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A Study On Effects Of Food And Drug Interaction On Pharmacokinetics And Pharmacodynamics Action Of Drug

Seema Jain[1*], Nargis Khan[1], Nitin Kumar[1], Paras Jain[1], Pankaj Gupta[2], Ram Dayal Gupta[1], Prasoon Kumar Saxena[1], Hemendra Gautam[3], Mohit Gupta[4]

[1]Sunder Deep Pharmacy College, NH-9, Delhi-Hapur Highway, Dasna, Ghaziabad, Uttar Pradesh 201002, India.
[2]School of Pharmaceutical Sciences, Maharishi University of Information Technology, Noida, Uttar Pradesh, 201304, India.
[3]Professor and Dean, Faculty of Pharmaceutical Sciences, Future University, Bareilly, Uttar Pradesh, 243503, India.
[4]Professor and HOD, Department of Pharmaceutical Chemistry, School of Pharmacy and Research, Dev Bhoomi Uttarakhand University, Dehradun, Uttarakhand, 248007, India

ABSTRACT

Objectives: *The importance of drug-food and drug-drug interactions to practice has been acknowledged considerably more slowly, despite the fact that drug-drug interactions are well known and recognized. However, the long use of drugs has led to an increase in drug-food interactions. In addition to being aware of these kinds of interactions, food-drug interactions are very important for assessing the proper time, dosage, and formulation of novel medication candidates. Variation in intestinal transport and metabolism, or systemic drug distribution, metabolism or excretion, are the mechanisms by which drug-food interactions occur. Additionally, pregnant women, those with major health issues, those with a poor diet, and children are more likely to experience food and medicine interactions. Basic details regarding the significance, categories, enzymes of drug and food interactions are provided in this article.*

Keywords: *Drug interaction, grape fruit juice, antibiotic, habituation, Pharmacokinetics, Pharmacodynamics, Diet.*

INTRODUCTION :

Medicines are used to cure, treat and prevent the huge range of health conditions but all medicaments should be used very carefully to ensure their safety and efficacy. Medicaments should be carefully prepared so that their effect have the same predicted effects for all kind of patients, it also be unaffected by concurrent food or other medications with linear potency, must be totally non-toxic in whatever dosage form , and require just a single dose to effect a long time cure. [1].

So many medicament are available which consist of potent compound that bind with the drug present in human body in unique method. Diet and lifestyle could also have a substantial effect on medicine effectiveness. A medicine interaction is like a circumstance in which an interaction can influences the activity of a drug, i.e. the efficacy of medicament can be increased or lessened, or together they can produced a new impact that neither can see before. However, interactions between both of medications and foods, as well as drugs and plants can be seen.

These all happens due to the lack of knowledge or information about the therapeutic moiety contained in the particular substances. Food and drug interactions may unintentionally decreases or enhanced the impact of the medications. Some frequently used vegetable herbs and fruits, and alcohol may cause the impact to fail, leading to serious health issues for the patient. Mostof clinically important food-drug interactions result from food-induced alterations in drug's bioavailability [2].

Some diets (foods) have a significant impact on drug absorption, including fatty foods, protein containing diet, and fibrous food. Bioavailability is a critical parameter that is connected with the clinical efficacy of various medicines. However, if anyone want to verify the clinical importance of a food and drug interaction, the effect of food intake on the drug's clinical effect should also be considered [3].

The most relevant effect are those that enhances the probability of treatment failure because of lower bioavailability in the fed situation. Chelation mechanism with dietary food is one of the common source of these interactions. Further, the physiological signal to meal intake, specifically gastric acid secretion, may decrease or increase the bioavailability of some medicaments [4].

Drug interactions can also affect the pharmacokinetics and pharmacodynamics activity. A pharmacodynamics effect of a drug interactions can be antagonistic in nature, additive effect or it can be synergistic effect. Drug interactions may be an important source of pharmaceutical negative impact [5].

The concomitant use of various medicines with a large surface area on that the drug components could be slicked or bind. Change gastric pH, may change gastrointestinal motility activity, or may cause problem in transportation of proteins like P-glycoprotein may have an effect on absorption of drug in the area of gut. A reduction in absorption of drug rate may have minute clinically significant, however a drop in the amount of absorption is clinically advantageous if it results in sub therapeutic serum levels [6].

DRUG AND FOOD INTERACTION:

A. PHARMACOKINETIC INTERACTIONS

1. Effect of Drug-absorption on food and drug Interactions [7]

Food can influence absorption of drugs in the gastrointestinal (GI) tract by changing factors such as pH of gastric area, stomach secretion Gastro-intestinal motility and transit time. These alterations can modify the rate and extent of medicaments absorption, thereby reducing treatment efficacy or increasing toxicity [8]. Examples are as below:

a) Antibiotic effect:

Azithromycinwhen taken with food, the absorption of azithromycin decreases, leading to a 43% reduction in bioavailability [9].

b) Effect of Theophylline:

Consuming high-fat foods with sustained-release theophylline can result in dosage dumping, which is when the medicine is suddenly released in huge quantities. This can lead to high theophylline levels, which increases the risk of poisoning. Children and kids are more susceptible to these kind of drug interaction than adults [10].

c) Effects of Food-drug interaction on Bioavailability of Drug:

Food can affect medication bioavailability through multiple ways. It causes a viscous environment in the gastrointestinal (GI) tract, which can limit medication dissolution and diffusion with the absorbing membrane. Furthermore, medications can attach to food particles or react with gastrointestinal liquids generated in reaction to meals, affecting their absorption. [11].

d) Effect on viscosity in gastrointestinal contents:

Food increases the viscosity of gastrointestinal contents, slowing medication breakdown. A fluid environment reduces the absorbing surface area, resulting in delay in drug absorption.

e) Changes in the rate of gastric emptying:

High fat, substantial meals inhibit stomach emptying, causing delayed medication absorption and activity. Hot , greasy meals can delay the effects of certain medications [12].

f) Stimulation of Gastrointestinal Secretions:

Food boosts stomach secretions, impacting medicine stability and absorption rate. Chemical hydrolysis and enzymatic metabolism can affect medication bioavailability. Surface-active substances such as bile salts can improve medication absorption by speeding up dissolution. Bile salts can improve the absorption of Griseofulvin [13].

g) Competitive Inhibition of Drug Absorption by Food Components

Some medications are structurally similar to nutrients and compete for the same absorption pathways. Levodopa competes with dietary amino acids for absorption, lowering its bioavailability [14].

h) Drug or Dietary Component Complexation: Certain medications generate insoluble or nonabsorbablecom pounds with food components, resulting in reduced absorption. Examples: Tetracycline can form compounds with calcium ions in milk, decreasing medication absorption. Iron rich foods can reduce medication bioavailabi lity through complex formation. This impact occurs when a medication develops irreversible or unobservable compounds with food components [15].

2. Effect of Drug -distribution on food and drug Interaction

Food can influence drug distribution by changing parameters such as plasma protein binding, lipid solubility, and blood flow. Some medications attach to plasma proteins such as albumin, and certain meals might compete for these binding sites, increasing the free (active) drug content and potentially improving its effects or toxicity. High-fat containing foods can improve the distribution of lipophilic (fat-soluble) medications by boosting their

storage in fatty tissues, resulting in longer pharmacological action [16].Furthermore, food-induced alterations in blood flow, particularly in the liver and intestines, might influence how soon a medicine reaches its target location. Certain minerals, like as calcium and iron, can bind to medications (e.g., tetracycline), reducing their availability for distribution. These types of connection can have a negative effect on the drug's efficacy and safety, thus dietary considerations must be considered when taking drugs [17].

3. Effect of Drug-metabolism on food and drug Interactions

Food can affect how the liver processes certain drugs, leading to changes in their effectiveness and side effects like Grapefruit Juice Interaction. Grapefruit juice can improve the bioavailability of some medicaments by reducing liver enzymes (cytochrome P-450). Example: When taken with grapefruit juice. Felodipine absorption increased by up to 469%, leading to lower blood pressure and a faster heart rate [18].

- Nifedipine absorption also increased but to a lesser extent (up to 169%).
- Side effects included headaches, flushing, and dizziness.
- Orange juice did not have this effect.[19]

Citrus juices are commonly drunk with breakfast, thus patients should be advised about this interaction.

4. Effect of food on first-pass Metabolism:

Some medications undergo first-pass metabolism in the area of liver, lowering their bioavailability. Like, when propranolol and metoprolol are taken with food, their absorption increases, making them more effective.

Tyramine and MAO inhibitors:

Monoamine oxidase (MAO) inhibitors (used to treat depression) interact with tyramine, a chemical contained in certain diets. The body normally breaks down tyramine, but MAO inhibitors hinder this, resulting in elevated blood pressure (hypertensive crisis). All should avoid foods like as long time stored pickled fish, cheeses, some extracts of yeast, red wine, and some types of beer that not contain alcohol and fermented food items [20].

5. Drug Excretion and Food Interactions:

Foods can alter urine pH, affecting the activity and excretion of certain medicines. Changes in urine pH can drastically affect drug half-lives. Acidic medicines have a longer half-life in acidic urine because they remain in their unionized form, which facilitates reabsorption. However, in alkaline urine, acidic medicines become ionized, resulting in faster excretion and a shorter half-life [21].

6. Pharmacokinetic interactions of actual dietary supplements

a) Alcohol contain drink

Advanced evidence of the cardio-protective advantages of alcohol containing drink has encouraged some moderate alcohol intake as a main part of a healthy lifestyle. Alcoholic liquids, like beer and wine are high in flavonoids contents and other polyphenols compounds, which have some antioxidant effects and can also effect CYP action via pathways unrelated to ethanol. However, evidence on enteric CYP3A blocking by tea and sometimes alcoholic liquids like wine, beer are limited, and their clinical advantages has yet to be known [22, 23, and 24].

b) Red wine

There have been numerous research looking into the connections between wine, red made from the common fruits like grape. Red wine's effect on the pharmacokinetics of CYP3A substrates but it may vary depending on the percentage used and type eaten. It is also hard to differentiate between the effects of ethanol and wine ingredients. Chemical trans-resveratrol and other chemical such as Gallic acid are two strong chemical components of red wine that have been known to effect in vitro to inhibit hepatic CYP3A in a mechanism-based and non-competitive, reversible manner. However, the mechanism of intestinal suppression by red wine is not yet well understood [25].

c) Beer

Beer contain various kinds of phenolic acids and other phenyl-flavonoids, but few of them are used initially as a flavoring agents and some are as to preserve the beer. An experiment of the inhibitory effect of a long range of lagers, scales, beers, ciders, and non-alcoholic drinks on CYP systems represented that some beers produced the blocking of CYP3A4-related metabolism by up to 77-81%. Somehow, there are a large variations in alcohol and hop acids components. Resulting, a strong relationship between inhibition and hops ingredients levels could not be produced. Some other studies with individual compounds are in support with the clinical studied [26, 27].

d) Tea

Tea is one of the famous and popular liquid drink after water in the world. The type of fermentation and variety of tea produced by the different tea plant like *Camellia sinensis* are evaluated by the processing procedure used for its green parts like leaves. Green tea have less oxidation during processing, as a result in it has a high concentration of polyphenol. The most common polyphenolic chemicals are catechins, which are known to help to stopped and to treat cancer, cardiac illness, and obesity. Currently, the major use of controlled clinical trials predicting the effect of repeated green tea intake on CYP activity have failed to show clinically relevant interactions [28].

e) Drug-grapefruit juice interactions

The initial study of this type of interaction found that juice obtained from grape fruits, (orange juice avoided), enhanced mean plasma area under the curve (AUC) of Felodipine compared to water in patients of borderline hypertensive disease [40]. Blood pressure of person was decreased, heart rate increased, and vasodilation-related adverse events occurred more frequently. Juices obtained from grapefruits generally enhanced the plasma peak concentration (Cmax) of drug but it did not alter the systemic elimination half-life (t1/2) [29, 30]. Juice obtained from grape fruits have not effect on intravenous pharmacokinetics of Felodipine [31], implying that the interaction with juice of grapefruits was caused by inhibition of pre-systemic drug metabolism [32].

f) Antimicrobials

In case of antivirals, the authors determined that simultaneous grapefruit juice treatment increased the pH of stomach area and delays absorption of Indinavir, but it has no consistent effect on Indinavir's systemic bioavailability in HIV-infected people [33]. In the same manner, clinical studies have suggested that grapefruit juice has no special effect on Amprenavir kinetics. This behavior could be because of medications' primary metabolism that occurs outside of the small intestine [34].

Grapefruit juice, among all antimalarial drug, considerably enhances the oral bioavailability of drug known as Artemether but it does not protect us from the time-dependent drop in bioavailability as well as elimination half-life, implying a role for intestinal enzyme CYP3A4 in Artemether pre-systemic metabolism [35, 36]. Same findings were also seen after a single dosage of orally taken Praziquantel with 200 ml juice obtain from grape fruits [37].

g) Antihistamines and Serotonin Analogs

Many scientific research have indicated that a one full glass of grape juice produced an individual-dependent, variable that increase in the systemic bioavailability of drug like Cisapride by blocking of enzyme present in intestine Cytochrome P450 3A4 (CYP3A4) activity [38]. Thereby it is suggested that frequent use of high amount of juice of grape with Cisapride should be not be used, especially in those patients who have high risk factors of cardiac arrhythmia [39]. The effect of these kind of juice on racemic Nitrendipine was found to increase its bioavailability and it was also seen that it blocks the Stereo-selective metabolism of Nitrendipine in human body [40].

h) Some other examples of food and drug interactions are

- **Warfarin**

Warfarin is widely prescribed to prevent or treat thromboembolic in patients [41]. Patients who are using warfarin are especially vulnerable to interactions with dietary supplements, however roughly 32% utilize herbal and natural product from plants and used as a supplements on a daily routine [42]. Warfarin can interact with a high-protein meal. Increased dietary protein consumption has been hypothesized to increase blood albumin percentage and cytochrome P450 activity, resulting in a reduce in international normalized ratios [43].

Some plant food like spinach, broccoli, sprouts, Brussels, kale and parsley are full of vitamin K. Taking large amount of these plant vegetables could create problems in the effectiveness and safety of warfarin treatment [44]. Eating charbroiled foods may lower warfarin activity, eating cooked onions may enhance it. Soy meals have been indicated to both boost and decrease warfarin activity. The importance of the latter three interactions is uncertain. The mixture of some drugs like warfarin medication and cranberry juice could create problems without bleeding in an old age patient [45].

- **Antibiotics**

Antibiotics drugs are provided to treat the bacterial infections in patient. So many types of antibiotics are there. They deplete biotin, folacin, vitamin K, mycobacterium such as Lactobacillus acidophilus, and Bifidobacterium.

These are some micro bacteria that collects in the digestive system and motivates good digestion as well immunity of system. During and after some time of taking this medication, patient should take a supplement to replace the probiotic microorganisms. Some mineral supplements like calcium, magnesium, selenium zinc, iodine and iron should be provided at least few hours apart from taking antibiotics, as they could attach to the therapeutic substances (drug) and impair the mechanism of absorption [46].

When some antibiotics like penicillin and erythromycin are taken with meal, acid released from stomach breaks them down. So it works nicely when taken in empty area of stomach. However, some food items can lower the likelihood of stomach distress that can be caused by these drugs. If substantial gastrointestinal problems occurs, these medicaments can be provided with some food, this will change the action like pharmacokinetics of the dosage form. Furthermore, before taking milky products, one should carefully note that as milk products are one of the richest sources of riboflavin, and they can also easily ingested and economical protein source [47].

In this review, the author concluded the up growing risk of food and drug interactions that focus on their effect on medication metabolism and therapeutic efficiency. They emphasized the importance of understanding these interactions in order to take medications safely and effectively.

B. PHARMACODYNAMICS INTERACTIONS

Foods can interfere with medicaments by changing their pharmacologic activities. For example, diets with high vitamin K can reduce the effectiveness of warfarin, an anticoagulant, by antagonizing its effects. Foods full of phyllo Quinone consisting plant leafy vegetables like spinach, broccoli, fenugreek, coriander, turnip greens, Brussels sprouts, green tea cauliflower, chickpeas, beef liver and pork liver.

C. EFFECT OF FOODS ON pH OF URINE.

a) Alkalizing foods include milk, veggies, and citrus fruits.

b) Acidifying foods include meat, fish, cheese, and eggs.

Foods can also impact the renal excretion of certain drugs. Sodium and lithium fight for tubular reabsorption in the organ called as kidney. A diet with high amount of salt increases lithium excretion, decreasing its effectiveness, whereas a low-salt diet reduces lithium excretion, resulting in higher lithium levels in the blood, thus elevating the risk of toxicity [48].

Alcoholic beverages can boost the depressive effects of certain drugs on the central nervous system (CNS), including benzodiazepines, antihistamines, antidepressants, antipsychotics, muscle relaxants, opioids, and any other sedative. This can result in increased sleepiness, dizziness, and poor coordination [49].

Some foods can potentially increase the effectiveness of drugs. For example, caffeine in coffee has an additive impact on theophylline, a bronchodilator. Caffeine has been shown in studies to boost levels of serum theophylline in the range of 25%-35% and prolong its half-life by slowing rate of clearance, resulting in symptoms such as nervousness, tremors, and insomnia [50]. Because caffeine has bronchodilator properties, it can improve the action of theophylline, necessitating the adjustment of theophylline dosage in individuals who consume considerable amounts of coffee (more than six cups per day) [51].

ROLE OF PHARMACISTS TO CURE AND PREVENT DRUG-FOOD INTERACTIONS

Pharmacists always have an important role in detecting and preventing drug and food interactions. They must be attentive in checking potential interactions and informing patients about which meals and beverages to avoid while taking specific drugs. Staying up to date on the latest drug interactions is critical for delivering correct counselling [52]

When dispensing medications, pharmacists should inform patients about:

a. Read medicine labels carefully and ask clarifying questions if confused.

b. Checking medicine labels and inserts for warnings and interactions, including over-the-counter drugs [53].

c. Take medicine with one glass of water.

d. Don't mix medications with food or open capsules unless recommended by a doctor.

e. Avoid taking vitamins concurrently with medications to avoid potential interactions.

f. Avoiding mixing medicine with hot liquids, which may diminish its effectiveness.

g. Never consume alcohol while taking medicine.

h. Consulting with a pharmacist to learn how diet affects specific prescriptions.

PRECAUTIONS:

Certain drugs should be taken before, with, or after meals to ensure optimal absorption.

If health issues persist, see a doctor.
Pregnant or breastfeeding mothers should get medical advice before taking any medication, as it may damage their infant [54, 55]

CONCLUSION:

Food & medications are equally necessary for optimal health, but using both at the same time can cause side effects and hazards. Identifying and understanding these interactions is critical for ensuring safe and effective pharmaceutical use.

In most circumstances, eating reduces a medicine's bioavailability, but it can also affect drug clearance. Additionally, medicines might affect food taken, digestion, absorption, and excretion. Some study are required to better understand these interactions, and chemists shows an important role in monitoring and informing patients about potential drug-food interactions. While some interactions can be detrimental, others can be beneficial, aiding in drug absorption or reducing side effects. Recently, medication interference with grapefruit juice have attracted a lot of attention. As new medications are created, recognizing these interactions remains crucial to safe medication usage.

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