



## Techniques Adopted for Extraction of Natural Products

### Extraction Methods: Maceration, Percolation, Soxhlet Extraction, Turbo distillation, Supercritical Fluid Extraction

Komal Patel, Namrata Panchal, Dr. Pradnya Ingle\*

Associate Professor Department of Chemical Engineering, Shivajirao S. Jondhale College of Engineering, Dombivli (East), 421201, University of Mumbai, India.

**\*Corresponding Author:** Pradnya Ingle, Associate Professor, Department of Chemical Engineering, Shivajirao S. Jondhale College of Engineering, Dombivli (East), 421201, University of Mumbai, India.

**Abstract:** From thousands of years there has been great importance of Natural Medicines. Natural products are important sources for pharmaceutical industries. There are wide variety of natural products with wide range of application and is considered as boon to Ayurvedic study. These days, the use of bioactive natural products in medicines is quite low and decreasing day by day. So, it is very significant to develop effective method of Extraction of Natural Products. In this paper, Extraction methods for Natural products are explained in brief along with their applications.

**Keywords:** Natural medicines, Natural products, Extraction methods, Applications.

#### 1. INTRODUCTION

From olden days diseases were alleviated and treated with the help of natural products obtained from plants, animals, micro-organisms. The use of natural extracts for medicinal use is from about 60,000 years back. From early times, Extraction of Natural products has presented great challenges and has developed a positive impact on the development of human civilization. These Extracts not only provide primary treatment of health in developing countries, but have attracted the developed countries due ever increasing health care cost. About most of the population use natural medicines for the treatment and prevention purpose [1]. From about 80 years, almost 50% of chemical drugs approved by FDA are inspired and derived by natural products [2, 3]. In terms of chirality, functional groups and structural complexity, natural products show more drugs like features [4, 5].

The quantity of Natural products obtained from sources is fairly low. The intensive and time consuming extraction and separation process has been the disadvantage for the application in drug. So, there is a need to develop extraction methods and isolation process. A comprehensive review on classification of natural products, variety of methods for extraction, application of extracts is provided in this paper.

#### 2. NATURAL PRODUCTS

Natural Products are found in wide range of diversity and with mutli-dimensional chemical structures, also use of natural products are biological function modifiers has also been developed. There are sequential development of application of natural products in the drug production and has advanced chemicobiology [6-8]. These extracts are prepared by chemical synthesis and the applications extended to commercial use such as dietary supplements, cosmetics, food products without artificial reagents.

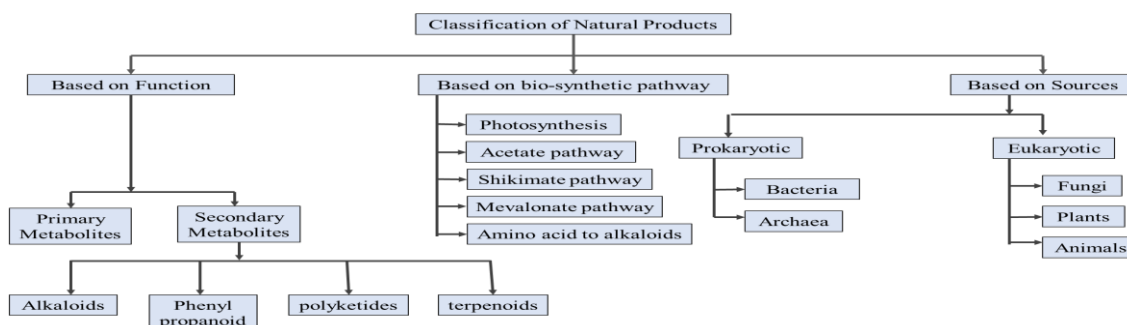
In recent years, the cancer treatment is influenced with the natural products. The 52% anti-cancer of the drugs are derived from the natural products. The examples are terpene pacticaxel from *Taxus baccata* and Vinca alkaloids from *Cantharanthus roseus* are the anticancer drugs derived from plants [9,10]. Numerous and varied biological targets are achieved due to the meaningful and interesting development of natural products and some of them are very important in health care system [11,12,13]. For example, small molecules from plants, animals and microorganisms play an important role in

discovery of drugs. Between the period 2005-07 there were 69 small molecules discovered, amongst 13 were natural products which were important in drug development [9, 14].

### 3. CLASSES

Natural products are anything that is produced by life [15, 16]. Based on the sources they are classified as biotic materials (e.g. wood, silk), bio-based materials (e.g. bioplastics, cornstarch), bodily fluids (e.g. milk, plant exudates), and other natural materials (e.g. soil, coal). These extracts can be defined as organic compound that is synthesized by living organisms [17].

These are also classified based on biosynthetic pathways, biological function, etc.



#### 3.1. Classification Based on Function

There are two major classes of Natural products based on function namely, Primary Metabolites and Secondary Metabolites [18, 19]. The metabolites that have an intrinsic function are the primary metabolites i.e. the survival of organisms that produce them. The metabolites that have an extrinsic function that mostly affect the organisms.

##### 3.1.1. Primary Metabolites

The components having basic metabolic which are essential or life. These have important cellular functions such as energy production, nutrient assimilation and growth/development. Carbohydrates, lipids, amino acids and nucleic acids are included in primary metabolites [20]. Those metabolites involved with production of energy include photosynthetic and respiratory enzymes. Enzymes comprise of amino acid and non-peptide cofactors [21]. The basic structure of organisms and cells comprise of primary metabolites. These include cell walls (e.g. peptidoglycan, chitin), cell membrane (e.g. phospholipids) and cytoskeleton (proteins) [22].

The following table (Table3.1.) represents the primary metabolite enzymatic cofactors. It basically includes the members of vitamin B family.

**Table3.1.**

VITAMIN	COENZYME	CONSTITUENTS and FUNCTION
Vitamin B1	Thiamine diphosphate	Pyruvate dehydrogenase, 2-oxyglutarate dehydrogenase and transketolase which are involved in carbohydrate mechanism
Vitamin B2	FMN and FAD	riboflavin which are necessary for many redox reaction.
Vitamin B3	NAD <sup>+</sup> and NADP <sup>+</sup>	Nicotinic or niacin which are required in electron transport in Kreb's Cycle, Oxidative Phosphorylation and many other reactions.
Vitamin B5	Coenzyme A	Pantothenic acid which are the basic components of carbohydrate and amino acid mechanisms.
Vitamin B6	Transaminases	Pyridoxol, pyridoxal and pyridoxamine which involve in amino acid mechanisms.
Vitamin B12	Enzyme containing corrin ring	cobalamines

Nucleic acid primary metabolites include DNA and RNA that stores genetic information [21].

Signaling molecules are the first messengers that control the metabolism and do the function of cellular differentiation. The signaling molecules include factors that are composed of biogenic amines, peptides, steroid hormones, gibberellins, auxins, etc. these first messenger with the help of cellular receptors activate the secondary receptors which convey the extracellular message to intracellular targets. Cyclic nucleotides, diacyl glycerol are included in the signaling molecules [23].

### 3.1.2. Secondary Metabolites

Secondary metabolites are not essential for survival and dispensables. There is limited Species distribution of secondary metabolites. These metabolites are regarded as waste products without physiological functions for plant. The compounds of secondary metabolites are classified into four groups according to the biosynthetic origin such as, alkaloids, phenylpropanoids, polyketides and terpenoids.

#### 3.1.2.1. Alkaloids

The naturally occurring compounds that contain nitrogen as a base are alkaloids. Some neutral [24]and weakly acidic compounds are also present in alkaloids [25]. Elements such as C, H, N along with O, S and rarely Cl, Br and P are found in alkaloids [5]. Fungi, Bacteria, plants and animals are the sources of alkaloids.

Alkaloids have wide range of pharma applications as shown in the table3.2. [26-30]

**Table3.2.**

Disease	Alkaloids used for treatment
Anticancer	Homoharringtonie
Cholinomimetic	Galantamine
Vasodilatory	Vincamine
Analgesic	Morphine
Antibacterial	Chelerythrine

#### 3.1.2.2. Phenylpropanoid

These are the organic compounds synthesized from plants (i.e. amino acids phenylalanine and tyrosine) [1]. These names are derived by phenyl group and propene tail of coumaric acid. Coumaric acid is the central intermediate in biosynthesis of phenylpropanoid. The natural productsconsisting of phenylpropanoid are found throughout the plant kingdom. Hence in plants they provide protection against UV light, herbivores and pathogens and mediate plant pollinators attraction as floral pigment and fragrant compounds.

Some Examples of Phenylpropanoid are given in the table shown below (Table3.3).

**Table3.3.**

PHENYLPROPANOID	EXAMPLES	APPLICATION
Hydroxycinnamic acids	Tyrosine	Precursor to Neuro transmitter used in pharmaceutical industry, dietary supplements and food additives.
Cinnamic aldehyde and monolignols	Safrole	Used in synthesis of insecticide, in drug industries, toothpaste, soap,etc.
Coumaric and flavonoids	Umbelliferone	Used as screen agent.

#### 3.1.2.3. Polyketide

Large group matabolites containing alternate carbonyl and methylene group are called as polyketide. These have antimicrobial properties. Generally synthesized in Bacteria, Fungi, Plants and certain marine Animals.

Examples: Polyether are used in antibiotic monensin, Macrolides used in insecticides, etc.

#### 3.1.2.4. Terpenoids

These are the muti-cyclic structures containing oxygen groups are terpenoids. Flavours to cinnamon, ginger, and cloves, yellow colour to sunflower and red colour to tomatoes are contributed by terpenoids

### 3.2. Classification Based on Biosynthetic Pathways

The classes of natural products are as follows [31, 32]:

- Photosynthesis
- Acetate Pathway
- Shikimate Pathway
- Mevalonate Pathway
- Amino acid to alkaloids

### 3.3. Classification Based on Sources

Natural products can be extracted from tissues, cell, plants, animals, etc. the extracted product from any of this sources differ in properties and chemical constituents [33].

#### 3.3.1.1. Prokaryotic

- Bacteria

These produce anti-infective natural products

Examples [34-36]:

**Table3.4.**

BACTERIA	DRUG CONSTITUENT ITS AND USES
Streptomycin griseus	Streptomycin, used as antifungal and anti-microbial agents
Clostridium botulinum	Botulinum toxin, used as anti-infectives
Paenibacillus polymyxa	Polymyxins
Rifamycins	Amycolatopsis rifamycinica

- Archaea

In extreme environment like polar region, acidic springs, hot springs, and deep oceans are adapted by Archaea and their enzymes are functional in unusual condition. Generally used in food, pharmaceutical and chemical industries.

Examples: amylases, cellulases, xylanases, alcohol dehydrogenase, etc.

#### 3.3.2. Eukaryotic

- Fungi

Example [37, 38, 32]:

**Table3.5.**

ARCHAEA	DRUG CONSTITUENTS AND ITS USES
Penicillium chrysogenum and Cephalosporium acremonium	Cephalosporins, used as antibacterial drug
Griseofulvin	Penicillium griseofulvum, used as antifungal drug
Pleurotus ostreatus	Lovastatin, used in drug for lowering the cholesterol levels

- Plants

Source of natural products from plants are complex and diverse structure chemical compounds i.e. phytochemicals.

Classes of photochemical are phenol, polyphenols, tannins, terpenes and alkaloids [39].

Example [40-42]:

**Table3.6.**

PLANT SPECIES	PRODUCTS	USES
Taxus brevifolia and Cephalotaxus harringtonii	Paclitaxel and omacetaxine mepesuccinate	Anticancer agent
Artemisia annua	Artemisinin	Antimalarial agent
Galanthus	Galantamine	Antimalarial agent

- Animals

Animals are also the source of Natural Products. Especially venomous animals have attracted much attention as they contain constituents such as peptides, enzyme, lipids, and nucleotides.

For Example, teprotide is venom isolated from Bothrops jararaca.

Also, marine species contribute for natural products.

For Example,  $\omega$ -conotoxin from marine snail *Conus magus* is used to relieve severe and chronic pain [43, 44].

#### 4. EXTRACTION

Extraction is the first step to separate the potential portion or substance from their sources (animals and plants) using selective extraction techniques. Extraction produces desired and undesired compounds in pure stage [45]. The conventional extraction methods, including maceration, percolation and reflux extraction, Some modern or greener extraction methods such as super critical fluid extraction (SFC), pressurized liquid extraction (PLE) and microwave assisted extraction (MAE), are adopted for extracting desired components from natural products. The required purpose for extraction of natural products can be to use as herbal medicines, to use in testing of biological activities of secondary metabolites, to isolate known mixture of compounds [46].

##### 4.1. Maceration

It is very simple extraction method with the disadvantages of long extraction time. Maceration is an isocratic extraction method and cold extraction methods [44]. It is suitable for extraction of thermo labile compounds. This method involves extraction of constituent materials from plants in solvent by immersing the plant sample in a particular solvent. It is done at room temperature at steady state.

###### 4.1.1. Procedure of Maceration:

**STEP 1:** Cleaned and air dried crushed plant material or coarsely powdered is dipped in an appropriate solvent called menstruum in a closed container and allowed to stand still for 4-6 days under complete steady state at room temperature with occasional agitation and opening the lid times to times to release the developed pressure and shake until the soluble matter has dissolved [46].

**STEP 2:** The damp solid material is filtered off using a funnel with a cotton plug and then the marc is further pressed to recover as much as occluded solution as possible. Sufficient time is provided for coagulation and settling and the settled matter is then filtered using filter paper [46].

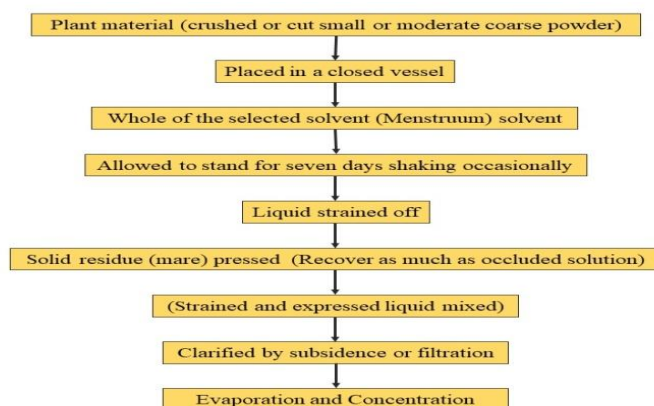
**STEP 3:** The resultant extract is then concentrated under reduced pressure to obtain the crude extract of the plant [46].

**STEP 4:** The extracted crude is used for further analysis.

As the system is stationary in the maceration process, the extraction process works on principle of molecular diffusion which is a time consuming process and ensues dispersal of the concentrated solution accumulation around the surface of the particles and bringing fresh solvent to the surface of particles for further extraction. Also a closed process is used to avoid the evaporation of solvent from the process [46].

The solvent used for maceration methanol, methanol water or any other organic solvent

Following is the Figure showing the flow for process of Maceration:



#### 4.1.2. Types of Maceration:

- Simple Maceration: Simple Maceration is basically used for organized and unorganized crude drugs.
- E.g. tincture of orange, lemon, and squill [48].
- Double Maceration [49]: It is used for concentrated infusion of orange.
- Triple Maceration: The maceration process may be carried out with the help of heating or stirring
- E.g. concentrated infusion of Quassia and Senna [48].

#### 4.1.3. Merits and Demerits:

Maceration requires small sample size. It has strong swelling properties or high mucilage and it is an energy saving process. But on the other hand unable to extract the drug exhaustively, It is very slow process and the amount of solvent required is more.

### 4.2. Percolation

It is continuous downward displacement of the solvent through the bed of crude drug material to get extract. It is most frequently used to extract active ingredients in the preparation of tinctures and fluid extracts [50]. It is a method of short successive maceration or process of the displacements [43]. A percolator (a narrow, cone-shaped vessel open at both ends) is generally used.

#### 4.2.1. Steps in Percolation:

**STEP 1:** Size reduction: The drug to be extracted is subjected to suitable degree of size reduction, usually from coarse powder to fine powder [43].

**STEP 2:** Imbibition: During imbibition the powdered drug is moistened with a suitable amount of menstruum and allowed to stand for four hours in a well closed container [43].

**STEP 3:** Packing: After imbibition the moistened drug is evenly packed into a percolator [43]

**STEP 4:** Maceration: After packing sufficient menstruum is added to saturate the material. The percolator is allowed to stand for 24-25 hours to macerate the drug [43].

**STEP 5:** Percolation: The lower tap is opened and liquid collected therein is allowed to drip slowly at a controlled rate until 3/4th volume of the finished product is obtained [43].

#### 4.2.2. Types of Percolation:

- Simple Percolation [ 48]:



E.g. Tincture of Belladonna and compound tincture of cardamom.

- Modified Percolation: Repeated maceration is more effective than simple one. Multiple maceration-solvent is divided into equal multiple time considering the solvent retained by plant tissue. It is basically used to prepare concentrated preparation.
- Reserved Percolation: In this case the extraction is done through the general percolation procedure [47]. At the last, evaporation is done under reduced pressure in equipment like a climbing evaporator to the consistency of a soft extract (semi solid) such that all the water is removed. This is then dissolved in the reserved portion which is strongly alcoholic and easily dissolves the evaporated portion with any risk of precipitation [48].

#### 4.2.3. Merits and Demerits:

It requires less time than maceration. Extraction of thermolabile constituents can be possible. But it requires more time than any other type of extraction [48]. Requires more solvent and skilled persons.

### 4.3. Soxhalation (Soxhlet Extraction)

The Soxhlet extractor is a type of continuous extraction of a component from a solid mixture. Boiling solvent rise up through the larger side arm [36]. Condensed drop of solvent falls into the porous cup, dissolving out the desired component from a solid mixture. When the smaller side-arm fills to overflowing, it initiates a siphoning action. The solvent, containing the dissolved component, is siphoned into the boiler below residual solvent then drains out of the porous cup, as fresh solvent drops continue to fall into the porous cup. And the cycle repeats [49]. The Following

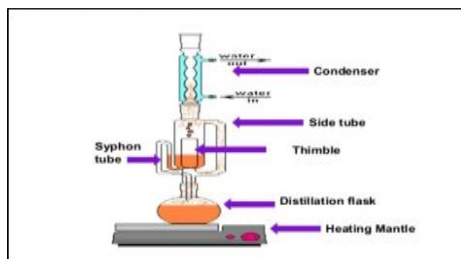


Figure4.1. Shows the Soxhlet Extraction Apparatus.

#### 4.3.1. Merits And Demerits

Large amount of drug can be extracted with much smaller quantity of solvent. Tremendous economy in terms of time, energy and ultimately financial inputs. It is a small scale used as batch process and becomes more economical when converted into continuous extraction. On the other hand the it holds some demerits such as physical nature of drug, solvent, chemical constituents of drug, etc [33].

### 4.4. Turbo Distillation Extraction:

Turbo distillation is suitable for hard-to-extract or coarse plant material, such as bark, roots, and seeds. In this processes the plants soak in water and steam is circulated through this plant and water mixture. Throughout the entire process, the same water is continually recycled through the plant material. This method allows faster extraction of essential oils from hard to extract plant material [33].



Figure4.2.

In recent years new extraction techniques with significant advantages over conventional methods have been developed for extracting analytes from solid matrices, e.g. reduction in organics solvent consumption and in sample degradation, reduction of extraction and clean-up times or even elimination of additional sample clean-up and concentration steps, improvement in extraction efficiency, selectivity, and/or kinetics, ease of automation [49].

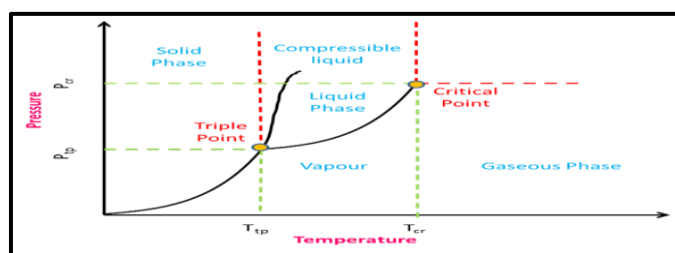
### 4.5. Supercritical Fluid Extraction

Supercritical fluid extraction represents an alternative technique to conventional solid liquid extraction with lower solvent consumption and lower working temperature [51]. It is form of liquid extraction where the usual liquid solvent phase has been replaced by a supercritical fluid- a substance that is above its critical point. Amongst a wide variety of supercritical fluids, carbon-dioxide is essentially the only convenient supercritical extraction solvent used because of its comparatively low critical temperature

(31.1OC) and pressure (73.8 bar /7.38MPa).

An organics solvent (also called modifier) may be added to the supercritical fluid to enhance its solvating properties. In case of CO<sub>2</sub> as the supercritical fluid, extraction can be performed under mild condition, thus reducing both the risks of thermal degradation and poor collection efficiencies of volatile analytes. CO<sub>2</sub> is most effective for dissolving organic compounds particularly molecules displaying some degree of lipophilicity, such as esters and lactones. The modifier component may introduce into the fluid either using a separate pump and suitable mixing devices or may be added to the sample matrix in the extraction cell prior to pressuring with CO<sub>2</sub> [51]. Frequently, an off-line valve is incorporated between the pump and the extraction vessel and between the vessel and the restrictor. In this set-up static or dynamic extraction or a combination of the two may be performed. The restrictor maintains the pressure within the extractor vessel by the flow control [53]. The use of SFE both at the analytical and processing scales is quite widespread in the food industry for extraction of fats and oils from seeds, foodstuffs, and other materials, the technique has also been applied to the extraction of the active compounds from medicinal plants, such as steroids, terpenes, alkaloids, various oxygen containing heterocyclic compounds, as well as aromatics and phenolic compounds.

Graph of Pressure Versus Temperature showing triple point and Critical Point (Supercritical curve) [52,53]: (Fig4.3.)



**Figure4.3.**

## 5. COMPARISON BETWEEN EXTRACTION PROCESSES

METHOD	SOLVENT	TEMPERATURE	PRESSURE	TIME	VOL. OF ORG. SOLVENT CONSUMED	POLARITY OF PRODUCT EXTRACTED
Maceration [54]	Water, aqueous and non-aqueous solvents	Room temperature	Atmospheric	Long	Large	Dependent on extracting solvent
Percolation [54]	Water, aqueous and non-aqueous solvents	Room temperature, occasionally under heat	Atmospheric	Long	Large	Dependent on extracting solvent
Soxhalation [54]	Organic solvents	Under heat	Atmospheric	Long	Moderate	Dependent on extracting solvent
Supercritical Fluid Extraction [54]	Supercritical fluid (usually S-CO <sub>2</sub> ), sometimes with modifier	Near room temperature	High	Short	None or small	Nonpolar to moderate polar compounds

## 6. APPLICATION








The table given below describes the application of the following different types of process such as Maceration Extraction, Percolation Extraction, Soxhlet Extraction, Supercritical Fluid Extraction, Turbo Distillation, etc. In Maceration Extraction, catechins are extracted from *Arbutus unedo* L. fruits, which can be used as an anti-viral effect on much disease; also it acts as enzymes [54]. The more better example of Maceration Extraction are Polyphenols from *Serpylli herba* and *Cajanus cajan* leaves



**Techniques Adopted for Extraction of Natural Products Extraction Methods: Maceration, Percolation, Soxhlet Extraction, Turbo distillation, Supercritical Fluid Extraction.**

which can be used as an anti-microbial, anti-proliferative properties and for treatment of hepatitis, diabetes, respectively. Similarly, examples for Percolation, Soxhlet, Supercritical Fluid Extraction and Turbo Distillation are mentioned in the table given below. (Table6.1.)

**Table6.1.**

EXTRACTION PROCESS	NAME OF SPECIES	APPLICATION	IMAGE
MACERATION EXTRACTION	catechins from <i>Arbutus unedo</i> L. fruits [54]	Anti-viral effect on many disease, acts as enzyme, also used as natural anti-oxidant, and as an anti-microbial agent, dietary supplements.	
	polyphenols from <i>Serpylli herba</i> [54]	Anti-microbial, acetylcholine-esterase inhibiting and anti-proliferative properties.	
	<i>Cajanus cajan</i> leaves [54]	Treatment of hepatitis, diabetes and chicken pox	
PERCOLATION EXTRACTION	Fucoxanthin from <i>Undaria pinnatifida</i> [54]	Prevention of hyperglycemia, separation of chemically induced mammary tumors, inhibition of anti-hypertension and anti-obesity.	
SOXHLET EXTRACTION	ursolic acid from the TCM <i>Cynomorium</i> ( <i>Cynomorii Herba</i> ) [54]	Herbal tonic to supplement the primordial “Yang Essence” for both men and women	
SUPERCritical FLUID EXTRACTION	essential oil from rosemary ( <i>Rosmarinus officinalis</i> ) [36]	Used as externally as supportive therapy for rheumatic diseases, circulatory problems to improve the liver and gall bladder functions and for dyspeptic complaints.	
TURBO DISTILLATION	Essential oils from garlic ( <i>Allivum sativum</i> ) and onion ( <i>Allium septa</i> ) [32]	Anti-bacterial and anti-oxidant	

**7. CONCLUSION**

The contribution of natural products to drug development in past few years has been increasing tremendously. The isolation processes are time consuming and however have hindered the application of natural products. Due to their tremendous increase in application of these extraction methods more and more new automatic and rapid techniques have been developed to extract and separate natural products.

The modern extraction methods such as SFE are of much attention in recent years. Due to their high extraction yield selectivity, stability of target extracts and process safety merits. Expectations regarding these techniques and trends will be increasing in newer future as they are mostly motivated by emerging consumer demands and by safety regulatory and environmental issues.

#### REFERENCES

- [1] WHO traditional medicine strategy: 2014–2023; [http://www.who.int/medicines/publications/traditional/trm\\_strategy14\\_23/en/](http://www.who.int/medicines/publications/traditional/trm_strategy14_23/en/). Accessed 29 Dec 2017.
- [2] Newman DJ, Cragg GM. "Natural products as sources of new drugs from 1981 to 2014". *J Nat Prod*. 2016;79(3):629–61.
- [3] Newman DJ, Cragg GM. "Natural products as sources of new drugs over the 30 years from 1981 to 2010". *J Nat Prod*. 2012;75(3):311–35.
- [4] Atanasov AG, Waltenberger B, Pferschy-Wenzig EM, Linder T, Wawrosch C, Uhrin P, Temml V, Wang L, Schwaiger S, Heiss EH, et al. Discovery and resupply of pharmacologically active plant-derived natural products: a review". *Biotechnol Adv*. 2015; 33(8):1582–614.
- [5] Cragg GM, Newman DJ. Natural products: a continuing source of novel drug leads". *Biochim Biophys Acta Gen Subj*. 2013; 1830(6):3670–95.
- [6] Hong, J.Y. "Natural product diversity and its role in chemical biology and drug discovery". *Curr. Opin. Chem. Biol*. 2011, 15, 350–354.
- [7] Rosén, J.; Gottfries, J.; Muresan, S.; Backlund, A.; Oprea, T.I. Novel "chemical space exploration via natural products". *J. Med. Chem*. 2009, 52, 1953–1962.
- [8] Butler, M.S. "Natural products to drugs: Natural product-derived compounds in clinical trials". *Nat. Prod. Rep*. 2008, 25, 475–516.
- [9] Newman, D.J.; Cragg, G.M.; Snader, K.M. "Natural Products as Sources of New Drugs over the Period 1981–2002". *J. Nat. Prod*. 2003, 66, 1022–1037.
- [10] Li-Weber, M. "New therapeutic aspects of flavones: The anticancer properties of Scutellaria and its main active constituents", *Wogonin, Baicalein and Baicalin*. *Cancer Treat. Rev*. 2009, 35, 57–68.
- [11] Zhu, F.; Ma, X.H.; Qin, C.; Tao, L.; Liu, X.; Shi, Z.; Zhang, C.L.; Tan, C.Y.; Chen, Y.Z.; Jiang, Y.Y. "Drug discovery prospect from untapped species: Indications from approved natural product drugs". *PLoS ONE* 2012, 7, e39782.
- [12] Winter, J.M.; Tang, Y. "Synthetic biological approaches to natural product biosynthesis". *Curr. Opin. Biotechnol*. 2012, 23, 736–743.
- [13] Li, J.W.; Vederas, J.C. Drug discovery and natural products: End of an era or an endless frontier?", *Science* 2009, 325, 161–165.
- [14] Ngo, L.T.; Okogun, J.I.; Folk, W.R. "21st Century natural product research and drug development and traditional medicines". *Nat. Prod. Rep*. 2013, 30, 584–592.
- [15] Samuelson G (1999), "Drugs of Natural Origin: A Textbook of Pharmacognosy", *Taylor & Francis Ltd*. ISBN 9789186274818.
- [16] Bhat S V, Nagasampagi B A, Sivakumar M (2005), "Chemistry of Natural Products", Berlin; New York; *Springer*. ISBN 81-7319-481-5.
- [17] Hanson JR (2003), "Natural Products: the Secondary Metabolite", *Cambridge: Royal Society of Chemistry*. ISBN 0-85404-490-6.
- [18] Kliebenstein DJ (2004), "Secondary metabolites and plant/environment interactions: a view through Arabidopsis thaliana tinged glasses", *Plant, cell and Environment*. 27 (6) : 675-684.
- [19] Boal D (2006), "Mechanics of cell (4<sup>th</sup> ed.)", *Cambridge, UK: Cambridge University Press*. ISBN 978-0-52179681-1.
- [20] Rogers K (2011), "The components of life: from Nucleic acid to carbohydrates (1<sup>st</sup> ed.)", New York, NY : *Britannica Publishing in association with Rosen Educational Services*. ISBN 978-1-61530-324-3.
- [21] Cox DL, Nelson MM (2013), "Lehninger Principles of Biochemistry (6<sup>th</sup> ed.)", New York, N. Y. : *W. H. Freeman*. ISBN 978-1-4641-0962-1.
- [22] Boal D (2006), *Mechanics of the cell (4<sup>th</sup> printing ed.)* Cambridge, UK: *Cambridge University Press*. ISBN 978-0-521-79681-1.
- [23] Sitaramayya A (1999), "Introduction to Cellular Signal Transduction", *Boston: Birkhauser*. ISBN 978-0-8176-3982-2.

- [24] "IUPAC, Compendium of Chemical Terminology", 2nd ed. (the "Gold Book") (1997). Online corrected version: (2006-) "alkaloids". doi:10.1351/goldbook.A00220.
- [25] R. H. F. Manske. The Alkaloids. Chemistry and Physiology. Volume VIII. – *New York: Academic Press*, 1965, p. 673
- [26] Kittakoop P, Mahidol C, Ruchirawat S (2014). "Alkaloids as important scaffolds in therapeutic drugs for the treatments of cancer, tuberculosis, and smoking cessation". *Curr Top Med Chem*. 14 (2): 239–252.
- [27] Russo P, Frustaci A, Del Bufalo A, Fini M, Cesario A (2013). "Multitarget drugs of plants origin acting on Alzheimer's disease". *Curr Med Chem*. 20 (13): 1686–93.
- [28] Raymond S. Sinatra; Jonathan S. Jahr; J. Michael Watkins-Pitchford (2010). The Essence of Analgesia and Analgesics. *Cambridge University Press*. pp. 82–90.
- [29] Cushnie TP, Cushnie B, Lamb AJ (2014). "Alkaloids: An overview of their antibacterial, antibiotic-enhancing and antivirulence activities". *Int J Antimicrob Agents*. 44 (5): 377–386.
- [30] Qiu S, Sun H, Zhang AH, Xu HY, Yan GL, Han Y, Wang XJ (2014). "Natural alkaloids: basic aspects, biological roles, and future perspectives". *Chin J Nat Med*. 12 (6): 401–406.
- [31] Bhatt S V, Nagasampagi BA, Sivakumar M (2005), "Chemistry of Natural Products", Berlin, *New York : Springer*. ISBN 81-7319-481-5.
- [32] Devik PM (2009), "Medicinal Natural Products: Biosynthetic Approach (3<sup>rd</sup> ed.) *Chichester : Wiley*. ISBN 978-0-470-74167-2.
- [33] Strobel G, Daisy B (December 2003). "Bioprospecting for microbial endophytes and their natural products". *Microbiology and Molecular Biology Reviews*. 67 (4): 491–502.
- [34] Procópio RE, Silva IR, Martins MK, Azevedo JL, Araújo JM (2012). "Antibiotics produced by *Streptomyces*". *The Brazilian Journal of Infectious Diseases*. 16 (5): 466–71.
- [35] Cochrane SA, Vederas JC (January 2016). "Lipopeptides from *Bacillus* and *Paenibacillus* spp.: A Gold Mine of Antibiotic Candidates". *Medicinal Research Reviews*. 36 (1): 4–31.
- [36] Saxena A, Kumari R, Mukherjee U, Singh P, Lal R (2014). "Draft Genome Sequence of the Rifamycin Producer *Amycolatopsis rifamycinica* DSM 46095". *Genome Announcements*. 2 (4): e00662–14.
- [37] Zaffiri L, Gardner J, Toledo-Pereyra LH (April 2012). "History of antibiotics. From salvarsan to cephalosporins". *Journal of Investigative Surgery*. 25 (2): 67–77.
- [38] Beekman AM, Barrow RA (2014). "Fungal metabolites as pharmaceuticals". *Aust J Chem*. 67 (6): 827–843.
- [39] Crozier A, Clifford MN, Ashihara H (2006). "Chapters 1, 3 and 4". *Plant Secondary Metabolites: Occurrence, Structure and Role in the Human Diet*. *Oxford, UK: Blackwell Publishing Ltd*. pp. 1–24, 47–136
- [40] Kittakoop P, Mahidol C, Ruchirawat S (2014). "Alkaloids as important scaffolds in therapeutic drugs for the treatments of cancer, tuberculosis, and smoking cessation". *Current Topics in Medicinal Chemistry*. 14 (2): 239–52.
- [41] Kano S (May 2014). "Artemisinin-based combination therapies and their introduction in Japan". *Kansenshogaku Zasshi*. 88 (3 Suppl 9–10): 18–25.
- [42] Russo P, Frustaci A, Del Bufalo A, Fini M, Cesario A (2013). "Multitarget drugs of plants origin acting on Alzheimer's disease". *Current Medicinal Chemistry*. 20 (13): 1686–93.
- [43] Bowersox SS, Luther R (November 1998). "Pharmacotherapeutic potential of omega-conotoxin MVIIA (SNX-111), an N-type neuronal calcium channel blocker found in the venom of *Conus magus*". *Toxicol*. 36 (11): 1651–8.
- [44] Prommer E (June 2006). "Ziconotide: a new option for refractory pain". *Drugs of Today*. 42 (6): 369–78.
- [45] Amir Muhammad Khan et al (2011), Phytochemical analysis of selected medicinal plants of Margalla Hills and surroundings, *J. Med. Plants Res*. 5(25), pp. 6017-.
- [46] A. Das Talukdar et al, (2010) Phytochemical screening and TLC profiling of plant extracts of *Cyathea gigantea* (Wall. Ex. Hook.) Hatt. And *Cyathea brunoniana*. Wall. ex. Hook. (Cl. & Bak.) Assam University Journal of Science & Technology: Biological and Environmental Sciences Vol. 5 Number I, 70-74.
- [47] Diaz, J. G., Ruiz, J. G., and de la Fuente, G. (2000) Alkaloids from *Delphinium staphisagria*. *J. Nat. Prod*. 63, 1136–1139.
- [48] Mukharji Pulok K. 2002, Quality Control of Herbal Drugs, 1st edition Published by Business Horizon, p.p 380-421.
- [49] Cooper J.W, Gunn's Colin 2010-2011 ,Register of General Pharmacy p.p.308-393.
- [50] Rangari v.d , 2002 ,Pharmacognosy and Phytochemistry ,1st edition Published by Vallabh Prakashan, p.p150-167.

- [51] John R. Dean, Extraction techniques in Analytical Sciences, The Graduate School and School of Applied Sciences Northumbria University, Newcastle, UK.
- [52] G. N. Sapkale, S. M. Patil, U. S. Surwase, P. K. Bhatbhage, "Super Critical Fluid Extraction", ASPM, S K. T. Patil College of Pharmacy, Osmanabad, India.
- [53] Abbas, K.A., A. Mohamed, A.S. Abdulmir and H.A. Abas, "A Review on Supercritical Fluid Extraction as New Analytical Method", Faculty Food Science and Technology, University Putra Malaysia (UPM), Malaysia.
- [54] Qing- Wen Zhang, Li- Gen Lin and Wen- Cai Ye, "Techniques for extraction and isolation of natural products: a comprehensive review", *Zhang et al. Chin Med* (2018).

**Citation:** Pradnya Ingle, et.al , (2019). "Techniques Adopted for Extraction of Natural Products ,Extraction Methods: Maceration, Percolation, Soxhlet Extraction, Turbo distillation, Supercritical Fluid Extraction, ". *International Journal of Advanced Research in Chemical Science (IJARCS)*, 6(4), pp.1-12. DOI: <http://dx.doi.org/10.20431/2349-0403.0604001>.

**Copyright:** © 2019 Authors. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.