food Consumption on Drug Metabolism

Many medications' metabolism (mainly hepatic) can be influenced by food. Concentrated grape fruit juice, for example, increases the bioavailability of antihypertensive medicines felodipine and nifedipine when given together. Flavonoid chemicals in grape fruit juice concentrate are thought to impede felodipine and nifedipine metabolism by cytochrome P-450. This combination has the potential to boost the efficacy as well as the toxicity of these medications. Citrus fruit or juice is a typical breakfast item, so it has a lot of therapeutic relevance. This probable interaction should be disclosed to patients [43].

2. 22. Effects of Food Consumption on Drug Excretion

Many food items can change the pH of the urine, resulting in a decrease or increase in the amount of medicine taken by the patient. As a result, the half-life of acidic drugs is longer in acidic urine (caused by foods such as meats, fish, cheese, and eggs) because the drug remains in its unionized form in the acidic medium, and the half-life of an acidic drug in alkaline urine (caused by milk, vegetables, and citrus fruits) is shorter because the drug is in its ionized form. Lithium and salt also compete in the kidney for tubular reabsorption. A high-salt diet causes more lithium to be expelled, whereas a low-salt diet causes less lithium to be eliminated by the kidneys and a higher lithium level in the blood [44].

2. 23. Factors affecting Food Drug Interaction

2. 23. 1. Timing of Medication Administration and Food

Certain foods have the potential to boost the bioavailability of drugs and/or reduce gastrointestinal adverse effects. A manufacturer's recommendation for a medication to be taken with or shortly after a meal may exist in some cases. For example, it is common to suggest that carvedilol should be taken with food, as this can slow down absorption, thereby decreasing the likelihood of orthostatic hypotension. Alfuzosin should be taken as soon as possible after a meal [45]. Lovastatin should be taken with a meal in the evening, whereas tamsulosin should be taken one half hour after a meal [46]. To reduce gastrointestinal irritation, ferrous sulfate, nonsteroidal anti-inflammatory drugs (aspirin, ibuprofen, naproxen), nitrofurantoin, prednisone, and potassium chloride tablets should be given with food or milk [29].

Posaconazole oral solution, posaconazole delayed-release tablets, rivaroxaban, and ziprasidone should all be taken with food, according to manufacturer recommendations [38]. Many other common medications should be taken on an empty stomach as well. Because zolpidem and eszopiclone's absorption is slowed by food, they should not be taken with or immediately after a meal [47]. Thyroid supplements, such as levothyroxine, should be taken 30 to 60 minutes before a meal. The oral antihistamines fexofenadine, loratadine, and cetirizine are most effective when taken on an empty stomach for optimum absorption [3]. Tropsium should be taken with water and at least one hour before a meal on an otherwise empty stomach[48]. Isoniazid should not be used with food because several studies have shown that it reduces bioavailability. Food in the stomach can reduce the absorption of angiotensin-converting enzyme inhibitors by up to 40%, hence captopril and moexipril should be taken one hour before meals.

Penicillamine capsules should be taken on an empty stomach at least one hour before or two hours after meals, and at least one hour before or after any other medication, food, or milk [45]. Oral cyclosporine capsules or oral solution should be taken on a regular schedule that is consistent in terms of time of day and meal timing [48]. Specific dose formulations of some medications have varied food-drug problems. The immediate-release glipizide pills should be taken 30 minutes before meals, whereas the extended-release glipizide tablets should be taken with breakfast or the first meal of the day [49].

3. CONCLUSIONS

The effects of drug interactions with food on the medication's therapeutic efficacy are the most important. Food has an effect on drug bioavailability, either increasing or decreasing the therapeutic agent's systemic absorption. Drug toxicity and adverse effects can occur as a result of interactions that result in enhanced bioavailability. Those with lower availability, on the other hand, can lead to therapeutic failure and tolerance. To obtain the intended therapeutic outcomes, drug-food interactions must be monitored and dose regimens evaluated, as well as patient counseling. To aid in the successful treatment of patients, appropriate information about potential interactions in the dose regimen should be provided. This review provides some information on the impact of food on medicine administration. The information is needed by healthcare providers, pharmacists, and nursing staff in order to guide patients and monitor future interactions while evaluating potential outcomes.

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