UNIT 11 PHARMACOGNOSTICAL STUDIES AND HERBAL FORMULATIONS

Structure

11.1 INTRODUCTION

The present unit deals with the study of adulterations in herbal drugs, methods for their evaluations, herbal formulations and herbal drug interactions. Herbal medicine is the oldest form of health care known to man kind used by all cultures throughout the history. It played a vital role in the development of modern civilizations. Use of herbal drugs depends upon the assessment of the quality, safety and efficacy of drug. Adulterated drug means one which does not confirm to the official standards. Drug evaluation involves parameters to confirmation the identity, purity and quality of herbal drug. Herbal formulations are the medicinal products containing as active substances exclusively herbal drugs or herbal drug preparations. The most common message, consumer get from herbal products is that these products are natural

and they assume that natural is safe. It is much needed to continuously review and access the safety of botanical, with an emphasis on surveillance of the use of these products to identify unknown hazards or risks and address them expeditiously. Herbal drug interactions refer to "an alterations of the affect of one drug caused by the presence of a second drug". Drug interactions may be beneficial or detrimental.

Objectives

After studying this unit, you should be able to:

- describe drug adulterations – their reasons and drawbacks;
- explain the drug evaluation;
- list various drug formulations; and
- discuss herbal drug interactions and their mechanisms.

11.2 ADULTERATION OF DRUG

Before we study about the adulteration of drugs, let us first understand the meaning of the term drug.

Drug may be defined as an article recognized in an official compendia (*e.g.*- Indian Pharmacopoeia (I.P.), National Formulary of India (N.F.I.) intended for use in diagnosis, cure, mitigation, prevention or treatment of disease in humans or other animals or intended to alter a bodily function or structure of humans or other animal.

An adulterated drug means one, which does not conform to the official requirements. Adulteration involves incorporation of impurities, spoilage, deterioration, admixture, sophistication and substitution. Adulteration can be accidental or deliberated/intentional.

11.2.1 Reasons for Adulteration

There are number of reasons for adulteration, some of which are listed below:

i) **Collection**

Adulteration may be due to faulty collection, as in some cases, active constituents reach a maximum at a particular season, stage of development, or age.

ii) **Imperfect Preparation**

Collection of other parts along with genuine parts, imperfect drying or faulty treatment may also cause adulteration.

iii) **Incorrect Storage**

The adulteration may also caused by improper storage of raw material of drugs.

- The quality, value or usefulness of the drug may be affected or destroyed by the action of microorganisms, insects, rodents etc. due to improper storage of drug material.
- Factors such as temperature, moisture and sunlight may also affect the proper storage.

11.2.2 Types of Deliberate Adulteration

Generally, the herbal drugs are adulterated by substitution with substandard commodities varieties, inferior drugs or artificially manufactured commodities.

Generally, there are five types of deliberate adulteration *i.e.*:

i) Confusion of Common Vernacular Nomenclature

ii) Cross Substitution with Different Plant Material

iii) Substitution with Artificially Manufactured Substances

iv) Substitution with Exhausted Drugs

v) Addition of Foreign Matter

Let us discuss each of them briefly.

i) **Confusion of Common Vernacular Nomenclature**

This type of adulteration is due to common vernacular name of different plants in different regions of India *e.g.* in most of the states "Brahmi" is obtained from plant *Hydrocotyle asiatica* while in certain parts of India, the plant "*Herpestis monniera*" is used as "Brahmi". The plants *Evolvulus alsinoides*, *Convolvulus microphyllus* and *Clitoria ternatea* are sold by the name "Shankhpushpi".

ii) **Cross Substitution with Different Plant Material**

In place of genuine drugs, substituted products of same appearance are available in market. These substituents are identical in appearance. For example: Material Ashoka bark (*Saraca indica*) can be substituted by *Trema orientalis* bark or Indian senna by Arabian senna.

iii) **Substitution with Artificially Manufactured Substances**

Some substances resembling original drugs are artificially manufactured are used as substitutes. *e.g.* Paraffin wax made yellow coloured and substituted for Bees wax and compressed chicory used in place of coffee.

iv) **Substitution with Exhausted Drugs**

Sometimes exhausted material (after isolation of active constituents) may be used entirely or in part as a substitute for genuine drug. *e.g.* exhausted drugs like clove, ginger, tea etc.

v) **Addition of Foreign Matter**

Mixing of adventitious matters, or naturally occurring materials with the drug in excessive amount or parts of plant other than which constitute the drugs *e.g.* lower plants like moss, liver worts and epiphytes growing on bark portion are mixed with cascara or cinchona. Similarly pieces of amber coloured glass in colophony, limestone in asafoetida, lead shots in opium etc are used. Powdered bark is frequently found to be adulterated with brick powder. Exhausted ginger powder may be used in powdered colocynth or ginger.

Besides these above practices, other methods are also employed like use of synthetic chemicals to enhance the natural character. For example, addition of benzyl benzoate to balsum of peru, citral to citrus oils, like oil of lemon and orange oil etc.

SAQ 1

Give the reasons for adulteration.

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11.3 DRUG EVALUATION

Drug evaluation means confirmation of its quality and determination of its quality and purity and deterioration of nature of adulteration. Such an evaluation is carried out to know:

- biochemical variation in a drug
- deterioration due to treatment or storage
- substitution and adulteration.

Following techniques are involved in standardization or evaluation of crude drugs.

i) Morphological or organoleptic evaluation
ii) Microscopic evaluation
iii) Chemical evaluation
iv) Physical evaluation
v) Biological evaluation

11.3.1 Morphological or Organoleptic Evaluation

Morphological or Organoleptic evaluation refers to evaluation of drugs by colour, odour, taste, size, shape and special features like touch, texture etc. It is a technique of qualitative evaluation based on study of morphological and sensory profiles of whole drugs hence, called *organoleptic evaluation*. Organoleptic evaluation means conclusions drawn from studies resulted due to impressions on organs of senses. For example aromatic odour of umbelliferous fruits, sweet taste of Liquorice, pungent tastes of ginger and capsicum, wavy shape of rauwolfia and ribbon shape of tragacanth.

11.3.2 Microscopic Evaluation

In the identification of crude drugs, it is often necessary to examine the anatomical structure. This involves the microscopical examinations of sections of material. In some drugs, transverse and longitudinal sections are taken and arrangement of tissue is observed.

There is a considerable variation in the amount or extent of different regions of detailed appearance of cells, trichomes, calcium oxalate crystals and this becomes the criteria for drug evaluation. Size, shape, relative positions of different cells and tissue chemical nature of cell walls, are determined.

Quantitative evaluation of drugs powders is done by counting specific histological features such as stomatal number, stomatal index, palisade ratio, vein-islets, vein termination numbers etc. which are highly constant for a given species.

- **Stomatal number:** It is average number of stomata per sq. mm of epidermal cells of the leaf.
- **Stomatal index:** It is the percentage which number of stomata forms to total no. of epidermal cells (each stomata being counted as one cell).
- **Palisade ratio:** Palisade ratio is average number of palisade cells beneath one epidermal cell of a leaf.
- **Vein islet number:** The number of vein islet per sq. mm of the leaf surface midway between the midrib and the margin.
- **Vein termination number:** The number of vein termination per sq.mm of the leaf surface midway between midrib and margin of lamina.

Vein Islet Number
Indian Senna: 15 to 29.5 and Alexandrian Senna: 19.5 to 22.5.

11.3.3 Chemical Evaluation

Determination of active constituents in a drug by chemical process is referred to as chemical evaluation. Thus, chemical evaluation can be used as method for the analysis of active constituents. It comprises of different chemical tests and chemical assays. The isolation, purification and identification of active constituents are chemical methods of evaluation.

Vein Termination Number
Cassia Senna: 32.7 to 40.2, Alexandrian Senna: 25.9 to 32.8.

The purity of crude drugs is ascertained by quantitative estimation of active chemical constituents present in them.

Chemical evaluation also covers

- Procurement of raw material and quality control.
- Extraction, purification and characterization of constituents of pharmaceutical interest.
- Investigation of biosynthetic pathways.
- Quantitative estimation.

Similarly, various tests are carried out for saponins, volatile oil, fixed oil (seed oil), phytosterol, phenolic compounds etc.

11.3.4 Physical Evaluation

Evaluation of the drugs on the basis of important physical properties of active constituents is known as physical evaluation.

Physical standards are to be determined for herbal drugs, whenever possible. These are rarely constant for crude drugs, but may help in evaluation, specifically with reference to moisture content, specific gravity, density, optical rotation, refractive index, melting point etc. Various parameters are taken into account for physical evaluation as different drugs possess different constant values for different parameters which account for physical evaluation.

- *Foreign matter:* Any thing present in drug, which is not complying with the authentic drug, may be considered as foreign matter. Improper harvesting, deliberately addition and improper storage are main reasons for foreign matter. Various official compendia's provide limits for percentage of foreign matter, which should not be exceeded.
- *Moisture content:* Moisture enhances (increases) the enzymatic activity and growth of microbes which leads to drug deterioration.
- *Ash values:* Remnants of crude drugs after incineration contains mostly inorganic salts called ash. Ash values vary in cases of many crude drugs and its study gives an idea about quality and purity of drugs during evaluation.
- *Extractive values:* In crude drugs, sometimes, the active chemical constituents cannot be determined and thus the water, alcohol or ether soluble extractive values are determined for evaluation of such drugs. These values are given in various pharmacopoeias.
- *Volatile oil content:* Efficacy of volatile oil containing drugs like cardamom, clove, and fennel depends upon amount of volatile oil content present in drugs. Volatile content is generally determined by hydro distillation method.

11.3.5 Biological Evaluation

The drugs which cannot be assayed satisfactorily by chemical or physical means, are evaluated by biological methods. Thus, potency of crude drug or its

preparation is determined by means of its effects on living organism like bacteria, fungi, animal tissue or entire animal, and it is called *bioassay*. This method is done for conformity of therapeutic activity of raw material or finished product.

SAQ 2

Name the various methods to determine moisture content.

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11.4 HERBAL DRUG FORMULATION

World Health Organization (WHO) currently encourages, recommends and promotes traditional herbal remedies in national health care programmes because such drugs are easily available at low cost. These are comparatively safe and the people have faith in such remedies. Researches have been carried out on medicinal plants and many of the major pharmaceutical corporations have renewed their strategies in favour of natural products drug discovery. The Research and Development thrust in the pharmaceutical sector is focused on development of new innovative / indigenous plant- based drugs through investigation of leads from the traditional system of medicine.

According to study, 70-80% of people living in rural areas are dependant on herbal medicine for the treatment of day to day diseases. According to one estimate, more than 700 mono and poly-herbal preparations in the form of tincture, tablets and capsules from more than 100 plants are in clinical use. Ayurveda, Unani and traditional Chinese medicine are the important system of medicines largely based on medicinal plants. The general public's use of herbal drugs has increased over the past 10 years.

Herbal drugs are getting popularized in developing and developed countries owing to their natural origin and lesser side effects. Herbal medicines are being manufactured on a large scale in mechanical units, where manufacturers come across many problems such as availability of good quality raw material, authentication of raw material, availability of standards, proper standardization methodology of single drugs and formulations, quality control parameters, etc. Herbal medicines are prepared from a variety of plant materials, leaves, stems, root and bark etc. They usually contain active constituents which are used for the treatment of disease.

11.4.1 Classification of Herbal Formulations

The herbal formulations are classified broadly as:

A) Herbal medicines

B) Herbal cosmetics.

A) **Herbal Medicines**

The herbs are considered to be medicinally important if they possess the pharmacological activities of possible therapeutic use. The use of herb is varied as Naturopathic Medicines, Unani, Siddha and Homoeopathic Systems of Medicine. All of these differ in how diseases are diagnosed and which herbal remedies are prepared from a variety of plant materials or are isolated phytoconstituents from stems, roots, bark, fruits, leaves, bark etc. Some of important ayurvedic formulations are as

i) *Anjan/ Varti (Eye Preparations):* These are medicated fine powder intended to be used in eyes for their local effect.

ii) *Araks (Distillate):* These are distilled essences or liquors made by soaking drugs in water for 24-48 hours and then distilling the same. The distillate collected is called 'Araks'.

iii) *Aristas (Fermented Preparations):* These are weak alcoholic preparations prepared by making a decoction of the drugs and then allowing them to undergo fermentation by the help of raw sugar or honey.

iv) *Asavas (Fermented Preparations):* These are medicated alcoholic liquors prepared by the fermentation of raw vegetable juices with honey or jaggery or treacle.

v) *Avalehas (Linctus):* These are thick extracts of the drugs.

vi) *Bhasmas (Calcinated residue):* These are ashes which are prepared from vegetable and mineral substances.

vii) *Churnas (Powders):* These are powdered mixtures prepared by mixing dry mineral, animal or vegetable substances in a pestle-mortar.

viii) *Ghritas (Medicated ghee and oils):* These are medicated ghees or clarified butter. The ghritas or clarified butter is heated on a fire to remove water. A little turmeric juice is then added to purify it.

ix) *Gutikas/ Vati (Tablets and Pills):* These are large pills. These are prepared from pill mass.

x) *Manda:* It is a decoction which is prepared in 14 parts of water and one part of cereal, usually rice.

xi) *Peya:* It is decoction which is prepared by boiling one part of a cereal in 14 parts of water till it becomes thicker than that of Manda.

xii) *Rasas:* These are preparations of metals containing mercury in any form. These preparations contain various kinds of poisons.

xiii) *Tailas (Medicated ghee and oils):* These are medicated oils which are prepared by boiling drugs in water, milk or other liquid substances mixed with oil until water content is evaporated.

B) **Herbal Cosmetics**

The substances specially prepared to enhance beauty and increase the attractiveness of a person are known as cosmetics. Herbal cosmetics are prepared from plants, their products and other natural drugs like animals and minerals etc. Herbal cosmetics can be further classified on basis of

a) **dosage forms,** and
b) **part or organ of the body to be applied for**

a) **Dosage Forms:** Different dosages form of the cosmetics and their examples are given below:

- *Emulsions*: cold cream, vanishing cream.
- *Powders*: face powders, talcum powder, tooth powder
- *Cakes:* rouge compacts, make up cake
- *Oils*: hair oil
- *Mucilage*: hand lotion
- *Jellies:* hand jelly
- *Suspensions*: cosmetic stocking
- *Paste*: tooth Paste
- *Soaps:* shaving soaps
- *Solutions*: after shave lotions and lotions

b) **Part or organ of the body to be applied for**

- **For skins**

  i) Powders ii) Creams iii) Lotions
  iv) Deodorants v) Cleansing products vi) Make up preparations
  vii) Suntan preparations

- **For hairs**

  i) Shampoos ii) Tonics iii) Hair waving preparations
  iv) Beard softeners v) Hairs dressing vi) Shaving cream
  vii) Depilatories for removing unwanted hairs

- **For nails**

  i) Nail polishes ii) Polishes removers

- **For teeth and mouth**

  i) Tooth paste ii) Dentifrices iii) Mouth washes

- **Borderline preparations**

  i) Eye preparations ii) Foot powders
  iii) Insect repellents iv) Miscellaneous products

11.4.2 Some Herbal Formulations

Ingredients of some herbal formulation are given in Appendix I in the end of this unit.

SAQ 3

a) Which one is thicker, Peya or Manda?

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b) How are Araks (distillate) prepared?

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11.5 HERBAL DRUG INTERACTION

Almost a century has passed and it has witnessed limitations of allopathic system of medicine. Lately, herbal medicine has gained momentum with the evidence that it has no side effects. Ayurveda, Unani and homeopathy medicine are the important systems of medicines largely based on medicinal plants.

Aside from the need to appraise these products for safety and efficacy, health care providers and the public need to know whether interactions might occur when these products are used in combination with conventional drugs. Not only has the prevalence of use of herbal medicine increased, but the pattern of use has also changed. Self-directed herbal use increased by 10% from 1997-2002. According to survey it has been estimated that 18% of patents who took prescription medications also used herbal products. As a result, an estimated about 15 million people were at risk for dietary supplement drug interactions. However, the prevalence of clinically significant interactions between herbals and medication is unknown. A factor that may account for lack of data on the true prevalence of herbal-drug interaction is that the following:

i) A lack of information concerning the "contents" of the herbal products

ii) Incomplete or inaccurate product information

iii) Multiple ingredients.

11.5.1 Overview of Drug Interaction

There is concern regarding the perceived safety of these products, particularly with respect to the lack of research and knowledge on botanicals drug interaction potential and significance. Drug-drug interaction refers to an alteration of the effect of one drug caused by the presence of a second drug. Drug nutrient interactions similarly refer to the alteration of the effect of drug or nutrient caused by the presence of a second agent. Drug interaction may be beneficial or detrimental.

11.5.2 Drug Interaction

Drug-drug interaction occurs when two or more drugs react with each other. This drug-drug interaction may cause you to experience unexpected side effects. For example, mixing a drug you take to help you sleep (a sedative) and a drug you take for allergies (an antihistamine) can slow your reaction and make driving a car or operating machinery dangerous.

Drug-food/beverage interactions results from drugs reacting with foods or beverages. For example, mixing alcohol with some drugs may cause you to feel tired or slow your reactions.

Drug-condition interactions may occur when an existing medical condition make certain drugs potentially harmful. For example, if you have high blood pressure, you could experience an unwanted reaction if you take Nasal decongestant.

11.5.3 Mechanism of Herbal Drug Interaction

The interaction between pharmacologically active botanicals and drug involve the same pharmacokinetic and pharmacodynamic mechanism as drug-drug interaction. Pharmacokinetic interactions may involve alteration in absorption, distribution, metabolism or excretion of the drug. Pharmacodynamic

interaction on the other hand, is named after the relationship between the drug concentration and the pharmacological response for a drug or botanical.

i) **Altered Pharmacokinetics**

a) ***Drug Absorption***

There was a report of an interaction between aspirin and tamarind, an Asian fruit used not only as an Ayurvedic medicine, but also as a flavouring ingredient for cooking, in six healthy volunteers, tamarind significantly increased the extent of absorption of a single 600 gm dose of aspirin, which might result in toxicity if a large amount of acetylsalicylate was ingested concurrently with tamarind.

b) ***Drug Distribution***

Changes in distribution of drugs resulting from altered protein binding of highly protein bound drugs have been studied intensively. However, the clinical significance of interactions based on this mechanism is usually minor and transient, unless accompanied by impaired metabolism and/or excretion that almost always result in persistently elevated blood concentrations of the affected drug.

c) ***Drug Metabolism***

Inhibition: Inhibition refers to effect when two substances have opposite effects on a process. The decreased anticoagulant effect of warfarin seen when vitamin K intake is increased, is a negative example of this type of interaction. Warfarin therapy frequently requires adjustment because of such inhibition, especially when patients suddenly increase their intake of green leafy vegetables rich in vitamin K. This is a real hazard of patients who are avid gardeners and whose vitamin K intake can vary drastically from season to season.

Induction: The term “induction” has evolved to include any mechanism that results in increased tissue concentration of catalytically active protein involved in drug metabolism. This increased enzyme activity results in greater systemic clearance and lower bioavailability of extensively metabolized drugs. The resulting lower drug concentrations often result in therapeutic failure.

d) ***Drug Excretion***

It is possible that botanicals with diuretic effects can increase drug excretion; most botanical diuretics are not as potent as furosemide and are unlikely to result in significant interactions. Most botanical also do not affect urinary pH significantly, and hence are unlikely to affect renal tubular reabsorption of drugs.

ii) **Altered Phramacodynamics**

In addition to pharmacokinetic botanical-drug interaction, pharmacodynamic interactions can also occur, resulting in either an augmented or attenuated response. Phramacodynamics interactions are based on patient cases or clinical experience.

iii) **Adverse Drug Reactions**

An adverse drug reaction can be defined as an unexpected diminished or enhanced pharmacological activity of a drug or noxious response to a drug, when used alone in humans at doses used for prophylaxis, diagnosis, or therapy. Adverse type reactions are classified as type A and B, Type A (augmented) reactions are normal pharmacological effects of the drug exaggerated to the point of being undesirable or intolerable for patients. Example of drugs indicated type A reactions include warfarin or heparin, which cause bruising. Type B reactions have more severe adverse effects unrelated to the unknown Pharmacologic action of the drug and include most immunologic reactions. Example of a type B reaction is an anaphylactic reaction to Penicillin.

11.5.4 Classification of Drug Interactions

There are three types of drug interactions:

i) Drug-Drug Interactions
ii) Drug-Nutrient Interactions
iii) Herbal-Drug Interactions

i) **Drug-Drug Interactions**

Drug-drug interactions can be defined as the modulation of the pharmacological activity of one drug (*i.e.*, the object drug) by the prior or concomitant administration of another drug (*i.e.* the precipitant drug). In these reactions, the pharmacological properties of the drugs can be either enhanced or diminished. The interaction can be expressed as antagonized when the resulting effect is less than the combined effects of the two drugs when used separately. The interaction may be synergistic or potentiated, when the combined effect of the two drugs is greater than the total effect of the drugs used separately. Sometimes, the drug-drug interactions are beneficial because they result in lower doses of the drugs being administered while still achieving therapeutic serum drug levels. For example, when probenecid is administered with the penicillin drug it elevates serum levels of penicillin and prolongs its half-life. The causes and significance of drug interaction are various and include drug dose, serum drug level, route of administration, duration of therapy, drug absorption, drug metabolism, patient factors, (age, gender, weight, genetic factors etc.). These interactions are frequently associated with antagonism, synergism or altered cellular transport and effect receptor sites.

ii) **Drug-Nutrient Interactions**

When drugs are administered along with foods, the drug interaction may occur and can modify the activity of the drug or impair the nutritional benefit of the foods. Mostly in this type of interaction drug, absorption are effected. Food can decrease the rate of absorption of drug or decrease the extent of absorption of numerous drugs. Vitamin K found in green leafy vegetables, tomatoes, beaf liver, green tea and nonprescription vitamin mineral products, can antagonize the anticoagulant activity and lowered prothrombin time. Vitamin B_6 found in beans, peas, sweet pototoes, beaf liver, pork and some nonprescription vitamin mineral products increases the metabolism of Levodopa, producing decreased blood levels of dopamine and antiparkinsonism effects. Liquid nutritional supplements and Calcium in vitamin-mineral products interact with ciprofloxacin antibiotics and reducing their bioavailability resulting in decreased antibiotic activity.

iii) **Herbal-Drug Interactions**

These types of interaction take place when allopathic drugs are administered with herbal drugs. One important factor that increases the likelihood of having an herbal-drug interaction is concomitant use of an herbal with drugs that have a narrow therapeutic index. The example of such type of drugs includes digoxin, antiepileptic drugs, antineoplastic agents, immunosuppressants and warfarin etc. These type of interaction are occur commonly in elderly, critical care patients, patients with undergoing surgical procedures, patients with renal disease or receiving multiple medications. For example, warfarin is known to interact with many drugs and owing to its narrow therapeutic index and results in fatal consequences *i.e.* bleeding complications or subtherapeutic levels occur. Some such interactions are given in Table 11.1 and Table 11.2.

Table 11.1: Interaction involving herbal drugs

Name of Herb	Some Common Uses	Possible Side Effects or Drug Interactions
Ephedra	Ephedra is also called Ma-Huang. It is used in many over-the-counter diet aids as an appetite suppressant. It is also used for asthma or bronchitis.	Ephedra may interact with certain antidepressant medications or certain high blood pressure medications to cause dangerous elevation in blood pressure or heart rate. It could cause death in certain individuals.
Garlic	Garlic is used for lowering blood cholesterol,	Garlic may increase bleeding, especially in patients already taking

	triglyceride levels and blood pressure.	certain anti-clotting medications.
Ginger	Ginger is used for reducing nausea, vomiting and vertigo	Ginger may increase bleeding, especially in patients already taking certain anti-clotting medications.
Ginkgo	Ginkgo, also called ginkgo biloba, is used for increasing blood circulation and oxygenation and for improving memory and mental alertness.	Ginkgo may increase bleeding, especially in patients already taking certain anti-clotting medications.
Ginseng	Ginseng increases physical stamina and mental concentration.	Ginseng may cause decreased effectiveness of certain anti-clotting medications. Persons using ginseng see increased heart rate or high blood pressure. It may cause bleeding in women after menopause.
Licorice	Licorice is used for treating stomach ulcers.	Certain licorice compounds may cause high blood pressure, swelling or electrolyte imbalances.
St. John's Wort	St. John's Wort is used for mild to moderate depression or anxiety and sleep disorders.	St. John's Wort may prolong the effect of certain anesthetic agents.
Valerian	Valerian is used as a mild sedative or sleep-aid. It is also a muscle relaxant.	Valerian may increase the effects of certain anti-seizure medications or prolong the effects of certain anesthetic agents.

Table 11.2: Interaction involving herbal with allopathic medicine

Adverse Drug Effects/Drug Interactions of Selected Herbal or Food Products		
Drug	**Herbal/Food**	**Adverse Effects/Drug Interactions Reported**
Alprazolam	Kava	Synergistic CNS activity of alprazolam
Amantadine	Quinine	Elevated serum drug levels of amantadine and risk of toxicity (ataxia, mental confusion)
Astemizole	Grapefruit (juice)	Increased bioavailability of astemizole
	Quinine	Elevated serum drug levels of astemizole, and increased risk of cardiotoxicity
Buspirone	Grapefruit (juice)	Increased serum drug levels of buspirone
Calcium channel blockers, Carbamazepine, Cyclosporine	Grapefruit (juice)	Increased serum drug levels.
Digoxin	Quinine	Elevated serum digoxin levels
	Licorice	Elevates serum digoxin levels
	Ginseng (Siberian)	Elevates serum digoxin levels
	St. John’s wort	Decreases serum digoxin concentration
Estrogen	Grapefruit (juice)	Increased serum drug levels
	Herbal tea	Increased serum drug levels
Lithium	Herbs with diuretic properties (broom, buchu, dandelion, juniper)	Increased serum drug levels of lithium

Midazolam	Grapefruit (juice)	Increased serum drug levels of midazolam
Phenalzine	Ginseng (Siberian)	Insomnia, tremulousness, tension headaches, irritability, and visual hallucinations
Phenobarbital	Quinine	Elevated serum phenobarbital levels
Quinidine	Grapefruit (juice)	Reduced and delayed cardiac effects
Spironolactone	Licorice	Mineralocorticoid of licorice blocked; hypokalemia and muscle weakness
Theophylline	St. John's wort	Increases serum theophylline concentration
Triazolam	Grapefruit (juice)	Increased serum drug levels of triazolam
Warfarin	Dashen	Increased anticoagulant activity or increased INR
Warfarin	Ginkgo biloba, garlic, feverfew, and cayenne	Platelet aggregation inhibitor effects and increased risk of bleeding/bruising
	Ginseng (Siberian)	Decreased anticoagulant activity or decreased INR
	Liquorice	Increased anticoagulant activity or increased INR
	Alfalfa	Decreased anticoagulant activity or decreased INR
	Vitamin E	Increased anticoagulant activity and increased platelet aggregation inhibition, increased risk of bleeding
	Ginger	Increased anticoagulant activity, increased INR, prolonged bleeding
	Quinine	Increased anticoagulant activity or increased INR

SAQ 4

a) Pharmacokinetic drug interactions involve the alteration in ……..., …… , …… and …… of a drug.

b) Herbal drug interactions are: ……. and ……

c) How garlic can interact with anti-clotting medications?

d) Ephedra may interact with certain …… medication.

e) Quinine may ……. the serum digoxin level by about 75%.

SAQ 5

What is adverse drug reaction?

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11.6 SUMMARY

Now we will summarize, what all has been discussed about herbal standardization and formulations. Herbal adulteration involves incorporation of impurities, spoilage, deterioration, admixture, sophistication and substitution. The reasons for adulteration may be accidental like fault in collection, preparation, storage or it may be intentionally for the purpose of profits.

Drug's identity, quality and purity can be evaluated by different techniques of morphological, microscopic, chemical, physical and biological evaluation.

Herbal formulations are various medicinal preparations ready for the administration where, herbs or herbal products or its phytoconstituents are integral part of it. These can be classified as herbal medicines and herbal cosmetics.

Since, majority of world's population uses herbs or herbal products and they generally considered it as safe, however it is not always true, as they may have some problems of adverse effects and herbal drug interaction. The mechanism involve herbal interaction is ether altered pharamacokinetics or altered pharmacodynamics. Herbal interaction involves the interaction of herbal preparation with food, allopathic drugs and also with other herbal preparation. The results of interaction may be beneficial of detrimental.

11.7 TERMINAL QUESTIONS

1. What is drug evaluation?
2. Name the various parameter used in physical methods of drug evaluation.
3. What is herbal-drug formulation?
4. What is herbal-drug interaction?
5. Give the classification of herbal-drug interaction.

11.8 ANSWERS

Self Assessment Questions

1. Faulty collection, Imperfect preparation and incorrect storage.
2. Some important physical and chemical methods used to determine moisture content are:-
   - Loss on drying
   - Azeotropic Distillation Method
   - Karl Fischer Method
3. a) Manda
   b) These are distilled essences or liquors made by soaking drugs in water for 24-48 hours and then distilling the same. The distillate collected is called 'Araks'.
4. a) Absorption, Distribution, metabolism and Excretion
   b) Beneficial and Detrimental
   c) Garlic may increase bleeding, especially in patients already taking certain anti-clotting medications.
   d) Antidepressant Medications
   e) Elevate

5. An adverse drug reaction can be defined as an unexpected diminished or enhanced pharmacological activity of a drug or noxious response to a drug, when used alone in humans at doses used for prophylaxis, diagnosis, or therapy. Adverse type reactions are classified as type A and B.

Terminal Questions

1. **Drug Evaluation** means confirmation of its quality and determination of its quality and purity and deterioration of nature of adulteration.
2. **Physical Evaluation**
   - Evaluation of the drugs on the basis of important physical properties of active constituents is known as physical evaluation.
   - Physical standards are to be determined for herbal drugs, whenever possible. These are rarely constant for crude drugs, but may help in evaluation, specifically with reference to moisture content, specific gravity, density, optical rotation, refrective index, melting point etc. various parameters are taken into account for physical evaluation as different drugs possess different constant values for different parameters which accounts for physical evaluation.

     i) Foreign matter

     ii) Moisture content

     - Loss on drying
     - Azeotropic Distillation Method
     - Karl Fischer Method

     iii) Ash values

     iv) Extractive values

     v) Volatile oil content
3. The herbal-Drug Formulation is the formulation of herbal medicine from a variety of plant materials, leaves, stems, root and bark etc in appropriate quantity for the treatment of disease.
4. Herbal-drug interactions can be defined as the modulation of the pharmacological activity of one drug (*i.e*., the object drug) by the prior or concomitant administration of another drug (*i.e*. the precipitant drug). These types of interaction take place when a allopathic drugs are administered with herbal drugs.
5. Herbal-Drug interaction can be classified as

   i) Drug-Drug interaction ii) Drug-Nutrient Interaction

   iii) Drug-disease Interaction iv) Herbal -Drug Interaction

11.9 SUGGESTED READINGS

1. Pharmacognosy (Pharmacognosy and Phytochemistry), Vol. 1, Mohammad Ali, 1st Edn., CBS Publisher and Distributors, N. Delhi, India, 2008.

2. Quality control of herbal drugs and approach to evaluation of Botanicals; Pulok, K. Mukherjee, 1st edn., Business Horizons, Pharmaceutical Publishers, New Delhi, India, 2002.

3. Textbook of Industrial Pharmacognosy; A.N. Kalia, 1st edition, CBS Publisher and Distributors, New Delhi.

4. Textbook of Pharmacognosy; S.S. Handa and V.K. Kapoor, 2nd Edn., Vallabh Prakashan, New Delhi, 2003.

APPENDIX I

Formula of cold cream

Ingredients	By weight (in gm)
White Beeswax	10.00
Vegetable Lard	15.00
Sesame oil	20.00
Almond oil	20.00
Borax	35.00
Rose water	100.00

Lubricating Cream

Ingredients	By weight (in gm)
Heavy white petrolatum	30.00
Honey	20.00
Code liver oil	45.00
Borax	01.50
Water Q.S. to make……..	100.00

Herbal Cream

Ingredients	By weight
Olive oil	15.00 gm
Oil of cade	15.00 gm
Cetyl alcohol	10.00 ml
Cocoa butter	10.00 gm
Lanolin	15.00 gm
Ammonium sulfo-ichthyolate	5.00 gm
Oil of wintergreen	1.00 ml
Petrolatum Q.S. to make……..	100.00 gm

Sunburn cream

Ingredients	By weight (in gm)
Oxyquinoline benzoate	0.15
Camphor-phenol	3.50
Linseed oil	21.50
Olive oil	20.00
Cholesterin absorption base Q.S. to make….	100.00

Burn cream

Ingredients	By weight (in gm)
Glyceryl monosterate	15.00
Cetyl alcohol	5.00
Lanolin	2.50
Lecithin	1.50
Linseed oil	15.00
Glycerin	10.00

Para-chloro-meta-cresol	0.05
Distilled water Q.S. to make……..	100.00

Scar remover cream

Each 100 gm contains

Wheat germ oil	3.50 ml
Curcuma longa linn.	20.00 gm
Azadirachta indica	2.00 ml
Santalum album linn.	1.00 ml
Tulsi oil	2.00 ml
Citrus sinensis rind	2.00 gm
Rosemary oil	5.00 ml
Aloe vera gel	2.00 ml
Crocus sativa	1.00 gm
Cream base Q.S. to make…….	100.00 gm

Fairness cream

Rose water	25.00 mg
Orange oil	25.00 mg
Aloe vera gel	50.00 mg
Walnut leaves extract	20.00 mg
Cream base Q.S. to make…….	1.00 gm

Face Pack

Ingredients	**By weight**
Brewer's yeast	120.00 gm
Witch hazel extract	7.50 ml
Peppermint Extract	7.50 ml
Lemon juice	4.00 ml

Witch Hazel Skin Tonning Lotions

Sunflower oil	45.00 ml
Wheat germ oil	7.50 ml
Witch hazel extract	25.00 ml
Sodium benzoate	5.00 gm
Lanolin Q.S. to make ……	100.00 gm.

Astringent Lotion

Boric acid	1.50 gm
Witch hazel	15.50 gm
Rose water	15.00 ml
Alcohol	10.00 ml
Orange flower water Q.S. to make…..	100.00 ml

Bleaching Lotions

Lawsonia innermis paste	9.50 g
Curcuma longa	0.50 gm
Benzoin tincture	1.00 ml
Perfume	0.30 ml
Rose water Q.S. to make…..	100.00 ml

Methi-Shikakai Shampoo

Trigonella foenum greacum	250.00 gm
Shikakai	1.00 Kg.
Orange peels	handful
Purified water Q.S. to make…….	2.00 litres.

Neem Shampoo

Gram flour	1.00 kg
Sandalwood powder	245.00 gm
Neem leaves powder	165.00 gm
Shikakai powder	1.00 kg
Purified water Q.S. to make…….	2.50 litres.

Herbal Hair Tonic

Castor oil, sulfonated	10.00 gm
Oil of Bergamot	1.10 ml
Oil of cinnamon	0.10 ml
Oil of clove	0.10 ml
Oil of Lavender	0.75 ml
Tincture of capsicum	0.75 ml
Alcohol 90% Q.S. to make……	100.00 ml

Suntan oil

Peanut oil, refined	45.00 gm
Sesame oil	5.00 gm
Oil of thuja	1.00 ml
Perfume	1.00 ml
Coconut oil Q.S. to make ……..	100.00 gm.

Herbal Mouth Wash

	By volume
Eucalyptol	1.50
Menthol	1.50
Clove oil	0.50
Wintergreen oil	0.10
Heliotropine	0.01
Cholorophyll alcohol soluble	0.20
Alcohol	45.00
Purified water Q.S. to make……..	100.00 ml

Herbal Toothpaste

Triphla	45.00 gm
Colloidal clay	2.50 gm
Gum tragacanth mucilage	2.50 gm
Glucose	4.00 gm
Honey	17.50 gm
Water	30.00 ml
Methyl parahydroxybenzoate	0.20 gm
Milk of magnesia	24.00 gm

Black peeper	30.00 gm
White powder soap	2.00 gm
Glycerine of tragacanth	10.00 gm
Clove oil	1.00 ml
Saccharine	0.10 gm
Flavor	0.80 ml
Distilled water Q.S. to make……	100.00 gm

Herbal Syrups

Liv52 Syrup (Himalaya Laboratories)

Each ml contains	
Himsra	17 mg
Kasani	17 mg
Kakamachi	8 mg
Arjuna	8 mg
Kasamarda	4 mg
Biranjasipha	4 mg
Jhavaka	4 mg

Processed in Bringraja, Bhumyaamlaki, Punarnava, Guduchi, Daruharidra, Mulaka, Amalki, Chitraka, Vidanga, Haritaki, Purpata.

Charak (Health forever ---- naturally)

Livomyn (syrup)

Each 5 ml syrup contains extracts of the following	
Phyllanthus niruri	100 mg
Triphala	90 mg
Amoora rohituka, *Boerhavaavia diffusa* and *Cichorium intybus* each	75 mg
Adhatoda vasica and *Eclipta alba* each	50 mg
Zingiber officinale	35 mg
Berberis arustata	25 mg
Fumaria officinale, *Emblica ribes*, *Tephrosia purpurea*, and *Tinospara cardifolia* each	15 mg
Aloe barbadensis and *Coriandrum sativum* each	10 mg
Andrographis paniculata and Picrorrhiza *Kurrooa* each	3 mg
Flavoured syrup base	Q.S.
Preservatives – Sodium benzoate, Sodium methyl paraben and Sodium propyl paraben	

Koflet (Himalaya Laboratories)

Each 5 ml contains	
Madhu (meldespumatum) purified	1.25 mg
Gugglu (purified) *Balsamodendron mukul*	35 mg
Extract	
Draksha (*Vitis Vinifera*)	35 mg

Vishnu priya (*ocimum sanctum*)	25 mg
Jufa (*Hyssopus officinalis*)	25 mg
Guduchi (*Tinospara cordifolia*)	20 mg
Vasaka (*Adhatoda vasica*)	15 mg
Jaatipatree (*Myristica fragrans*)	15 mg
Yasti-madhu (*Glycyrrhiza glabra*)	15 mg
Gojiha (*Onosma bracteatun*)	10 mg
Neelapushpa (*Violet otorata*)	10 mg
Triphla	9 mg
Trikatu	9 mg
Vidanga (*Embelia ribes*)	8 mg
Kantakari (*Solanum xanthocarpum*)	8 mg
Taja (*Cinnamomum cassia*)	8 mg
Navasagra	3 mg

Processed in Gojiha (*Onosma bracteatun*), Gul-khair(*Malva sylvestris*), Rajbadar (*Zizyphus sativa*), Dhamasa(*Fagonia cretica*), Yawanika(*Ptychotis ajowan*).
Preservative: methyl paraben, propyl paraben.

Jufex Syrup (Aimil Pharmaceuticals)

Each 10 ml syrup contains

Bharngi	300 mg
Bansapatar	300 mg
Sunlata	200 mg
Kantkari	200 mg
Anjeer	200 mg
Hansraj	200 mg
Bahera	100 mg
Karasingi	100 mg
Jufa	100 mg
Khubbaji	50 mg
Gulbanfa	50 mg
Kaiphal	25 mg
Nasvar	30 mg
Appamargasher	25 mg
Pudhina	5 mg
Kapoor	5 mg
Syrup base	Q.S.

Tablet

Liv 52 Tablets (Himalaya Laboratories)

Each Tablet contains

Himsra	65 mg
Kasani	65 mg
Mandur bhasma	33 mg
Kakamachi	32 mg
Arjuna	32 mg
Kasamarda	16 mg

Biranjasipha	16 mg
Jhavaka	16 mg

Processed in Bringraja, Bhumyaamlaki, Punarnava, Guduchi, Daruharidra, Mulaka, Amalki, Chitraka, Vidanga, Haritaki, Purpata.

Mentat (Himalaya Laboratories)

Each Tablets contains

Brahmi	136 mg
Mandukaraparani	70 mg
Ashvgandha	52 mg
Vishnu karantha	52 mg
Jatamansi	52 mg
Tagar	50 mg
Vidanga	50 mg
Votadha	50 mg
Vacha	42 mg
Haritaki	36 mg
Amalki	36 mg
Gudichi	36 mg
Jyotismati	32 mg

Septilin (Himalaya Laboratories)

Each Tablet contains

Powders

Guggulu	0.32 mg
Shankh basma	64 mg

Extracts

Maharanadi quath	130 mg
Guduchi	98 mg
Manjistha	64 mg
Amalaki	32 mg
Shigra	32 mg
Yasti-madhu	12 mg

Cystone (Himalaya Laboratories)

Each Tablet contains

Shilapushpa(*Didymocarpus pedicullata*)	130 mg
Manjistha (*Rubia cordifolia*)	32 mg
Nagarmusta(*Cyperus scariosus*)	32 mg
Apamarga(*Achyranthus aspara*)	32 mg

Extract

Gojiha(*Onosma bracteatum*)	32 mg
Sahidevi(*Vernonia cinera*)	32 mg
Hajrul jahid bhasma	32 mg
Shilajeet	26 mg

Powders

Divya Gashar Churna (Antiflatulence) (Divya Pharmacy)

Each 5.00 gm contains	
Trachyspermum ammi	1.50 gm
Piper nigrum	0.50 gm
Black rock salt	0.50 gm
Terminalia chebula	1.00 gm
Carum carvi	0.75 gm
Sodium bicarbonate	0.25 gm
Ammonium chloride	0.25 gm
Citric acid	0.15 gm
Ferula foetida	0.10 gm