UNIT 7 NUTRIENT AND DRUG INTERACTION

Structure

7.1 Introduction

7.2 Nutrient and Drug Interaction: Basic Concept

7.3 Effect of Nutrition on Drugs

7.4 Drug Effects on Nutritional Status

7.5 Drug and Drug Interaction

7.6 Clinical Significance and Risk Factors for Drug-Nutrient Interactions

7.7 Guidelines to Lower Risk and Wise Use of Drugs

7.8 Let Us Sum Up

7.9 Glossary

7.10 Answers to Check Your Progress Exercises

7.1 INTRODUCTION

Modern medicine has given us many useful drugs that not only prolong and save lives but in fact improve the quality of our lives. Have you ever thought that the beneficial effects of the drugs that we take can be affected by some of the foods in our diet? Many drugs have powerful ingredients that interact with the human body in different ways. Diet and lifestyle can sometimes have a significant impact on a drug's ability to work in the body. Certain foods, beverages, alcohol, caffeine and even cigarettes can interact with drugs. These food and drug interactions can have dramatic, even dangerous effects on the way our bodies react to drugs. The purpose of this unit is to present the most common food and drug interactions, to see that we get the best results from the drugs that we need to take.

Objectives

After studying this unit, you will be able to:

- define nutrient drug interactions,
- describe the effect of nutrients and food on drugs and the effect of drugs on the nutritional status,
- identify the clinical significance and risk factors associated with nutrient drug interaction, and
- list handy guidelines for safe and wise use of drug.

7.2 NUTRIENT AND DRUG INTERACTION: BASIC CONCEPT

Medicines can treat and cure many health problems. Nevertheless, do you recall your doctor advising or recommending certain medications to be taken with food whereas others on an empty stomach. Have you given a thought as to why this is being advised?

Well, this for the simple reason that medicines can be effected by the food we eat. Well, not all medications are affected by food, but many can be affected by what we eat and when we eat it. Sometimes, taking medications at the same time we eat may interfere with the way our stomach and intestines absorb medication. Other medications are recommended to be taken with food. A food-drug interaction can occur when the food we eat affects the ingredients in a medication we are taking, preventing the medicine from working the way it should. Some nutrients can affect the way we metabolize certain drugs by binding with drug ingredients, thus reducing their absorption or speeding their elimination. For example, the acidity of fruit juice may decrease the effectiveness of antibiotics such as penicillin. Dairy products may blunt the infection-fighting effects of tetracycline. Anti-depressants called MAO inhibitors are dangerous when mixed with foods or drinks that contain tyramine (beer, red wine, and some types of cheese).

So then, can you now define or explain what we mean by drug-nutrient interaction? *Drug-nutrient interaction include specific changes in the process by which a drug is absorbed, distributed, metabolized, and eliminated by the body, caused by a nutrient(s) or changes to the kinetic(s) of a nutrient(s) caused by a drug.* In fact, nutrient-drug interaction is a broader term that also includes the effect of a medication on nutritional status. Nutritional status, you may already know, refers to the condition of health of an individual as influenced by the utilization of nutrients. Nutritional status may be impacted by the side effects of a medication, which could include an effect on appetite or the ability to eat.

Hence, a study of these interactions is important as it enables the health cure professionals and patients to work together to avoid or minimize problems. The benefits of minimizing drug nutrient interaction, you would notice, would go a long way in ensuring:

- medications achieve their intended effect,
- continuity of the prescribed drug by the patient,
- fewer nutrient or caloric supplement is required,
- optimal nutritional status is maintained,
- disease complications are minimized, and
- cost of health care services is reduced.

The extent of the effects of any food and drug interaction can vary. Potential effects depend on the dose and the form in which the drug is taken (pill, liquid, etc.). It also varies with an individual's age, sex, body weight, nutritional status and specific medical condition. The number of potential food and drug interactions is almost limitless. Interaction problems most often occur with the use of diuretics, oral antibiotics, anti-coagulant (blood-thinning) drugs, anti-hypertensive drugs, thyroid and sodium compounds, and alcohol.

Generally, administering oral medication along with the food or at a mealtime is a convenient manner of drug dosing. However, drug interactions can occur that modify the activity of the drug (decrease or increase drug effects) are referred to as *drug-drug interactions* or impair the nutritional benefit of certain food are called as a *drug-nutrient interaction.* While the effect of food or a nutrient on a drug or medication is a *nutrient-drug interaction.* The most commonly observed type of drug-food interaction affects the drug absorption.

Such interactions raise concerns that medications may lead to nutritional deficiencies or a poor diet may change how a medication works. This does not mean that if one is taking a medication, one needs to use a vitamin and or mineral supplement. There is a little chance that taking a medication for a short time (such as a ten day treatment), will affect the nutritional status, However, use of some medications for months or years may affect the nutritional health,

Drug and nutrient relationship can be categorized into two aspects:

1. *Effect of nutrition on drugs:* the influence of nutritional factors on drug absorption, action and effectiveness, and.
2. *Effect of drugs on nutrients:* the influence of drugs on nutritional intake, metabolism, excretion and requirements.

We will study about these interactions in the subsequent sections. We will also briefly review the drug and drug interactions. So let us get started. We shall begin first with effect of nutrition on drugs.

7.3 EFFECT OF NUTRITION ON DRUGS

Pharmacokinetics is the study of the time course of a drug in the body involving the absorption, distribution, metabolism and excretion of the drug. The movement of the drug through the body during absorption, distribution, metabolism etc. can be influenced by food or nutrients in the diet. These influences are reviewed next.

Food's Effect on Drug Absorption

The pharmacological effect of a drug depends on the rate and extent to which it is absorbed from the gastrointestinal tract. Food can decrease a drug's rate of absorption and/or increase the extent of absorption of numerous drugs. Examples include penicillin, tetracycline (TCN). The possible reasons for this may include:

- delayed gastric emptying,
- altered gastrointestinal pH,
- competition for binding sites with the nutrients,
- adsorption or the adhesion of food or a food component,
- chelation (combining) of drugs by food cations, and
- dietary fats impeding the absorption of hydrophilic drugs.

Gastric emptying may be delayed by the consumption of high-libre meal and meals with high fat content. *Chelation* reactions occur between certain medications and divalent or trivalent cations (a positively charged ion), such as iron, calcium, magnesium etc. and the absorption of the drug may be reduced by chelation (combining) with one of these metal ions. To illustrate, the antibiotic tetracycline form insoluble complexes with calcium in dairy products thus preventing or reducing the absorption of both drug and nutrient. *Adsorption* is another mechanism by which drug absorption is slowed or reduced. An example of this mechanism is the cardiovascular drug digoxin which should not be taken with high phytate food (such as what bran, oatmeal etc.).

The presence of food in the stomach enhances the absorption of some medication. Drugs whose absorption increases when taken with food include drugs such as *spironolactone, griseofulvin* and *itraconazole*. With some drugs, this food-drug interaction may be utilized to achieve higher serum drug levels or to use lesser amounts of drug per dose. For example, administration of the drug *ketoconazole* with acidic beverages such as colas, leads to increased and prolonged serum levels for the drug. This mechanism is based on changes in the gastrointestinal pH. Generally, tliese interactions have an insidious onset and may not be clinically evident except for the failure to achieve the therapeutic goals of therapy or loss of disease control. Continuous long-term monitoring of patients is needed when drugs and food must be taken together. An example to substantiate this aspect is as follows:

- The calcium in milk and milk products such as yoghurt and cheese decreases the absorption of certain antibiotics, including tetracycline. Therefore, these foods

should not be eaten at the same time this drug is taken, so that the full dosage of the drug is available for adequate treatment of the infection.

- Tyramine is a vasoconstrictor that raises blood pressure. Significanl ingestion of high-tyramine food, such as aged cheese and cured meats, by individuals while being treated with mono-amine oxidase inhibitors (MAOI) – an antidepressant, can cause a hypertensive crisis such as increased heart rate, flushing, headache, stroke and even death.
- Caffeine in foods or beverages increases the adverse effects of stimulant drugs such as amphetamines, methylpheniclate, causing nervousness, tremor and insomnia.

In addition to affecting absorption of drugs, food can interact with drugs in a variety of other ways. These are highlighted in Box 7.1.

Box 7.1 Other Examples of Drug-Food Interactions

1) Vitamin K found in green leafy vegetables, tomatoes, coffee, beef liver, green tea etc., and some non prescription vitamin-mineral products can antagonize the anticoagulant effect of warfarin, resulting in decreased anticoagulant activity and lowered prothrombin time (PT); laboratory blood tests.

2) Vitamin B_6 (pyridoxine) found in avocados, beans, peas, sweet potatoes, bacon, pork, tuna, and some non prescription vitamill-mineral products, increases the metabolism o i levodopa, producing decreased blood levels of dopamine and antiparkinsonism effects. We will learn more about this later in Unit 17.

3) Calcium, magnesium and aluminium found in food supplements or antacid compounds bind (chelate) with ciprofloxacin and tetracycline to form an insoluble complex resulting in significantly decreased absorption of these antibiotics and decreased antibiotic effect.

4) Calcium in vitamin-mineral products and liquid enteral nutritional supplements inleract with some fluoroquinolone antibiotics and with phenytoin, reducing their bioavailability and resulting in decreased antibiotic activity and loss of seizure control, respectively.

Next, let us review the effect of food on drug transport in the body.

Foods Effect on Drug Transport

Many drugs are transported in blood bound to plasma proteins. Severe malnutrition or diseases affecting the synthesis of plasma proteins (such as liver disease) may reduce the body's ability to transport drugs and hence impair their effectiveness. Albumin is the most important drug-binding protein in the blood. Low serum albumin levels (due to inadequate protein intake and poor nutrition), therefore, provides fewer binding sites for some highly protein-bound drugs such as warfarin and anticonvulsant phenytoin, which may lead to risk of excessive anticoagulation and bleeding or toxicity, respectively.

Next, we move on to the effect of food on drug metabolism.

Food Effects on Drug Metabolism

The general tendency of the process of metabolism is to transform a drug from a lipid-soluble to a more water-soluble compound so that it can be handled more easily by the kidneys and excreted in the urine. Food can both inhibit and enhance the metabolism of drugs by altering the activity of the enzyme systems operating in the body. To illustrate, scientists discovered that grapefruit contains natural substances that can affect the way certain prescription medications are broken down (metabolized) by an

enzyme, known as *CYP3A4* (cytochrome P-450 3A4). This means that if a person drinks grapefruit juice and takes drugs (such as felodipine, zocor) orally, more of the drug may enter the bloodstream than would have under normal circumstances resulting in a greater pharmacologic effect and possible toxicity. Factors, which affect the deactivation or conjugation of a drug, can thus alter its pharmacological or toxic effects.

Periods of short-term starvation or prolonged periods of nutritional inadequacy can influence the effectiveness or safety of drugs. The amount of a drug required to produce a certain pharmacological effect is determined by the body weight. Sudden reduction in weight or dehydration may therefore result in over dosage. Undernutrition also reduces the activity of rnicrosomal drug metabolizing enzymes and this can diminish a drug's effectiveness (by reducing its rate of excretion). These are additional reasons for ensuring nutritional adequacy during illness, particularly since this is when pharmacological drug use is most likely to be needed.

Alcohol, which is also a drug in its own right often affects microsomal enzyme activity and can potentiate the action of some hypoglycemic drugs or central nervous system (CNS) depressants. The action of certain drugs such as propanolol may be reduced by alcohol.

Certain nutrients can also have a direct influence on drug metabolism. Vitamin K reduces the anticoagulant effect of warfarin and the dosage has to be sufficient to counteract the effects of habitual vitamin K intake. Any significant alteration may necessitate adjustment in warfarin dosage.

Sodium intake inversely affects serum levels of the mood stabilizer lithium carbonate and since this drug has a narrow range of therapeutic effectiveness, dietary sodium intake must be kept to a constant level in patients receiving this treatment.

Next, we move on to drug utilization.

*Foods Effect on **Drug** Utilization*

The following illustrations highlight the effect of food on drug utilization.

Liver and green leafy vegetables can decrease the effect of anticoagulants (blood-thinning drugs). These foods contain vitamin K, which helps promote blood clotting. On the other hand, aspirin and aspirin-containing compounds can enhance the effect of the blood-thinning drug and promote excessive bleeding.

- One of the most hazardous food and drug interactions is between monoamine oxidase (MAO) inhibitors and aged or fermented foods. MAO inhibitors are used to treat depression and high blood pressure. They decrease the metabolism in the body of compounds called monoamines. MAO inhibitors can react with a substance called tyramine (a monoamine) in foods such as aged cheese, fava beans and others. As a result blood pressure can rise to dangerous levels causing severe headaches, brain hdemorrhage and, in extreme cases, death.

- Natural licorice contains a substance which can increase blood pressure when eaten in large amounts. Long-term use of licorice and licorice-flavoured candy or drugs can counteract the effect of medication used for treating high blood pressure.

Finally, let us review the effect of food on drug excretion.

*Food Effects on **Drug** Excretion*

Food and nutrients can alter the reabsorption of drugs from the renal tubes. Urinary acidity affects drug reabsorption from the renal tubules. Hence, a change in urinary pH by food may change the amount of drug existing in the nonionic state, thus increasing or decreasing the amount of drug available for tubular reabsorption. Supplemental intakes of nutrients, which increase urinary acidity (e.g., large amounts of vitamin C intake), can decrease the excretion of salicylate drugs such as asprin.

In our discussion, so far we focused on the effect of food or nutrients on drugs absorption, utilization, metabolism, excretion etc. Let us now move on to the effects of nutrient supplements on drugs.

Effect of Nutrient Supplements on Drugs

A nutrient or nutrient supplement can alter the pharmacological action of a drug by enhancing the drug effect or by opposing it. These can result in drug-nutrient interactions. To illustrate, warfarin, is an oral anticoagulant that reduces the production of vitamin-K dependant clotting factors by inhibiting the conversion of vitamin K to a usable form. Because, this is a competitive interaction, the ingestion of vitamin K in the usable form (supplement) will oppose the action of warfarin and allow the production of more clotting factor. Therefore, to achieve an optimal level of coagulation, a balance must be maintained between the dose of the drug and the ingestion of vitamin K. On the other hand, ingestion of other nutrients like vitamin E in doses greater than 400 IU may enhance the anticoagulant effect of warfarin. Enhancement of the anticoagulation effects of warfarin may lead to serious bleeding events.

Further, in excessive amounts, vitamins and minerals act like drugs instead of nutrients. Nutrients in excessive amounts may interact with other nutrients or may even be toxic. For example, large amounts of zinc can interfere with copper and iron absorption. Similarly, large amounts of iron can interfere with zinc absorption.

Effect of feeding method on drug availability

The form in which a drug is administered or enters the body can influence its absorption, metabolism or excretion. This becomes more pronounced among critically ill patients who can not consume drugs orally and are on enteral food support. If the drug has to be administered though the enteral feeding tube it needs to be either crushed or dissolved in a solvent. Crushing oral preparations to pass down the tube may alter their absorption time/activity. Some of the drugs can not be added to the food infusion as it may alter their stability. Several drugs are available only in the form of tablets or capsules, dissolving these in feed, water, alcohol or sorbitol may not always be feasible. Drug such as cimetidine, aluminium hydroxide, metaclorpromide are physically incompatible with enteral foods. Certain drugs like phenytoin form complexes with calcium and protein thereby resulting in markedly reduced absorption of this medication. Such drugs need to given only by stopping enteral feed infusions for 1-2 hours. Patients on total parenteral nutrition generally have a separate tube (catheter) for infusion of drugs. Toxicity/overdosage of drugs is frequently observed in case of certain drugs administered directly into the blood.

With this, we end our study on effect of nutrient on drugs. Next, we shall explore the relationship between drug and food and the impact of medication on nutritional status. We would however take a break here and revise what we have learnt so far by answering the questions given in check your progress exercise 1.

Check Your Progress Exercise 1

1 What is drug nutrient interaction? Why is tlie study of these interactions important?

.....

.....

.....

2. What are the different categories into which nutrient drug relationships can be categorized? Explain briefly, giving examples.

.....

.....

.....

3. Food can decrease or increase a drug's rate of absorption. Comment on the statement giving suitable examples.

.....

.....

.....

4. Give two examples of the effect of food on drug utilization.

.....

.....

.....

Let us now get to know about the effect of drugs on the nutritional status.

7.4 DRUG EFFECTS ON NUTRITIONAL STATUS

Drugs can affect nutritional status in a number of ways i.e. by enhancing excretion of certain nutrients, by interfering with nutrient absorption, or by decreasing the body's ability to change nutrients into usable forms. These effects are gradual so that the effects will be greater in persons taking drugs over a long period of time. For these people, vitamin and mineral deficiencies may result. Here are some examples of drug effects on nutrients in the body:

- Abuse of antacids can lead to phosphate depletion. This can lead to a vitamin D deficiency in severe cases. Some patients have developed osteomalacia or softening of the bones due to loss of calcium because of a vitamin D deficiency.
- The excessive use of diuretics ("water pills") may result in the loss of electrolyles, mainly potassium. This may put people with heart problems at higher risk for serious heart rhythm problems. People taking diuretics regularly should eat foods which are good sources of potassium: tomatoes, tomato juice, oranges, orange juice, bananas, raisins, pmnes, potatoes, sweet potatoes and winter squash.
- Women who take oral contraceptives over a long period of time may develop folic acid and vitamin C deficiencies if their diets are inadequate in these nutrients. The best sources of folic acid are spinach and other greens, asparagus, broccoli and lima beans. Excellent vitamin C sources include oranges, grapefruits, lemons and limes, strawberries, tomatoes, potatoes, cabbage and green peppers.
- Anticonvulsant drugs, prescribed to prevent seizures, can lead to vitamin D and folic acid deficiencies. The use of vitamin supplements by patients taking these drugs should be medically monitored.
- The anti-hypertension drug hydralazine can deplete the body's supply of vitamin B_6. This vitamin is widely distributed in foods. Some good sources are chicken, fish, liver, whole grain breads and cereals, egg yolks, bananas and potatoes. Consumption of these foods should be encouraged.
- Several drugs, including colchicine (used to treat acute gout), oral antidiabetic agents, and the antibiotic neomycin can impair absorption of vitamin B_{12}. Persons who do not eat any animal products (vegans) may have poorer vitamin B_{12} status and may be at greater risk for a deficiency when taking one of these drugs.

It is, therefore, evident that use of certain drugs can lead to deficiency conditions and poor nutritional status. It is also common to find that certain drugs cause altered taste or dysgeusia, change in appetite, have gastrointestinal effects and some may lead to organ system toxicity. We shall review these changes briefly next.

Drug Effects on Food Intake

Food intake may be reduced because of drugs which:

- have an *anorexic effect,* either as a direct effect of the drug on appetite e.g., some antibiotics or because of side-effects such as drowsiness or lethargy e.g., tranquilizers. Drugs can suppress appetite, leading to undesired weight changes, nutritional imbalances, and growth retardation. Most central nervous system stimulants, including amphetamine mixture and melhylphenidate, supress appetite or cause frank anorexia.

- cause *nausea* and *vomiting:* This is a common side effect of many drugs, particularly the antineoplastic drugs, used to treat cancer.

- affect *the gastrointestinal tract:* Gastrointestinal irritation and ulceration are serious problems with many drugs. You may be aware that Non-steroidal anti-inlammatory drugs (NSAIDs) such as aspirin or ibuprofen often cause stomach irritation, indigestion, heartburn, gastritis, ulceration and sudden serious gastric bleeding. Other drugs may produce gastrointestinal side effects such as bloating or early satiety. Drugs can also cause changes in bowel function that can lead to constipation or diarrhoea. Narcotic agents such as codeine and morphine cause a nonproductive increase in smooth muscle tone of the intestinal muscle wall, thereby decreasing peristalsis and causing constipation. On the other hand use of certain drugs can lead to the destruction of intestinal bacteria leading to diarrhoea.

- causes taste *changes:* Several drugs can cause an alteration in taste sensation, reduced acuity of taste sensation or leave an unpleasant after taste, any of which can affect food intake. Common drugs that cause alteration in taste sensation include the antihypertensive drug captopril, the anticonvulsant phenytoin.

- cause *dry mouth (xerostomia)* : Lack of saliva makes it difficult to masticate and swallow foods, especially those of a dry or fibrous consistency. Dry mouth immediately causes loss of taste sensation. If dry mouth condition prevails for a long-term it can cause dental carries and loss of teeth, gum diseases and nutritional imbalance and undesired weight loss. The drugs to watch out in this case are anticholinergics, which include tricyclic antidepressants such as diphenhydramine, antihistamines (e.g. benadryl), and antispasmodic bladder control drugs such as oxybutyanin (ditropan). These anticholinergic drugs compete with the neurotransmitters acetylcholine for its receptor sites, thereby inhibiting transmission of parasympathetic nerve impulses. This results in decreased secretions, including salivary secretion causing dry mouth.

- cause *sore or painful mouth* : This is a common side effect of chemotherapy and can significantly affect food intake. Antineoplastic drugs, used in chemotherapy for cancer, affect the mucous membrane as well, causing inflammation or mucositis. This may manifest as stomatitis (mouth inflammation), glossitis (tongue inflammation) or cheilitis (lip inflammation and cracking).

- *Confusion* : Drugs, which impair memory or cause confusion can result in people forgetting to eat. Central nervous system side effects can interfere with the ability or desire to eat, Drugs that cause drowsiness, dizziness, ataxia, confusion, headache, weakness, and neuropathy can lead to nutritional compromise, particularly in older patients and chronically ill patients.

From our discussion above, it must be evident to you, that any of these problems, which are mentioned above from dry mouth to gastrointestinal irritation to constipation or diarrhoeas, can negatively affect food intake and absorption and thus have an impact on the nutritional status of the patient. This is one side of the coin. You must understand that drugs may also increase food intake. This is because they can:

- *stimulate appetite*: This is a common side effect of corticosteroids, insulin and psychotropic drugs, and
- *induce cravings for particular types of foods,* particularly carbohydrates. Some psychotropic drugs have this effect.

Next, let us learn about the effect of drugs on the absorption, metabolism and excretion of nutrients.

Drug Effects on Absorption

Many drugs can impair, prevent or reduce absorption of nutrients due to:

- *Formation of insoluble complexes*: many drugs can chelate with minerals and trace elements e.g., antibiotics ciprofloxacin and tetracycline form insoluble complexes with calcium, magnesium, zinc or iron, thus preventing or reducing the absorption of these vital nutrients..
- *Competition for binding sites*: e.g., salicylate drugs such as aspirin competes with vitamin C.
- *Damage to the absorptive surface of the intestinal mucosa*: drugs used in chemotherapy can cause villous atrophy, resulting in malabsorption.
- *Lack of bile acids*: the absorption of fat-soluble vitamins such as vitamin A,D, E and K, will be impaired by bile salt binding drugs such as cholestyramine.
- *Increased intestinal mobility*: drugs, which cause diarrhoea or stimulate peristaltic activity may result in nutrient losses.

Drug effects oiz Metabolism

Drugs can affect the metabolism of various essential nutrients in the body. These impairments are highlighted herewith:

- *Carbohydrate metabolism:* Hypoglycemic drugs such as insulin and sulphonylureas are prescribed because of their ability to increase carbohydrate utilization, and their action has to be balanced with carbohydrate intake in order to maintain glycemic control. Other drugs such as oral contraceptives and corticosleroids have adverse effects on carbohydrate metabolism and worsen glucose intolerance.
- ***Lipid*** *metabolism:*Some drugs are used to correct lipid metabolism, whilst others such as chlorpromazine and phenobarbitone can induce hyperlipidemia.
- *Vitamin and mineral metabolism*: Micronutrients are required as cofactors or coenzymes in many metabolic pathways, including those by which drugs are metabolized. Increased activity of these pathways because of drug metabolism may therefore increase micronutrient requirements.

Drugs can also compete with, or inhibit, the metabolic conversion of some micronutrients to their active metabolites, particularly folate. Methotrexate (used in the treatment of some cancers) directly antagonizes folic acid metabolism by inhibiting the activity of enzyme *dehyrofolate reductase*. Similarly, anticonvulsants impair vitamin D metabolism with consequent disturbances in calcium metabolism which adversely effects on bone.

- *Dietnry Components*: Drugs may also affect the metabolism of dietary components such as MAOI, as we have discussed earlier in section 7.3.

Finally, let us get to know how drugs can have an impact on nutrient excretion.

Drugs Effects on Excretion

Use of certain drugs can influence the excretion of certain substances. For example, besides their intended increase in sodium excretion, diuretic drugs can also result in enhanced losses of other elements such as potassium, calcium, magnesium and zinc. Tetracycline increases the urinary excretion of vitamin C.

So far, we have covered the relationship or the interaction of drug with nutrients and the effect of food on drug absorption, metabolism, utilization and excretion. Let us now move on to the study of the effect of a drug on the other drug i.e. the drug and drug interaction.

7.5 DRUG AND DRUG INTERACTION

In the discussions above, we reviewed the effect of food on drug metabolism. Interestingly, not only can drugs interact with food and alcohol, they can also interact with each other. Some drugs are prescribed together on purpose for an added effect, like codeine and acetaminophen for pain relief. However, other drug-to-druginteractions may be unintended and harmful. Prescription drugs can interact with each other or over-the-counter (OTC) drugs, such as acetaminophen, aspirin, etc.

Sometimes, the effect of one drug may be increased or decreased. For example, tricyclic antidepressants can decrease the ability of a hypotensive to lower blood pressure. In other cases, the effects of a drug can increase the risk of serious side effects. For example, some antifungal medications can interfere with the way some cholesterol-lowering medications are broken down by the body. This can increase the risk of a serious side effect.

We hope this brief discussion may have helped you understand the interaction between drugs and their usefulness and ill effects. With this, we end our discussion on the interactions between drugs and nutrients, drugs and drugs and nutrients and drugs. Let us check your understanding of the subject so far. Answer the questions given in the check our progress exercise 2. Thereafter, move on to review the clinical significance of these interactions.

Check Your Progress Exercise 2

1. How is drug nutrient interaction different from a nutrient drug interaction and a drug-drug interaction?

.....

.....

.....

.....

2. Enumerate any three effects of drug on food intake.

.....

.....

.....

.....

.....

3. How do drugs influence the absorption of nutrients in the body? Explain very briefly.

.....

.....

.....

4. What are drug and drug interactions? Explain giving example.

.....

.....

.....

Let us now quickly review the clinical significance and risk factors associated with these interactions.

7.6 CLINICAL SIGNIFICANCE AND RISK FACTORS FOR DRUG-NUTRIENT INTERACTIONS

We are already aware of the fact that poor nutritional status can impair drug metabolism and the drug treatment can have a detrimental effect on the nutritional status.

Not all drug-nutrient interactions are clinically significant. In many instances, any losses in nutrient availability or drug action will be small in scale and may be of short duration. Drugs, which are most likely to have diuretic implications, are those which:

- have a narrow range between therapeutic effect and toxicity,
- need to be taken for a prolonged period,
- have implications in terms of the timing of food intake,
- necessitate dietary restrictions or regulation,
- have side-effects which influence appetite or gastro-intestinal function, and
- compete directly with a nutrient.

People who are at risk from drug-nutrient interactions are the:

- Persons who have *a poor diet* or in other words have a *poor tiutritional status.* Existing malnutritionplacespatients at greater risk. Protein alteration, particularly low albumin level, as you may recall studying earlier, can effect drug disposition,
- Persons who have *serious health problems.* Patients with active neoplastic diseases (cancer) or active acquired immunodeficiency syndrome (AIDS) with significant anorexia and muscle wasting are at special risk.
- *Body composition*: This is an important consideration in determining drug response. In obese or older patients, for instance, the proportion of adipose tissue to lean body mass is decreased. Accumulation of a drug and its metabolite in adipose tissue is greater, and may result in prolonged clearance and increased toxicity.
- *Foetus, growing children, pregnant women:* These individuals are at high risk for drug nutrient interaction.
- The physiological changes that occur with age, such as a decrease in lean body mass and body water, fall in plasma protein concentration, and a general decline

in renal and liver Function, mean that the risk of adverse drug reactions is much higher. Elderly people are also more likely to be given the types of drugs with powerful effects and which are most likely to have an impact on nutrition e.g., cytotoxic drugs, anti-Parkinson's drugs and antidiabetic drugs. Diminished salivation may make it more difficult to swallow tablets and oesophageal motility disorders may lead to bulky drugs sticking in the oesophageal mucosa. Other problems such as failing memory, poor hearing and vision, and difficulty with opening containers may mean that drug regimens are not followed correctly, particularly if they are complex. Many of these factors are likely to coexist in elderly people.

- Persons taking two or more medications at the same time.
- Persons using prescription and over-the counter medications together.
- Persons not following medication directions.
- Persons taking medications for long periods of time.
- Persons who drink alcohol or smoke excessively.

Now that we are aware of the clinical manifestations and the risk factors involved, it is important that we use the drugs wisely and lower the risk of drug nutrient interaction. To help you do that, here are some handy guidelines.

7.7 GUIDELINES TO LOWER RISK AND WISE USE OF DRUGS

There can be no two views regarding the a c t that the management of many diseases require drug therapy. I-Iowever, they must be taken properly to ensure that they are safe and effective. Many medicines, as we have learnt so far, have powerful ingredients that interact with the human body in different ways, and diet and lifestyle can sometimes have a significant impact on a drug's ability to work in the body. To help you in this task and equip you to take wise decisions here are a few handy guidelines. Infact, you may want to advocate these guidelines to the patients as well who shall come to you for dietetic advice.

Guidelines to Help Use Drugs Wisely

By now, you are aware that the interaction of foods and drugs is a complex problem. Researchers cannot always predict whether a new drug will react with a food or if a drug that has been in use for some time will react with a new food. Moreover, you, as the consumer, cannot be expected to know everything about the drug. Then, what can we do to get the greatest benefit from drugs with the least risk? The following guidelines will assist us in preventing problems and getting the most from the medicines that one must take:

- When the doctor prescribes a medicine, be sure to mention every other drug taken including alcohol and over-the-counter agents such as aspirin, antacids and laxatives. If you don't know the amount and types of drugs you are taking, take the bottles with you when you visit the doctor.

- Be sure you understand when and how the drug/supplement/product should be taken and then follow directions (for example, with meals, before meals, or after meals). You could perhaps paste labels on the bottle(s) to remind you when and how the drug should be taken.

- Tell the doctor about any changes or ill effects you have after taking the drug and any unusual symptoms that occur after eating certain foods. Use the telephone, Donot wait until your next visit.

- Taking drugs with a full glass of water is generally the safest way and in many cases, it may help prevent irritation of the stomach lining.
- Do not mix medication into hot drinks, because the heat from the drink may destroy the effectiveness of the drug.
- Do not take vitamin pills at the same time as taking the medication; vitamins and minerals can interact with some drugs.
- Do not stir medicine into your food or take capsules apart (unless directed by your physician). This may change the way the drug works.
- If you take any drug, do not use alcohol without checking with the doctor first to see if it will be safe.
- If you have been taking a drug for a long time, ask the doctor if you should be concerned about any vitamin or mineral deficiencies.
- Read directions, warnings and interaction precautions printed on all medicine labels and package inserts.
- When buying any over-the-counter medicine, be sure to read the label and the package insert for directions and warnings. If in doubt about the product, ask the pharmacist.
- Finally, use the least number of drugs possible and take them as directed to reduce the chances of developing a drug/drug or food/drug interaction.

How to Lower the Risk of Drug-Nutrient Interactions

- Eat a healthy diet using the food guide pyramid.
- Follow directions on how to take medication (prescription and over-the-counter)
- Read warning labels on both prescription and over-the-counter medications.
- Do not take over-the-counter medications frequently on your own.
- Tell the physician about any other medications being taken, including over-the-counter medications and alcohol.
- Tell the physician about any new or intensified symptoms that develop when taking a medication.
- Keep a list of all medications (prescription and over-the-counter) being used.
- If you have questions, ask your physician for answers.

Besides the handy tips listed above, you will find some useful tips regarding the usage of certain drugs along with food and alcohol highlighted in Table 7.1. Read this information carefully. This will help you during patient counseling.

Table 7.1: Nutrient and drug interaction - handy tips

S. No.	Drugs	Interaction with	
		Food	Alcohol
1.	Antihistamines	Best on empty stomach	Increase drowsiness and slow mental and motor performance.
2.	Analgesics/ Antipyretics	Best on empty stomach	Increase risk of liver damage or stomach bleeding
3.	Non-steroidal Anti-inflammatory Drugs (NSAIDS)	Best with food or milk	Increase risk of liver damage or stomach bleeding.
4.	Corticosteroids	Besl with food or milk	–
5.	Narcotic Analgesics	–	Increases sedative effects of medication
6.	Bronchodilators	Can result in side effects such as nausea, vomiting, headache and irritability. Caffeine containing foods or beverages can stimulate control nervous system	Increase risk of side effects such as nausea, vomiting/headache and irritability.
7.	Diuretics	Cause loss of K, Ca and Mg. Also can lead to hyperkalemia resulting in irregular heart beat and heart palpitations	–
8.	Beta Blockers	–	Lowers the blood pressure
9.	Nitrates	–	Lowers the blood pressure
10.	Angiotensin Converting Enzyme (ACE) inhibitors	Decreases absorption Avoid foods rich in potassium	–
11.	HMG CoA Reductase Inhibitors	Absorption enhances with food intake	Increase the risk of liver damage
12.	Anticoagulants	Vitamin K reduces effectiveness	–
13.	Antibiotics	–	–
14.	Antifungals	Depends on an individual's tolerance. Avoid Ca-containing foods. Caffeine leads to excitability and nervousness	–
15.	MAO inhibitors	Avoid foods rich in tyramine	Avoid Alcohol
16.	Anti-anxiety drugs	Caffeine-rich foods cause excitability, nervousness and hyperactivity	Impair mental and motor performance
17.	Anti-depressant drugs	With or without food	Affect mental ox motor skills
18.	Histamine blockers	With or without food caffeine-rich foods irritate the stomach	Irritate the stomach and delays the healing process.

Check Your Progress **Exercise 3**

1. Who are the people who are the most at risk of nutrient drug interaction?

.....

.....

.....

2. Give one important clinical manifestation of drug nutrient interaction.

.....

.....

.....

3. Give any five handy guidelines that you will advocate to patients to use drugs wisely.

.....

.....

.....

4. What points would you keep in mind to lower the risk of drug nutrient interaction in your life?

.....

.....

.....

7.8 LET US SUM UP

Certain foods, beverages, alcohol, caffeine, and even 'cigarettes can interact with medicines. This may make them less effective or may cause dangerous side effects or other problems. On the other hand, certain medicines and drugs have powerful ingredients that interact with the human body in different ways, and these can sometimes significantly influence the absorption, metabolism and utilization of nutrients in the body leading to poor nutritional status. These nutrient drug interactions, therefore, were the focus of this unit.

We learnt about the different ways in which the food effects drug absorption, metabolism. Further, the relationship between drugs and the nutritional status was also explored. The factors by which the drug influences food intake and the effect of drug on nutrient absorption, utilization and excretion were highlighted.

The unit finally dwelt upon the risk factors associated with nutrient drug interaction(s) and presented handy guidelines for wise use of drugs and measures to adopt to reduce the risk from nutrient drug interactions.

7.9 GLOSSARY

Anti convulsants	:	drugs used to prevent or treat convulsions (seizures) such as in case of epilepsy.
Anti **fungals**	:	drugs that treat fungal infection.
Anti histamines	:	drugs that treat symptoms of allergies.
Bronchodilators	:	drugs that widen the airways of the lungs to ease breathing difficulties.

Dysgeusia : an impairment or dysfunction of the sense of taste.

MAO Inhibitors : mono-amine oxidase inhibitors are medicines that relieve certain types of mental depression.

Neuropathy : a problem in peripheral nerve function (any part of the nervous system except the brain and spinal cord) that causes pain, numbness, tingling, swelling, and muscle weakness in various parts of the body.

Osteomalacia : disease occurring mostly in adult women that results from a deficiency in vitamin D or calcium and is characterized by a softening of the bones with accompanying pain and weakness.

Prothrombin : a plasma protein that is converted into thrombin during blood clotting.

7.10 ANSWERS TO CHECK YOUR PROGRESS EXERCISES

Check Your Progress Exercise 1

1. Drug nutrient interaction refers to specific changes in the process by which a drug is absorbed, distributed, metabolized and eliminated by the body due to the presence of nutrient (s). The study of the effect of drugs on various nutrient and vice-versa help us in understanding and minimizing these interactions which can help in gaining maximum benefit from particular drug dosage without disturbing the nutritional homeostasis in the body/deteriorating the existing nutritional status. This would also help in minimizing the expenditure on health care services and the incidence of various disease complications or side effects.

2. The inter-relationship between drugs and nutrients is generally categorized as of two types viz.:

   - Nutrient drug interactions i.e. the effect of food or nutrient(s) on the structure or chemical properties of a drug/medicine.
   - Drug-nutrient interactions i.e. the impact of a drug on the digestion, absorption, excretion of nutrient (s), structure/function of gastrointestinal tract or the intake/consumption of food.

3. Foods can decrease or increase a drugs rate of absorption due to delayed gastric emptying altered gastrointestinal pH, competition for binding sites with the nutrients, adsorption of a food, chelation of drug as in the case of antibiotic tetracycline etc.

4. a) *The **two examples** include*: Green leafy vegetables can decrease the effect of anticoagulants, as these foods contain vitamin K which promote blood clotting.

   b) MAO inhibitors are used to treat blood pressure and depression. These substoances can interact with tyramine in foods such as aged cheese, beans and decrease their metabolism.

Check Your Progress Exercise 2

1. Several forms of interaction can develop between drugs and nutrients because both drugs and food are absorbed, metabolized and excreted from similar sites and in similar ways. Thus, the three key forms of interaction can be:

   a) Drug Nutrient Interactions i.e. the influence of nutritional factors on drug absorption, action and effectiveness.

b) Nutrient drug interaction refers to the influence of drugs on the nutritional intake, metabolism, excretion and requirement i.e. on the entire nutritional status of an individual.

c) Drug-drug interactions occur when two or more drugs react with each other. Such interactions may make a drug less or more effective and /or elicit unexpected side effects.

2. Drugs may affect food intake in several forms:

- Stimulate appetite or induce craving for particular type of foods such as the effecl produced by cortico-steroids and psychotropic drugs.
- Affect the gastrointestinal tract thereby eliciting indigestion, heartburn/ gastritis, abdominal pain or diarrhoea associated with food intake e.g. non-steriodal anti-inflammatory drugs.
- Reduce appetite such as antibiotics, cyto-toxic drugs and some tranquillizers.

3. Drugs can influence the absorption of nutrients by forming insoluble complexes, affecting the structure/ function of gastrointestinal tract, reducing digestive secretions or competing for binding sites. For example: antacids, laxatives, anti-bacterial agents such as sulfasalzine may cause nutrient malabsorpton. Drugs used in the treatment of tuberculosis such as rifampicin and isoniazid interfere with the normal metabolism of vitamin D and hence impair calcium absorption.

4. Drug-drug interaction refers to the reactions which may develop between two or more drugs that may result in altered structure of the parent compound(s) and development of new compound(s). This may in turn elicit unexpected side effect(s) which may cause sever morbidities and even mortality in isolated cases. Some examples of dnig-drug interaction include: antiemetics may interact with sedatives and tranquilizers, aspirin can interact with alcohol to cause stomach bleeding.

Check Your Progress Exercise 3

1. The risk of developing nutrient – drug interactions is high among: Individuals having a poor nutritional status susceptible age groups such as children, pregnant] lactating women and elderly, Immuno-compromised patients or those who are suffering from chronic degenerative diseases), individuals consuming multiple drugs at one time etc.

2. One of the most important clinical interactions is that of MAOIs (Monoamine Oxidase Inhibitors) and Tyramine. In a normal cycle tyramine is metabolized by monoamine oxides before it enters body's systemic circulation. When MAO inhibitors are consumed, foods high in Tyramine can potentially reach systemic circulation, resulting in acute increase in blood pressure. In severe cases it can cause hypertensive emergencies as well. Foods rich in Tyramine are: avocados, bananas, chocolate, coffee, raspberries and raisins.

3. Look up section 7.7 and list any five useful guidelines.

4. Nutrient and drug interactions can be minimized by adhering to "directions for use" mentioned on the "manufacturer's insert" of each medicine. Some general guidelines are listed in section 7.4 Read them carefully and write the answer.