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Advance Herbal Technology

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Abstract

Recently peoples are getting attracted towards herbal medicines due to many advantages. Herbal formulation has reached extensive acceptability as therapeutics agents for several diseases. Although, most of these applications are unorthodox, it is however a known fact that over 80% of the world population depends on herbal medicines and products for healthy living. This rise in the use of herb- al product has also given rise to various forms of abuse and adulteration of the products leading to consumers and manufacturers disappointment and in some instances fatal consequences. The developmant of authentic analytical method which can reliably profile the phytochemical composition, including quantitative analyses of marker/bioactive compounds and other major constituents, is a maj- or challenge to scientists. Standardization is an important step for the establishment of a consistent biological activity, a consistent chemical profile, conventional methods as well as newer advances are described.

ADVANCED HERBAL TECHNOLOGY

INTRODUCTION

Herbal medicine is oldest remedies known to mankind. Herbal drug technology is used for converting botanical material into medicine.[1]

The major drawback of modern medicine is their side effect which may leads to lived threatening of patient. Herbal medicine have their list of side effect like any other synthetic drug.[1]

Plant materials are used throughout the developed and developing world as home remedies, in over-the-counter drug products, and as raw material for the pharmaceutical industry. Plants, herbs, and ethnobotanicals have been used since the early days of humankind and are still used throughout the world for health promotion and treatment of disease.[1]

Recently peoples are getting attracted towards herbal medicines due to many advantages. Herbal formulations have reached extensive acceptability as therapeutic agents for several diseases. Although, most of these applications are unorthodox, it is however a known fact that over 80% of the world population depends on herbal medicines and product for healthy living. This rise in the use of herbal product has also given rise to various forms of abuse and adulteration of the products leading to consumers' and manufacturers' disappointment and in some instance's fatal consequences. The development of authentic analytical methods which can reliably profile the phytochemical composition, including quantitative analyses of marker/bioactive compounds and other major constituents, is a major challenge to scientists. Standardization is an important step for the establishment of a consistent biological activity, a consistent chemical profile, or simply a quality assurance program for production and manufacturing of herbal drugs. In present review article various conventional methods as well as newer advances are described. Recent advancements includes DNA fingerprinting, metabolomics technique, differential pulse polarography, chemometric, X-ray diffraction...etc are observed. Capillary electrophoresis and chromatographic techniques contributions towards standardization of herbal drugs is also reported.[2]

Identification, Authentication and Extraction of Herbs

1) Introduction to herbal technology

Herbal Technology- Herbal Technology encompasses all the myriads of ways of utilizing the multifarious potentialities of plants for human welfare.[3]

There are presently five main branches such as Medicinal plants, Natural dyes, Bio pesticides, Biofertilizers and Biofuel in this discipline, though more and more may be added later.[3]

Medicine is a substance that has nutritive, curative, or preventive properties, while the term "herbal" refers to a botanical or plant-based preparation. Hence, the term "herbal medicine" is used for plant-based substances that consist of nutritive, curative, or preventive properties. Herbal medicine is an interdisciplinary branch between herbal medicine and Ayurveda as it covers all fields of herbal medicine related to botany, medicinal plant research, pharmacognosy, phytochemistry, phytotherapy, botanical medicines, Ayurveda, natural chemistry, agriculture science, Unani medicine, biotechnology, and biochemistry. A person who deals with herbs, especially medicinal herbs, is known as an herbalist. Herbal journals deal with the use of plants in the treatment of disease.[21]

2) Different method for identification of plant

1) Expert Determination:- The method of identification is expert determination in terms of reliability or accuracy. In general, the expert have prepared treatment (monograph, revision, synopses) of the group in question, and it is probable that the more recent floras or manuals include the expert's concept of taxa.[1]

2)Recognition:- This is based on extensive, past experience of the identifier with plant group in question.[1]

3) Comparison:- A third method is by comparison of an unknown with named specimens, photograph, illustrations or descriptions.[1]

4) The Use of Keys and Similar Devices:-This is by far the most widely used method and does not require the time, material or experience involved in comparison and recognition.[1]

3) Authentication of plant

Herb authentication is a quality assurance process that ensures the correct plant species and plant parts are used as raw material for herbal medicines. The proper authentication of herbal raw materials is critically important to the safety and efficacy of herbal medicines. Morphological, anatomical, chemical and DNA markers solve the problem by differentiating the genuine material from the adulterant, substitutes and spurious drugs.[1]

Macroscopic examination- They involved the comparison of morphological characters that are visible with the naked eye or under low magnification with descriptions of the plant or botanical drug in floras or monograph. Characters such as size, shape, and colour of leaves, flowers or fruits are commonly used in macroscopic identification.[1]

Microscopic examination- They focuses on anatomical structure in the plant material that are visible only with the help of a microscope. Features such as trachoma shape and structure the arrangement of stomata in the epidermis, the presence or absence of compound such as mucilage, starch or lignin, or the presence of tissues with characteristics cells might be used in the microscopic identification of herbal drugs.[1]

4) Extraction of herbal plant

Extraction of medicinal plants is a process of separating active plant materials or secondary metabolites such as alkaloids, flavonoids, trepans, saponin, steroids, and glycosides from inert or inactive material using an appropriate solvent and standard extraction procedure.[1]

Maceration - This is an extraction procedure in which coarsely powdered drug material, either leaves or stem bark or root bark, is placed inside a container; the menstrum (The solvent used for the extraction of medicinal plants) is poured on top until completely covered the drug material. The container is then closed and kept for at least three day.[1]

Infusion:-Infusion is a chemical process that uses botanical (dried herbs, flowers) that are volatile and release their active ingredients readily in water, oil or alcohol. In this process, a liquid is typically boiled and poured over the herbs[1].

Digestion - This is a form of maceration in which gentle heat is used during the process of extraction. It is used when the moderately elevated temperature. The solvent efficiency of the menstrum is increased.[1]

Decoction - Decoction involves first drying the plant material; then cutting the material to allow for maximum dissolution; and finally boiling in water to extract oils.[1]

Reflux extraction-Reflux extraction is more efficient than percolation or maceration and requires less extraction time and solvent. It cannot be used for the extraction of thermolabile natural products.[18]

Soxhlet extraction- Soxhlet extraction method integrates the advantages of the reflux extraction and percolation, which utilizes the principle of reflux and siphoning to continuously extract the herb with fresh solvent. The Soxhlet extraction is an automatic continuous extraction method with high extraction efficiency that requires less time and sol-vent consumption than maceration or percolation. the high temperature and long extraction time in the Soxhlet extraction will increase the possibilities of thermal degradation.[18]

In advanced herbal technology include following extraction process:-

1) Supercritical fluid extraction.

2) Microwave assisted extraction.

3) Ultrasound assisted extraction.

4) Solid phase&microwave assisted extraction.

Supercritical fluid extraction

It is the process of separating one component (the extractant) from another (the matrix) using supercritical fluid as the extracting solvent. Extraction is usually from a solid matrix and also be from liquid.[6]

Supercritical fluid extraction(SFE) is a green method that can be used as an alternative method to traditional solvent extraction. SFE(Fig 1) is a method in which a gas is delivered to an extraction vessel at a temperature and pressure above its critical temperature.[4]

Critical point is defined as the characteristic temperature (Tc) and pressure (Pc) above which distinctive gas and liquid phases do not exist.[5]

Carbon dioxide is considered as an ideal solvent for SFE. The critical temperature of CO_2 (31^0C) is close to room temperature, and the low critical pressure (74 bars) offers the possibility to operate at moderate pressure, generally between 100 and 450 bar.[5]

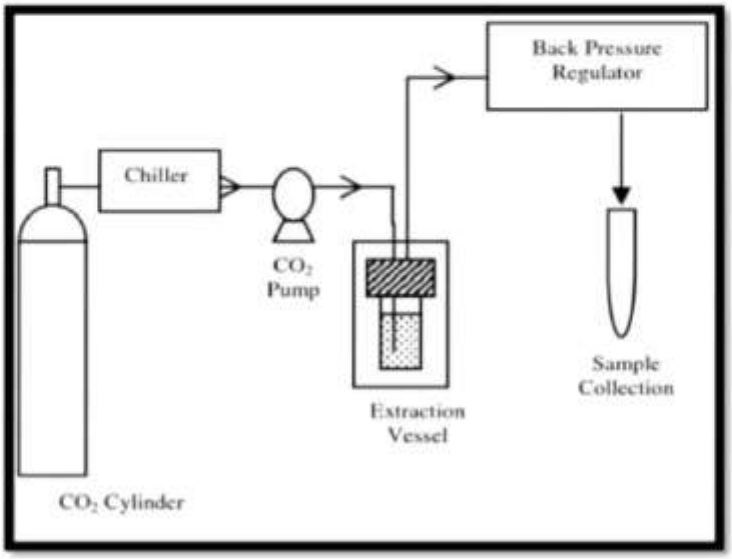

Fig.1 Super Critical Fluid

Application-

- Processing and preservation of food product.
- It helps in purification of vitamin intermediates.
- Separation of aromas and oils from spices.[6]

Microwave assisted extraction

Principle- The basic principle of this method includes: The target for heating of mixture traces of moistures presents in the cell of dried plant materials. The heating up of this moisture is due to microwave effect that resulted in evaporation and generated tremendous pressure on the cell wall and the cell wall ruptured due to cell wall pushed materials from the inside (Fig.2)[6]

The microwave-assisted extraction is also considered as a novelmethod for extracting soluble products into a fluid from a widerange of materials using microwave energy.[5]

They consist of two perpendicularly oscillatory fields namely: Electric Field and Magnetic Field, which can also be called as Microwave. These waves are used as energy vectors or information carriers. Electromagnetic waves are absorbed by the material and converted to heat energy. This is a Microwave Energy.[7]

Microwaves are electromagnetic fields in the frequency range from300 MHz to 300 GHz.[5]There are two mechanisms for conversion of electromagnetic energy to calorific energy or heat: Ionic Conduction and Dipole Rotation.[7]

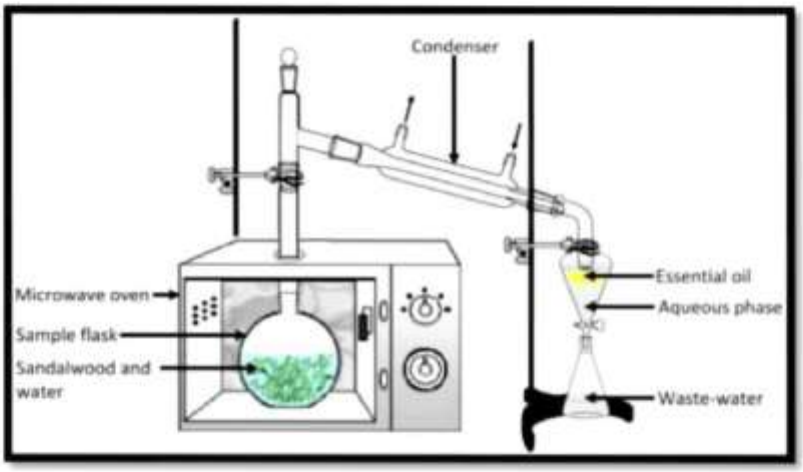

Fig.2 Microwave Assisted Extraction

Advantages:-

- No loss of volatile substances and very less volume of solvent are required.
- Not required any addition of solvent repeatedly.
- Risk of air-borne contamination is low.

Ultrasound assisted extraction

This method is modified method of maceration.This method is based on the use of ultrasound.[6]Ultrasound is a special type of sound wave beyond human hearing.[5] Ultrasound frequencies ranging from 20 to 2000 kHz are used in UAE (Fig.3)[4]

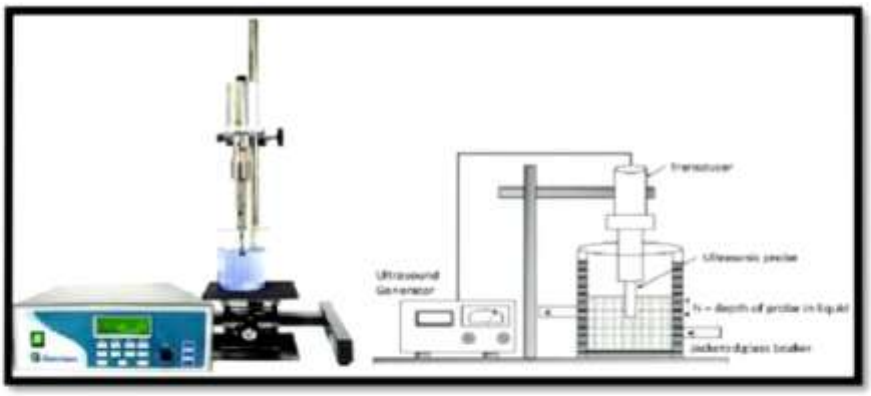

Fig.3 Ultrasound Assisted Extraction

Applications:-

- Ultrasound extraction is used in crude oil desulfurization and cell disruption.
- Sonication can also be used to initiate crystallization processes and even to control polymorphic crystallization.
- This method is also used in production of biofuels, production of nanoparticles such as Nano emulsion and liposomes as well as for waste water purification extraction of plant oil.[7]

Solid Phase Micro Extraction

This method of extraction involves the use of a fiber coated with an extracting phase that can be a liquid or a solid. It extracts both volatile and non-volatile compound by used liquid or gas phases but mainly used for volatile analytes. The microextraction process is considered complete when the analyte concentration is reached distribution equilibrium between the sample matrix and the fiber coating.(Fig.4)[6]

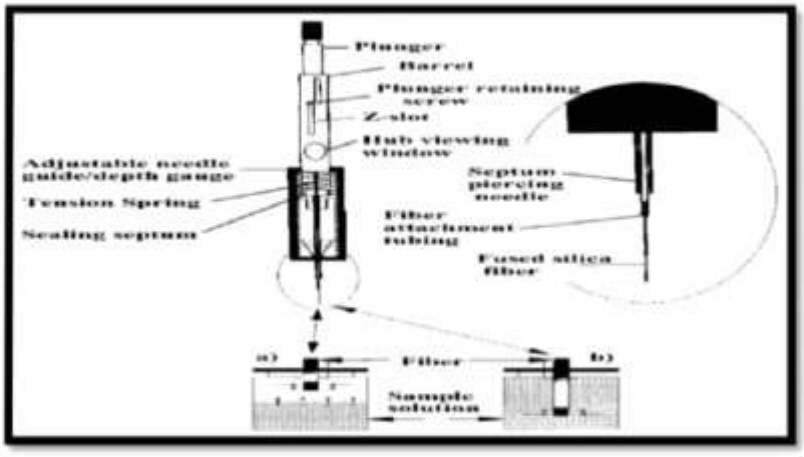

Fig.4 Solid Phase Micro Extraction

Advantages:-

- The extraction is the fast and simple.
- Extraction is performed without solvents.

Isolation and purification techniques

1) General Isolation Techniques

Isolation is a separation technique in which we can obtain a purified compound. Isolation is also called as purification.[3]

General Techniques for isolation-

1) Column chromatography

2) Paper chromatography

3) Ion exchange chromatography

4) Thin layer chromatography

5) High pressure liquid chromatography (HPLC)

6) Gas liquid chromatography (GLC)

7) High performance thin layer chromatography (HPTLC)

Chromatographic Techniques:-

It is a new physical technique of separation, identification and purification of components of a mixture.

2)Different Chromatographic Techniques

1)Thin Layer Chromatography:-

Where mixture components are separated between mobile phases by differential affinities between the two phases.[3]

TLC is the most popular and simple planer chromatographic techniques used for separation of compounds from the plant extract.[6]

Thin-layer chromatography (Fig.5) is a "solid-liquid adsorption" chromatography. In this method stationary phase is a solid adsorbent substance coated on glass plates.[8]Mobile phase is a developing liquid which travels up the stationary phase, carrying the samples with it.[9]

Components of the samples will separate on the stationary phase according to how much they adsorb on the stationary phase versus how much they dissolve in the mobile phase.[9]

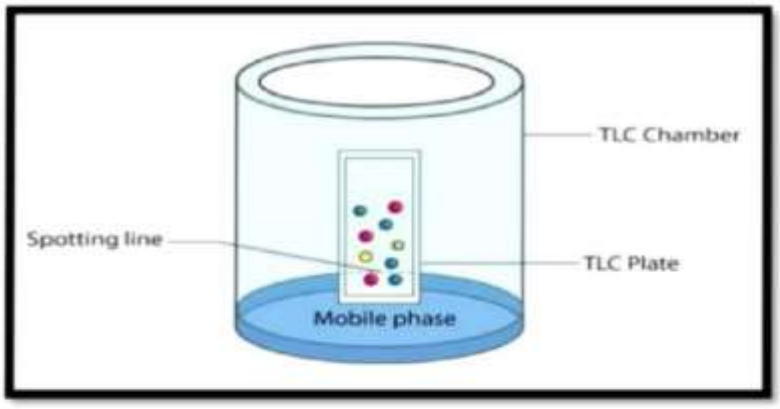

Fig.5 Thin Layer Chromatography

Procedure-

Thin Layer Chromatography Plates-Ready-made plates are used which are chemically inert and stable. The stationary phase is applied on its surface in the form of a thin layer. The stationary phase on the plate has a fine particle size and also has a uniform thickness.

Thin Layer Chromatography Chamber-Chamber is used to develop plates. It is responsible to keep a steady environment inside which will help in developing spots. Also, it prevents the solvent evaporation and keeps the entire process dust-free.

Thin Layer Chromatography Mobile Phase-Mobile phase is the one that moves and consists of a solvent mixture or a solvent. This phase should be particulate-free. The higher the quality of purity the development of spots is better.

Thin Layer Chromatography Filter Paper-It has to be placed inside the chamber. It is moistened in the mobile phase.

1) To apply sample spots, thin marks are made at the bottom of the plate with the help of a pencil.

2) Apply sample solutions to the marked spots.

3) Pour the mobile phase into the TLC chamber and to maintain equal humidity, place a moistened filter paper in the mobile phase.

4) Place the plate in the TLC chamber and close it with a lid. It is kept in such a way that the sample faces the mobile phase.

5) Immerse the plate for development. Remember to keep the sample spots well above the level of the mobile phase. Do not immerse it in the solvent.[10]

Application:-

- To find the adulteration or substitution present in the original plant sample.
- It helps in purification process as it separates all the compound present in particular plant extract.
- To keep a check on the performance of other separation processes.[6]

2) Column chromatography:-

Column chromatography (Fig.6) in chemistry is a chromatography method used to isolate a single chemical compound from a mixture. Chromatography is able to separate substances based on differential adsorption of compounds to the adsorbent; compounds move through the column at different rates, allowing them to be separated into fractions. The technique is widely applicable, as many different adsorbents (normal phase, reversed phase, or otherwise) can be used with a wide range of solvents. The technique can be used on scales from micrograms up to kilograms. The main advantage of column chromatography is the relatively low cost and disposability of the stationary phase used in the process. The latter prevents crosscontamination and stationary phase degradation due to recycling. Column chromatography can be done using gravity to move the solvent, or using compressed gas to push the solvent through the column.[21]

Since proteins have difference characteristic features as size, shape, net charge, stationary phase used,and binding capacity, each one of these characteristic components can be purified using chromatographic methods. Among these methods, most frequently column chromatography is applied. This technique is used for the purification of biomolecules. Column (stationary phase) firstly the sample to be separated, then wash buffer (mobile phase) are applied (Figure 1). Their flow through inside column material placed on a fiberglass support is ensured. The samples are accumulated at the bottom of the device in a time, and volume-dependent manner.[8]

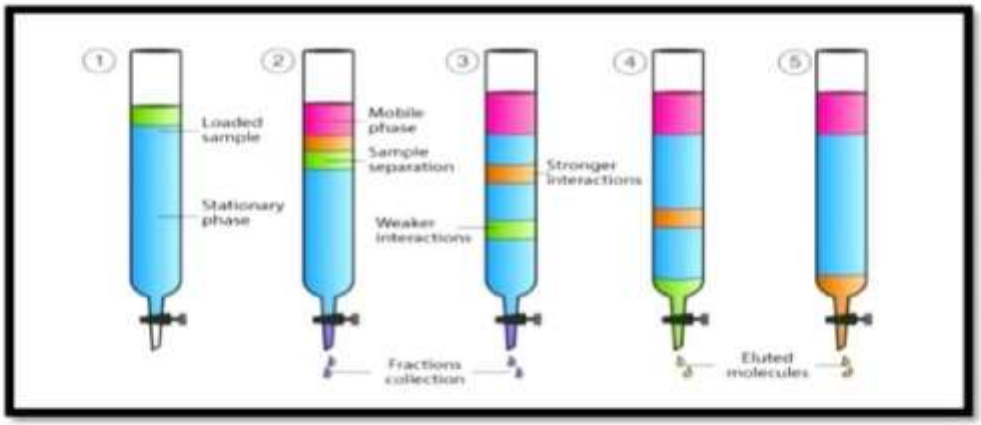

Fig.6 Column Chromatography

Type of column chromatography:-

1. Adsorption column chromatography – Adsorption chromatography is a technique of separation, in which the components of the mixture are adsorbed on the surface of the adsorbent.[22]

2. Partition column chromatography – The stationary phase, as well as mobile phase, are liquid in partition chromatography.[22]

3. Gel column chromatography – In this method of chromatography, the separation takes place through a column packed with gel. The stationary phase is a solvent held in the gap of a solvent[22].

4. Ion exchange column chromatography – A chromatography technique in which the stationary phase is always ion exchange resin.[22]

3)Paper Chromatography:-

Paper chromatography is a type of analytical tool which is used for separation of colored components. The principle involved may be separation and partition of components based on their affinity towards stationary phase.[11]

In this method a thick filter paper comprised the support, and water drops settled in its pores made up the stationary "liquid phase." Mobile phase consists of an appropriate fluid placed in a developing tank. Paper chromatography is a "liquid-liquid" chromatography.[8]

Types of Paper Chromatography:-

1) **Ascending paper chromatography**:-
Here the solvent travel up the chromatographic paper. It is used for separation of organic and inorganic substance.[12]

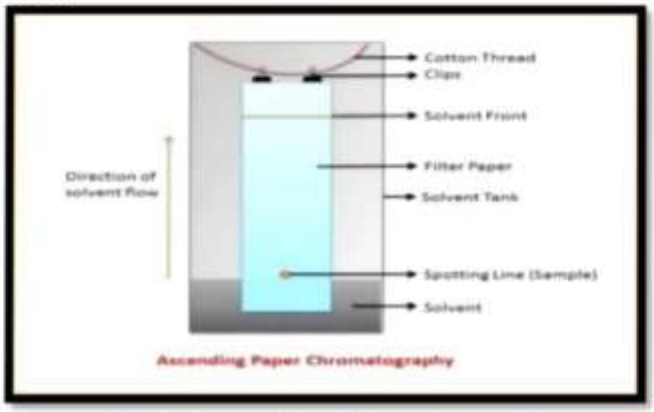

Fig.7 Ascending Chromatography

2) **Descending paper chromatography:-**
In this type, development of chromatogram is done by allowing the solvent to travel down the paper. Mobile phase is placed in the solvent holder at the top.[12]

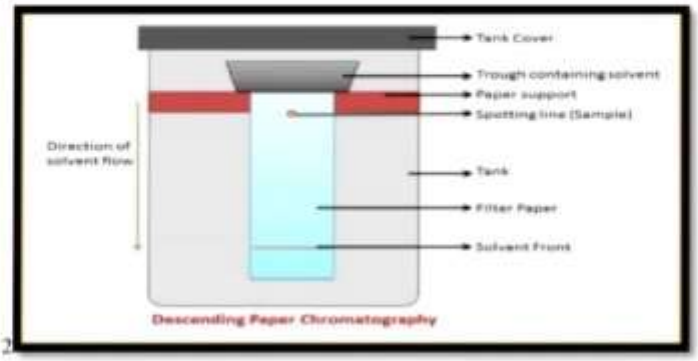

Fig.8 Descending Chromatography

3) **Ascending-Descending Chromatography:-**
The upper part of ascending chromatography can be folded over the rod in order to allow the paper to become descending after cross the rod.[12]

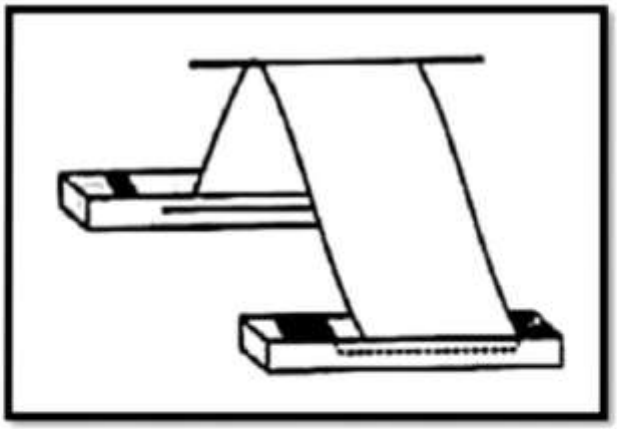

Fig.9 Ascending & Descending Chromatography

4) Radial paper chromatography:-

It is also called circular chromatography. Here a circular filter paper is taken and the sample is deposited at the center of the paper. After drying the spot, the filter paper is tried horizontally on a petri dish containing solvent, so that the wick of the paper is dipped in the solvent.[12]

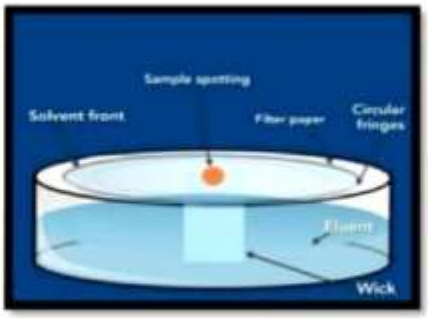

Fig.10 Radial Chromatography

5) Two-dimensional paper chromatography:-

In this technique a square or rectangular paper is used. Here the sample is applied to one of the corners and development is performed at right angleto the direction of the first run.[12]

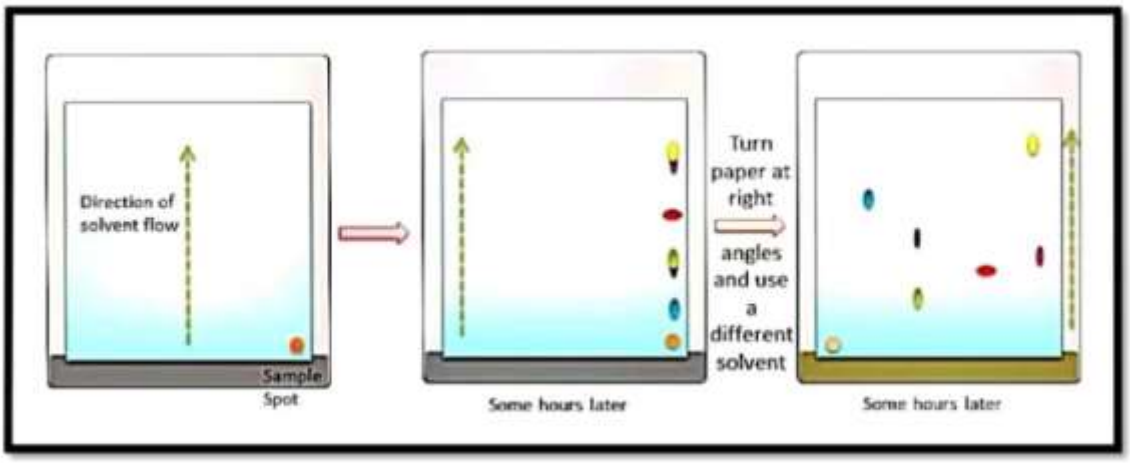

Fig.11Two-Dimensional Chromatography

Procedure -

1- Selecting a suitable type of development: It is decided based on the complexity of the solvent, paper, mixture, etc. Usually, ascending type or radial paper chromatography is used as they are easy to perform. Also, it is easy to handle, the chromatogram obtained is faster and the process is less time-consuming.

2- Selecting a suitable filter paper: Selection of filter paper is done based on the size of the pores and the sample quality.

3- Prepare the sample: Sample preparation includes the dissolution of the sample in a suitable solvent (inert with the sample under analysis) used in making the mobile phase.

4- Spot the sample on the paper: Samples should be spotted at a proper position on the paper by using a capillary tube.

5-Chromatogram development: Chromatogram development is spotted by immersing the paper in the mobile phase. Due to the capillary action of paper, the mobile phase moves over the sample on the paper.

6- Paper drying and compound detection: Once the chromatogram is developed, the paper is dried using an air drier. Also, detecting solution can be sprayed on the chromatogram developed paper and dried to identify the sample chromatogram spot.[10]

Application:-

- Separation of mixture of drugs.
- Identification of impurities.
- Detection of adulterants.[12]

4)High Performance Liquid Chromatography:-

Principle:- HPLC technique is modified version of TLC method and based on adsorption principle. It is quantification or qualitative identification or separation of two components or multi component mixture.[6]

HPLC contains two basic phases, a liquid mobile phase to transport the analyte through the column and a stationary phase which is packed with a stationary phase material by applied high pressure. HPLC is based on other mechanisms also as; size exclusion and ion exchange, depend on the type of stationary phase used.[10]

Fig.12 HPLC

Components of HPLC-

The Pump-The development of HPLC led to the development of the pump system. The pump is positioned in the most upper stream of the liquid chromatography system and generates a flow of eluent from the solvent reservoir into the system.

Injector- An injector is placed next to the pump.The simplest method is to use a syringe, and the sample is introduced to the flow of eluent.The most widely used injection method is based on sampling loops.

Column- The separation is performed inside the column.Most column housing is made of stainless steel since stainless is tolerant towards a large variety of solvents.

Detector- Separation of analyses is performed inside the column, whereas a detector is used to observe the obtained separation.This difference is monitored as a form of an electronic signal. There are different types of detectors available.

Recorder- The change in eluent detected by a detector is in the form of an electronic signal, and thus it is still not visible to our eyes

Degasser- When gas is present in the eluent, this is detected as noise and causes an unstable baseline. Degasser uses special polymer membrane tubing to remove gases.

Column Heater- In order to obtain repeatable results, it is important to keep consistent temperature conditions. Also, for some analysis, such as sugar and organic acid, better resolutions can be obtained at elevated temperatures (50 to 80°C).Thus columns are generally kept inside the column oven.

Application-

- The method is used in determination of quality and consistency in soft drink.
- It is used for the assay of pharmaceutical drugs.[12]

5)High performance thin layer chromatography-

Principle-

The HPTLC works on the same principles as TLC such as the principle of separation is adsorption. The mobile phase or solvent flows through the capillary action. The analyses move according to their affinities towards the stationary phase (adsorbent). The higher affinity component travels slower towards the stationary phase.[10]

This technique is an advanced technology to TLC, with better efficiency and resolution, an auto sampler and automated visualization of spots and capability to allow for quantitative analysis. This technique does not use columns but rather, chambers which contain the separation plates.[20]

A low-affinity component travels rapidly toward the stationary phase. On a chromatographic plate, then, the components are separated.[11]

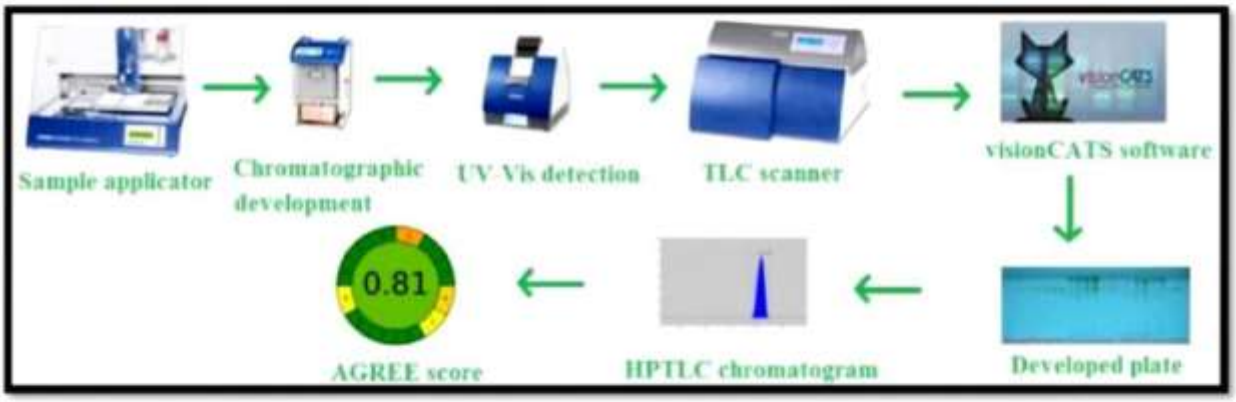

Fig.13 HPTLC

Procedure:-

1.Sample Preparation: This requires a highly concentrated solution since much less sample quantity needs to be applied. The plates solvents must be non-polar of the volatile type.

2.Selection of Chromatographic Layers: The layer of HPTLC is available in the form of very fine particle size silica gel pre-coats which is widely used as adsorbent.

3.Pre-Washing: To water vapor or volatile impurities, the plates must be cleaned. It may be clean with a suitable solvent such as methanol.

4. Conditioning: Plates are placed in an oven at 120 ° C for 15 to 20 minutes to perform conditioning.

5. Sample Application: The size of the sample spot is not greater than 1 mm in diameter. There are various methods for spotting samples in HPTLC. One is a self-loading capillary in which small quantities of samples can apply on the HPTLC plate.

6. Pre-Conditioning: Saturation is necessary for highly polar mobile phases although there is no need for saturation for low polarity mobile phases.

7. Mobile Phase of HPTLC: Through trial and error, the mobile phase of the suitable solvents is to be selective.

8. Chromatographic Development: The linear development method in high-performance thin-layer chromatography is the most common technique here the plate is positioned vertically

in an appropriate container with a solvent or mobile phase. The mobile phase is generally fed by capillary action and both sides may produce chromatograms.

9. Detection of spot and Scanning: The HPTLC instrument has attached to computer and data recording devices. The development of spots is viewed as peaks at wavelengths of selected UV regions.[10]

Applications-

- High-performance thin-layer chromatography is used to analysis of molecules in both qualitative and quantitative terms.
- HPTLC can estimate the concentration of components although TLC can only separate components.
- HPTLC can analyze a complex structure or a very small number of compounds.
- This method is used in the food industry to evaluate nutrients, beverages, vitamins, and pesticides in fruit, vegetables, and other foodstuffs.
- HPTLC is useful in forensic detection of substances, including adulteration, overdose, counterfeit drugs, and drug misuse.[11]

3)Purification techniques for isolated phytoconstituents

Phytoconstituents are defined as the chemical compounds that can be found naturally in plants.Examples of phytoconstituents are fats, sugars, tannins etc..[15]

Isolation and purification of phytoconstituents is the most difficult and complex operation in phytopharmaceutical research. Plant extracts are complex mixtures which contain hundreds or thousands of different constituents. Plant constituent's presence in a crude extract make the isolation and measurement of active constituents more difficult.[15]

Modern chromatographic techniques such as thin layer chromatography, column chromatography and high-speed counter-current chromatography are used for the isolation and purification of phytoconstituents.[15]

The identification and isolation of bioactive compounds from herbal extracts is the starting point for drug development for potentially new mechanisms against human diseases.[19] To purify, samples are subjected to a range of solvents of varied polarities and then separated using chromatographic techniques.[20]

1. **Thin layer chromatography:-**
   Thin layer chromatography (TLC) is one of the most common and easiest method for purifying components. It is a technique where a solute will undergo distribution between two phases: stationary phase and mobile phase.
   Example, the photosynthetic pigments can be extracted from kiwi fruit chloroplasts by breaking up the fruit tissue in a very small amount of suitable solvent. The different pigments can be separated by thin layer chromatography by usingdifferent solvent

mixture. Thin layer chromatography for the isolation of biologically active natural products.[15]

2. **Column chromatography:-**

   Column chromatography (CC) is useful in the isolation and purification of phytoconstituents.The phytoconstituents from the methanolic extract of Limoninacidosis can be isolated using column chromatography. The common name of Limoninacidosis is wood apple due to the hard shell of the fruit.[15]

3. **High-speed counter chromatography:-**

   High-speed counter-current chromatography (HSCCC) instrument is one of the types of counter-current chromatography apparatus. HSCCC also known as the hydrodynamic counter-current chromatography column. It uses liquid-liquid partition chromatographic technique or two-phase solvent system. It consists of stationary phase and mobile phase in where the liquid used for both of these phases should be immiscible solvents.

   High-speed counter-current chromatography (HSCCC) is suitable for the preparative isolation and purification of anthocyanins from the purple sweet potato (Ipomoea batatas). Anthocyanins are color pigments that can be found in plants and under the classification of flavonoids. Other phytoconstituents that can be isolated from HSCCC include purification of flavonoids from mulberry leaves and isolation and purification of isoflavones from Pueraria lobata.[15]

Some other techniques for purification of phytoconstituents are:-

1)Acid-base extraction: This method is of liquid-liquid extraction type, typically used to separate organic compounds based on their acid-base properties. The process is based on the hypothesis that most organic compounds are more soluble in organic solvents than water. The compounds containing acidic or basic functionalities can easily be converted into cations or anions, either by adding acid or base making them more soluble in water.[16]

2) Crystallization: It is a unique separation technique used to obtain purified compounds out of the super-saturated liquid. For natural crystallization, the plant extract is dissolved in sparingly soluble solvent, in which heat is used to dissolve the extract.[16]

3)Sublimation: Sublimation is one of the phase transitions of a solid substance to gaseous state without passing through liquid state. It is an endothermic process that occurs at temperatures and pressures below a substance's triple point in its phase diagram. The reverse process of sublimation is deposition or DE sublimation, in which a substance passes directly from a gas to a solid phase, crystallized on a cold surface.[16]

4) Liquid-liquid partitioning extraction (LLC): In general, liquid-liquid partitioning is the most efficient method for doing repeated extractions. This indicates that the separation features of extraction systems may be translated to liquid-liquid chromatography. The practically infinite number of phase systems available in LLC is a significant benefit such as the ability to retain and to select a precise blend of components. The analytesare partitioned between two immiscible solutions with differing polarities in LLC.[16]

Methods for standardization of herbal drugs

Standardization:-

Standardization of drug means confirmation of its identity and determination of its purity and detection of nature of adulterant by various parameters like morphological, microscopical, physical, chemical and biological observations.

Standardization is numerical value or specify property that quantifies the purity and quality of drugs and formulations.[3]

Importance of standardization:-

- Standardization is the process of setting quality parameters.
- Standardization gives rise to uniformity and consistency in quality of product.
- Properly standardized formulations are more effective with fewer side effects.[13]
- Reduces the variations of the process and improve the quality of product and processes.[3]

Need of Standardization:-

Modern system of medicine is based on sound experimental data, toxicity studies and human clinical studies. But, Pharmacopeial standards on raw material / finished products are not available. CGMP for herbal industry are not well defined nor the barest minimum standards of medicinal plant products are maintained or regulated.

The lack of quality standards has resulted in mild to serious adverse effects ranging from hepatic toxicity to death. Hence, herbal ingredients require for determining the identity, purity and quality and have to be technically sufficient, rapid and cost effective with GMP equipment's.

World health organization has set specific guidelines for the assessment of safety, efficacy and quality of herbal medicines. Standardization of herbal drug is not an easy task as numerous factors influence the bio efficacy, reproducible therapeutic effect. In order to obtain quality oriented herbal product care should be taken right from the proper identification of plants, season, area of collection, their extraction and purification and rationalizing the combination in case of polyherbal drugs.[14]

WHO Guidelines:-

1) Quality control of crude drugs:- Material, plant preparations and finished products.
2) Stability assessment and shelf life.
3) Safety assessment:- Documentation of safety based on experience or toxicological studies.
4) Assessment of efficacy:- By ethnomedicalinformation's and biological activity evaluations.

The bioactive extract should be standardized on the basis of active principles or major compounds along with the chromatographic fingerprints (TLC, HPTLC, HPLC, and GC).

1) Quality Control of Herbal Drugs

Quality control for efficacy and safety of herbal products is of paramount importance. Quality can be defined as the status of a drug that is determined by identity, purity, content, and other chemical, physical, or biological properties, or by the manufacturing processes. Quality control is a term that refers to processes involved in maintaining the quality and validity of a manufactured product. The term "herbal drugs" denotes plants or plant parts that have been converted into phytoconstituentsby means of simple processes involving harvesting, drying, and storage . Hence, they are capable of variation. This variability is also caused by differences in growth, geographical location, and time of harvesting.

2) Stability Assessment and Shelf Life

The past decade has seen a significant increase in the use of herbal medicines. As a result of WHO promotion of traditional medicine, countries have been seeking the assistance of the organization in identifying safe and effective herbal medicines for use in national health care systems. It is recommended that in case of an herbal medicinal product containing a natural product or an herbal drug preparation with constituents of known therapeutic activity, the variation in component during the proposed shelf-life should not exceed ± 5% of the initial assay value, unless justified to widen the range up to ±10 per cent or even higher.

3) Safety assessment

Herbal medicines are generally regarded as safe based on their long use in various cultures. However, there are case reports of serious adverse events after administration of herbal products. In a lot of cases, the toxicity has been traced to contaminants and adulteration. However, some of the plants used in herbal medicines can also be highly toxic. As a whole, herbal medicines can have a risk of adverse effects and drug-drug and drug-food interactions if not properly assessed. Assessment of the safety of herbal products, therefore, is the first priority in herbal research. These are various approaches to the evaluation of safety of herbal medicines.

4) Assessment of toxicity

Toxicity investigation will also be required because the analysis alone is unlikely to reveal the contributions to toxicity itself. In assessing toxicity of an herbal medicine, the dose chosen is very important. Toxicity assessment involves one or more of the following techniques- In vivo techniques, in vitro techniques, cell line techniques, micro- array and other modern technique Standardization techniques to adequately model toxicity.

5) Assessment of efficacy

Herbal medicines are inherently different from conventional pharmacological treatments, but presently there is no way to assess their efficacy other than by currently used conventional clinical trial methodologies, in which efficacy is conventionally assessed by clinical, laboratory, or diagnostic outcomes: Clinical outcomes include meters such as improved morbidity, reduced pain or discomfort, improved appetite and weight gain, reduction of blood pressure, reduction of tumorsize or extent, and improved quality of life.[14]

Standardization and quality control parameters for evaluation of herbal crude drugs

Macroscopic Examination: In case of whole drugs, the macroscopic and secondary characters are sufficient for identification of right variety and search of adulterants.

Microscopic Examination: These are valuable both for powders and ungrounded drugs for identification of right variety and search of adulterants.

Solubility: The solubility, especially exceptional behavior toward solvent, is useful in examination of many oils and olio - resins.

Physical Constituents: Physical constituents such as specific gravity, optical rotation, viscosity and refractive index are especially valuable for the evaluation of facts, oleo resins, balsams and similar substances.

Foreign Organic Matter: Remove off matter other than source plant to get the drug in pure form.

Swelling Index: It measures the swelling property of the medical plant.

Ash Values: It is criteria to judge the identity and purity of crude drug - total ash, sulfated ash, water soluble ash and acid insoluble ash etc.

Extractive Values: These are indicating the approximate measure of chemical constituents of crude drug.

Moisture Content: To check moisture content helps prevent degradation of product.

Crude Fiber: To determine excessive woody material. Criteria for judging purity.

Chromatographic examination: Include identification of crude drug based on use of majorchemical constituent as marker.

Qualitative Chemical Evaluation: Covers criteria for identification and characterization of crude drug with respect to phytochemical contents.

Quantitative Chemical Evaluation: Covers criteria to estimate the number of active constituents.

Volatile Oils: It covers the measurement of the volatile content of the plant.

Bitterness Value: The bitter properties of plant material are determined by comparing the threshold bitter concentration of an extract of the materials with that of a dilute soluble of guanine hydrochloride R.

Hemolytic Activity: The hemolytic activity of plant materials, or a preparation containing saponins, is determined by comparison with that of a reference material, saponin R.

Foaming Index: The foaming ability of an aqueous decoction of plant materials and their extracts is measured in terms of a foaming index

Pesticide Residues: It measures the pesticide residues in the plant.

Arsenic and heavy metals: Contamination of medicinal plant materials with arsenic and heavy metals can be attributed to many causes including environmental pollution and traces of pesticides.

Microorganisms: Current practices of harvesting, handling and production may cause addition contamination and microbial growth.

Aflatoxins: Minute presence in crude drug can be toxic and hence their presence is being tested.

DNA Fingerprinting: Technique is useful for identification of phytochemically indistinguishable genuine drug from substituted or adulterated drug.

Chemical Fingerprinting: To allow the detection of all the components in extracts.

Biological Profiling: It identifies the biological active plants allowing highly sophisticated standardization and quality control.

Radioactive Contamination: A certain amount of exposure to ionizing radiation cannot be avoided since they are many sources, including radio nuclides occurring naturally in the ground and the atmosphere.[17]

CONCLUSION

Plant materials are used throughout the developed and developing world as home remedies, in over-the-counter drug products, and as raw material for the pharmaceutical industry.Plants, herbs, and ethnosbotanicals have been used since the early days of humankind and are still used throughout the world for health promotion and treatment of disease. Plants and natural sources form the basis of today's modern medicine and contribute largely to the commercial drug preparations manufactured today. About 25% of drugs prescribed worldwide are derived from plants. Still, herbs, rather than drugs, are often used in health care. For some, herbal medicine is their preferred method of treatment. For others, herbs are used as adjunct therapy to conventional pharmaceuticals. However, in many developing societies, traditional medicine of which herbal medicine is a core part is the only system of health care available or affordable. Regardless of the reason, those using herbal medicines should be assured that the products they are buying are safe and contain what they are supposed to, whether this is a particular herb or a particular amount of a specific herbal component. Consumers should also be given science-based information on dosage, contraindications, and efficacy. To achieve this, global harmonization of legislation is needed to guide the responsible production and marketing of herbal medicines. If sufficient scientific evidence of benefit is available for an herb, then such legislation should allow for this to be used appropriately to promote the use of that herb so that these benefits can be realized for the promotion of public health and the treatment of disease.

Cost of some operational apparatus and equipment may be a limiting factor in extraction and isolation. A combination of simpler and cheaper methods could overcome this limitation. Due to a variety of compounds in plants for potential drug development, a single method may not be ideal to extract and to isolate them. Sometimes, efficiency may be achieved when two or more methods at the extraction and isolation stages are combined. Structural elucidation is already done in combination of various techniques for meaningful interpretation of spectral data. However, there is need for a single robust piece of equipment that can do all the techniques at once to determine structures of compounds.

The limitation to this work was that it did not include quick test methods available commercially on the market. This limitation does not affect the methods described because even the quick test methods still employ fundamentals described in this report.

In conclusion, there is a clear and increasing interest in the extraction and isolation of natural products and their advantageous applications. The specific applications are also conditioning the employed extraction methods and novel stationary phases and mobile phases to be used by these techniques. It is thus expected that these trends will be maintained in the near future as they are mostly motivated by emerging consumer demands and by safety, environmental and regulatory issues.

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