History of medicinal plants

The oldest written evidence of medicinal plants’ usage for preparation of drugs has been found on a Sumerian clay slab, approximately 5000 years old. It comprised 12 recipes for drug preparation referring to over 250 various plants, some of them alkaloid such as poppy (*Papaver somniferum*), henbane (*Hyoscyamus niger*), and mandrake (is the root of a plant, historically derived either from plants of the genus *Mandragora* found in the Mediterranean region.

The Chinese book on roots and grasses “Pen T’Sao,” written by Emperor Shen Nung circa 2500 BC, 365 drugs (dried parts of medicinal plants), many of which are used even nowadays such as the following: camphor, , ginseng, jimson weed, cinnamon bark, and ephedrine extracted from ephedra which used for treat the bronchitis.

The Indian holy books Vedas mention treatment with plants, which are abundant in that country. Reserpine compound which isolated from *Rauvolfia serpentine* roots and used to treat the nervous system problems and high pressure during Indian civilization.

Khelin compound which extracted from *Ammi visnaga* fruits and used to treat the kidney stones and increase the diuretic. This happen during Egypt civilization longtime ago.

Early 19th century was a turning point in the knowledge and use of medicinal plants. The discovery, substantiation, and isolation of alkaloids from poppy (1806), ipecacuanha the dried root of *Cephaelis ipecacuanha*, (1817), quinine (1820), pomegranate (*Punica granatum*) (1878), and other plants, then the isolation of glycosides, marked the beginning of scientific pharmacy. With the upgrading of the chemical methods, other active substances from medicinal plants were also discovered such as tannins, saponosides, etheric oils, vitamins, hormones, etc.
Classification of medicinal and aromatic plants.

Classification of medicinal plants is organized in different ways depending on the criteria used. In general, medicinal plants are arranged according to their active principles in their storage organs of plants, particularly roots, leaves, flowers, seeds and other parts of plant.

Medicinal plants are classified in many ways. Some of them are

1. According to the usage.
2. According to the active constituents.
3. According to the period of life.
4. According to their taxonomy.

1- According to the usage

The herbs are classified in four parts: Medicinal herbs, culinary herbs, Aromatic herbs, Ornamental herbs.

A. Medicinal Herbs

Medicinal herbs have curative powers and are used in making medicines because of their healing properties like milk thistle (*Silybum marianum*).

B. Culinary Herbs

Culinary herbs are probably the mostly used as cooking herbs because of their strong flavors like mint (*Menthe spicata*), parsley (*Petroselinum crispum*) and basil (*Ocimum basilicum*).

C. Aromatic Herbs

Aromatic herbs have some common uses because of their pleasant smelling flowers or foliage. Oils from aromatic herbs can be used to produce perfumes, toilet water, and various scents. For example: mint, rosemary (*Rosmarinus officinalis*), basil etc.
D. Ornamental Herbs

Ornamental herbs are used for decoration because they have brightly colored flowers and foliage like lavender, chive.

2- According to the active constituents

The herbs are divided into five major categories: Aromatic (volatile oils), Astringents (tannins), Bitter (phenol compounds, saponins, and alkaloids), Mucilaginous (polysaccharides), and Nutritive (foodstuffs).

A. Aromatic Herbs

Aromatic Herbs, the name is a reflection of the pleasant odor that many of these herbs have. They are used extensively both therapeutically and as flavorings and perfumes. Aromatic herbs are divided into two subcategories: stimulants and nerviness

Stimulant Herbs increase energy and activities of the body, or its parts or organs, and most often affect the respiratory, digestive, and circulatory systems. E.g. fennel (*Foeniculum vulgare*), ginger (*Zingiber officinale*), garlic (*Allium sativum*), lemon grass (*Cymbopogon citratus*).

Nerving Herbs are often used to heal and soothe the nervous system, and often affect the respiratory, digestive, and circulatory systems as well. They are often used in teas or in encapsulated form, e.g. catnip (*Nepeta cataria*).

B. Astringent Herbs

Astringent Herbs have tannins, which have the ability to precipitate proteins, and this "tightens," contracts, or tones living tissue, and helps to halt discharges. They affect the digestive, urinary, and circulatory systems, and large doses are toxic to the liver. They are analgesic, antiseptic. For example: peppermint, red raspberry.
C. Bitter Herbs

Bitter Herbs are named because of the presence of phenols and phenol glycosides, alkaloids, or saponins, and are divided into four subcategories: laxative herbs, diuretic herbs, saponin-containing herbs, and alkaloid-containing herbs.

Laxative Bitter herbs include, antipyretic, hypotonic, blood purifier. For example: yucca, barberry, Gentian.

Diuretic Herbs induce loss of fluid from the body through the urinary system. The fluids released help cleanse the vascular system, kidneys, and liver. They are antibiotic, antipyretic, and antiseptic, and blood purifier. For example: blessed thistle (*Silybum marianum*) and parsley.

Saponin-containing Herbs are known for their ability to produce frothing or foaming in solution with water. The name "saponin" comes from the Latin word for soap. They emulsify fat soluble molecules in the digestive tract, and their most important property is to enhance the body's ability to absorb other active compounds.

Saponins have the ability to effectively dissolve the cell membranes of red blood cells and disrupt them. They are alterative, ant catarrhal, antispasmodic, and aphrodisiac, emmenagogue, cardiac stimulant, and increased longevity in nature. For example: alfalfa, yucca, and ginseng.

D. Mucilaginous Herbs

Mucilaginous herbs derive their properties from the polysaccharides they contain, which give these herbs a slippery, mild taste that is sweet in water. All plants produce mucilage in some form to store water and glucide as a food reserve. Since most mucilage are not broken down by the human digestive system, but absorb toxins from the bowel and give bulk to the stool, these herbs are most effective topically as poultices, and are also used topically in the digestive tract. When used as extracts, they have a demulcent action on the throat.
They eliminate the toxins from the intestinal system, help in regulating it and reduce the bowel transit time. They are antibiotic, demulcent, and detoxifier in nature. For example: (Marshmallow) *Althaea officinalis* and *Aloe vera*.

**E. Nutritive Herbs**

These herbs derive both their name and their classification from the nutritive value they provide to the diet. They are true foods and provide some medicinal effects as fiber, mucilage, and diuretic action. But most importantly they provide the nutrition of protein, carbohydrates, and fats, plus the vitamins and minerals that are necessary for adequate nutrition. For example: apple, asparagus, banana, barley grass, broccoli, cabbage, carrot, lemon, oat straw, onion, orange, papaya, pineapple, red clover.

2-According to the period of life

Herbs also can be classified as annuals, biennials, and perennials. Annuals bloom one season and then die. Biennials live for two seasons, blooming the second season only. Once established, perennials live over winter and bloom each season.

**Annual herbs** complete their life cycle in one year; start them from seed. Annual herbs include:

Fennel • Marjoram • Parsley  Anise • Basil • Borage • Chamomile

**Perennial herbs** grow for more than one season and include sweet marjoram, parsley, mint, sage, thyme and chives.

**Biennial herbs** are plants, which live two seasons and bloom in the second season only. Include for example: Caraway (*Carum carvi*).
According to their taxonomy:

Plants are divided into families in which similarly related plants are grouped together based on the clear similarity of morphological characteristics. Families may contain one genus or a large number. A genus may similarly contain one species or a large number of related individuals – for example, the Rosmarinus genus contains just two species.

Most of the medicinal and aromatic plants belong to the following families:
- Compositae
- Labiatae
- Umbelliferae
- Leguminosae
- Roseaceae
- Rutaceae
- Solanaceae
- Cruciferae
- Liliceae
- Caryophyllaceae
- Boraginaceae
- Ranunculaceae
- Papaveraceae
- Malvaceae
- Cucurbitaceae
- Verbenaceae
- Scrophulariceae
- Phytolaccaceae
- Poaceae.

A. Medicinal plants of the Compositae family

The Compositae family, also known as the Asteraceae family, contains the highest number of medicinal plants as compared to other families. Medicinal plants belonging to this family include for example:

❖ **Chamomile: Matricaria chamomilla**

Is an annual herb found in Europe, North Africa and northern Asia. Chamomile comes from the Greek words chamos meaning ground and milos meaning apple.

**Medicinal Uses and Health benefits**

Chamomile is often used to treat nervous disorders such as insomnia, anxiety and nervous tension, as anti-allergy and chamomile to treat digestive problems.

**Parts Used:** The entire above ground portion of the plant can be used. The flowers are edible and can be used raw to top salads.

❖ **Chicory: Cichorium intybus**

**Habitat:** Chicory is found growing wild in Europe, North Africa, and West Asia. It has been introduced to North America, where it has locally become naturalized.

**Plant Parts Used:** It is primarily the root that is used, but occasionally the whole plant.

**Medicinal Uses and Health benefits**
In today’s herbal medicine chicory is considered to be of particularly great value as a tonic for the liver and gastrointestinal tract.

❖ **Milk thistle, holy thistle, blessed thistle: *Silybum marianum.***

**Habitat:** *Silybum marianum* is native to a narrow area of the Mediterranean, but has been naturalized throughout Europe and along the chaparral coastal area of California in the United States. Its preferred habitat is a dry, sunny area.

**Plant Parts Used:** Commonly, the seeds; however throughout history virtually all the aboveground parts of the plants have been used as both food and medicine.  
The active constituents of milk thistle are flavonoids (silybin, silydianin, and silychristin).

**Medicinal Uses and Health benefits**

Milk thistle seeds have been used for the treatment of liver disease. Milk thistle is referred to in the earliest Greek writings as a liver-protecting herb.

**B. Medicinal plants of the Labiatae family**

A very important medicinal plant family is the Labiatae family, also known as the mint family. Plants in this family are herbs or shrubs often with an aromatic smell. They are common in the Mediterranean countries for the fact that some of them produce a high amount of essential oil that enables them to survive the hot summer season. Some examples from this family include the spearmint and rosemary.

**Examples:**

❖ **Rosemary: *Rosmarinus officinalis***

**Habitat:** Rosemary is native to the Mediterranean countries, but is now grown worldwide as a spice and medicinal herb. The plant thrives best in a warm sunny climate.

**Plant Parts Used:** Leaves, flowers, stems, branches.

**Medicinal Uses and Health benefits**

1-Rosemary has long been thought to prevent premature balding and even aiding new hair growth.

2- It has been infused into many shampoo products as an aid in fighting dandruff.

3- Rosemary has had a long-lived reputation for improving memory.
Some studies claim that the carnosic acid found in rosemary may shield the brain from free radicals. Lowering the risk of strokes and neurodegenerative diseases like Alzheimer’s disease, dementia.

❖ **spearmint: *Mentha spicata***

**Habitat:** The spearmint plant is native to Europe, but it grows well in most temperate climates. Its common name is related to the pointed shape of its leaves that resemble a spear

**Plant Parts Used:** The leaves are the parts of the plant that are used for their essential oils that contain menthol and flavonoids.

**Medicinal Uses and Health benefits:**
Speeds Wound Healing, Relieves Spasms and Disinfectant.

C. **Medicinal plants of the Umbelliferae also known as Apiaceae family**

The Umbelliferae or carrot family consists of plants with a characteristic umbrella-arranged fruit. These plants usually produce an essential oil, an asset to survive during the hot summer days. In fact the oil has a cooling effect on the plant. Some examples anise (*Pimpinella anisum*), parsley (*Petroselinium crispum*), and hemlock (*Conium maculatum*) which consider One of the most poisonous.

❖ **parsley (*Petroselinium crispum*)**

**Habitat:** Originally, parsley was probably endemic to Southwest Asia and the Mediterranean (Turkey, Algeria, Sardinia, and Lebanon). The herb has been cultivated since ancient times and was early on widely grown in most parts of Europe. Today, the plant is extensively used as a spice and cultivated all over the world.

**Plant Parts Used:** The whole plant is utilized either as medicine or food. The leaves are used fresh or dried as a seasoning and garnish while the root and seeds are primarily used as herbal medicine.

**Medicinal Uses and Health benefits:**

1- A diuretic Herb.
2- useful in the treatment of anemia (anemia). The herb also contains the much needed folic acid, a vital building block of the red blood cells.
3- Studies have shown that vitamin K is vital in bone formation, protects against osteoporosis.

❖ Coriander: *Coriandrum sativum*

Habitat: Coriander is indigenous to the Mediterranean countries and today most of the commercial supply of the herb comes from Morocco, Romania, and Egypt.

**Plant Part Used:** Seeds, and leaves.

**Medicinal Uses and Health benefits:**

1- is considered a natural treatment for high cholesterol levels.
2- As an appetizer and has been used to increase appetite in those suffering from anorexia.

❖ fennel: *Foeniculum vulgare*

Habitat: Fennel is circumpolar (that is, can be found all over the globe). It is most often found in dry stony calcareous soils near the sea.

**Plant Parts Used:** Primarily the seeds and an essential oil extracted from them; leaves and root are also used.

**Medicinal Uses and Health benefits:**

to treatment of irritable bowel syndrome (IBS), gout, motion sickness, cramps, and spasms. Fennel is thought to be an effective herbal remedy for respiratory congestion and is a common ingredient in cough remedies.

D. Medicinal plants of the fabaceae family

The Leguminosae or pea family consists of large number of plants, both native and naturalized, that have been cultivated for fodder, food and ornamental purposes. Amongst these plants, alfalfa (*Medicago sativa*) and fenugreek (*Trigonella foenum-graecum*).

❖ *Trigonella foenum-graecum.*
**Habitat:** Fenugreek is native to the Mediterranean countries and western Asia and is undoubtedly one of the oldest cultivated plants.

**Plant Parts Used:** The leaves and seeds. The leaves are picked in the summer and used fresh.

**Medicinal Uses and Health benefits:**
1. The Fenugreek leaves and seeds are used as a remedy for kidney stones.
2. Fenugreek has been used for skin irritation, such as ulcers, eczema, dandruff.

**E. Medicinal plants of the Solanaceae family**
A family with several poisonous, but medicinally-important herbs is the Solanaceae or potato family. A species in this family that is widely cultivated (*Solanum tuberosum*). Other cultivated edible crops are the tomato (*Lycopersicum esculentum*) and the aubergine (*Solanum melongena*). The potato is only edible when ripe, as green potatoes were found to be poisonous. Mediterranean natives in this family include the Mediterranean withania (Withania somnifera) and garden thorn apple (Datura metel). Other important species include black nightshade (*Solanum nigrum*).

- Mediterranean withania (*Withania somnifera*).
- Stramonium (*Datura stramonium*).
- Black nightshade (*Solanum nigrum*).

**F. Medicinal plants of the Cruciferae family**
The Cruciferae or cress family is characterised by plant that have flowers with cross-like petals. This family groups a large group of medicinal plants that include: Shepherd's purse (*Capsella bursa-pastoris*), Black mustard (*Brassica nigra*), Arugula (*Eruca sativa*), London rocket (*Sisymbrium irio*), Wild radish (*Raphanus raphanistrum*).

**Two examples:**
- **London rocket Sisymbrium irio**

**Habitat:** is native to southern Europe, North Africa and temperate Asia but has been carried by migrants to North America, Australasia and South Africa.
Plant Parts Used: seeds and leaves.

Medicinal Uses and Health benefits: London rocket is used in the Middle East to treat coughs and chest congestion, to relieve rheumatism, to detoxify the liver and spleen, and to reduce swelling and clean wounds.

❖ Shepherd's purse: *Capsella bursa-pastoris*

Habitat: The plant is probably native to Europe and parts of Asia, but now it can be found in temperate regions around the world.

Plant Parts Used: All of the above-ground parts of the plant are used in herbal medicine. It is collected when it is in bloom and can be dried for later use.

Medicinal Uses and Health benefits:
1- Shepherd’s Purse uses to stop bleeding and as a healing agent.
2- Shepherd’s purse is mainly used in Chinese herbal medicine to “cool the blood,” and as a treatment for dysentery, high blood pressure and excessive bleeding after birth.

G- Medicinal plants of the Poaceae family
Grass family (Poaceae), one of the largest plant families with almost 12,000 species, is the most important plant family in economical view. Today, grasses are used also in pharmaceutical industry and in cosmetical industry, in products like powders and various creams. Plant drugs of grass family are recognised as medically and therapeutically useful, and with further research their use in medicine will be more important. For example: lemon grass (*Cymbopogon citratus,*)

❖ lemon grass: *Cymbopogon citratus*

Habitat: perennial grass, which is native to India and tropical regions of Asia.

Part used: leaves

Medicinal Uses and Health benefits:
1- Lowers Cholesterol  
2- Detoxifies the Body
3- Prevents Cancer (Research conducted to prove the anti-cancerous activity of lemongrass has shown promising outcomes in the prevention of skin cancer.)
Lower plants: Medicinal uses

The lower plants are thought by most people to be quite useless members of the plant kingdom. Being a group of lower plants, it remains unattended and their useful aspects are largely ignored. However, these can be used for food, fiber, crafts, building material, abrasives, decoration and also as medicine.

Members of Bryophytes used as medicinal plants as follows

**Marchantia polymorpha**

**Medicinal uses:** Against inflammation: The entire thalli is washed thoroughly with water, ground into fine paste and applied externally on inflammation.

**Riccia**

**Medicinal uses:** Against ringworms in children: The thallus in washed and ground to paste and mixed with jiggery and given to the children affected by the ringworms.

**club moss, Lycopodium clavatum**

**Medicinal uses:** Spores are used against rheumatism, cramps.

The plant is chewed to induce vomiting in case of food poisoning.

**field horsetail, (Equisetum arvense)**
Horsetail is native to both North America and Europe. It is one of only a few Equisetum survivors from the dinosaur era.

**Plant Parts Used:** The above ground parts of the green summer shoots are collected and used fresh. The lower dark portion of the stem should be removed before the plant is dried.

**Medicinal uses:**

1- repair broken bones and as an herbal remedy for arthritis.

2- to treat inflammation of the prostate gland, or benign enlargement of the prostate (benign prostatic hyperplasia, BPH).

3- as an herbal treatment of kidney stones.

**Seaweeds**

Seaweeds offer a wide range of therapeutic possibilities both internally and externally. The term Seaweeds in this case refers only to macrophytic marine algae, both wild and cultivated, growing in saltwater.

**1-Bull Kelp** *Nereocystis luetkeana*

Rich in Calcium, Magnesium, Sodium, Iodine, Potassium, Bromine, Phosphorus, Iron, Bulk fibre, Vitamin A B complex, C D E and K.
Medicinal uses:

To treat Attention Deficit Disorder (ADD), Schizophrenia, Minerals Depletion.

2) Kombu (*laminaria* spp.) includes *L. digitata*

Medicinal Uses of Kombu:

Anti-viral, Relives sore joints and Muscles, Lowers Treats certain thyroid problems, Aids weight loss, inhibits tumours.

3) Bladderwrack (*Fucus* spp.) includes *F. gardneri*

Medicinal Uses of Bladderwrack:

Stimulates the Thyroid, Detoxifies, Aids in weight loss, Fatigue, Strengthen the bones, Reduces Inflammation, Improves moods such as Anxiety, Depression, Forgetfulness.

4) Giant Kelp (*Macrocystis integrifolia*)

Medicinal Uses of Macrocystis:

Supports a healthy thyroid, Regulates hormones and metabolism, Supports the immune system, Antioxidant, Heart healthy.
field horsetail, *(Equisetum arvense)*  

club moss, *(Lycopodium clavatum)*

*Marchantia polymorpha*

Bull Kelp *Nereocystis luetkeana*  

Giant Kelp *Macrocystis integrifolia*
Kombu *laminaria* spp.  

Bladderwrack *Fucus* spp
Secondary metabolism

In all organisms, there are two types of metabolism which synthesize complex molecules from simple molecules with the help of catalysts. These metabolisms are called primary and secondary metabolism.

Primary metabolism, also known as basic metabolism, is very significant for organisms, because the compounds produced in primary metabolic pathways are used in vital functions. While primary metabolites play roles in development and growth functions, compounds synthesized in secondary metabolism do not enter into these types of reactions.

However, Secondary metabolites compounds have important functions including interactions between organisms and their environments. These secondary metabolites are often necessary so that organisms can survive in their ecosystem.

Although primary and secondary metabolites are different, they can have overlapping biosynthetic pathways and primary metabolites often serve as precursors for the production of secondary metabolites. When these metabolisms compared with each another, it is seen that primary metabolites are present in greater quantities than secondary metabolites. This feature is important because primary metabolites can serve as substrates in secondary metabolic pathways. In the primary metabolic pathway of carbon, different compounds, such as pyruvate and acetyl-CoA produced in intermediate steps, used as precursors to produce secondary metabolites. For example, the glucose generated by photosynthesis converted to pyruvate by glycolysis. The pruvate can converted into aliphatic amino acids, which are precursors for alkaloid production. Alternatively, the pruvate can be used to make acetyl-CoA which have a role in flavonoid, terpenoid and wax production. If Malonic acid produced by acetyl-CoA, this product can give flavanoids or waxes according to two different pathways. However, if acetyl-CoA turns into mevalonic
acid, this product can be utilized as an intermediate compound to synthesize terpenoids. The ecological functions affect plant survival profoundly, and it reasonable to adopt the less pejorative term “plant natural products” to describe secondary plant metabolites that act primarily on other species.

<table>
<thead>
<tr>
<th>Plant primary metabolites</th>
<th>Plant Secondary metabolites (Plant natural products)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Organic compounds produced in the plant kingdom</td>
<td>1. Organic compounds produced in plant kingdom</td>
</tr>
<tr>
<td>2. Have metabolic functions essential for plant growth and development</td>
<td>2. Don’t have apparent functions involved in plant growth and development</td>
</tr>
<tr>
<td>3. Produced in every plant</td>
<td>3. Produced in different plant families, in specific groups of plant families or in specific tissues, cells or developmental stages throughout plant development.</td>
</tr>
<tr>
<td>4. Include carbohydrates, amino acids, nucleotides, fatty acids, steroids and lipids</td>
<td>4. Include terpenoids, special nitrogen metabolite (including, non-protein amino acids, amines, cyanogenic glycosides, glucosinolates, and alkaloids), and phenolics.</td>
</tr>
</tbody>
</table>

Functions of Secondary Metabolites in Plant

When the pathways of secondary metabolism are studied, it is seen that synthesis of secondary metabolites is very costly for plants and other organisms which have secondary metabolism. ‘Costly’ means that secondary metabolism requires high concentrations of ATP. Because high levels of ATP are needed during secondary metabolite production. The functions of secondary metabolites reveals. In plants, these metabolic compounds have ecological functions for plants and other organisms related to plants.
Relationships between primary metabolic pathways and secondary metabolic pathways. Secondary metabolites are shown in boxes.
The functions of secondary metabolites in plants.

1- **Secondary metabolites protect plants against microbial pathogens and viruses.**

Secondary metabolites used as antibiotics against pathogens; they are active at all times, because these components are part of the constitutive defence mechanism and are usually localized in the cell wall or in the vacuole. However, in the inducible defense system, defence compounds formed after infection by the pathogen. These responses include the production of different secondary metabolites such as steroid glycol alkaloids. Moreover, secondary metabolic compounds serve as signal agents during infection. When a plant infected by a pathogen, it can become resistant against the pathogen that infected the plant. This defense system called systemic acquired resistance (SAR). SAR generally induced by secondary metabolites such as salicylic acid.

2- **Plants having secondary metabolites are also to protected against herbivores.**

A part from defense functions against pathogens, protect plants from herbivores because of their toxicity effects. Plants also use toxic secondary metabolites to compete with other individuals of the same or different species. This type of toxic compound called an ‘allelopathic substance, For instance, two plants which share the same territory, will compete for insufficient water or nutrients. Under these conditions, allelopathic substances play an important role.

3- **Moreover, secondary compounds provide a defence system against abiotic environmental stresses.**

Moreover, plants have to defend themselves against abiotic stresses such as temperature, light level and water level. These abiotic stresses cause oxidative stress in plants. Oxidative stresses can also occur because of air pollutants, UV radiation, and radioactive deposition. In addition to
protection against oxidative stresses, some phenolics such as flavanoids act as an UV protection shield.

4- Some secondary metabolites attract insects for pollination and seed dispersal. In addition, they used for interactions between plants and symbiotic microorganisms. In addition to these functions, some secondary metabolites serve to attract insects or animals for pollination and seed dispersal. Generally, secondary metabolites serve as flower pigments, scent, taste compounds, and attract other organisms. For example, terpenes and aromatic compounds known as attractive compounds because of their volatility. In addition, flavonoids used as colour pigments in flower petals to attract the attention of insects or animals.

5- Furthermore, these compounds are important in a plant’s relations with other plants.

6- Another function of secondary compounds is to give signals for symbiotic interaction. These metabolites serve as signal agents to provide communication between a host plant and symbiotic microorganisms. The interaction between Agro-bacterium or Rhizobium and a plant given as an example of symbiotic interaction. For instance, some phenolic compounds derived from flavanoids used to attract Rhizobium bacteria to plant roots for formation of nodules. When the bacterium can form nodules and live on the plant, the plant also benefits by using the soil nitrogen that have been fixed by the bacterium. In addition, secondary compounds have an important role for plants, other organisms and the balance of nature.

7- In addition to all these functions, secondary metabolites utilized as plant growth regulators at the cellular level and as regulators of gene expression.
Importance of Plant Secondary Metabolites for Humans

Secondary Metabolites are very important for humans. They are used for different purposes such as in medicine, the building sector, agriculture, the food sector, and the cosmetics, soap and shampoo industries.

In recent years, it has been found that secondary metabolites can have antioxidant, anticarcinogenic, anti-inflammatory, antiallergenic, and antimicrobial effects on human health. Because of these functions, they have been attractive for medicine and used as drugs. Therefore, some secondary metabolites are called natural drugs.

1- One of their most important functions is an antioxidant function. Most secondary metabolites such as flavanoids, beta-carotene, and lycopene have antioxidant functions. This function protects humans from oxidative stress. It is known that oxidative stress damages humans because of ROS (reactive oxygen species). Generally free radicals, which are a kind of ROS, can interact with lipids, proteins, low-density lipoproteins, and DNA. When free radicals join one of these biomolecules such as a lipid, some modifications in the biomolecule occur due to the unpaired electrons of ROS. These modifications can cause some diseases in humans such as cardiovascular disease, cancer, and atherogenesis. Secondary metabolites prevent these types of damages to humans, because they can scavenge all elements of ROS due to their antioxidant function.

The antioxidant and also anticancer functions of secondary metabolites, these compounds are:

1- Phenolic antioxidants can be used in cancer therapy due to their functions.
2- Generally, polyphenols have an important role as anti-inflammatory, antimicrobial, and antibacterial compounds in medicine. The most polyphenols, which act as antioxidants, protect humans against genomic instability and cancer due to their ability to protect DNA from oxidation.
3- Flavopiridol used in medicine as an anticancer. Especially, flavone found to be inhibitory to respiratory syncytial virus.
4- In addition, other phenolic acids inhibit some different viruses, bacteria and fungi.
5- Indicated that alkaloids used to inhibit the HIV virus.

Table 1. Shows some other secondary metabolites that used in medicine.

<table>
<thead>
<tr>
<th>PSM</th>
<th>Major Sources</th>
<th>Therapeutic application</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tannin</td>
<td>vascular woody plants</td>
<td>Anticancer applications</td>
</tr>
<tr>
<td></td>
<td>ferns</td>
<td>Cardioprotective effects</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Antimicrobial effects</td>
</tr>
<tr>
<td>Saponin</td>
<td>higher plants</td>
<td>Anticancer applications</td>
</tr>
<tr>
<td></td>
<td>some marine animals</td>
<td>Immunomodulatory applications</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cardioprotective effects</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Antidiabetic effects</td>
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<td></td>
<td></td>
<td>Analgesic</td>
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<tr>
<td></td>
<td></td>
<td>Anti-inflammatory effects</td>
</tr>
<tr>
<td>Mimosine</td>
<td>\textit{Leucaena leucocephala}</td>
<td>Anticancer applications</td>
</tr>
<tr>
<td></td>
<td>\textit{Mimosa pudica}</td>
<td>Anti-inflammatory effects</td>
</tr>
<tr>
<td>Phytoestrogens</td>
<td>leguminous forage seeds</td>
<td>Anticancer effects</td>
</tr>
<tr>
<td></td>
<td>foods</td>
<td>Prevention of prostate cancer</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Prevention of colon cancer</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cardioprotective effects</td>
</tr>
</tbody>
</table>

Because of all these functions, secondary metabolites referred to as drugs for human health in medicine. However, secondary compounds used in different sectors such as in agriculture, building, food, cosmetics, soaps and shampoos. In agriculture, humans use some secondary metabolites as herbicides. Also in the building sector, two known secondary compounds, lignin and cellulose utilized in building materials. Moreover, most secondary compounds are very important for the taste and colour of
plant foods. Furthermore, several secondary metabolites such as essential oils used for perfume, soap and shampoo in the cosmetic, soap and shampoo industries.

**Major Classes of Secondary Metabolites**

Plants generally classified according to the secondary metabolites, which they produce. This classification called ‘chemotaxonomy’. However, secondary metabolites classified according to their carbon skeletal type or biosynthetic organs. Generally, classification of secondary metabolites based on carbon skeletal type.

Table 2. Shows the major classifications of plant secondary metabolites with examples of compounds in each class.

<table>
<thead>
<tr>
<th>Major class of SM</th>
<th>Subunits of SM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Terpenoids</td>
<td>Hemiterpenes</td>
</tr>
<tr>
<td></td>
<td>Monoterpenes</td>
</tr>
<tr>
<td></td>
<td>Sesquiterpenes</td>
</tr>
<tr>
<td></td>
<td>Diterpenes</td>
</tr>
<tr>
<td></td>
<td>Triterpenes</td>
</tr>
<tr>
<td></td>
<td>Tetraterpenes</td>
</tr>
<tr>
<td></td>
<td>Polyterpenes</td>
</tr>
<tr>
<td></td>
<td>Meroterpenes</td>
</tr>
<tr>
<td>Phenolics</td>
<td>Phenolic acids</td>
</tr>
<tr>
<td></td>
<td>Lignin</td>
</tr>
<tr>
<td></td>
<td>Lignan</td>
</tr>
<tr>
<td></td>
<td>Flavanoids</td>
</tr>
<tr>
<td></td>
<td>Coumarins</td>
</tr>
<tr>
<td></td>
<td>Furanocoumarins</td>
</tr>
<tr>
<td></td>
<td>Stilbenes</td>
</tr>
<tr>
<td></td>
<td>Tannin</td>
</tr>
<tr>
<td>Nitrogen and sulfur containing</td>
<td>Glucosinolates</td>
</tr>
<tr>
<td>Nitrogen containing</td>
<td>Alkaloids</td>
</tr>
<tr>
<td></td>
<td>Glycoalkaloids</td>
</tr>
</tbody>
</table>
Plants generally classified according to the secondary metabolites, which they produce. This classification called ‘chemotaxonomy’. However, secondary metabolites classified according to their carbon skeletal type or biosynthetic organs.

**Major Classes of Secondary Metabolites**

**Alkaloids**

- The most important nitrogen containing secondary products, they produced from the Shikimate pathway.
- They are being found in more than 15,000 compounds found in 20% of vascular plants.
- Nitrogen is usually part of a heterocyclic ring with N and C atoms
- Large pharmacological effects on animals
- Most effective at deterring mammalian herbivores
- Some examples: morphine, codeine, Cocaine, nicotine, and caffeine used as stimulants and sedatives.

![Dopamine](image)

**Terpenoids**

- They produced from the mevalonic acid pathway
- Building block- 5 C isoprene unit.
- They function as herbivore deterrents
- They can be produced in response to herbivore feeding, and to attract predatory insects and parasites of the feeding herbivore.
- They are constituents of essential oils.
- They are classified by the number of isoprene units: monoterpenes-1, diterpenes-4.
Phenolics

 ✓ Secondary metabolites which contain a hydroxyl functional group on an aromatic ring
 ✓ They are heterogenous group.
 ✓ Many serves as defense compounds against herbivores and pathogens
 ✓ Other function in attracting pollinators and fruit dispensers
 ✓ They produced from the malonic acid pathway.

![Phenol](image)
Plants remain the main source of medicines for a large proportion of the world’s population, chemically synthesized drug gained popularity and became the basis of pharmaceutical industry. Several problems not applicable to synthetic drugs often influence the quality of herbal drugs. For instance:

1. Herbal drugs are usually mixtures of many constituents.
2. The active principle(s) is (are), in most cases unknown.
3. Selective analytical methods or reference compounds may not be available commercially.
4. Plant materials are chemically and naturally variable.
5. Chemo-varieties and chemo cultivars exist.
6. The source and quality of the raw material are variable.

Plant preparations have a very special characteristic that distinguishes them from chemical drugs: a single plant may contain a great number of bioactive phyto-
compounds and a combination of plants even more. This complexity is one of the most important challenges to phytoscientists attempting to identify a single bioactive phytocompound or chemical group in the enormous universe that comprises a single crude extract.

By following Standardization flow chart (Fig. 1), we can see the methods from extraction to identification of bioactive phytocompounds:

(1) **Plants can be chosen** either randomly, based on the literature or following consultation with local healers. After choosing the right material, plant collection must be followed by botanical identification and a voucher specimen must be placed in the local herbarium. All data about the collection must be observed and documented, such as climate conditions, season, geographical localization, environmental conditions, etc. in order to elucidate future differences in bioactivity compared with other results found. Any plant part can be used but consultation of the literature or with local healers is very useful to reduce research time.

(2) **Primary extraction**

   **A- Extraction methods**

   Collected plant material can be used fresh or dried. Several studies have started extractions with both fresh and dried material in order to compare the chemical composition of the extracts. They must be ground to optimize the solvent contact during the extraction process. Weight standardization must be used (i.e. 300 g of plant material to 1000 mL of solvent).
Fig. 1. Standardization flow chart
More than 90% of the studies for antimicrobial activity in the literature start extraction with methanol, ethanol or water because it is proved that ethanol extraction is more effective in isolating the bioactive phytocompound. The primary extractions methods are very variable but the idea is to research activity cited in popular use, and to choose the same extraction method. This is especially useful to corroborate the in vivo activity found in popular use.

Variation in extraction methods are usually depend on the length of the extraction period, solvent used, pH of the solvent, temperature, particle size of the plant tissues and the solvent-to-sample ratio. The basic principle is to grind the plant material (dry or wet) finer, which increases the surface area for extraction thereby increasing the rate of extraction. In the study by Eloff, 5 min extractions of very fine particles of diameter gave higher quantities than values obtained after 24 h in a shaking machine with less finely ground material. Earlier studies reported that solvent to sample ratio of 10:1 (v/w) solvent to dry weight ratio has been used as ideal.

The extraction method that has been widely used by researchers is plant tissue homogenization in solvent. Dried or wet, fresh plant parts are grinded in a blender to fine particles, put in a certain quantity of solvent and shaken vigorously for 5 - 10 min or left for 24 h after which the extract is filtered. The filtrate then may be dried under reduced pressure and re-dissolved in the solvent to determine the concentration. Some researchers however centrifuged (approximately 2500 rpm for 30 min) the filtrate for clarification of the extract.

Another common method is serial exhaustive extraction, which involves successive extraction with solvents of increasing polarity from a non-polar (hexane) to a more polar solvent (methanol) to ensure that a wide polarity range of compound could be extracted. Other researchers employ soxhlet extraction of dried plant material using organic solvent. This method cannot be used for thermo labile compounds.

**B - Choice of solvents**

Successful determination of biologically active compound from plant material is largely dependent on the type of solvent used in the extraction procedure. Properties of a good solvent in plant extractions include low toxicity, ease of evaporation at low heat, promotion of rapid physiologic absorption of the extract, preservative action and inability to cause the extract to complex or dissociate. As the product in extraction will contain traces of residual solvent, the solvent should be non-toxic and should not interfere with the bioassay. The choice will also depend on the targeted compounds to be extracted. Initial screening of plants for possible antimicrobial activities typically begins by using the crude or alcohol extractions and can be prolonged
heating may lead to degradation of compounds. Followed by various organic solvent extraction methods.

Water is universal solvent, used to extract plant products with antimicrobial activity. Though traditional healers use primarily water but plant, extracts from organic solvents have been found to give more consistent antimicrobial activity compared to water extract. In addition, water-soluble flavonoids (mostly anthocyanins) have no antimicrobial significance and water-soluble phenolics only important as antioxidant compound. A study reported that extraction of tannins and other phenolics was better in aqueous acetone than in aqueous methanol.

In another study, among the twenty different solvents evaluated, chloroform was found to be the best solvent for the extraction of non-polar biological active compounds. Since nearly all of the identified antimicrobial compounds from plants are aromatic or saturated organic compounds, they are most often obtained through initial ethanol or methanol extraction. Thus, the most commonly used solvents for preliminary investigations of antimicrobial activity in plants are methanol, ethanol and water.

Examined a variety of extract ants for their ability to solubilize antimicrobials from plants, rate of extraction, ease of removal, toxicity in bioassay and acetone received the highest overall rating. Though there is a wide diversification in the usage of solvents, it is necessary to focus on a standardized extraction method and solvent system for a wide variety of researchers working in diverse settings to minimize the variability in the antimicrobial efficacy reports.

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Polarity index</th>
<th>Boiling point (°C)</th>
<th>Viscosity (cPoise)</th>
<th>Solubility in water (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n-Hexane</td>
<td>0.0</td>
<td>69</td>
<td>0.33</td>
<td>0.001</td>
</tr>
<tr>
<td>Dichloromethane</td>
<td>3.1</td>
<td>41</td>
<td>0.44</td>
<td>1.6</td>
</tr>
<tr>
<td>n-Butanol</td>
<td>3.9</td>
<td>118</td>
<td>2.98</td>
<td>7.81</td>
</tr>
<tr>
<td>iso-propanol</td>
<td>3.9</td>
<td>82</td>
<td>2.30</td>
<td>100</td>
</tr>
<tr>
<td>n-Propanol</td>
<td>4.0</td>
<td>92</td>
<td>2.27</td>
<td>100</td>
</tr>
<tr>
<td>Chloroform</td>
<td>4.1</td>
<td>61</td>
<td>0.57</td>
<td>0.815</td>
</tr>
<tr>
<td>Ethyl acetate</td>
<td>4.4</td>
<td>77</td>
<td>0.45</td>
<td>8.7</td>
</tr>
<tr>
<td>Acetone</td>
<td>5.1</td>
<td>56</td>
<td>0.32</td>
<td>100</td>
</tr>
<tr>
<td>Methanol</td>
<td>5.1</td>
<td>65</td>
<td>0.60</td>
<td>100</td>
</tr>
<tr>
<td>Ethanol</td>
<td>5.2</td>
<td>78</td>
<td>1.20</td>
<td>100</td>
</tr>
<tr>
<td>Water</td>
<td>9.0</td>
<td>100</td>
<td>1.00</td>
<td>100</td>
</tr>
</tbody>
</table>
(3) After extraction the volume must be concentrated by lyophilization or another concentration technique before screening. Usually, after the lyophilization process ground powder is obtained. This must be resuspended in water at a higher concentration for initial drop test screening. The high concentration of the extract guarantees the identification of the bioactivity, if present. Using low concentrations in drop tests may lead to false negative results.

(4) Due to the complex composition of the extract primary separation may be used to facilitate the identification process. Micromolecules can be separated from macromolecules (proteins and carbohydrates) by very simple techniques such as ethanol precipitation (30% v/v), centrifugation (10 000 rpm for 10 min) and filtration systems such as Centricon and Amicon (Millipore). Supernatant and precipitate phases are obtained and can be separated in drop tests. As discussed previously, antimicrobial activity is commonly present in micromolecules (supernatant) phase.

(5) The antimicrobial screening by drop test (formerly disk diffusion agar assay) is the most efficient and inexpensive assay to identify antimicrobial activity. The extract is dropped (i.e. 15 μL) onto an agar surface previously inoculated with the desired microorganism. Note that is very important to count by McFarland scale or New Bauer chamber the microorganism inoculums; this permits the antimicrobial activity to be compared within antibiotic controls and between different microorganism groups.

(6) When antimicrobial activity is detected the minimum inhibitory concentration (MIC) must be determined to continue other antimicrobial assays of interest. The MIC is usually established by the broth dilution method. The use of 96-microwell plates to minimize costs is very effective, reducing the culture media quantities drastically and enhancing the test capacity.

(7) Bio-guided chromatography techniques such as bio autography preceded by solvent separation is essential to initiate the bioactive phytocompound identification process; fraction collection with HPLC or FPLC assays, preparative TLC are also valid techniques. Bio-guided fraction and purification confirms previous results leading to isolation of a bioactive phytocompound.

The methods of harvesting, drying, storage, transportation, and processing (for example, mode of extraction and polarity of the extracting solvent, instability of constituents, etc.) also affect herbal quality. At present no official standards are available for herbal preparations. Those manufacturers, who are currently doing some testing for their formulations, have their own parameters, many of which are very preliminary in nature. Presently it is very difficult to identify the presences of all the ingredients as claimed in a formulation. Hence the first important task is to evolve such parameter by which the presence of the entire ingredient can be identified, various chromatographic and spectrophotometric methods and evaluation of physicochemical properties can be tried to evolve pattern for identifying the presence of different ingredient. Wherever possible these methods can be applied for
quantitative estimation of bioactive group of compounds like alkaloids, flavonoids, polyphenolic components or estimation of particular compound.

Table 3: (Solvent used for active component extraction)

<table>
<thead>
<tr>
<th>Water</th>
<th>Ethanol</th>
<th>Methanol</th>
<th>Chloroform</th>
<th>Dichloromethanol</th>
<th>Ether</th>
<th>Acetone</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Pattyacid</td>
</tr>
<tr>
<td>Tannins [16]</td>
<td>Polyacetylenes [31,35]</td>
<td>Saponins</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saponins [33]</td>
<td>Flavonol [35,36]</td>
<td>Tannins [40]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Terpenoids</td>
<td>Terpenoids [37]</td>
<td>Xanthosyllines</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Polyphenoids</td>
<td>Sterols [38]</td>
<td>Totarol [40]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lectins</td>
<td>Alkaloids [39]</td>
<td>Quassinoinds [41]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

These compounds in bold are commonly obtained only in one solvent.

Standardization and quality control of herbal crude drugs – Processes and procedures According to WHO (1996a and b, 1992), standardization and quality control of herbals is the process involved in the physicochemical evaluation of crude drug covering aspects, such as selection and handling of crude material, safety, efficacy and stability assessment of finished product, documentation of safety and risk based on experience, provision of product information to consumer and product promotion. Attention is normally paid to such quality indices such as:

1. Macro and microscopic examination: For Identification of right variety and search of adulterants.
2. Foreign organic matter: This involves removal of matter other than source plant to get the drug in pure form.
3. Ash values: These are criteria to judge the identity and purity of crude drug – Total ash, sulphated ash, water soluble ash and acid insoluble ash etc.
4. Moisture content: Checking moisture content helps reduce errors in the estimation of the actual weight of drug material. Low moisture suggests better stability against degradation of product.
5. Extractive values: These are indicative weights of the extractable chemical constituents of crude drug under different solvents environment.
6. Crude fibre: This helps to determine the woody material component, and it is a criterion for judging purity.
7. Qualitative chemical evaluation: This covers identification and characterization of crude drug with respect to phytochemical constituent. It employs different analytical technique to detect and isolate the active constituents. Phytochemical screening techniques involve botanical identification, extraction with suitable
solvents, purification, and characterization of the active constituents of pharmaceutical importance.
8. Chromatographic examination: Include identification of crude drug based on the use of major chemical constituents as markers.
9. Quantitative chemical evaluation: To estimate the amount of the major classes of constituents.
10. Toxicological studies: This helps to determine the pesticide residues, potentially toxic elements, safety studies in animals like LD50 and Microbial assay to establish the absence or presence of potentially harmful microorganisms.

(8) By TLC assays, Rf values can be determined and polarity or even chemical groups elucidated (Fig. 1.3).

(9) NMR, HPLC/MS, and GC/MS are used to identify a bioactive phytocompound.

Table 1:

<table>
<thead>
<tr>
<th>S.No</th>
<th>Scientific Name</th>
<th>Family</th>
<th>Extract</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Acacia nilotica</td>
<td>Fabaceae</td>
<td>Ether, Alcohol, Aqueous</td>
</tr>
<tr>
<td>2.</td>
<td>Ageratum conyzoides</td>
<td>Asteraceae</td>
<td>Methanol, Aqueous</td>
</tr>
<tr>
<td>3.</td>
<td>Boerhavia diffusa</td>
<td>Nyctaginaceae</td>
<td>Aqueous, Alcoholic</td>
</tr>
<tr>
<td>4.</td>
<td>Cynodon dactylon</td>
<td>Poaceae</td>
<td>Aqueous, Methanol</td>
</tr>
<tr>
<td>5.</td>
<td>Cleome viscosa</td>
<td>Cleomraceae</td>
<td>Aqueous</td>
</tr>
<tr>
<td>6.</td>
<td>Datura stramonium</td>
<td>Solanaceae</td>
<td>Ether, Aqueous</td>
</tr>
<tr>
<td>7.</td>
<td>Euphorbia hirta</td>
<td>Euphorbiaceae</td>
<td>Methanol, Aqueous</td>
</tr>
<tr>
<td>8.</td>
<td>Ficus bengalensis</td>
<td>Moraceae</td>
<td>Aqueous</td>
</tr>
<tr>
<td>9.</td>
<td>Hyptis suaveolens</td>
<td>Lamiaceae</td>
<td>Aqueous</td>
</tr>
<tr>
<td>10.</td>
<td>Hibiscus rosa sinensis</td>
<td>Malvaceae</td>
<td>Ethanol, Aqueous</td>
</tr>
<tr>
<td>11.</td>
<td>Jatropha gossypifolia</td>
<td>Euphorbiaceae</td>
<td>Aqueous</td>
</tr>
<tr>
<td>12.</td>
<td>Pueraria roxburghii</td>
<td>Euphorbiaceae</td>
<td>Aqueous</td>
</tr>
<tr>
<td>13.</td>
<td>Phyllanthus niruri</td>
<td>Euphorbiaceae</td>
<td>Methanol, Aqueous</td>
</tr>
<tr>
<td>14.</td>
<td>Prosopis juliflora</td>
<td>Fabaceae</td>
<td>Aqueous</td>
</tr>
<tr>
<td>15.</td>
<td>Polyscias longifolia</td>
<td>Annonaceae</td>
<td>Aqueous</td>
</tr>
<tr>
<td>16.</td>
<td>Sida cordifolia</td>
<td>Malvaceae</td>
<td>Aqueous</td>
</tr>
<tr>
<td>17.</td>
<td>Tephrosia purpurea</td>
<td>Fabaceae</td>
<td>Aqueous</td>
</tr>
<tr>
<td>18.</td>
<td>Tridax procumbens</td>
<td>Euphorbiaceae</td>
<td>Aqueous, Methanol</td>
</tr>
<tr>
<td>19.</td>
<td>Zizyphus jujuba</td>
<td>Rhamaceae</td>
<td>Aqueous, Methanol</td>
</tr>
<tr>
<td>20.</td>
<td>Solanum nigrum</td>
<td>Solanaceae</td>
<td>Acetone, Aqueous</td>
</tr>
</tbody>
</table>
SECRETORY STRUCTURES IN PLANTS

The complex nature of these chemicals, which are usually produced in various types of secretory structures, is also influenced and controlled by genetic and ecological factors and significantly, by the mode of extraction from the plants. The type of secretory structure is an important characteristic of a plant family. Detailed anatomical description of these structures is relevant to the market value of the plants. The verification of authenticity of a given species and for the detection of substitution or adulteration. It also provides a guide to the method of processing.

Microscopically investigation of plant structures is an important part of the complex biological research process which includes plant growth and development genetics and breeding. There is endless variability in form and structure; observing these with the microscope allows us to discover Nature in one of its most powerful forms.

Plant chemicals classed as primary or secondary metabolites. Depending on whether or not they have an essential role in plant metabolism and are universally present in all plants. Primary metabolites include sugars, Amino acids, Nucleic acids and the chlorophylls. Secondary metabolites make up all the remaining plant chemicals from alkaloids to phenols.

Secretion is a common feature of living cells and involves the discharge of substances to the exterior (exotropic secretion) or into special intercellular Cavities (endotropic secretion). These are specialized cells and the secreted material may contain various salts, Latex, Waxes, Fats, Flavonoids, sugars, gums, mucilage, essential oils and resins. It has been assumed that these products are biosynthesized in situ and direct evidence for the biosynthetic capacity of gland cells has become available relatively recently with the development of procedures
for gland isolation. These methods have yielded definitive proof of the presence of enzymes specifically with gland cells.

**BASIL - Ocimum basilicum**

Trichomes present on the leaf surface and other secretory tissues. It can be examined by using light scanning or transmission electron microscopy which enables detailed observation of major stages in the development of secretory cells. Including their membrane system and nuclei. The overall size of the gland and the amount of material released into the subcuticular cavity.

Essential oils with or without accompanying resins and gums, are most commonly found in special secretory structures either on the surface of the plant or within the plant tissues. The type of structure is family or species specific. This can be useful in identification of plant material and verifying the authenticity of the plant source in the case of suspected adulteration.

**SECRETORY CELL**

The most secretory structure is a single secretion-containing cell. It is only the actual content that distinguishes from adjacent non-secretory cells. However, it may also be larger than the other cells or have a thick cuticularized lining. This cell type is found in many different plant tissues: in the leaf parenchyma of lemongrass
(Andropogon spp), in the seed coat of cardamom (Elettaria cardamonunnn), in the rhizome of ginger (Zingiber officinale) and Curmeric (Curcuma longa), in the fruit wall of pepper (Piper nigrum), capsicum and chillies (Capsicum annum), in the perisperm and embryo of nutmeg (Myristica fragrans), in the bark of cassia (Cassia angustifolia) and cinnamon (Cinnamomum zeylanicum) and in the root of valerian (Valeriana officinalis).

**GINGER - Zingiber officinale**

**OSMOPHORES**

Osmophores are areas of flower tissues with secretory cells differing structurally from the adjacent cells (e.g. isodiametric cells in orchids).
SECRETROY CAVITIES

These cavities are more or less spherical structures that can be formed in two ways: the parenchyma cells can separate one from another leaving intercellular spaces called lumina or lacuna, or an actual cell can disintegrate leaving a cavity within the tissue. These spaces are lined with secretory cells or an epithelium that produces the essential oils. In high oil yielding plants several layers of these secretory cells are formed. The cavities continually enlarge and some become filled with cells with thin, convoluted walls which also store the oil produced from within their plastids. Included in this group are fruits and leaves of plants in the Citrus family (*C. aurantifolia*, *C. aurantium*, *C. bergamia*, *C. sinensis*) as well as *Eucalyptus* spp. and buchu leaves.
Citrus peel oils are confined in oblate to spherical-shaped oil cavities (glands), sometimes called oils sacs, that are located irregularly in the exocarp of the fruit. These cavities have no walls and are embedded at different depths in the flavedo (the coloured outer portion or skin of the fruit). The glands of grapefruit lie deeply in the flavedo and those of mandarin are likely to be nearer the surface. Fruits and leaves of these plants are covered by a thick cuticle which is waterproof and also the primary means of water conservation. Being shiny and reflective it is capable of deflecting some of the excess solar radiation in tropical and subtropical regions; it also reflects ultraviolet light, thereby protecting the DNA from the mutagenic effects of sunlight. It is an excellent protection against fungi and bacteria since they have no enzymes capable of digesting cut in. Secretory cavities are also present in the flower buds of cloves (Syzygium aromaticum), the fruit walls of pimento (Pimento dioica), and in the elongated cavities in the bark of frankincense (Boswellta spp.).
SECRETORY DUCTS

Ducts are elongated cavities. They can often branch to create a network extending from the roots through the stem to the leaves, flowers and fruits. They are composed of an epithelium which surrounds a central cavity. Several predisposed cells within the parenchyma undergo asynchronous division and in doing so they expand the initial space in the middle where the cells are all adjacent to form a cavity. Some of these cells forming the wall of the cavity will change into secretory epithelial cells. The oils are biosynthesized within their leucoplasts and move via the endoplasmic reticulum into the cavity. These cavities then become joined to form ducts. They can be found in all of the Umbelliferae family including fennel (*Foeniculum vulgares*). In the case of celery (*Apium graveolens*) they can branch to create a network extending from the roots, through the stem to the leaves then to the flowers and finally to the fruits where they are known as vittae (*sing. vitta*). They are also present in the Pinaceae, Compositae, Hypericaceae and Coniferae families. The resin ducts in the xylem of Coniferae can reach 4-10
cm in length with between 2 and 7 ducts per leaf.

GLANDULAR TRICHOMES

Glandular trichomes are modified epidermal hairs and can be found covering leaves, stems and even parts of flowers such as the calyx in many plants of the Labiatae family. These include basil (*Ocimum basilicum*), lavender (*Lavandula spp.*), marjoram and oregano (*Origanum spp.*), mint (*Mentha spp.*) and thyme (*Thymus sp.*). The secretory cells are attached by a single stem or basal cell in the epidermis. The outer surface of the gland is heavily cutinized. A toughened cuticle in which no pores or perforations are present, usually completely covers the Trichomes. The essential oils accumulate in subcuticular spaces and it is thought that they diffuse outwards through the cuticle. The glandular cells differ from normal plant cells in that they have a very large nucleus and a dense protoplasm that lacks a large central vacuole. There are numerous plasmodesmata across the walls of the gland cells especially between the stalk cell and the collecting cell. In the very young gland the intracellular organization is almost identical to that of the adjacent cells but as the secretory cells develop complex changes occur. The membrane system progressively degenerates and in the

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Plate 29: Seed (T/S) showing 4 primary and 2 commissural vittae situated beneath the seed coat (SEM, CPD) [x39].
fully-developed glands only a fine granular cytoplasm remains. Cells in the multicellular heads usually have nuclei with double the normal numbers of chromosomes (endopolyploidy) and in fully-mature glands, mitochondria are the most abundant organelles which might reflect a high energy requirement. There is also a well-developed endoplasmic reticulum. Essential oils accumulate in the subcuticular cavity.

All these changes in the glands occur at a very early stage of the leaf development and the glandular hairs are fully-formed by the time the leaves are about 5 mm long. The formation and transformation of the essential oils, however, takes place continuously from the formation of the gland until senescence. The essential oil biogenetic precursor isopentenyl pyrophosphate is with high probability, synthesized in the leucoplasts.

There are two main types of glands that can exhibit minor variations:

1- Peltate glands with one basal cell, a short stalk and a large six- to eight-celled head.

2- Capitate trichomes with either-

A) one basal cell, a short monocellular stalk and a two-cellular head.
b) one basal cell, a multicellular stalk and a small globose, unicellular head.

In every species there are distinctive variations in the size and shape of the glands. For example, yarrow (*Achillea millefolium*) secretory trichomes of the floret produce azulene and occur mainly in the corolla lobes of the ray and disk florets and also on the leaves. When a floret reaches 0.25 mm, fully-mature trichomes are present having developed from protodermal cells. They have 10 cells including a pair of basal cells, a pair of stalk cells and 3 pairs of glandular cells. In *Cannabis sativa* a variety of glandular trichomes occur, including bulbous (small glands with a single-celled head and a unicellular stalk), capitate-sessile (a gland with a head of 8 or more cells on a very short stalk) and capitate-stalked (similar to previous type but with a substantial multicellular stalk). These glands are considered to be the main location of the nareotic cannabinoids. It is possible to isolate an individual gland from the leaf surface and analyse its content for chemical composition and presence of specific enzymes.

Essential oils obtained from flowers are not usually secreted by glandular hairs but merely diffuse through the cytoplasm, the cell walls and the cuticle to the outside. They yield of essential oils from these species is generally very low. Examples include rose (*Rosa spp.*), 0.075% (w/v), acacia (*Acacia spp.*) 0.084% (w/v) and jasmine (*Jasminum spp.*) 0.04% (w/v).

Buds of a number of plant species (e.g. *Aesculus, Alnus, Betula, Populus, Prunus and Rhamnus*) also secrete lipophilic substances, mainly flavonoid aglycones mixed with essential oils. Secretion here occurs from epidermal cells which are covered by a cuticle. The secreted material is first eliminated into a space formed between the outer walls of the cells and the cuticle covering them, forming a blister that subsequently bursts.
Herbs & Natural Supplements

What is a Dietary Supplement?

A dietary supplement is a product taken by mouth that contains a "dietary ingredient" intended to supplement the diet.

Herbal supplements, sometimes called botanicals. However, herbal supplements haven't been subjected to the same scientific scrutiny and aren't as strictly regulated as medications. However, guarantee that herbal supplements are safe for anyone to use. Because many supplements contain active ingredients that have strong effects in the body, these products can pose unexpected risks. For example, taking a combination of herbal supplements or using supplements together with prescribed medications could lead to harmful, even life-threatening results. For this reason, it's important to talk with your doctor before using herbal supplements.

Who shouldn't use herbal supplements?

If you have health issues, it's essential that you talk with your doctor before trying herbal supplements. In fact, in some high-risk situations, your doctor will likely recommend that you avoid herbal supplements altogether.

It's especially important that you talk to your doctor before using herbal supplements if:

1. **You're taking prescription or over-the-counter (OTC) medications.** Some herbs can cause serious side effects when mixed with prescription and OTC drugs, such as aspirin, blood thinners or blood pressure medications. Talk to your doctor about possible interactions.

2. **You're pregnant or breast-feeding.** Medications that may be safe for you as an adult may be harmful to your fetus or your breast-feeding infant. As a general rule, don't take any medications —
prescription, **OTC or herbal** — when you're pregnant or breastfeeding unless your doctor approves.

3. **You're having surgery.** Many herbal supplements can affect the success of surgery. Some may decrease the effectiveness of anesthetics or cause dangerous complications, such as bleeding or high blood pressure. Tell your doctor about any herbs you're taking or considering taking as soon as you know you need surgery.

4. **You're younger than 18 or older than 65.** Older adults may metabolize medications differently. And few herbal supplements have been tested on children or have established safe doses for children.

**Daily Dosage:**

Dosing of herbal preparations is highly dependent on a variety of factors, such as growing and harvesting conditions, plant parts, extraction methods used and the dosage form chosen by the manufacturer. Standardization to single constituent makers has proven unreliable. Since no official standards have been established to date to regulate production of herbal medicines in the United States, dosage ranges must be employed as guidelines.

For example: Preparations equivalent to 4.5 to 7 g drug may be used. When used internally, the daily dosage must not exceed 0.1 micrograms of pyrrolizidine alkaloids with 1.2 unsaturated necine structure including their N-oxides. When used externally, the maximum daily dosage should not exceed 10 micrograms of pyrrolizidine alkaloids with 1.2 unsaturated necine structure including their N-oxides. Tea should not be used.
Safety using of herbal supplements.

- **Follow supplement instructions.** Don't exceed recommended dosages or take the herb for longer than recommended.

- **Keep track of what you take.** Take only one supplement at a time to determine if it's effective. Make a note of what you take — and how much for how long — and how it affects you.

- **Be cautious about supplements manufactured outside the United States.** Herbal products from some European countries are highly regulated and standardized. But toxic ingredients and prescription drugs have been found in supplements manufactured elsewhere, particularly China, India and Mexico.

- **Check alerts and advisories.** The FDA and NCCAM maintain lists of supplements that are under regulatory review or that have been reported to cause adverse effects. Check their websites periodically for updates.

- **Dietary supplements** are unnecessary if one eats a balanced diet.

The "dietary ingredients" in these products may include: vitamins, amino acids, minerals and herbs or other botanicals, and substances such as enzymes, organ tissues, glandular.

**Water Soluble Vitamins**

It’s best to get your vitamins and minerals from food rather than supplements,

- B₁, thiamine, B₂, riboflavin ,B₆, pyridoxamine , B₁₂ , Biotin , Panothenic acid ,Niacin , Folacin , Vitamin C

**1- Minerals**

- **Issues**
  - Absorption
  - Bioavailability
Percent of Body weight

- Calcium: 2%
- Phosphorus: 1%
- Potassium: 0.3%
- Sulfur: 0.2%
- Sodium: 0.1%
- Chloride: 0.1%
- Magnesium: 0.05%
- Iron: 0.04%

2- Herbs

Ginkgo to improve memory. Flax seed to lower cholesterol. Echinacea to prevent colds. The list of herbal remedies goes on and on.

Ginkgo biloba

Ginkgo is an herb. The leaves are generally used to make “extracts” that are used as medicine. However, a few medicines are made from the seed.

**effective for...**

- Alzheimer’s disease and other forms of dementia.
- Improving thinking problems caused by old age.
- Improving thinking in young people.
- Painful response to cold especially in the fingers and toes (Raynaud’s syndrome).

Ginkgo seeds contain substances that might kill the bacteria and fungi that cause infections in the body. The seeds also contain a toxin that can cause side effects like seizure and loss of consciousness.
Alfalfa

Alfalfa is an herb. People use the leaves, sprouts, and seeds to make medicine.

People also take alfalfa as a source of vitamins A, C, E, and K4; and minerals calcium, potassium, phosphorous, and iron.

effective for...

- **Lowering cholesterol in people with high cholesterol.** Taking alfalfa seeds seems to lower total cholesterol and “bad” low-density lipoprotein (LDL) cholesterol in people with high cholesterol levels.

Alfalfa seems to prevent cholesterol absorption in the gut. Alfalfa leaves are **POSSIBLY SAFE** for most adults. But taking alfalfa seeds long-term is **LIKELY UNSAFE**. Alfalfa seed products may cause reactions that are similar to the autoimmune disease called lupus erythematosus. Alfalfa might also cause some people's skin to become extra sensitive to the sun. Wear sunblock outside, especially if you are light-skinned.

Aloe Vera

Aloe is used as :

1- A folk or traditional remedy for a variety of conditions, including diabetes, asthma, epilepsy, and osteoarthritis.

2- It is also used topically for osteoarthritis, burns, sunburns, and psoriasis.

3- Aloe vera gel can be found in hundreds of skin products, including lotions and sunblocks.
4- The Food and Drug Administration (FDA) has approved aloe vera as a natural food flavoring.

Aloe leaves contain a clear gel that is often used as a topical ointment. The green part of the leaf that surrounds the gel can be used to produce a juice or a dried substance (called latex) that is taken by mouth.

**Belladonna**

Belladonna is a plant. The leaf and root are used to make medicine. The belladonna berry juice was used historically in Italy to enlarge the pupils of women. This was not a good idea, because belladonna can be poisonous. Effective for...

- Colds.
- Hay fever.
- Parkinson's disease.
- Motion sickness.
- Arthritis-like pain.
- Nerve problems.

**Chamomile**

Chamomile is used as a folk or traditional remedy for sleeplessness, anxiety, and gastrointestinal conditions such as upset stomach, gas, and diarrhea. It is also used topically for skin conditions and for mouth ulcers resulting from cancer treatment.

**Ginseng, American**

American ginseng is an herb. The root is used to make medicine. American ginseng is used for stress, to boost the immune system, and as a general tonic and stimulant. American ginseng is often used to fight infections such as colds and flu.
There is some evidence that it might help prevent colds and flu and make symptoms milder when infections do occur.

**How does it work?**

American ginseng contains chemicals called ginsenosides that seem to affect insulin levels in the body and lower blood sugar. Other chemicals, called polysaccharides, might affect the immune system.

**Fish Oil**

Inside your cells, you have a balance of omega-6 and omega-3 fatty acids. Most people’s diets are heavy in omega-6 fatty acids (especially from cheap vegetable oil), which throws the balance off. A great source for omega-3 fatty acids are fatty fish, and eating these fish or supplementing directly with the fish oil itself can improve overall health.

The most noticeable results from fish oil supplementation include benefits for severe depression, joint pain reduction, and a powerful triglyceride reducing effect. Fish oil’s effect on triglycerides is so potent that it’s also sold as pharmaceutical grade fish oil, under the brand name Lovaza.

Bottom line: Unless you eat a decent amount of fatty fish (e.g. salmon), fish oil is a solid option for providing a variety of health benefits.

**Vitamin D**

There are two numbers to think about with vitamin D - the minimum, and the ideal amount.

Most people get a minimum amount of vitamin D (otherwise they would have rickets). But they do not get the ideal amount.

Vitamin D supplementation can improve mood and provide long-term protection against cognitive decline and bone deterioration. It stacks very well with vitamin K2 and magnesium.

Vitamin D’s effects are sometimes exaggerated, but that doesn’t mean it’s ineffective - it simply went from underused to overhyped. While it isn’t a cure-all, vitamin D is cheap, safe, and effective for long term
supplementation. People in cold places or overcast areas should possibly take it.

Many studies have shown that most people are not in the optimal range for vitamin D. Vitamin D supplementation works to improve your health.

**Creatine**

If you follow sports, you may have heard of creatine being compared to steroids or other drugs.

This couldn’t be further from the truth! Creatine is naturally found in meat, and even the IOC (International Olympic Committee) has said that creatine is 100% legal.

Creatine is basically a source of energy for your cells. Extra energy means extra effort, which means better results!

Creatine has a lot of evidence to support its safety, and it’s cheap and can be supplemented indefinitely. Plus creatine isn’t just limited to benefiting physical performance and muscle growth - it also shows promise for brain-related conditions like major depression.

Bottom line: Creatine works. It is especially powerful if you are vegetarian.

**Turmeric/Curcumin**

According to nutrition research career, noting that the curcumin in turmeric needed an absorption enhancer or else it wouldn’t be able to cross through the intestine and enter circulation. But a decade later, evidence has come out that sometimes you want the curcumin to stay inside your intestine (for example, if you have intestinal inflammation). Turns out grandma was right, turmeric is healthy, and it doesn’t have to come in a fancy absorbable pill. So while there’s nothing wrong with getting that curcumin into systemic circulation in order to possibly help other parts of the body, that’s not necessarily the only way turmeric can help you. As Hippocrates famously said, “All disease begins in the gut”.

∧
Melatonin

This hormone had a pretty defined role until recently - it helps sleep. But then marketers started latching onto papers exploring other characteristics of melatonin, and suddenly it became a magic pill.

For example, cherries naturally contain melatonin, as do a few other foods. And lo and behold, alternative medicine websites have just started to note the benefits of cherries on a huge variety of different conditions, due to their melatonin and phytochemical content. In reality, the evidence for melatonin is either mixed or negative for most non-sleep related conditions.

And even for the tried-and-true benefit of better sleep, melatonin mostly helps you fall asleep (especially if you insist on exposing yourself to computer or TV light before bed ... in which case we strongly recommend you change your habits!). So for those who have problems waking up at night, issues with anxiety or intrusive thoughts, or other sleep issues, melatonin may not be the magic bullet. But if you had a late night out and need some temporary sleep help, go ahead and grab some melatonin.

BONUS: N-Acetylcysteine

N-Acetylcysteine (NAC) stands out from the crowd of antioxidants on the supplement store shelf because it’s actually effective when supplemented. NAC is needed to produce the antioxidant enzyme called glutathione, which exerts a general protective effect on the body.

NAC can also be supplemented for a variety of cognitive benefits, which include the treatment of drug addiction, reducing irritability and obsession, and protecting against cognitive decline.

NAC is also one of the few supplements that might actually remove heavy metals from the body. Though many detoxifying supplements are claimed to have this effect, NAC is one of the few that delivers.
Methods of Preparing Herbal Remedies

In traditional herbal medicine systems, herbal remedies are prepared in several ways, which usually vary based on the plant utilized, and what condition is being treated. Some of these methods include infusions (hot teas), decoctions (boiled teas), tinctures (alcohol and water extracts), and macerations (cold soaking). Others include preparing plants in hot baths (in which the patient is soaked in it or bathed with it), inhalation of powdered plants, or steam inhalation of various aromatic plants boiled in hot water.

Types of extraction:

1-Water extracts:
In this method the water could be used for extraction and the resulted extract called water extract and it could be called crude due to water which is high polar solvent similar to ethanol and methanol which extract all chemical compounds in the plant part. Water could be used as cold or hot and called hot or cold water extract. In this type of extraction glycosides could be extracted.

2- Alcoholic extraction:

There are 2 types of alcoholic extraction:

a- Alcoholic extraction by shaking:

In this type of extraction 250 ml of solvent put in beaker and 50 g of plant powder put over it and mix them well, then covered it and leave it for 24h, then filtrate by using muslin cloth then by using filter papers and the supernatant put in petri dishes and put it in oven 40 C° or using vacuum evaporator to evaporate the solvent, and the extract kept in refrigerator until use. The extract called according to the organic solvent used when we used ethanol called crude ethanolic extract....etc.

b- Alcoholic extraction by using soxhlet apparatus:

In this type of extraction 200 ml of solvent and 10 g of plant powder put in soxhlet apparatus and extracted for 8h, then the extract put in rotary evaporator at 40 C° to concentrate the extract. The resulted extract called crude alcoholic extract.

3- Steam water extraction:
This type of extraction could be used to extract volatile oils by using Clevenger apparatus.

4- Oil extraction:

Volatile oil found in aromatic plant parts such as flowers and leaves, and it is volatile in room temperature, and extracted by steam water in Clevenger apparatus. While fixed oil found in seeds, bark, and root and they are not volatile in room temperature and extracted by using soxhlet apparatus with hexane or diethyl ether.

**Preparing of Remedies or herbal drugs.**

When a plant is finely ground, it usually makes a stronger remedy as more surface area of the plant is available to extract in the solvent. Extra time filtering is normally required when working with plant powders, but many herbalists prefer working with powders instead of bulky cut herbs since they make stronger remedy extracts. It is also recommended to use distilled or purified water when extracting medicinal plants. Regular tap water can contain chlorine and other chemicals, which might have an interaction or chain reaction with one, or more of the many chemicals found in plants. Instructions for the main extraction methods are as follows.

1-Macerations

This method of extraction is certainly the easiest. The fresh or dried plant material is simply soaked in cool water overnight. The herb is strained out and the liquid is taken. Normally this is used for very tender plants, or those with delicate chemicals that might be disfigured by heating or which might be degraded in strong alcohol.
2- Infusions

Infusions are typically used for fresh/dried leaves and tender herbs or plants. Preparing an infusion is much like making a cup of tea. Water is boiled and then poured over an herb (or combination of herbs), cover the cup and allow to sit/steep for 10-15 minutes or more (get the liquid and leave the sediment in the bottom of the cup). The ratio of herb to water can vary depending on the remedy and the plant. Generally using 30-60 g of herb in 180-240 ml water is sufficient, while the proper dosages are (2-3) cup daily.

3- Decoctions

Decoctions are usually used with tougher and more fibrous plants, barks and roots (and which have water soluble chemicals). Instead of just steeping it in hot water, Use 500 ml. of water for every 30 gm of dried herb. Cover the container and boil the plant material for a longer period of time 15-20 min. to soften the harder woody material and release its active constituents.

A tincture is an alcohol and water extract which is used when plants have active chemicals that are not very soluble in water, and to prepare a concentrate plant extract (in its chemical component) for longer term storage. Properly prepared plant tinctures can last several years or more without losing therapeutical potency (shelf life). To prepare a tincture with a shelf-life of at least one year, by using a minimum of 40% alcohol, in addition to a clean, dark and glass bottle with tight fitting lid. A standard (1:4) tincture usually means 1 part herb to 4 parts liquid (or as above, 1 ounce herb to 4 ounces of liquid). Seal the container and
store at room temperature away from direct sunlight. Shake the bottle/jar at least once daily for at least two weeks. If using a powdered plant for the tincture, three days will be sufficient and the powder will settle to the bottom. Dosages needed for tinctures are usually much less than infusions and decoctions. Average dosages for tinctures are about 1-2 milliliters (about 30 to 60 drops) two to three times daily. The tincture can be placed directly in the mouth for immediate absorption, or placed in a small amount of water or juice.

5- Compresses

Compresses are simply soaking a cloth in a prepared infusion, tincture or decoction and laying the cloth onto the affected part of the body/skin. Or even chewing up fresh leaves or roots and spitting them out onto the skin.

6- Bathing Remedies

Medicinal plants are added to a bath water and the patient is soaked in it. The skin is a wonderful organ capable of absorbing plant chemicals (and even synthetic chemicals) directly thru the skin, and into the underlying fat tissue, then into the bloodstream.

7- Pills (Honey Pills)

Pills can be made by mixing thoroughly the powdered drug with equal quantity of honey cooked to bright red syrup. The moment the mixture starts to cool off, it can be rolled to desired tubular strands and cut into small pieces.

8- Ointment:
Herbal creams and ointments are natural remedies that are mainly used for skin conditions (wounds and burns) or muscle and joint aches.

1. Start by preparing the herbs. Chop any fresh herbs and then weigh them.

2. Melt 600 ml of emulsifying ointment (as olive oil) in the glass dish over low heat.

3. Add 270 ml of glycerol and 300 ml of water.

4. Then add 120 g of herbs and simmer for 3 hours, stirring occasionally. If the water runs low, top it up again.

**Introduction**

- It is becoming an increasingly challenging undertaking.
- Facts of Drug discovery and development:
  1. Time 10-15 years
  2. Cost $800 million-$1 billion
  3. Drugs tested 5000-10,000
  4. Subjects tested 1000-5000
  5. Drugs approved 1
  6. Modern drug discovery is the product of cooperation.
  7. Both public and private organizations play unique roles in translating basic research into medicine.
  8. Major biopharmaceutical companies are the primary source funding for new medicines.
Smaller companies conduct basic research, drug discovery, preclinical experiments and, in some cases, clinical trials.

**Steps involved**

The production of a new drug involves following steps:

1. Discovery
2. Preclinical Testing
3. Clinical Trials
4. NDA and Approval
5. Manufacture
6. Post-Marketing Surveillance

### III. Clinical Trials

- This phase is the longest one in drug development ranging from 2-10 years.

- A suitable clinical trial design is developed. These include:

  1. Placebo controlled trials
2. Randomized trials

3. Double blinded studies

• Clinical trials comprise of three phases-
  • Phase 1
  • Phase 2
  • Phase 3

Phase 1 trials:

• The candidate drug is tested in people for the first time.

• These studies are usually conducted with about 20 to 100 healthy volunteers.

• Usually last 6 months to 1 year (30% of drugs fail Phase 1 testing)

• Used to determine
  1. Pharmacokinetic data
  2. Pharmacodynamic data
  3. Max. tolerated dose

Adverse reactions profile

Phase 2 trials:

• In Phase 2 trials researchers evaluate the candidate drug’s effectiveness in about 100 to 500 patients with the disease or condition under study

• Usually last Few weeks - 2 years (37% of drugs fail Phase 2 testing)
• Used to know

1. Preliminary evidence of efficacy
2. Pharmacodynamic effects in patients
3. Optimal dosage ranges and dosing schedule

• Phase 2 trials are followed by a meeting with FDA to Obtain agreement on Phase 3 adequate and well controlled study design and analysis plan

Phase 3 trials:

• In Phase 3 trials researchers study the drug candidate in a larger number (about 1,000-5,000) of patients.
• Usually last 3 years (6% fail Phase 3 testing)
• Used for
  • Confirmation of efficacy
  • Establishment of complete safety profile
  • Base of regulatory information (labeling)
  • Asseessment of risk/benefit
• Phase 3 trials are both the costliest and longest trials.
• Hundreds of sites around the world participate in the study to get a large and diverse group of patients.
• Coordinating all the sites and the data coming from them is a monumental task.

IV. NDA and Approval
• Once all three phases of the clinical trials are complete, the sponsoring company analyzes all of the data. If the findings demonstrate that the experimental medicine is both safe and effective, the company files a New Drug Application (NDA) with the FDA requesting approval to market the drug.

• The NDA includes an integrated summary of efficacy (ISE) and of safety (ISS).

• NDA contains all the pre-clinical and clinical data from previous 7-10 years of study.

• NDA contains several thousands of pages of reports.

Conclusion

• The discovery and development of new medicines is a long, complicated process.

• Research-based pharmaceutical companies are committed to advancing science and bringing new medicines to patients.

• Increased support from Governments and Organizations may help in development of safer and cost effective medicines.

References

