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Review

Review of extraction of medicinal plants for pharmaceutical research

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Abstract

Techniques of maceration, percolation and infusion have been traditionally used for making galenicals and tinctures from medicinal and aromatic plants (MAPs). This article describes the underlying principles and mechanisms of these extraction techniques, and discusses the various modifications made for the small- and large-scale extraction of MAPs, the factors affecting the selection of extraction process, and the quality of the extracts produced.

Keywords: Extraction process, Medicinal plants, Phytochemicals, Thermolabile

INTRODUCTION

A natural product is a chemical compound or substance produced by a living organism that is found in nature. Natural products that can be isolated or produced from plants are called phytochemicals. They are non-nutritive but are needed by plants for purposes such as disease and pathogen defence and control. Studies have shown that phytochemicals are important in human health. This is because they display different biological activities such as anti-oxidant, anti-inflammatory, anti-cancer and anti-bacterial activities. Most of these biochemicals are ingested in food such as fruits, vegetables and whole grains. This is why people are advised to eat more fruits and vegetables so that they can prevent many health conditions such as cancer, diabetes, high blood pressure and cell ageing. Main phytochemicals falls under two broad categories which are flavonoids and caretonoids. However some important phytochemicals, especially ones in traditional medicinal plants, are not available to people as they do not eat these plants. Ways in which these phytochemicals can be extracted from the said plants thus have to be devised to make the chemicals available for use.

Phytochemical extraction techniques follow a more or less standard protocol. A typical phytochemical extraction procedure is as follows:

Homogenisation

Homogenisation is synonymous to size reduction. This is where plant tissues and cells are disrupted so that they release the chemicals. This is mainly done using pestle and mortar under liquid nitrogen. Plant tissues can also be air dried usually at room temperature in well aerated room temperatures and then the dry tissue is crushed using pestle and mortar. The disruption gives the samples more surface area for extraction.

Extraction of medicinal plants

What follows what can be referred to as the actual extraction. This is where the homogenised plant tissue is immersed in a solvent. Different solvents can be used depending on the kind of phytochemicals that are targeted for extraction. Solvents differ in polarity, just like phytochemicals. There are three polarity strengths of solvents and they are polar, medium-polar and non-polar. Polar solvents will extract polar chemicals and the same is true for non-polar solvents. Polar solvents include methanol, ethanol and water, medium-polar solvents examples are ethyl acetate, acetone and dichloromethane and non-polar solvents include toluene, chloroform and hexane. Thus in a sample, different solvents can be mixed for extraction or they can be used in sequence in the same sample material.

Extraction efficiency

Extraction efficiency can be aided by what is referred to

as different extraction methods; the most simple and easy to use of these methods are maceration, hydro distillation using steam and soxhlet extraction. In maceration, the homogenised plant sample is soaked in a solvent in a closed container and it is left at room temperature. The solvent is then decanted and filtered to remove debris. In hydro distillation the plant sample, which can be dry or wet, is placed in a flask and immersed in water. The flask is then connected to a condenser and heated. The distillate is collected in a tube that is connected to the condenser. It comes out as a mixture of oils and water and they are collected separately. Hydrodistillation is good for extraction of volatile phytochemicals. For soxhlet extraction, the homogenised plant sample is placed in a cellulose thimble in an extraction chamber. The chamber is then placed on top of a collection flask which is placed beneath a condenser. A solvent of choice is then added to the sample which gets heated up under reflux. The condensed solvent with extracts is collected in the flask underneath. There are other extraction methods that can be used such as sublimation, percolation, ultrasound-assisted extraction and so on that are not discussed in this note.
After extraction, to concentrate the extracts, the extract is left open at room temperature, ideally in a fume hood to evaporate the solvent. Then afterwards a measured volume of solvent can be used to dissolve the extract to required working concentrations. The extract is then used for metabolic profiling and also tested for different biological activities or any other analysis as required.

Medicinal plant extracts

Extraction, as the term is used pharmaceutically, involves the separation of medicinally active portion of plant or animal tissues from the inactive or inert components by using selective solvents in standard extraction procedures. The products so obtained from the plants are relatively impure liquids, semisolids or powders intended only for oral or external use. These include classes of preparation known as decoctions, infusions, fluid extracts, tinctures, pilular (semisolid) extracts and powdered extracts. Such preparations popularly have been called galenicals named after Galen, the second century Greek physician. The purpose of standardized extraction procedures for crude drugs is to attain the therapeutically desired portion and to eliminate the inert material by treatment with a selective solvent known as menstruum. The extract thus obtained may be ready for use as a medicinal agent in the form of tinctures and fluid extracts, it may be further processed to be incorporated in any dosage form such as tablets or capsules, or it may be fractionated to isolate individual chemical entities such as ajmalicine, hyoscine and vincristine which are modern drugs. Thus standardization of extraction procedures contributes significantly to the final quality of the herbal drug.

General Methods of Extraction of Medicinal Plants

Maceration

In this process, the whole or coarsely powdered crude drug is placed in a stoppered container with the solvent and allowed to stand at room temperature for a period of at least three days with frequent agitation until the soluble matter has dissolved. The mixture then is strained, the marc (the damp solid material is pressed, and the combined liquids are clarified by filtration or decantation after standing.

Digestion

This is a form of maceration in which gentle heat is used during the process of extraction. It is used when moderately elevated temperature is not objectionable. The solvent efficiency of the menstruum is thereby increased.

Infusion

Fresh infusions are prepared by macerating the crude drug for a short period of time with cold or boiling water. These are dilute solutions of the readily soluble constituents of crude drugs.

Decoction

In this process, the crude drug is boiled in a specified volume of water for a defined time; it is then cooled and strained or filtered. This procedure is suitable for extracting water-soluble, heat-stable constituents. This process is typically used in preparation of Ayurvedic extracts. The starting ratio of crude drug to water is fixed, e.g. 1:4 or 1:16; the volume is then brought down to one-fourth its original volume by boiling during the extraction procedure. Then, the concentrated extract is filtered and used as such or processed further.

Percolation

This is the procedure used most frequently to extract active ingredients in the preparation of tinctures and fluid extracts. A percolator (a narrow, cone-shaped vessel open at both ends) is generally used (Figure I). The solid ingredients are moistened

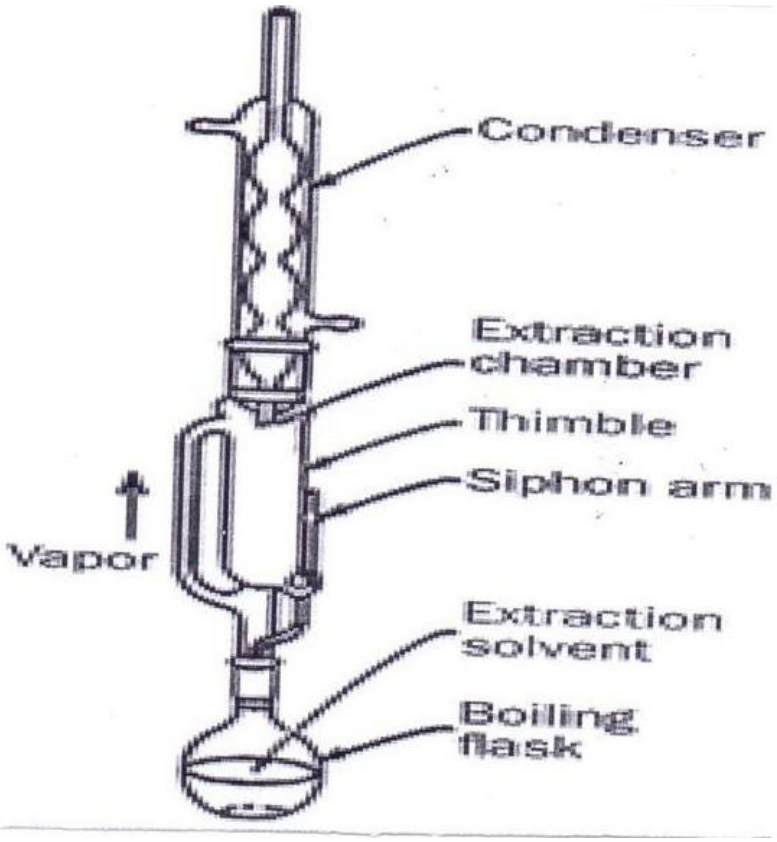

Figure 1. Soxhlet apparatus

with an appropriate amount of the specified menstruum and allowed to stand for approximately 4 h in a well closed container, after which the mass is packed and the top of the percolator is closed. Additional menstruum is added to form a shallow layer above the mass, and the mixture is allowed to macerate in the closed percolator for 24 h. The outlet of the percolator then is opened and the liquid contained therein is allowed to drip slowly. Additional menstruum is added as required, until the percolate measures about three-quarters of the required volume of the finished product. The marc is then pressed and the expressed liquid is added to the percolate. Sufficient menstruum is added to produce the required volume, and the mixed liquid is clarified by filtration or by standing followed by decanting.

Hot Continuous Extraction (Soxhlet Extraction)

Conventional Solvent Extraction

Principles and Mechanisms

Classic techniques for the solvent extraction of active constituents from medicinal plant matrices are based on the choice of solvent coupled with the use of heat or agitation. Existing classic techniques used to obtain active constituents from plants include: Soxhlet, hydrodistillation and maceration with an alcohol-water mixture or other organic solvents. Soxhlet extraction is a general and well-established technique, which surpasses in performance other conventional extraction techniques except for, in limited fields of application, the extraction of thermolabile compounds.

In a conventional Soxhlet system, as shown in Figure 1, plant material is placed in a thimble-holder, which is filled with condensed fresh solvent from a distillation fl ask. When the liquid reaches the overflow level, a siphon aspirates the solution of the thimble- holder and unloads it back into the distillation flask, carrying extracted solutes into the bulk liquid. Solute is left in the flask and fresh solvent passes back into the plant solid bed. The operation is repeated until complete extraction is achieved.

Advantages of Soxhlet Extraction

I. The displacement of transfer equilibrium by repeatedly bringing fresh solvent into contact with

Table 1. Some common solvents used for the extraction of medicinal and aromatic plants

Solvent	Boiling point (°C)	Miscibility with HO	Threshold limit values (ppm)
Acetone	56	∞	1000
Acetic acid	116 – 117	∞	10
Ethyl acetate	77	80%	400
Benzene	80	<0.01	25
2-Butanol	79.5	19%	2200
Cyclohexane	80.7	<0.01	300
Dichloromethane	39.7	1.35	2200
Choroform	61	8%	10
Carbon tetrachloride	765.77	0.8%	50
Hexane	69	<0.01%	-
Ethyl ether	34.6	1.2%	400
Petrol ether	30-50	-	500
Propanetriole	290*	∞	-
Methanol	64.7	∞	200
1-Propanol	91	M	400
2-Propanol	82.4	M?	400
Toluene	110.6	0.06	100

*With decomposition; M miscible; ∞ completely miscible

the solid matrix.
2.Maintaining a relatively high extraction temperature with heat from the distillation flask.
3. No filtration of the extract is required.

Disadvantages of Soxhlet Extraction

1. Agitation is not possible in the Soxhlet device.
2. The possibility of thermal decomposition of the target compounds cannot be ignored as the extraction usually occurs at the boiling point of the solvent for a long time. Worldwide, most of the solvent extraction units are based on the Soxhlet principle with recycling of solvents. Basic equipment for a solvent extraction unit consists of a drug holder-extractor, a solvent storage vessel, a reboiler kettle, a condenser, a breather system (to minimize solvent loss) and supporting structures like a boiler, a refrigerated chilling unit and a vacuum unit. (Figure 1, Table 1)

Accelerated Solvent Extraction

Principles and Mechanisms

Accelerated solvent extraction (ASE) is a solid-liquid extraction process performed at elevated temperatures, usually between 50**O** and 200°C, and at pressures between 10 and 15 MPa. Therefore, accelerated solvent extraction is a form of pressurized solvent extraction. Increased temperature accelerates the extraction kinetics and elevated pressure keeps the solvent in the liquid state, thus achieving safe and rapid extraction. Also, high pressure allows the extraction cell to be filled faster and helps to force liquid into the solid matrix. A typical accelerated solvent extraction system is illustrated in Figure 2. Although the solvent used in ASE is usually organic, pressurized hot water can also be used. In these cases, one refers to pressurized hot water extraction or sub-critical water extraction.

Advantages and Disadvantages of Accelerated Solve Extraction

Compared with traditional Soxhlet extraction, ASE presents a dramatic reduction in the amount of solvent and extraction time. Particular attention should be paid to ASE performed at high temperature, which .may lead to degradation of thermolabile compounds.

Parameters for Selecting an Appropriate Extraction Method

i) Authentication of plant material should be done before performing extraction. Any foreign matter should be completely eliminated.
ii) Use the right plant part and, for quality control purposes, record the age of plant and the time, season and place of collection.
iii) Conditions used for drying the plant material largely depend on the nature of its chemical constituents. Hot or cold blowing air flow for drying is

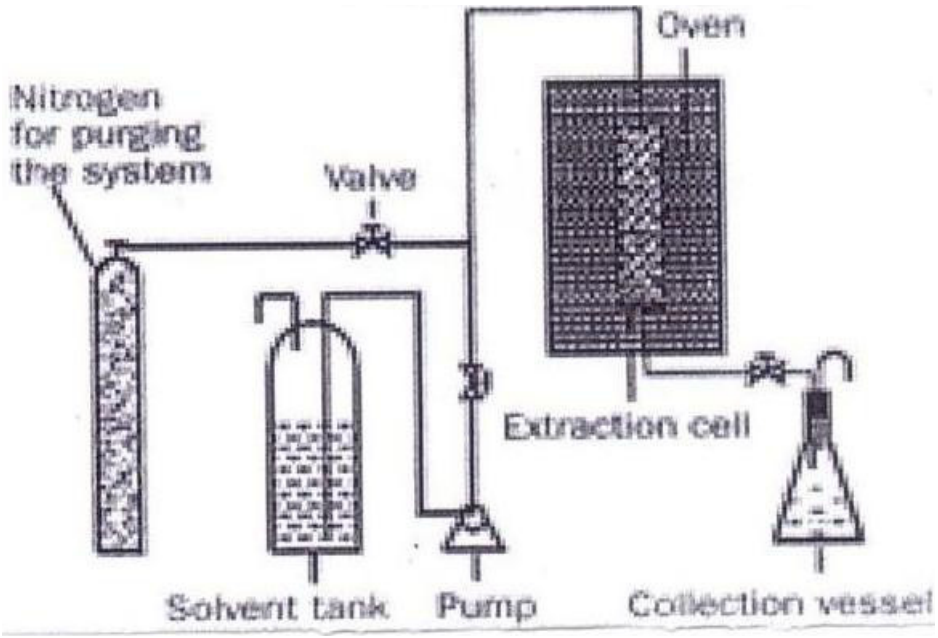

Figure 2. Accelerated Solvent Extraction

generally preferred. If a crude drug with high moisture content is to be used for extraction, suitable weight corrections should be incorporated.
iv) Grinding methods should be specified and techniques that generate heat should be avoided as much as possible.
v) Powdered plant material should be passed through suitable sieves to get the required particles of uniform size. vi) Nature of constituents:
a) If the therapeutic value lies in non-polar constituents, a non-polar solvent may be used. For example, lupeol is the active constituent of *Crataeva nurvala* and, for its extraction, hexane is generally used. Likewise, for plants like *Bacopa monnieri* and *Centella asiatica,* the active constituents are glycosides and hence a polar solvent like aqueous methanol may be used.
b) If the constituents are thermolabile, extraction methods like cold maceration, percolation and are preferred.
For thermostable constituents, Soxhlet extraction (if nonaqueous solvents are used) and decoction (if water is the menstruum) are useful.
c) Suitable precautions should be taken when dealing with constituents that degrade while being kept in organic solvents, e.g. flavonoids and phenyl propanoids.
d) In case of hot extraction, higher than required temperature should be avoided. Some glycosides are likely to break upon continuous exposure to higher temperature.
e) Standardization of time of extraction is important as:
• Insufficient time means incomplete extraction.
• If the extraction time is longer, unwanted constituents may also be extracted. For example, if tea is boiled for too long, tannins are extracted which impart astringency to the final preparation.
f) The number of extractions required for complete extraction is as important as the duration of each extraction.
vii) The quality of water or menstruum used should be specified and controlled.
viii) Concentration and drying procedures should ensure the safety and stability of the active constituents. Drying under reduced pressure (e.g. using a Rotavapour) is widely used. Lyophilization, although expensive, is increasingly employed.
ix) The design and material of fabrication of the extractor are also to be taken into consideration.
x) Analytical parameters of the final extract, such as TLC and HPLC fingerprints, should be documented to monitor the quality of different batches of the extracts.

Factors Affecting Selection of an Extraction Process

1.Nature of the drug: The selection of an extraction process mainly depends on the physical nature of the drug. (Table 2)
2. Cost of the drug
Costly drugs are extracted by percolation whereas cheaper drugs may be extracted by maceration. Cost involve in reduction (i.e. comminuting) of the drug should also be taken into consideration.
3.Stability of drugs

Table 2. Physical nature of the drug

Physical nature of the drug	Extraction procedure
Hard and woody	By percolation
Soft drugs	By maceration
Unorganized drug	By maceration and not by percolation because it may block the percolator

Table 3. Examples of maceration, percolation, infusion and decoction

Extraction Methods	Examples
A. MACERATION	i) Tincture of Orange
i) Simple maceration	ii) Tincture of Lemon
	iii) Tincture of Squill
ii) Maceration of unorganized drug /Mace-ration with adjustment	i)Tincture of Tolu Balsam ii)Compound Tincture of Benzoin
iii) Multiple Maceration	
a)Double maceration	i)Concentrated Infusion of orange ii)Concentrated Infusion of chirata
b)Triple maceration	iii)Concentration Infusion of gentian
	i)Concentrated Infusion of Quasela ii)Concentrated Infusion of Senna
B. PERCOLATION	i)Tincture of Belladona
i)Simple percolation	ii)Compound tincture of cardamom iii)Strong tincture of ginger etc Liquid extract of Liquorice
ii)Reserved percolation	i)Cantherdin from cantharides
iii)Continuous hot percolation/Soxhlation	ii)Alkaloids from seeds
C. INFUSION	Frsh Infusion of Quasela
i)Fresh Infusion	i)Concentrated compound Infusion of chirata
ii)Concentrated Infusion	ii)Concentrated compound Infusion of gentian
D. DECOCTION	No official preparations in IP or BP

Table 4. Difference between maceration and Decoction

Maceration	Decoction
1.Menstruum may be water or hydro-alcoholic solvent	Menstruum is water
2. The crude drug is macerated for 3-7 days	Just 10 to 15 minutes is required to complete the process
3.The drug is kept in contact with cold or warm menstruum.	Boiling water is passed through the crude drug
4. After extraction the marc is expressed	After extraction the marc is not expressed
5. Extra menstruum is not added to make up the required volume.	Extra menstruum is passed through the extracted drug to make up the volume
4. Alcohol acts as a preservative, hence it may be dispensed after 24 hours also	A freshly prepared decoction should be taken within 24 hours because microorganisms may grow in aqueous medium

Continuous hot extraction process should not be used for those drugs containing thermolabile active constituents.

5. Therapeutic value of the drug

The drug containing flavouring agents or bitter etc which does not have much therapeutic value may be extracted by maceration; but if the drug has considerable therapeutic value then percolation process should be used.

6. Nature of solvent

If the solvent is water maceration is generally adopted but, if the solvent is volatile then percolation process should be used.

7. Concentration of the product

Dilute preparations such as tinctures may be prepared by maceration but, concentrated preparations such as; liquid extracts should be prepared by percolation or reserved percolation process. (Table 3-4)

CONCLUSION

The spectrum of constituents obtained by steady-state extraction (simple maceration) differs from that obtained by exhaustive extraction (percolation). With maceration, one can achieve a spectrum of constituents similar to that of percolation. Different extraction procedures may be considered to be equivalent if they respect critical quality parameters and if the analysis of numerous production batches confirms their compliance with standards.

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