

**BP 603 T. HERBAL DRUG TECHNOLOGY (Theory)**

**UNIT – TWO**



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**UNIT-II            7 Hours**

**Nutraceuticals**

General aspects, Market, growth, scope and types of products available in the market. Health benefits and role of Nutraceuticals in ailments like Diabetes, CVS diseases, Cancer, Irritable bowel syndrome and various Gastro intestinal diseases.

Study of following herbs as health food: Alfaalfa, Chicory, Ginger, Fenugreek, Garlic, Honey, Amla, Ginseng, Ashwagandha, Spirulina

**Herbal-Drug and Herb-Food Interactions:**

General introduction to interaction and classification. Study of following drugs and their possible side effects and interactions:

Hypericum, kava-kava, Ginkobiloba, Ginseng, Garlic, Pepper & Ephedra

# **NUTRACEUTICALS**

## **NUTRACEUTICALS**

The term nutraceutical was coined from nutrition and pharmaceutical in 1989 by Dr. Stephen De Felice, USA.

Nutraceutical can be defined as a food or a part of food or a nutrient, which in addition to its nutrient values provides health benefits including promotion of health and prevention of disease. Most of the diseases such as diabetes, cardiovascular, obesity, etc occur due to incorrect diet and life style. Hence nutraceuticals play an important role in disease prevention as well as promoting health.

## **GLOBAL MARKET OVERVIEW AND GROWTH OF NUTRACEUTICAL SEGMENT**

- The nutraceutical market is predicted to record a revenue of USD 671.30 billion by 2024.
- Developing countries have a high prevalence of non-communicable diseases like cancer, diabetes, cardiovascular ailments, etc, therefore the demand for nutraceuticals is expected to rise in these nations.
- Nutraceuticals are also gaining global importance and have become a part of daily diet due to increased risk of diseases due to improper life style and people consciously adapting preventive healthcare measures.
- The gradually increasing healthcare expenses are also stimulating the demand for nutraceuticals.
- Developed countries like United States and Europe have seen an fast emerging segment of customised products especially functional foods and beverages.
- Nutraceuticals have become an opportunity for economic growth of many developing countries which have a rich source of medicinal herbs and traditional knowledge of such plants, especially India, China and South American countries.

## **SCOPE OF NUTRACEUTICALS**

Nutraceuticals are expected to deliver promising outcomes in the prevention and occurrence of various diseases resulting due to improper lifestyle and food habits. Various constituent of plants like catechins, carotenoids, lycopene, polyphenols, PUFA, etc have been very effective in the prevention and occurrence of various diseases like cardiovascular, arthritis cancer, gastrointestinal disorders, etc.

## **TYPES OF NUTRACEUTICAL PRODUCTS AVAILABLE IN THE MARKET**

The nutraceutical market is segmented into functional foods, functional beverages and dietary supplements which are again subcategorized into different products which are as follows

### **FUNCTIONAL FOODS**

CEREALS

BAKERY & CONFECTIONARY

DAIRY

SNACKS

FUNCTIONAL FATS, OILS

BABY FOODS

### **FUNCTIONAL BEVERAGES**

ENERGY DRINKS

SPORTS DRINKS

FORTIFIED JUICES

DAIRY & DAIRY BEVERAGES

TEA, COFFEE

### **DIETARY SUPPLEMENTS**

VITAMINS

MINERALS

BOTANICALS

ENZYMES

FATTY ACIDS

PROTEINS PROTEINS

PROBIOTICS

PREBIOTICS

## ROLE OF NUTRACEUTICALS IN VARIOUS DISEASES

Nutraceuticals play an important role in therapeutic areas such as arthritis, cancer, diabetes digestion, cholesterol, blood pressure, pain killers, depression and various other disorders. The following table depicts the role of few plants and their constituents in the prevention and management of diseases.

<b>Plant/ Constituents</b>	<b>Disease</b>
Anti Oxidant Vitamins(Vit-CE, Carotenoids) Tocopherols, Ascorbic Acid (Fruits, Vegetables)	Cancer, Cardiovascular Diseases Arthritis, Alzheimers Disease, Cataract
Polyphenols (Tea, Coffee)	Antimicrobial, Diabetes Anti-Inflammatory Cardioprotective, Neurodegenerative Disorders
Curcumin (Turmeric), Capsaicin (Capsicum). Gingerol (Ginger), Piperine (Pepper), Eugenol (Clove)	Digestive Inflammatory, Antimutagenic, Antiinflammay, Lower bad cholesterol,Antioxidant, Diabetic Neuropathy
Poly Unsaturated Fatty Acids (PUFA)	Cardio Vascular Disease, Dysmenorrhea, Diabetes, Anti Antithrombotic, Asthma, Hypolipedemic
Probiotics, Prebiotics	Gastrointestinal Disorders,Constipation, Anitumor, Toxin Neutralisation

## CLASSIFICATION OF NUTRACEUTICALS

They can be classified according to their chemical nature and therapeutic properties as follows:

- MINERALS
- ANTIOXIDANTS
- PUFA,s
- PROBIOTICS
- PREBIOTICS

➤ **DIETARY FIBRES**

**i. Inorganic mineral supplements**

Eg: calcium, magnesium, manganese, boron, copper, zinc, phosphorous, etc.

**ii. Antioxidants**

They are present in fruits, vegetables and fishes. They are used to prevent the reactive oxygen species and free scavenging radicals. Eg: Vit-E, C, A, Beta carotene.

**iii. Poly unsaturated fatty acids (PUFA)**

These are fatty acids which contain more than one double bond and include essential fatty acids. Eg: Omega-3-fatty acids, safflower oil, corn oil, soyabean oil, fish oil.

**iv. Probiotics**

These are living microorganisms, which when taken with or without food intestinal microbial balance and functioning of large intestine, Eg: Bifidobacterium, Lac chilli, Saccharomyces cerevisiae, etc improv

**v. Prebiotics**

These are non digestible substances that provide beneficial effects and protection to the probiotics from gastric acid and digestive enzymes. They also promote the growth of probiotic bacteria. Eg Oligo fructose, Inulin, Galacto-oligosaccharides, Lactulose.

**vi. Dietary fibres**

They are two types viz:- water soluble fibres and water insoluble fibres. They are present rats, vegetables, grains, legumes, etc. They are used to correct constipation, bowel irregularities, haemorrhoids.

## **HERBS AS HEALTH FOOD**

**a) Alfalfa**

**Source:** It is the entire plant of Medicago sativa belonging to the Family: Fabacene.

**Chemical constituents:**

Leaves, sprouts and seed contain vitamin-K, vitamin-C, copper, manganese, folate, thiamine riboflavin, magnesium and iron. One cup of sprouts contains one gram of protein and one gram of carbohydrates. It also has a high content of bioactive compounds like saponins coumarins, flavonoids, phytosterols, phytoestrogens and alkaloids.

## Uses

It is used as:

- Hypo cholestremic
- Anti hypertensive
- Diuretic.
- Galactogouge
- Anti arthritic.
- To treat kidney stones.
- Anti diabetic.
- To relieve menopausal symptoms.
- Antioxidant.

## **b) Chicory**

**Source:** It is obtained from the plant *Cichorium intybus*, belonging to the Family: Asteraceae.

### **Chemical constituents:**

Chicory contains a variety of nutrients which include carbohydrates, protein, vitamins, minerals, soluble fiber, phenolics, Inulin, coumarin, tannins, monomeric flavonoids, esquiterpene lactones and beta carotene.

**Uses:** The roots are used as

- A coffee substitute and additive.
- They are mixed in Indian filter coffee
- Used in high blood pressure, heart failure, loss of appetite stomach upset, constipation, cancer, liver and gall bladder disorden inflammation and\_hepatic\_toxicity

## **c) Ginger**

**Source:** It is the dried rhizomes of *Zingiber officinale*, belonging to the Family: Zingiberace

### **Chemical constituents:**

It contains volatile oils, minerals, resins. Ginger oil contains zingiberine, bisabolone, farnesene, sesquiphellandrene and curcumene. Resins contain phenolic ketones such as gingerols, shogaols, zingerone and other compounds.

### **Uses:**

Ginger is used as

- Stomachic.
- Aromatic.
- Carminative
- Stimulant.
- Flavouring agent.
- In ginger beverages
- Adsorbent of toxins from GIT
- To control parasitic infections.

### **d) Fenugreek**

**Source:** It consists of seeds of the plant *Trigonella foenum-graecum*, belonging to the Family: Leguminosae.

#### **Chemical Constituents**

It contains alkaloids (Gentiamine, Trigonelline), flavonoids, coumarins, proteins, amino acids and steroidal saponins.

#### **Uses**

- Demulcent
- Laxative
- Nutritive
- Expectorant
- Used in the treatment of anorexia, dyspepsia, gastritis, diabetes and high cholesterol

### **e) Garlic**

#### **Source**

It consists of dried bulbs of *Allium sativum*, belonging to the Family: Liliaceae.

#### **Chemical constituents**

Garlic contains, carbohydrates, proteins, fats, mucilage, volatile oils and minerals. The volatile oil contain allin, allicin, allyl propyl disulfide, diallyl disulfide. Minerals contain phosphorous, iron and copper.

## Uses

- Carminative
- Aphrodisiac
- Expectorant
- Stimulant
- Disinfectant.
- Anthelmintic
- Antibacterial.
- Antihypertensive.
- Hypocholesteremic.

## F) Honey

### Source

Honey is a sugar like secretion deposited in honeycomb by the bees *Apis mellifera*, *A. dorsata* and other species of *Apis*, belonging to the Family: *Apidae*.

### Chemical constituents

Honey is an aqueous solution containing 35% glucose, 45% fructose and 2% sucrose.

### Uses

It is used as demulcent sweetening agent, nutrient, antiseptic and expectorant

## g) Amla

### Source

It consists of fruits of the plant *Emblica officinalis* and *Phyllanthus emblica*, belonging to the Family: *Euphorbiaceae*

### Chemical constituents:

It contains Vitamin-C (ascorbic acid), calcium, iron and phosphorous

### Uses

It is used as Diuretic, Laxative.

Used in the treatment of

- Anaemia
- Diarrhoea.
- Jaundice



- Fruits are used to prepare shampoos and hair oils.

## h) **Ginseng**

### **Source:**

It consists of roots of the plant Panax ginseng and other species of Panax, belonging to the Family: Araliaceae.

### **Chemical constituents:**

Ginseng contains saponins, glycosides, volatile oils, sterols, polysaccharides, minerals, vitamin-B. B, B<sub>12</sub>, pantothenic acid and biotin.

### **Uses**

It is used as

- Adaptogenic.
- It relieves stress and fatigue.
- Used in hypertension, diabetes, psychogenic impotence and child psychiatric disorders.
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## i) **Ashwagandha**

### **Source**

It consists of dried roots and stem bases of the plant Withania somnifera, belonging to the Family: Solanaceae,

### **Chemical constituents**

It contains alkaloids and steroidal lactones. Alkaloids contain withanine, somniferine, somnine, tropine, two acyl steryl glucosides sitoindosine-7 and sitoindosine-8

### **Uses**

Used as

- Sedative.
- Hypnotic.
- Hypotensive.
- Respiratory stimulant.
- Immunomodulatory agent
- Anti-stress agent
- Anti-arthritis.

## j) **Spirulina**

### **Source:**

It is blue green algae obtained from Spirulina maxima or Spirulina platensis, belonging to the Family: Oscillatoriaceae.

### **Chemical constituents**

It contains 50-70% proteins, 5-6% lipids. Lipids contain essential fatty acids like linoleic acid, oleic acid, palmitic acid. It also contains glycolipids and sulfolipids, various vitamins like vitamin-B1, B2, B3, B. By and Es. It contains iron and an enzyme superoxide dimutase which has free radical scavenging effects and help full in atherosclerosis, arthritis, diabetes, cataract stress and aging.

### **Uses**

Used as

- Immune stimulant
- Anticancer Antiviral
- Hypocholestremic.
- Appetite stimulant.

## **HERB DRUG & HERB-FOOD INTERACTIONS**

Drug interaction is a reaction between two or more drugs or between a drug and a food beverage or supplement inside the body. A drug interaction can make the drug less effective increased activity or cause unwanted side effects.

### **TYPES OF DRUG INTERACTIONS**

- DRUG-DRUG INTERACTIONS
- DRUG-FOOD INTERACTIONS
- DRUG-DISEASE INTERACTIONS

#### **a) Drug-drug interaction**

These are the most common type of drug interaction. More the medications administered, greater is the chance of drugs interacting with each other. One drug may potentiate the activity of another or inhibit its activity or serious unexpected side effects may occur.

Eg: vicodin a pain killer when taken along with sedating antihistamine drug. Benadryl produce an additive effect of drowsiness,

#### **b) Drug-food interaction**

This is another type of drug interaction where drugs interact with food/ beverages and can produce various side effects.

Eg: grape juice reduces the enzyme activity in liver which are responsible for metabolising drugs thus resulting in increased blood levels of certain drugs such as cholesterol lowering drugs (statins), this leads to toxic effects of the drug such as muscle pain and muscle injury.

#### c) Drug-disease interaction

Sometimes drugs also interact with certain diseases where the disease alter the way a drug works.

Eg: oral decongestants like pseudoephedrine, phenylephrine may increase the blood pressure and can be dangerous in patients having hypertension

### MECHANISM OF DRUG INTERACTIONS

Drug interactions can occur in several different ways starting from its absorption up to its elimination from the body. Following are the various mechanisms by which drugs interact.

## **MECHANISMS OF DRUG INTERACTIONS**

1. PHARMACODYNAMIC
2. PHARMACOKINETIC
  - ABSORPTION
  - DISTRIBUTION
  - METABOLISM
  - EXCRETION

#### **Pharmacodynamic interaction**

This occurs when two or more drugs administered together act at the similar receptor sites leading to enhancement (additive or synergistic) effects or decreased (antagonistic) effects.

Eg chlorpromazine given to prevent nausea and vomiting interacts with antipsychotic medications like haloperidol and produce serious and possible fatal irregular cardiac rhythm.

#### **Pharmacokinetic interaction**

This occurs when drugs interact during the process of absorption, distribution metabolism or excretion.

##### ➤ Absorption interactions

Some drugs can alter the absorption of another drug for example calcium can bind with some drugs like tetracycline and HIV drug dolutegravir and block its absorption, hence such drugs should not be taken along with milk and antacids.

##### ➤ Distribution interactions

One or more drugs can compete with each other for plasma protein binding sites resulting in displacement of one drug thereby increasing its blood levels and toxicity. Eg fenofibric acid (cholesterol lowering agent) and warfarin (blood thinner) when administered together, compete for the protein binding sites leading to displacement and increased blood levels of warfarin thus resulting in bleeding.

➤ Metabolism interactions

Enzymes in the liver such as cytochromes are responsible for metabolising drugs and eliminating them from the body. Some drugs may alter the enzyme levels or its activity resulting in fast or slow metabolism of drugs.

Eg diltiazem (antihypertensive) inhibits the cytochrome enzyme responsible for metabolising simvastatin (hypocholesteremic) and elevates its blood levels resulting in serious liver and muscle side effects.

➤ Excretion interactions

Some non-steroidal anti-inflammatory drugs (NSAIDs) like indomethacin may lower the kidney function and reduce the excretion of lithium, a drug used for bipolar disorders. In such cases dose adjustment is required.

## **HERB DRUG/ FOOD INTERACTIONS**

Even though herbal medicines are obtained from natural sources, their active ingredients are potent chemicals which can give rise to herb-drug or herb-food interactions. Herbal supplements and nutraceuticals are often purchased over the counter (OTC) and may be labelled as "All Natural" but that does not mean they are always safe.

Herbal supplements are not subject to review by the FDA and their use can often be risky when taken along with other drugs or foods. Following are the general guidelines which help minimize herb-drug or herb-food interactions.

1. Avoid taking mucilage containing herbs like ispaggol, flax with other drugs, as mucilage can inhibit the absorption of many drugs. Even mucilage containing drugs can alter the blood sugar levels which have to be considered in case of diabetic patients.
2. Spicy substances such as ginger, capsicum, etc can enhance the absorption rate of some drugs, hence they need to be taken one hour after drug administration.
3. Heart tonic herbs such as hawthorn/ digitalis / cactus, should be avoided when taking heart medications.
4. Caffeine containing herbs like green tea, kola nut, coffee and herbal stimulants like ephedra should be avoided when taking heart medications or mood altering drugs or antidepressants.
5. Avoid herbs or formulations containing liquorice when using diuretics like furosemide because liquorice can cause potassium depletion from the body.
6. While taking antidepressants like mono amino oxidase (MAO) inhibitors, avoid African aphrodisiac herbs containing yohimbine.
7. Green vegetables like broccoli, spinach, cabbage, etc which have high vitamin-K content are reported to interact with anticoagulant drugs as vit-K has coagulation promoting effects.

8. Grape fruit juice interacts with calcium channel blockers (antihypertensives), lipid lowering drugs, psychiatric medications, oral contraceptives and antiallergic medications. Grape juice modifies the metabolism pattern of these drugs in the liver.

## **STUDY OF SOME COMMON HERBS AND THEIR INTERACTIONS**

### **I. Hypericum perforatum (St. Johns Wort)**

- ✓ It is a popular herb used to treat mild depression. The active constituent of this herb is known as "hypericin", which has similar effects on the brain as that of mono amino oxidase (MAO) inhibitors (antidepressants). If taken together, it may produce dangerous drug interactions resulting in rapid rise in blood pressure, severe head ache, collapse and death. Foods such as cheese, chicken liver, fish, legumes, soya sauce and beer should be avoided with this drug.
- ✓ Hypericin has also reported to produce interactions with immune suppressant drug cyclosporine, antiviral drug indinavir, oral contraceptives, digoxin and benzodiazepines resulting in increased sensitivity to light, anxiety, dizziness, dry mouth, fatigue and sexual dysfunction.

### **II. Kava (Piper methysticum)**

- ✓ It is an herb that has anti-anxiety, pain relieving muscle relaxing and anticonvulsant effects
- ✓ Kava should not be taken with drugs which act on nervous system such as barbiturates, antidepressants, antipsychotics and alcohol.
- ✓ It is reported that concomitant use of kava with central nervous system depressants can increase the risk of drowsiness and motor reflex depression
- ✓ Kava has also reported to produce hepatotoxic effects when taken with some drugs.

### **III. Ginkgo biloba (Maiden hair tree)**

- ✓ Ginkgo has been used to treat symptoms of Alzheimers dementia, Parkinson's > disease and to enhance the memory capabilities.
- ✓ Ginkgo is reported to decrease the antiviral effects of drugs used in HIV such as efavirenz or indinavir. Ginkgo can also alter the actions of drugs metabolized through liver such omeprazole, fluvastatin and donepezil.
- ✓ Ginkgo should be avoided in patients who are on anticonvulsants, blood thinners and antidiabetic drugs. Ginkgo is reported to interact with over 250 drugs, hence patient should take proper consultation before using it.

### **IV. Ginseng (Panax ginseng)**

- ✓ Ginseng is used to improve the body's resistance to stress, boost the immune system and improve the sense of well-being and stamina.
- ✓ It is also used to improve physical and mental performance and treat erectile dysfunction, hepatitis C, symptoms related to menopause, lowering of blood glucose and controlling blood pressure.
- ✓ Ginseng is reported to induce the activity of enzyme cytochrome P3A, in the liver which metabolises various drugs resulting in their decreased activity and faster excretion from the body.
- ✓ Ginseng decreases the effectiveness of warfarin (blood thinner) and increase the risk of clotting hence it should be avoided while taking anticoagulants.
- ✓ Ginseng is also reported to decrease the activity of anti-hypertensive resulting in high blood pressure.
- ✓ It is also reported to affect the activity of anti-diabetic drugs, hence should be avoided in such cases.

#### V. **Garlic (Allium sativum)**

- ✓ Garlic is used in various conditions like to lower blood sugar levels, reduce menstrual pain, lowering blood cholesterol levels and decrease blood pressure.
- ✓ Garlic does not interact with drugs at normal recommended doses, however exposure to concentrated garlic extracts for prolonged periods is reported to interact with several drugs.
- ✓ Garlic is reported to reduce the efficacy of drugs whose distribution is dependent on efflux transporter mechanism.
- ✓ Garlic is reported to affect the blood clotting hence should be avoided in patients taking blood thinning agents like aspirin and warfarin. Garlic alters the blood sugar level, hence used under supervision on patients with anti-diabetics.
- ✓ It is also reported that garlic supplements have decreased the blood levels of HIV protease inhibitors when used together.

#### VI. **Pepper (Piper migrsm)**

- ✓ Black pepper contains piperine as the chief active constituent. It is used as spices as well as carminative and to treat arthritis, asthma, stomach upset and sinus infection.
- ✓ Piperine is reported to inhibit various cytochrome enzymes, resulting in increased blood level of certain drugs like carbamazepine, midazolam, diclofenac, phenytoin and warfarin.
- ✓ Black pepper might increase the risk of bleeding when mixed with anticoagulants or blood thinning drugs like aspirin, clopidogrel, heparin and warfarin.
- ✓ Black pepper might produce additive effect with antidiabetic drugs and increase the risk of hypoglycaemia Black pepper might increase the blood level of cefotaxime and cyclosporine resulting in increased drug effects as well as side effects.
- ✓ Black pepper might also increase the blood levels thereby enhancing the effects as well as side effects of anti-cancer drugs, anti hypertensives, anti convulsants and some antibiotics.

## VII. Ephedra (Ephedra gerardiana)

- ✓ Ephedra is used to treat allergies, high fever, and respiratory tract conditions like bronchospasm, asthma and bronchitis.
- ✓ Ephedra contains ephedrine which is a potent drug and stimulates heart, lungs and nervous system.
- ✓ Overdose or improper use of ephedra results in various effects like high blood pressure, heart attack, muscle disorders, seizures, stroke, loss of consciousness and death.
- ✓ Ephedra may reduce the effectiveness of antihypertensives and could rise the blood pressure
- ✓ Ephedra should not be mixed with other central nervous system stimulants such as amphetamine and its derivatives as it may enhance hyperactivity and produce serious conditions.
- ✓ Ephedra should be avoided with blood thinning medications such as aspirin and warfarin, as it may induce bleeding.
- ✓ Ephedra may interact with anti depressants like imipramine, clomipramine, mirtazapine and mono amino oxidase (MAO) inhibitors and enhance their effects.
- ✓ Ephedra should be avoided in people suffering from seizures, as it may worsen the onset of seizures