INTERNATIONAL JOURNAL OF PHARMACEUTICAL RESEARCH AND BIO-SCIENCE

THE RISKS OF INTERACTION OF DRUGS WITH FOOD

NIRAJ KUMAR SINGH, AHSAS GOYAL, NEETU AGRAWAL

Institute of pharmaceutical research, GLA University, Mathura 281 406, Uttar Pradesh, India.

Accepted Date: 03/03/2015; Published Date: 27/04/2015

Abstract: Interactions between food and drugs can have profound influence on the success of treatment and on the side effects of many drugs. These interactions may not always be effecting negatively to the drug therapy but may be used to improve the therapy, by increasing absorption of drugs and minimizing the side effects. These interactions have received more attention since it was discovered that grape fruit juice affects the biotransformation of drugs and this resulted in sudden increase of literature in this field. The drug-food interactions may occur by increasing or reducing rate of absorption or through chemical and pharmacological effects. The food may enhance the bioavailability of some drugs. Chemicals or pharmacologic interactions may occur through various mechanisms like potentiating the drug effect or by antagonizing the desired effect of drugs. Perhaps the most feared food drug interaction is that of MAOI's and amino acid tyramine, which is an indirect sympathomimetic and may be found in seasoned cheese, fermented food or prickled food or beverages, leading to significant release of noradrenalin, resulting in marked hypertension, cardiac arrhythmia and cerebral hemorrhage. We are discussing these interactions and enlisting the drugs but absence of the name of any drug does not necessarily mean that it has no drug-food interaction.

Keywords: Drugs, Food, Interactions

Corresponding Author: MR. NIRAJ KUMAR SINGH

PAPER-QR CODE

Access Online On:

www.ijprbs.com

How to Cite This Article:

Niraj Kumar Singh, IJPRBS, 2015; Volume 4(2): 40-47

INTRODUCTION

Drugs are frequently taken with food, and patients often use mealtime to remind them to take their medication. However, food can have a significant effect on the bioavailability of drugs. Food or certain dietary items influence the activity of a drug. Food may influence drug absorption indirectly, through physiological changes in the GI tract e.g. delayed gastric emptying and increased gastric secretions. Viscous environment, which will reduce the rate of drug dissolution and drug diffusion to absorbing membrane and altered gastric pH also influence drug absorption. Food can also directly influence absorption of drugs by increasing splanchnic blood flow and through physical (adsorption) or chemical (chelation) interactions between the drug molecules and food components e.g. certain food contain tyramine, and interaction of tyramine with MAOIs is well known[1]. Similarly some cruciferous vegetables like cabbage, broccoli and brussels contains CYP_1A_2 and the drugs which require this subtype of cytochrome for metabolism will reduce their plasma concentrations. Some drugs like fexofenadine metabolized by CYP_3A_4 show decreased levels with grapefruit juice (use to mask the taste of alcohol). The probable reason for this is that grapefruit juice is inhibitor of some drug transporter and possibly affects organic anion transporting polypeptide (OATPs), although inhibition of P- glycoprotein has also been suggested[2].

Generally there is better absorption of drugs, when given empty stomach but the absorption of few drugs is actually promoted when administered after a meal. The absorption of riboflavin is greater when administered after meal; the absorption of griseofulvin is doubled when administered after a meal, containing high fat content. The bioavailability of chlorthiazide is increased when taken immediately after a meal compared to that found in fasting subjects[3]. Exact mechanisms of food-drug interactions are very complex and unpredictable. However, some of them are being discussed below, which may show how food may influence the bioavailability of drugs.

1. Increased viscosity of GI contents: The presence of food in the GIT will provide a viscous media which may result in reduction of rate of dissolution in the GI contents. In addition, the rate of diffusion may also be reduced by increased viscosity. Both phenomena will tend to reduce the absorption of drugs and ultimately decrease their bioavailability.[4, 10]

2. Alteration in the rate of gastric emptying: More the bulk of food, longer will be the gastric emptying time. Liquid meal takes less time than solid meal to pass the gastric region. High or low temperature of ingested food (in comparison to body temperature) reduces the gastric emptying rate and the drugs which are absorbed through gastric mucosa thus will have higher bioavailability. The drugs which will be absorbed through intestinal mucosa, will have delayed onset of action.[5]

3. Stimulation of GIT secretions: The secretion of GIT is stimulated by food. The gastric secretion includes hydrochloric acid and pepsin whereas intestinal secretion includes bile salts, bile acids, enzymes etc. These substances may influence the drug stability and the rate of absorption of drug. Degradation of drugs can take place in GIT due to chemical hydrolysis and enzymatic action, which may lead to reduced/abolished bioavailability of such drugs like penicillin, insulin etc. While bile acids increases the absorption of certain more fat soluble drugs, by increasing their rate of dissolution in GIT fluids, but bile salts may form insoluble or non-absorbable complexes with drugs like kanamycin, neomycin and nystatin.[4]

4. Competitive inhibition of drug absorption by food component: There are certain specialized absorption mechanisms for absorption of certain components of food. The drugs which have structural similarity with such components are also absorbed by same mechanism. Therefore, it is expected that there will a competition between drugs and these substances. Some of such examples are, that the absorption of levodopa is inhibited by certain amino acids likes phenyl alanine and tyrosine, which are metabolic products of food containing these proteins.[6]

5. Formation of non-absorbable complex of drugs with food components: In general, reduction in bioavailability due to complexation is observed only when drug forms an irreversible or non-absorbable complexes with components of food especially dairy products. The examples include chelation of tetracyclines, fluoroquinolones, penicillamine etc with micronutrients like `Ca^{+2}, Cu^{+2} Mg^{+2}, Zn^{+2}, Fe^{+2} etc. [8, 10]

6. Blood flow to the liver: Blood flow to the GIT and liver increases shortly after a meal. This increased blood flow to the liver will increase the rate at which drugs are presented to the liver, resulting in the reduction of first-pass metabolism of some drugs (propranolol, hydralazine,,dextropropoxyphen etc.), as the metabolism of such drugs is sensitive to their rate of reaching to liver, greater the rate of flow of such drugs to the liver, larger will be the fraction of the drug that escapes first-pass metabolism. This is due to the enzyme systems, responsible for their metabolisms, become saturated at that rate of presentation of drugs to the liver. [4]

Various ways by which absorption of drugs after meal may increase: Increased drug absorption following a meal could be due to one or more of the under mentioned reasons:

1. Increased time, for dissolution of a poorly soluble drug.
2. Enhanced solubility, due to GIT secretion like bile.
3. Prolonged residence time and absorption site contact of drug e.g. water soluble vitamins.
4. Increased lymphatic absorption e.g. acitretin[6].

Table 1 lists the drugs, the absorption of which may be influenced by food**,** whereas Table 2 enlists the drugs which should be taken empty stomach. However there are certain drugs which should be taken with food and some of these are listed in table 3.

Some important examples of drug interactions with different food materials:

Anti-infective agents and Food: The presence of food in GIT will reduce the absorption of many anti-infective agents (e.g. penicillin and tetracycline derivatives). Erythromycin stearate formulation should be administered at least 1 hr before meal or 2 hr after meal. There are many anti-infective agents like penicillin V, amoxicillin, doxycycline, minocycline etc., absorption of which are not affected by food. [8]

Alendronate & Risedronate and Food: Food and even coffee, orange juice and mineral water may markedly reduce the bioavailability of these drugs. It is recommended that these drugs should be administered early in the morning, but at least half hr before any food, medication, with plain water. [8]

Coumadin and Food: Leafy green vegetables high in vitamin K should not be taken in great quantities while taking coumadin. These vegetables could totally negate the effects of the drug and may cause blood clotting[9].

Caffeinated beverages and antiasthmatic drugs taken together can cause excessive excitability. Those taking cimetidine, quinolone antibiotics (ciprofloxacin) and even oral contraceptives should be aware that these drugs may cause their cup of coffee to give them more of a Java jolt than they expected. [3]

Captopril and Food: The presence of food in GIT has been reported to reduce the absorption of captopril by 30 to 40%. It is advisable to administer the drug 1 hr before the meal. [3]

Digoxin and Oatmeal: Large amounts of oatmeal and other high-fiber cereals should not be eaten when taking digoxin. The fiber can interfere with the absorption of the digoxin, and may decrease its bioavailability. [1]

Drugs and Grapefruit Juice: Grapefruit juice reduces the activity of many cytochrome P-450 enzyme synthesis in the gut wall, which are involved in the metabolism of certain calcium channel blockers (e.g. Amlodipine, Feloidipine, Nisoldipine Varapamil etc.), HMG-CoA reductase inhibitors (e.g. Lovastatin) and cyclosporine. As a result, larger amounts of un-metabolized drugs are reabsorbed, and serum concentrations are increased. Some of the drugs which may exhibit increased concentration are listed in table 4. [2, 5, 8, 9]

Drugs and Orange juice: Orange juice should not be consumed with antacids containing aluminum. This juice increases the absorption of the aluminum. Orange Juice and milk should be avoided when taking antibiotics. The shift in pH towards acidic side decreases the effectiveness of antibiotics, as does milk. [3, 9]

Laxatives and Milk: Milk also doesn't mix with laxatives containing bisacodyl (Correctol and Dulcolax). The laxative works much better if taken in the morning. [3]

MAOIs and Tyramine: There have been reports of serious hypertensive crisis reactions occurring in people being treated with MAOIs (e.g. Isocarboxazid, Phenelzine etc.) following ingestion of food with a high content of tyramine (e.g. aged cheese, wine, pickled fish, concentrated yeast extracts, broad-been pods etc). The interaction can cause a potentially fatal increase in blood pressure**.** [8, 9]

NSAIDs and Food: Regularly consuming a diet, high in fat while taking anti-inflammatory, anti-arthritis medications can cause renal toxicity and can leave the patient feeling of not well. [9]

Raspberries: Raspberries contain a natural salicylate that can cause an allergic reaction in salicylate sensitive people.

.**Theophylline and Food:** Generally food does not alter the activity of theophylline significantly when the drug is administered in an immediate release formulation. However, variation is seen with the controlled release formulation of theophylline, if taken with food. [8, 11]

Theophylline and Grilled meat: Grilled meats can lead to problems for those on antiasthmatic drugs containing theophyllines. The chemical compounds formed when meat is grilled, somehow prevent this type of medication from working effectively, thereby increasing the possibility of an unmanageable asthma attack. [3]

Tomato contains small quantities of a toxic substance known as solanine that may trigger headaches in susceptible people. They are also a relatively common cause of allergies. An unidentified substance in tomatoes and tomato-based products can cause acid reflux, leading to indigestion and heartburn. Individuals, who often have digestive upsets, should try eliminating tomatoes for 2 to 3 weeks, to see if there is any improvement. [3]

What clinical pharmacologist should do to reduce food-drug interactions?

- He should study the prescription label on the container. If he does not understand something, or think that more information is required, he should ask the physician.

- The directions, warnings, interactions and precautions printed on all medication labels and package inserts, should be read carefully. Even over-the-counter medications can cause problems. The same should be clearly communicated to the patient/attendant.
- The Patient should be directed that

➢ He should take the medicine with a full glass of water as the dosage form is taken without water may increase esophageal concentration of drug.

➢ The medication should not be mixed with food/hot drinks.

➢ The hard gelatin capsules should not be opened. This may change the clinical effect of the drug.

➢ Multivitamin, specially containing minerals should not be taken with medication. Some vitamins and minerals can interact/chelate with some drugs.

➢ The medication should be avoided with alcoholic drinks.

➢ He should be asked for all medications (both prescription and non-prescription drugs), he is taking.

Table 1: Effect of Food on Drug Absorption

Reduced Absorption	Delayed Absorption	Increased Absorption	Unaffected Absorption
Ethanol	Aspirin	Griseofulvin	Mehyldopa
Tetracycline	Digoxin	Diazepam	Sulfasomidine
Erythromycin	Diclofenac	Vitamins	Propylthiouracil
Levodopa	Acetaminophen	Propranolol	
Captopril	Furosemide	Metaprolol	
Atenolol	Sulfadiazine	Chlorthiazide	
Aspirin	Sulfixazole	Hydralazine	
Ampicillin	Nitrofurantoin	Lebetalol	

Table 2: Medications which should be taken on an empty stomach

Alendronate	**Ampicillin**	**Astemizole**	**Bethanechol**
Bisacodyl	Captopril	Cefibuten	Cilostazol
Demeclocycline	Dicloxacillin	Didanosine	Etidronate
Felodipine	Indinavir	Lansoprazole	Levothyroxine
loratadine	loracarbef	Methotrexate	Moexipril
Mycophenolate	Omeprazole	Oxacillin	Penicillamine
Perindopril	Repaglinide	Rifampin	Rifabutin
Riluzole	Roxithromycin	Sucralfate	Sulfamethoxazole
Sulfadiazine	Zalcitabine	Tolcapone	Zafirlukast

Table 3: Medications which should be taken with Food

Allopurinol	**Atovaquone**	**Augmentin**	**Aspirin**
Amiodarone	Baclofen	Bromocriptine	clofazimine
Carvedilol	Naproxen	Chloroquine	Cimetidine
Cefpodoxime	Diclofenac	Divalproex	Doxycycline
Felbamate	fenofibrate	Fiorinal	Fludrocortisone
fenoprofen	Griseofulvin	glyburide	Hydrocortisone
Sulindac	Indomethacin	Valproic acid	Itraconazole
Ketorolac	Lithium	Metronidazole	Misoprostol
methanamine	mebendazole	Prednisone	Naltrexone
Ticlopidine	Tolmetin	Trazodone	Troglitazone
Ritonavir	Nelfinavir	Nitrofurantoin	Niacin

Table 4: List of drugs which serum concentration may increase when taken with grapefruit juice

Amiodarone	**Astemizole**	**Atorvastatin**	**Alprazolam**
sBenzodiazipine	Buspirone	Carbamazepine	Carvedilol
Cerivastatine	Cilostazole	Clarithromycin	Clomipramine
Codine	Cyclosporine	Dapsone	Dextromethorphan
Diazepam	Diltiazem	Estrogens	Erythromycin
Felodipine	Fentanyle	Finesteride	Haloperidol
Indenavir	Lidocaine	Lovastatine	Lercanidipine
Midazolam	Methadone	Nelfinavir	Niifedipine
Ondansetron	Paclitaxel	Progestins	Progeseterone
Quinidine	Ritonavir	Salmeterol	Saquinavire
Simvastatine	Tacrolimus	Trazodone	Triazolam
Vinblastine	Vincristine	Zaleplon	Zelpidem

REFERENCES:

1. Sarah E, Bland. Drug-Food Interactions. Journal of the Pharmacy Society of Wisconsin. 1998: 28-35.

2. http://www.hoptechno.com/book10.htm

3. http://medicalcenter.osu.edu/patientcare/healthcare_services/emergency_services/non_traumatic_emergencies/food_drug_interactions/Pages/index.aspx

4. Venkateswarlu V. Biopharmaceutics and Pharmacokinetics. 2004; Ist edition; Pharma Med Press Hyderabad: 57-58.

5. Bennette P.N, & Brown M. J. Clinical Pharmacology. 2003; Ist edition: 111-112.

6. Brahmankar D.M, Jaiswal S.B, Biopharmaceutics and Pharmacokinetics A Treatise. edition 2009; Vallabh Prakashan: 73-74.

7. http://www.globalrph.com/drugfoodrxn.htm

8. Remington. The Science and Practice of Pharmacy. 2005; 21th edition, Volume ii, Pub by Wolters Kluwer (India) Pvt. Ltd.; New Delhi: 1889, 1893 & 1894.

9. Sharma H.L. & Sharma K.K. Principle of Pharmacology. 2007; Ist edition: Paras Medical Publisher Hyderabad: 950.

10. Harle, U.N. & Gairwaad, N.J. Principles & Industrial Application of Pharmaceutics & Biopharmaceutics. 2008; Nirali Prakashan, Pune

11. Sharma V.N. Essentials of Pharmacology Basic Principles and General Concepts. 2007; 3rd edition: CBS Publishers & Distributors, 44.