Abstract

Interaction between foods and drugs can have profound influence on the success of drug treatment and on the side effect profiles of many drugs. A drug interaction is defined as any alteration, pharmacokinetics and/or pharmacodynamics, produced by different substances, other drug treatments, dietary factors and habits such as drinking and smoking. These interactions can affect drugs, altering their therapeutic efficacy and causing toxic effects. The aim of this study was to conduct a review of available data about interactions between different therapeutic agents and food. After excluding different articles, the main results refer to interactions between drugs and food. Advising patients to remove some members of daily food from their diet when treatment with these drugs seems to be the best recommendation. Given these interactions and the associated potential adverse effects the anamnesis must include detailed information about the specific eating habits of the patients. Pharmacists in every practice setting need to be vigilant in monitoring for potential drug-food interactions and advising patients regarding foods or beverages to avoid when taking certain medications. It is imperative for pharmacists to keep up-to-date on potential drug-food interactions of medications, so that they may counsel properly to the patients.

Keywords: Therapeutic Agents; Food-Drugs Interactions; Daily Food; Diet.

DRUG-FOOD INTERACTIONS

According to the World Health Organization (WHO) reports, increased in daily fruit and vegetable intake could be beneficial to prevent the major chronic non-communicable diseases. It has been reported that low fruit and vegetable intake is among the top-10 risk factors contributing to mortality.[1] Increase in fruit and vegetable intake can also help to displace food high in saturated fats, sugar or salt. Observed drug-phytochemical interactions, additionally to interactions with dietary micronutrients indicate various possibilities for improved therapeutic strategies. However, several reports have observed the effects of herbal medicines and plant foods on drug bioavailability. It has been suggesting that important food
and phytochemical modulation of drug transporters and drug-metabolizing enzymes leading to potential important nutrient-drug interactions. [1] Drug-Food interactions can result in two main clinical effects; decreased in bioavailability of a drug resulted in treatment failure or an increased in bioavailability, moreover increases the risk of adverse events and may even precipitate toxicities. Drug metabolizing enzymes and drug transporters play vital roles in the alteration of ADME (drug absorption, distribution, metabolism, and elimination). Acting alone or in combination with each other, they can affect and alter the pharmacokinetics and pharmacodynamics of a drug. Interaction between the drug metabolizing enzymes and transporters is one of confounding aspect that has been recently shown to contributable for potential multifaceted drug interactions.[2]

*Syzygium Cumini (Jamun)*: Syzygium Cumini or Jamun (Hindi), Jamun fruit also called as Indian blackberry. Syzygium cumini (Family-Myrtaceae) at a dose level of 50 mg/kg also showed significant decrease in blood glucose level. Also, it has shown significant decrease in blood glucose levels of alloxan-induced diabetic rats. *S. cumini* act on glucose transporter (GLUT-4), PPAR gamma and PI3K involved in glucose transport. Activity suggests that *S. cumini* activate glucose transport in a PI3K-dependent manner. Shweta and her colleagues reported that oral administration of ethyl acetate and methanol extracts of *Syzygium cumini* (200 and 400 mg/kg) showed significant decrease in blood glucose level.[3] It has been reported that different solvent extracts extracted sequentially were analyzed for glucose uptake activity at each step, methanol extracts were found to be significantly active at 100 ng/ml dose comparable with insulin and Rosiglitazone.[4, 5] Jamun traditionally used as antidiabetic agent; so that it should be avoided and contraindicated during the treatment of diabetes because the administration of oral hypoglycemic agents along with Jamun may leads to severe hypoglycemia.

*Momordica Charantia (Karela)*: Bitter Melon or *Momordica Charantia*, also known as Karela or Balsam pear; is a Tropical vegetable and common food in Indian cuisine and has been used extensively in folk medicine as a remedy for diabetes.[6] The fruit of *Momordica Charantia* is considered as tonic, stomachic, stimulant, emetic and laxative. Also the fruit is useful in treatment of gout, rheumatism and sub-acute cases of the spleen and liver diseases as well it is supposed to purify blood and dissipate melancholia. It has also been shown to have hypoglycemic properties in the animal as well as effective in human studies.[7] It has been reports that *Momordica Charantia* intake increases the number of beta cells in the pancreas thereby improving the body’s ability to produce insulin. The fruit has also shown
the ability to promote insulin release by enhancing cells uptake of glucose and potentiate the effect of insulin.

Oral administration of fresh fruit juice (dose, 6 c.c./kg) decreases the blood glucose level in normal and alloxan-induced diabetic rabbits. Bitter melon’s hypoglycemic effects have been shown in animal and human studies. P-insulin, a polypeptide from the fruits and seeds, results in rapidly decreased and stabilized the blood glucose level in rats. It improves blood glucose levels by increasing glucose uptake and glycogen synthesis in the liver, muscles, and fat cells as well as it improve the insulin release from pancreatic beta cells and repair or promote new growth of insulin-secreting beta cells.[6] Extremely high doses of the juice (bitter melon) can cause diarrhea and abdominal pain. Bitter melon should not be used and avoided for small children or anyone with hypoglycemia, as it may trigger or worsen low blood glucose or hypoglycemia. The use of Momordica Charantia should be avoided in pregnant women as it stimulates the uterus and may cause premature birth. Administration of bitter melon may potentiate the action of insulin; produces synergistic effects with antidiabetic drugs and also may potentiate the cholesterol-lowering drugs. Moreover, the diabetic patients taking/receiving hypoglycemic drugs (likely Phenformin and chlorpropamide) or insulin, [6] the use of bitter melon should be avoided or taken with caution as it may potentiate the effectiveness of the drugs and may leading to severe hypoglycemia.

Garlic (Allium sativum): Garlic has been widely used for reducing the high cholesterol. Garlic has also been used for treating or myriad other disorders (such as atherosclerosis, diabetes, fungal infections, cancer, hypertension, myocardial infarction and peripheral vascular disease) with little scientific evidence supporting its benefits. Jain and Vyas had shown the hypoglycemic effect of garlic extracts with water or several other different organic solvents on the oral glucose tolerance in both normal and alloxan-induced diabetic rabbits. [8] Garlic oil shown hypoglycemic effect in diabetic animals as well as in humans has also been reported. [9-11] Co-administered of glimepiride with garlic resulted in tight glycemic control due to the hypoglycemic properties of garlic as well as glimepiride. [12] Sheela and Augusti reported that sulfur containing amino acid S-allyl cysteine sulfoxide (alliin) in garlic has more potential to control the diabetic condition in rat as compared to insulin and Glibenclamide. [13] Elidi et al. reported that oral administrations of the garlic extract had shown significant decrease in the levels of serum glucose, triglycerides and total cholesterol levels while shown increase in serum insulin levels in diabetic rats. It was
reported that the antidiabetic effect of the garlic extract was more effective than that observed with Glibenclamide administration (600 microg/kg). *Allium sativum* results in hypoglycemia when taken with chlorpropamide. Patients taking diabetes medications should be cautioned because of the possibility of hypoglycemia. [14] The use of garlic should be avoided or taken with caution as it may potentiate the effectiveness of the drugs and may lead to severe hypoglycemia.

**Interactions between food and alpha and beta-blockers**

Blockers of α1-adrenergic receptors causes a competitive and reversible blockage of those receptors, thus lessening or removing the actions of catecholamines mediated by way of the stimulation of those receptors. In regard to β-adrenergic blockers, these agents block competitively and reversibly the actions of catecholamines mediated by way of the stimulation of β-adrenergic receptors. Furthermore, some of these agents have vasodilator properties, which are associated with an increase in nitric oxide release or with the blocking of the α-adrenergic receptors. [15] With respect to doxazosin, the BA of a single dose of 8 mg by means of a controlled release gastrointestinal form under fasting conditions and after ingestion, and a single standard dose of 2 mg under fasting conditions have been studied comparatively. Under fasting conditions, Cmax was similar for both presentations, with a BA of 75% in the case of the sustained release form with respect to the standard one. In the case of the sustained release form, an administration with fat-rich food leads to a Cmax and AUC 31% and 18% higher respectively.[16]. Since the decreases of BP in hypertensive patients treated with urapidil are more pronounced in the inclined portion of the curve of serum concentration of the drug, maximizing that part of the curve, as is the case of administration of the sustained release capsule with breakfast, could be advantageous.[17] In the case of prazosin, an animal experimental work has shown that its administration at the paraventricular nucleus of the hypothalamus is able to reduce the SBP only in undernourished animals.[18] However, no studies concerning potential interactions between the drug and food in humans are developed. With respect to beta-blockers, the BA of bevantolol, metoprolol when administered as sustained release form, propranolol when administered as sustained release form and timolol is not affected by the simultaneous ingestion of food.[19-22] In the case of acebutolol and diacetolol there is a decrease of BA when administered with food but without relevant clinical effects.[23] The BA of propranolol may be increased with simultaneous food intake and specifically with a high-in-protein diet. Nevertheless no relevant clinical effects have been reported. Other diets (high-in-carbohydrates diet and low-
in-protein diet) do not modify the BA of propranolol.[24] In addition, the simultaneous intake of propranolol and garlic increases the BA without causing clinical effects.[25,26] With respect to metoprolol, a high in-protein diet seems to increase the BA but without relevant clinical effects.[27]

**Interactions between food and calcium-channel blockers**

These antihypertensive agents are drugs that reduce the tone of vascular smooth muscle and produce peripheral and coronary vasodilation, improving the coronary flow and reducing vascular resistance. There are three groups: a) dihydropyridine derivatives (nifedipine, amlodipine, nicardipine, felodipine, nisoldipine, barnidipine and isradipine), b) derived from phenylalkylamines (verapamil) and c) derived from benzodiazepines (diltiazem). [15] Felodipine has a delayed absorption when administered by sustained release forms along with food, which is attributed to increased drug retention in the stomach.[28] With respect to verapamil, a more rapid absorption by using a generic drug compared with the reference drug has been found when taken with food and using sustained release forms. In addition, an absence of BA changes in verapamil has been reported by taking it with rich-in-protein foods.[29,30] The use of sustained release capsules compared with the dispersion of the content of the capsules in food has not shown significant differences on the pharmacokinetics neither of verapamil nor of norverapamil.[31] With respect to nisoldipine, at the time of maximum plasma concentration the additional decrease in BP relative to baseline due to the food effect seems to be about 7-15% for DBP and 3-9% for DBP.[32] Considering nisoldipine coat-core, the concomitant use of other drugs, which may produce marked induction or inhibition of CYP3A4 is contraindicated. The concomitant intake of the coat-core tablet with high-fat, highcalorie foods results in an increase in the maximum plasma concentrations of nisoldipine. This “food effect” can be avoided by administration of the coatcore tablet up to 30 minutes before the intake of food.[33] The pharmacokinetic properties of barnidipine are unaffected by food.[9] With regard to the salt, it is known that a high intake of common salt (NaCl) plays a fundamental role in the development and maintenance of HT.[35,36] Nevertheless, the antihypertensive effect of felodipine, a calcium channel blocker with natriuretic properties, is maintained during high salt intake, at least when given at the maximal antihypertensive dose.[37] Isradipine, another calcium channel blocker, decreases the sitting SBP and the sitting DBP during a high salt diet with a lowest effect during the salt restriction.
With respect to sodium restriction, it must be noted that calcium antagonists may have better efficacy when prescribed to saltreplete hypertensive persons.

**Interactions between food and angiotensin-converting enzyme (ACE) inhibitors**

They are agents that act by blocking one of the steps in the formation of angiotensin II, a key effector of the renin-angiotensin-aldosterone system. ACE inhibitors are one of several groups of drugs capable of interfering with the renin-angiotensin-aldosterone system, others being inhibitors of renin and AT1 receptor blockers. ACE inhibitors inhibit competitively the angiotensin-converting [15] ACE inhibitors constitute a heterogeneous group of agents with pharmacologic, pharmacokinetic and therapeutic differences among them.[40] With respect to the classification, three groups are usually distinguished based on the existence of a sulfhydryl-, carboxyl- or phosphinyl-group.[41] In general, there are not any relevant food-drug interactions described for these agents. Thus, food seems not to affect the BA of lisinopril. [42, 43] With respect to captopril, the co-administration of food or antacids with this agent has been shown to diminish the BA of the latter and decrease its clearance, respectively. Nevertheless the decreased BA of captopril when taken with meals does not significantly alter clinical responses to the drug.[44,45] Considering enalapril, its BA is not modified when taken with meals [46] and benazepril can be taken any time of day, with or without food, this not being relevant for its BA.[47] Benazepril is rapidly converted to benazeprilat and despite foods delaying slightly the absorption of the first, the BA of the latter is not modified.[48] The absorption of quinapril is unaffected by food. Peak serum concentrations of quinapril and quinaprilat are achieved within one and two hours, respectively.[49] Moexiprilat, the active metabolite of moexipril, has shown an extended duration of action owing to a long terminal pharmacokinetic half-life and produces a persistent ACE inhibition. Although the pharmacokinetic is partly influenced by food intake, ACE inhibition is not affected. This might be explained by a second compartment directly related to the ACE which is less prone to food effects and the reaching of a ceiling in the sigmoidal concentration-effect curve, even with the lower Cmax concentrations associated with the postprandial state. [50] In general the BA of ACE inhibitors may be reduced by concomitant food or antacids, which may slow gastric emptying and raise gastric pH. [51] In the case of nifedipine, a low-fat (high-carbohydrate) meal slows the rate but does not alter the extent of nifedipine absorption. Insofar as certain side effects may be related to the high peak plasma levels associated with rapid absorption, administration with meals might serve to reduce the incidence of such effects. For the majority of patients on routine maintenance
Interactions between food and angiotensin II receptor blockers (ARBs)

Angiotensin II receptor blockers (ARBs) represent a class of effective and well tolerated orally active antihypertensive agents. The ARBs specifically block the interaction of angiotensin II at the AT1 receptor, thereby relaxing smooth muscle, increasing salt and water excretion, reducing plasma volume, and decreasing cellular hypertrophy. After oral administration, the ARBs are rapidly absorbed (time for peak plasma levels = 0.5-4 h) but they have a wide range of BA (from a low of 13% for eprosartan to a high of 60-80% for irbesartan). In general, food does not influence the BA, except for valsartan (a reduction of 40-50%) and eprosartan (increase). [53] The fact that most ARBs do not interact with food makes it oral administration very straightforward for this class of agents. Several of the ARBs, irbesartan and losartan, are metabolized by cytochrome P450 (CYP), and are therefore subject to potential drug-drug interactions with other drugs that alter CYP activity. [54] Despite the absence of general relevant effects of food intake on ARBs BA, foods retard the absorption and decrease the Cmax of losartan (5-10%) and telmisartan (10-20%). In addition, foods decrease the BA, Cmax and AUC (3,5%) of valsartan, although plasmatic concentrations are similar to those reached without food within the next eight hours. On the contrary, high-fat foods increase Cmax and AUC of eprosartan (80% and 55%, respectively). [55] Irbesartan is a specific AT1 receptor antagonist with rapid oral BA (peak plasma concentrations occurring at 1.5-2 h after administration) and a long half-life (11-15 h) that provides 24-h BP control with a single daily dose. The maximal BP fall occurs between 3 and 6 h after the dose. This antihypertensive agent is relatively unaffected by food or drugs. [56, 57]

Interactions between food and hydrazines

Hydralazine acts directly on arteriolar smooth muscle, where it activates the guanylyl-cyclase and increases the Antihypertensive drugs-food interactions [22]. It also inhibits the release of calcium from the sarcoplasmic reticulum induced by inositol-1,4,5-triphosphate (IP3). The result is a decrease in intravascular calcium concentration, which leads to a reduction of the peripheral vascular resistances and BP, whereas venous tone is nearly unmodified. [15] Hydralazine has been widely used in combination with other antihypertensive agents, particularly betablockers and diuretics. One of the main reasons for this combination relates to the pharmacological effects of hydralazine, such as fluid retention.
and reflex tachycardia. The logic behind the inclusion of a diuretic is the elimination of fluid retention, while the betablocker would control the tachycardia. [58] In a former study about the pharmacokinetics of hydralazine, the AUC and Cmax values were much higher under the fasted and enteral infusion conditions than under the standard breakfast or enteral bolus conditions, indicating that the absorption and/or disposition kinetics of hydralazine may be altered by food. In addition the rate of administration, but not necessarily the physical form, of the nutrients appeared to be a significant factor to determine the magnitude of the food effect. [59] In a former study, the peak blood hydralazine levels were reduced by food after both hydralazine and slowrelease hydralazine, by 69 and 66%, respectively. Time to peak blood hydralazine concentration was delayed significantly with the slow-release form and a statistically significant food-related reduction of area under blood hydralazine concentration versus time curves (AUC) only with hydralazine (by 44%) was observed. The AUC for slowrelease hydralazine was decreased only 29% by food. Authors concluded that hydralazine should be taken at a consistent time with respect to meals, [60] thus confirming another previous study. [61] With respect to endralazine, comparing a dose of 5 mg and 10 mg after a standard breakfast, in the case of 5 mg the peak endralazine concentration averaged 57.5% lower and the AUC decreased significantly by 49.9%, whereas after 10 mg the postprandial peak level and the AUC were 82.9% and 64.7%, lower. In the 5 mg study the mean arterial BP was decreased by 30 mmHg in the fasting subjects and by 21 mmHg in the postprandial group. For the 10 mg dose the corresponding values were 35 and 24 mmHg. The BP lowering effect was only weakly correlated with the food-related reduction in the plasma endralazine levels. The results suggested that endralazine has a similar kinetic interaction with food as that found for hydralazine. [62]

**Interactions between antihypertensive agents and grapefruit juice**

It was indicated that grapefruit juice acted by inhibiting the drug pre-systemic metabolism mediated by CYP, particularly the isoform CYP3A4 in the bowel. In addition, they reported that people with higher levels of CYP3A4 with liver failure and with clinical situations that predispose to increase the effects and toxicity of drugs would be more likely to suffer from the interaction of grapefruit juice with administered drugs. [63] Grapefruit juice acts on intestinal CYP3A4, which metabolizes more than 60% of commonly prescribed drugs, drug transporter proteins (such as P-gp) and transporter proteins of organic cations (OCT), all in the intestine. The hepatic CYP3A4 appears to not be inhibited and, on the other hand, the above-mentioned P-gp would be inhibited.[64] It must be noted that the intake of
grapefruit juice with drugs effectively inhibits P-gp, but the habitual intake of grapefruit juice could increase the expression of P-gp.[65] On the other hand, flavonoids (some of them like naringin and quercetin are present in grapefruit juice) may interfere with the P-gp not only at the binding site but also inhibiting OCT and organic anion transporter (OAT), transport systems of the basal membrane of intestinal epithelium.66,67] Grapefruit juice has different bioactive components such as flavonoids (flavanones, flavones, flavonols, anthocyanins), limonoid aglycones, glycosides, furanocoumarins (bergamottin, dihydroxybergamottin), ascorbic acid, folic acid, glucaric or saccharic acid, carotenoids, pectin and potassium. Traditionally, drug interactions have been attributed to furanocoumarins.[64,68,69] Inactivation of CYP3A4 seems to be irreversible, it occurs when taking 200-300 ml, and the effect of increasing the BA of the drugs, that may occur even after 24 hours of the intake, are particularly relevant.[70] After having described an increase in the levels of the dihydropyridine calcium channel antagonists felodipine and nifedipine when taken with grapefruit juice, [71] different drugs in this antihypertensive group have been seen to interact with grapefruit juice. Thus, amlodipine, azelnidipine, benidipine, cilnidipine, efonidipine, felodipine, manidipine, nicardipine, nifedipine, nimodipine, nisoldipine, nitrendipine and pranidipine. The result of the interaction is an enhancement of plasma concentration of these drugs.[72-83] With respect to barnidipine, minor increases in its availability may occur with concomitant use of alcohol or grapefruit juice, but these are unlikely to have clinical relevance.[34] Paine et al. have reported in an experimental design that furanocoumarins are the active ingredients of grapefruit juice responsible for enhancing the systemic exposure of felodipine and probably other CYP3A4 substrates that undergo extensive intestinal first-pass metabolism. [84] It has been suggested that felodipine-grapefruit juice interaction should be taken into account among elderly people [85] and that taking grapefruit juice should be separated by at least 2-3 days of the drug intake. [86] In addition, the existence of interindividual variability in the effect of that interaction has been noted [87] and also the fact that among calcium channel blockers felodipine is the one with the clearest interaction. [88] Finally, with respect to felodipine, one of the most recent studies concludes that previous research may have overestimated the effect of that interaction. [89] In other cases, the interaction between grapefruit juice and some drugs causes a reduction of Cmax, AUC and t1/2. This is the case of aliskiren, a renin inhibitor. Amlodipine seems to not be affected by the concomitant intake of grapefruit juice. [90]
With respect to diltiazem, a single intake of grapefruit juice (250 ml) has been found to cause a slight but statistically significant increase in the systemic exposure of diltiazem. The inhibition of intestinal metabolism and/or P-gp efflux transport might be responsible for this effect. Considering verapamil, grapefruit juice significantly increases the AUC and the Cmax. The increase in concentrations present for (R)- and (S)-enantiomers seems to be slightly greater for verapamil than for norverapamil. [91] Nevertheless, certain controversy remains with respect to verapamil- grapefruit juice interaction due to the previous study of Zaidenstein et al., in which a single administration of grapefruit juice with short-acting verapamil had no significant effect on the pharmacokinetics of verapamil. [92] With regard to angiotensin II receptor blockers, it must be noted that the AUC of losartan increased insignificantly when taken with grapefruit juice and the time to drug appearance in serum was prolonged. Grapefruit juice also caused a change in the pharmacokinetic properties of the pharmacologically active metabolite of losartan. The half-life of the metabolite as well as the mean retention time were significantly longer; however, the AUC was decreased. Losartan is thought to be primarily metabolized by CYP2C9, but the results of the study of Zaidenstein et al., show that grapefruit juice’s effect on CYP3A4 in the gut is able to alter the pharmacokinetics of losartan. [93] Among beta-blockers, talinolol absorption is modified by an inhibitory action of naringin on the P-gp and the OAT system. [94] After the intake of a glass of grapefruit juice a reduced BA of talinolol has been found as occurs with the repeated intake. The parameters affected are AUC, maximum plasmatic concentration and urinary excretion values.[95] However, the inhibitory action on the P-gp would result in an increased BA.[96] With respect to acebutolol and its major metabolite, diacetolol, the intake of grapefruit juice slightly decreases plasma concentrations by interfering with intestinal absorption, without significant clinical manifestations.[97] The reduced celiprolol concentrations when taken with grapefruit juice are probably caused by physicochemical factors that interfere with celiprolol absorption, although other mechanisms cannot be excluded. It must be noted that the grapefruit juice-celiprolol interaction is probably of clinical relevance.
Table 1: Examples of specific counseling on some drug-food interaction (98, 99-101)

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Counseling</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cephalosporins, penicillin</td>
<td>Take on an empty stomach to speed absorption of the drugs.</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>Don't take with fruit juice or wine, which decrease the drug's effectiveness.</td>
</tr>
<tr>
<td>Sulfa drugs</td>
<td>Increase the risk of Vitamin B₁₂ deficiency</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>Dairy products reduce the drug's effectiveness. Lowers Vitamin C absorption</td>
</tr>
<tr>
<td>Dilantin, phenobarbital</td>
<td>Increase the risk of anemia and nerve problems due to deficiency of folate and other B vitamins.</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>Reduce appetite and can lead to excessive weight loss</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>A low-salt diet increases the risk of lithium toxicity; excessive salt reduces the drug's efficacy</td>
</tr>
<tr>
<td>MAO Inhibitors</td>
<td>Foods high in tyramine (aged cheese, processed meats, legumes, wine and beer among others) can produce a hypertensive crisis.</td>
</tr>
<tr>
<td>Tricyclics</td>
<td>Many foods, especially legumes, meat, fish and foods high in Vitamin C, reduce absorption of the drugs.</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>Take on an empty stomach to improve the absorption of the drugs.</td>
</tr>
<tr>
<td>Alpha blockers</td>
<td>Take with liquid or food to avoid excessive drop in blood pressure.</td>
</tr>
<tr>
<td>Antiarrhythmic drugs</td>
<td>Avoid caffeine, which increases the risk of irregular heartbeat.</td>
</tr>
<tr>
<td>Beta blockers</td>
<td>Take on an empty stomach; food, especially meat, increases the drug's effects and can cause dizziness and low blood pressure.</td>
</tr>
<tr>
<td>Digitalis</td>
<td>Avoid taking with milk and high fiber foods, which reduce absorption, increases potassium loss.</td>
</tr>
<tr>
<td>Diuretics</td>
<td>Increase the risk of potassium deficiency.</td>
</tr>
<tr>
<td>Pseudoephedrine</td>
<td>Avoid caffeine, which increase feelings of anxiety and nervousness.</td>
</tr>
<tr>
<td>Theophylline</td>
<td>High protein diet reduces absorption. Caffeine increases the risk of drug toxicity.</td>
</tr>
<tr>
<td>Cholestyramine</td>
<td>Increases the excretion of folate and fat soluble vitamins.</td>
</tr>
<tr>
<td>Gemfibrozil</td>
<td>Avoid fatty foods, which decrease the drug's efficacy in lowering cholesterol.</td>
</tr>
<tr>
<td>Antacids</td>
<td>Interfere with the absorption of many minerals; for maximum benefit, take medication one hour after eating</td>
</tr>
<tr>
<td>Drug Class</td>
<td>Instructions</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Oral contraceptives</td>
<td>Salty foods increase fluid retention. Drugs reduce the absorption of folate, vitamin B₆ and other nutrients; increase intake of foods high in these nutrients to avoid deficiencies.</td>
</tr>
<tr>
<td>Steroids</td>
<td>Salty foods increase fluid retention. Increase intake of foods high in calcium, vitamin K, potassium and protein to avoid deficiencies.</td>
</tr>
<tr>
<td>Thyroid drugs</td>
<td>Iodine-rich foods lower the drug's efficacy.</td>
</tr>
<tr>
<td>Aspirin and stronger</td>
<td>Always take with food to lower the risk of gastrointestinal irritation; avoid taking with alcohol, which increases the risk of bleeding. Frequent use of these drugs lowers the absorption of folate and vitamin C.</td>
</tr>
<tr>
<td>nonsteroidal antiinflammatory drugs</td>
<td></td>
</tr>
<tr>
<td>Codeine</td>
<td>Increase fiber and water intake to avoid constipation.</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>Never take with alcohol. Caffeine increases anxiety and reduce drug's effectiveness.</td>
</tr>
</tbody>
</table>

**ROLE OF PHARMACIST IN PREVENTION AND COUNSELING ABOUT DRUG-FOOD INTERACTIONS**

Pharmacists in every practice setting need to be vigilant in monitoring for potential drug-food interactions and advising patients regarding foods or beverages to avoid when taking certain medications. It is imperative for pharmacists to keep up to date on potential drug-food interactions of medications, especially today’s new drugs, so that they may counsel properly.

In providing drug information to patients, pharmacists often discuss potential side effects and how the medication should be taken. It is important to provide information to patients on when to take their medications in relation to food intake. Consequences of drug-food interactions may include delayed, decreased or enhanced absorption of the drug. Food may also affect the bioavailability, metabolism and excretion of certain medications. The patient may experience an adverse side effect or toxicity or may not receive the full therapeutic benefit of the medication. The Joint Commission on the Accreditation of Healthcare Organizations (JCAHO) requires that a patient’s medication profile include potential drug-food interactions, that the pharmacist call the prescriber whenever the potential for a medication-food interaction exists and document the communication and follow-up action on the prescription or order form, and that patients be given instructions and
counseling regarding the potential for drug-food interactions before their hospital discharge. Elderly patients may be at a greater risk for drug-food interactions [102]
The following information can be given to the patients while dispensing the medicine. [103-104]
- Read the prescription label on the container. If you do not understand something or think you need more information, ask your physician or pharmacist.
- Read directions, warnings and interaction precautions printed on all medication labels and package inserts. Even over-the-counter medications can cause problems.
- Take medication with a full glass of water. Do not stir medication into your food or take capsules apart (unless directed by your physician). This may affect the efficacy of medication.
- Do not take vitamin pills at the same time you take medication. Vitamins and minerals can interact with some drugs.
- Do not mix medication into hot drinks because the heat from the drink may destroy the effectiveness of the drug.
- Never take medication with alcoholic drinks.
- Be sure to tell your physician and pharmacist about all medications you are taking, both prescription and nonprescription.
- Check with the pharmacist on how food can affect specific medications taken with the food. Examples of specific counseling on some drug-food interaction are summarized

**CONCLUSION**

As per our literature survey, we have found that the patients receiving medication are at higher risk of drug-food interactions as they are receiving multitherapies for the treatment of different complications and related disorders. So that the physician and other medical staff should aware and guide the patient about the medication, drug related problems, interaction with food and other drugs. This will help to prevent and stop the occurrence of the drug-food interactions. This review study summarized and highlights the various drug-food interactions as well as reports that the interaction between foods and drugs can have profound influence on the success of drug treatment and on the side effect profiles of many drugs. The clinical significance of drug-food interactions can be variable. Some foods greatly affect drug therapy, resulting in serious side effects, toxicity or therapeutic failure. In some instances, the interaction may have a beneficial effect by increasing drug efficacy or diminishing potential
side effects. The interactions are not always detrimental to therapy, but can in some cases be used to improve drug absorption or to minimize adverse effects. These interactions have received more attention recently, especially drug interactions with grapefruit juice. As new drug approvals occur with ever increasing speed, there is less information available about their adverse effects and interactions when the drugs reach the market. Pharmacists in every practice setting need to be vigilant in monitoring for potential drug-food interactions and advising patients regarding foods or beverages to avoid when taking certain medications. It is imperative for pharmacists to keep up to date on potential drug-food interactions of medications, especially today’s new drugs, so that they may counsel properly to the patients.

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