Review Article **ISSN: 2394 – 7403**

International Journal of Medicine and Health Profession Research

Journal home page: www.ijmhpr.com

DESIGN AND DEVELOPMENT OF EXTRACTION PROCESS IN THE ISOLATION OF PHYTOPHARMACEUTICALS FROM PLANT SOURCES

Sunil Kumar*[1]

*[1]Department of Pharmacy, Manav Bharti University, Solan, Himachal Pradesh, India.

ABSTRACT

Extraction is defined as the process of removing a substance or several substances from another substance. The process is extremely important in a wide range of technical applications, for instance biotechnology, the pharmaceutical and food industries as well as environmental protection. Extraction is a separating process which has the advantage of low energy consumption. Extraction is the process of separation of medicinally active substances of plant or animal from a mixture by a mechanical or chemical action such as by distillation or pressure. This separation is done with the help of dissolving one or more of the substances in a solvent in which it is easily soluble and is separated on the basis of their physical or chemical properties. Extraction is the withdrawing of a active agent or a waste substance from a solid or liquid mixture with a liquid solvent. The solvent is not or only partial miscible with the solid or the liquid. By intensive contact the active agent transfers from the solid or liquid mixture (raffinate) into the solvent (extract). After mixing the two phases are separated which happens either by gravity or centrifugal forces.

KEY WORDS

Extraction and Distillation.

Author of correspondence:
Sunil Kumar,
Department of Pharmacy,
Manav Bharti University, Solan,
Himachal Pradesh, India.

Email: sunilpharma0003@gmail.com.

INTRODUCTION

The recovery of the solvent and to get the active agent in pure form a further separation process is necessary (rectification or re-extraction). Depending on the phases following types of extraction exist:

- Solid – liquid extraction
- Liquid – liquid extraction
- The gas – liquid extraction is called absorption.

The main area of extraction is for hydro metallic processes, for pharmaceutical industry (producing active agents), for petroleum industry (production of monomers and aromates) and for cleaning of waste water to separate solved compounds[1].

Liquid-Liquid Extraction

Solvent extraction

Although solvent extraction as a method of separation has long been known to the chemists, only in recent years it has achieved recognition among analysts as a powerful separation technique. Liquid-liquid extraction, mostly used in analysis, is a technique in which a solution is brought into contact with a second solvent, essentially immiscible with the first, in order to bring the transfer of one or more solutes into the second solvent. The separations that can be achieved by this method are simple, convenient and rapid to perform; they are clean as much as the small interfacial area certainly precludes any phenomena analogous to the undesirable co-precipitation encountered in precipitation separations. Solvent extraction is one of the most extensively studied and most widely used techniques for the separation and pre-concentration of elements. The technique has become more useful in recent years due to the development of selective chelating agents for trace metal determination. With proper choice of extracting agents, this technique can achieve group separation or selective separation of trace elements with high efficiencies. In analytical applications solvent extraction may serve the following three purposes:[2,3]

- Pre concentration of trace elements.
- Elimination of matrix interference.
- Differentiation of chemical species.

The procedure is applicable to both, trace and macro levels. A further advantage of solvent extraction method lies in the convenience of subsequent analysis of the extracted species. If the extracted species are coloured, as is the case with many chelates, spectrophotometric methods can be employed. Alternatively, the solution may be aspirated for atomic absorption or ICP emission spectrometric analysis. If radiotracers are used, radioactive counting techniques can be employed. Before going in detailed discussion of fundamental principles of extraction, the three mostly used terms for expressing the effectiveness of extraction processes are being defined below. These terms are basic for understanding of theoretical as well as practical considerations of the subject.

Process Development

Most projects involve a pilot test to provide the basis for commercial plant design. Unlike distillation, which can often be designed by simulations alone, liquid-liquid extraction usually has many unknown factors such as stage efficiency, rates of diffusion, flood point, emulsion formation, interface behaviour, entrainment tendency and capacity data. Small trace impurities can have a significant impact on all of the above. For this reason, it is preferred to use only actual plant feed and solvent materials are best used for these tests. Before pilot testing begins bench scale tests are performed to generate the liquid-liquid equilibrium data. Besides supplying the equilibrium data, these tests can reveal information on emulsions or entrainment that help guide extractor selection[4-6].

Information from Testing

Bench Scale Tests Provide

- Equilibrium data
- Mixing characteristics
- Settling times
- Extractor type selection for pilot test

Pilot Scale Tests Provide

- Data for scale up> stage efficiency, throughput, agitation speed
- Demonstration of the entire process
- Process optimization
- Basis for performance guarantee

Select the appropriate extractor based on our review of each application. Pilot tests are then run to demonstrate the process performance as well as provide data for scale up. These pilot tests are performed in the same type of extractor planned for the commercial scale. In some cases, more than one type of extractor will be tested to compare performance[7].

Test Scale

Design of liquid-liquid extraction (LLE) equipment with any reasonable degree of accuracy remains very difficult without some type of pilot plant testing. This is due to the complexity of the process taking

place within an extraction column, e.g. droplet breakup and coalescence, mass transfer, axial mixing, and the fact that small amounts of impurities can dramatically affect performance. KMPS offers a broad range of laboratory and pilot plant liquid-liquid extraction equipment to assist you during feasibility studies, process development and equipment design stages of your project. The picture to the right shows a pilot scale extraction column. Typically we supply the column with internals mounted to a stainless steel support frame along with the variable speed drive[2,4,8].

Our equipment is available on either a sale or rental basis and includes the following:

Laboratory scale extraction columns to screen solvents, evaluate feed variables and determine the feasibility of liquid-liquid extraction for specific applications. Small pilot scale columns (static and dynamic designs) to optimize the extraction parameters and provide accurate data for scale up to commercial equipment. Large pilot columns for semi works or small scale production facilities. Portable units, which can be rented for testing on site. KMPS can provide trained service personnel to assist you in installing the pilot extraction column at your facility. KMPS is also available to help you set up an effective pilot plant test procedure and will work with you to optimize the column performance. We will also interpret the test results and apply them to the design of your commercial column.

Agitated Columns

KMPS offers a number of agitated liquid-liquid extraction columns. These columns are normally provided with a borosilicate glass shell for observation of the process. Such observation is critical for optimization of the column performance. The standard designs are the 1" diameter KARR® Reciprocating Plate Column and 3" diameter SCHEIBEL® and RDC columns[9].

Static Columns

KMPS also offers a 4" diameter static column packed with either SMV or SMVP extraction packing. This unique packing promotes good radial mixing while suppressing axial (back) mixing providing better plug flow characteristics and improving efficiency compared to random packing. The pilot column is offered with a glass shell (atmospheric pressure operation) and stainless steel shell (for operating at elevated pressures)[10].

Bench Top KARR® Column

For lab scale feasibility studies, KMPS can also provide a Bench Top KARR® Column that consists of a 5/8" diameter glass column with a 24" plate stack height. Two plate stack assemblies are included (316SS and Teflon perforated plates and spacers) with 1/2" plate spacing. An air motor is provided to regulate the agitation in the column. The unit comes in a stainless steel frame as shown in the picture below. KMPS has demonstrated that up to 2.7 theoretical stages per foot of agitated height can be achieved with this unit. Please contact us for ordering information[11].

Extraction Screening Unit

Sometimes the nature of process materials being handled prohibits testing at our pilot plant. In these cases, KMPS can deliver portable units and operating personnel to the plant for onsite testing. One such unit is our portable Extraction Screening Unit (ESU) ideally suited to simplify onsite testing, see picture to the right. This unit consists of a 3" diameter x 12 18 stage, SCHEIBEL® Column with glass shell and air drive motor. Two stainless steel tanks with sight glasses and roto meters for flow control are mounted with the column onto a portable frame. Powered by air or nitrogen, it is ideal for use in hazardous areas[7,12].

Extractor Design

During the pilot plant tests, the extractor separation performance is measured over a range of flow rates, solvent to feed ratios and effective heights. If the extractor selected is agitated then the agitation speed is also varied. At each flow rate, the agitation is increased until the flood point is reached. From this data, the conditions that give the optimum volumetric efficiency are determined. Shown in Figure No.1 and 2.

Next comes scale up to commercial size. Any scale up procedure must determine

1. How diameter varies with throughput and
2. How stage efficiency varies with diameter. For the agitated columns, there is an

additional parameter to be determined, namely

3. How the power input varies with column size.

Finally the extractor is sized with the active zone height, together with the top and bottom settler zones and instrumentation for control of the column interface as shown in Figure No.3 KMPS has a wide range of extractors to choose from, both static and agitated columns. See the column types below for more information on each (Table No.1).

In addition to the extractor, an extremely important aspect of any extraction application is the design of the system to recover and recycle the solvent. In most cases, these additional steps are accomplished by means of distillation, and when necessary, are also studied during the pilot tests. At KMPS, we often supply the extraction and distillation components as a complete modular system. Typical examples are illustrated on this page. Our team of experienced engineers is available to work together with you on your next liquid-liquid extraction application, from conceptualization through startup.

Advantages of Modular Construction[12,13]

1. Lower cost/lump sum bid
2. Schedule compression
3. Minimal plant site interruption
4. Construction proceeds while waiting for permits
5. Single source responsibility
6. Progress of work is not affected by weather conditions.

Supercritical fluid extraction

(SFE) is an alternative sample preparation method with general goals of reduced use of organic solvents and increased sample throughput. The factors to consider include temperature, pressure, sample volume, analyte collection, modifier (cosolvent) addition, flow and pressure control, and restrictors. Generally, cylindrical extraction vessels are used for SFE and their performance is good beyond any doubt[4].

The collection of the extracted analyte following SFE is another important step: significant analyte loss can occur during this step, leading the analyst to believe that the actual efficiency was poor[3,14].

There are many advantages to the use of CO2 as the extracting fluid. In addition to its favourable physical properties, carbon dioxide is inexpensive, safe and abundant. But while carbon dioxide is the preferred fluid for SFE, it possesses several polarity limitations. Solvent polarity is important when extracting polar solutes and when strong analyte matrix interactions are present. Organic solvents are frequently added to the carbon dioxide extracting fluid to alleviate the polarity limitations. Of late, instead of carbon dioxide, argon is being used because it is inexpensive and more inert. The component recovery rates generally increase with increasing pressure or temperature: the highest recovery rates in case of argon are obtained at 500 atm and 150° C[11,12].

Phytonics Process

A new solvent based on hydrofluorocarbon134a and a new technology to optimize its remarkable properties in the extraction of plant materials offer significant environmental advantages and health and safety benefits over traditional processes for the production of high quality natural fragrant oils, flavours and biological extracts. Advanced Phytonics Limited (Manchester, UK) has developed this patented technology termed “phytonics process”. The products mostly extracted by this process are fragrant components of essential oils and biological or phytopharmacological extracts which can be used directly without further physical or chemical treatment[15].

The properties of the new generation of fluorocarbon solvents have been applied to the extraction of plant materials. The core of the solvent is 1,1,2,2 tetrafluoroethane, better known as hydrofluorocarbon134a (HFC134a). This product was developed as a replacement for chlorofluorocarbons. The boiling point of this solvent is 25° C. It is not flammable or toxic. Unlike chlorofluorocarbons, it does not deplete the ozone layer. It has a vapor pressure of 5.6 bar at ambient temperature. By most standards this is a poor solvent. For example, it does not mix with mineral oils or triglycerides and it does not dissolve plant wastes[16].

The process is advantageous in that the solvents can be customized: by using modified solvents with HFC134a, the process can be made highly selective in extracting a specific class of phytoconstituents. Similarly, other modified solvents can be used to extract a broader spectrum of components. The biological products made by this process have extremely low residual solvent. The residuals are invariably less than 20 parts per billion and are frequently below levels of detection. These solvents are neither acidic nor alkaline and, therefore, have only minimal potential reaction effects on the botanical materials. The processing plant is totally sealed so that the solvents are continually recycled and fully recovered at the end of each production cycle. The only utility needed to operate these systems is electricity and, even then, they do no consume much energy. There is no scope for the escape of the solvents. Even if some solvents do escape, they contain no chlorine and therefore pose no threat to the ozone layer. The waste biomass from these plants is dry and "eco friendly" to handle[5].

Selection of the solvent

The solvent for extraction has to withdraw the active agent from a mixture.

- **Selectivity**: Only the active agent has to be extracted and no further substances which mean that a high selectivity is required.
- **Capacity**: To reduce the amount of necessary solvent the capacity of the solvent has to be high.
- **Miscibility**: To achieve simple regeneration of the solvent the miscibility of solvent and primary solvent has to be low.
- **Difference in density**: After extraction the two phases have to be separated in a separator and for this a high difference in density is positive.
- **Optimal surface tension**: σ low > low amount of energy for dispersing required; if surface tension < 1 mN/m stable emulsions are produced. σ > 250 mN/m > high amount of energy for dispersing and high tendency to coalesce
- **Recovery**: The solvent has to be separated from the extract phase easily to produce solvent free active agents.
- **Corrosion**: If the solvent is corrosive prices for construction increase
- **Low price**
- **No or low toxicity**
- **Flame temperature**: 25 °C higher than operating temperature
- **Vapour pressure**: To prevent loss of solvent by evaporation a low vapour pressure at operating temperature is required.
- **Viscosity:** A low viscosity of the solvent leads to low pressure drop and good heat and mass transfer[17].
- **Chemical and thermal stability**

Regeneration of the solvent

For all extraction processes the regeneration by further separation processes is necessary. By this way pure products are produced and the solvent can be recycled in the extraction process. In many cases the regeneration step is the most cost intensive part of the whole process. Following possibilities for separating of the solvent are available:[4,6,16]

- **Rectification:** The most common method
- **Evaporation:** The evaporation of the solvent is used if the active agent is very high volatile. The solvent should have a low boiling temperature and a low heat of evaporation.
- **Crystallization:** Cooling the solvent results in crossing the solubility and the active agent falls out and can be separated by mechanically separation processes.
- **Extraction:** A further extraction step with another solvent can be used to separate the active agent from the first solvent. But the by this way produced extract has to be separated once again.

Solid-liquid extraction (Leaching)

Principles The principle for the solid-liquid extraction is that the soluble compounds of a solid matter, existing of an inert matrix and the active agent, are extracted by a solvent. The extract can be included in the extraction matter in solid or liquid form. It can be included in cells like oil in oil seeds or as fine dispersion on the solid matter like caffeine in coffee. Following points are necessary for a economic extraction process:

- The extraction matter has to be prepared in this way that the extract can be solved by the solvent in short time. This is achieved by grinding, milling or rolling.
- Only the desired extract has to be solved and extracted. This is achieved by the selectivity of the solvent and the temperature.
- The extract should contain high concentrations of extracted compounds.

This is the reason why counter current extraction plants are preferred. Separation of the solvent from as well extract solution as extraction residual has to be economically. A total solid-liquid extraction process includes the preparation of the extraction material, separation and recovery of the solvent from extract and separation and recovery of solvent from extraction residual.

Liquid-liquid Extraction by Aqueous Two-phase Systems

In many bioengineering processes, the high cost of downstream processing methods for the recovery of the product is a key problem. Recent advances in biotechnology have opened up numerous possibilities for the large scale production of many bio products. An increased interest has arisen in the development of efficient downstream processing methods for the separation, concentration and purification from fermentation and cell culture media (Raghavarao*et al.*, 1998; Sinha*et al.*, 2000). The downstream processing of biological materials requires purification techniques that are delicate enough to preserve the biological activity. In conventional methods like centrifugation and even modern methods like electrophoresis and column chromatography, scales up problems are enormous, making them uneconomical or very expensive. There is therefore a need in the industry for efficient and economical approaches to the bio separation problems. Extraction using aqueous two phase is one such possibility[18].

THE PURIFICATION OF RECOMBINANT PHARMACEUTICAL PROTEINS

Human insulin like growth factor 1 (IGF1) accumulates in both folded and aggregated forms in the fermentation medium and cellular periplasmic space when expressed in *E. coli* with an endogenous secretary signal sequence. Due to its heterogeneity in form and location, low yield of IGF1 was obtained using a typical recovery strategy. To enhance recovery yield, a new procedure was developed to solve and extract IGF1 from cells while in fermentation broth (Hart *et al*., 1994). This method, called *in situ* solubilization, involves addition of chaotrope and reductant to alkaline fermentation broth and provides recovery of about 90% of all IGF1 in an isolated supernatant[19].

Then, an aqueous two phase extraction procedure was employed which partitions soluble nonnative IGF1 and biomass solids into separate liquid phases. The techniques of *in situ* solubilization and aqueous two phase extraction provide a new, high yield approach for isolating recombinant protein which is accumulated in more than one form during fermentation. To develop the extraction system further, Hart *et al*. (1995) used multi factorial experimental approach to simultaneously map the phase diagram and identify conditions to suitably partition IGF1 and cell remnants. It was found that the presence of urea in these systems tended to disrupt two-phase formation and solids sedimentation. This, in turn, constrained the concentrations of phase forming solutes which could be effectively used. Systems containing intermediate levels of salt (between about 4% and 7% w/w) and polymer (between about 10% and 18% w/w) formed two phases in which solids were enriched in the bottom phase. Systems were produced with a variety of different salts and polymers and all enriched nonnative IGF 1 in the top phase. Highest recovery yield (Table No.2) was obtained with systems composed of 5% sodium sulfate and 14% PEG8000.

Intracellular human recombinant interferon a1 (rhIFNa1) could also be purified using aqueous two-phase extractions (Guan *et al*., 1996). In the polyethylene glycol potassium phosphate aqueous two-phase system, the optimum condition was found to be 22% (w/w) synthesized PEG phosphate ester, 16% (w/w) potassium phosphate and 3% (w/w) NaCl at pH 6.9 with 10% (wet w/ w) biomass load. The corresponding top phase yield of rhIFNa1 was 99.6%. A back extraction system using 20% (w/w)

PEG phosphate ester and 10% (w/w) potassium phosphate system at pH 6.0 gives the yield of rhIFNa1 in the bottom phase. This newly established back extraction procedure avoids the use of a cumbersome gel chromatography while the yield achieved is fairly high (Table No.2). Menge*et al*. (1983) found that in PEG phosphate ester/ phosphate aqueous two phase system, the IFNb partitioned into the top phase while other proteins remained in the bottom phase. Using this system, the IFNb was purified, the purification factor reached 350, and the yield was 97%. With the PEG 8 000(14%)/Na_2SO_4 (5%) aqueous two-phase system, Datar*et al*. (1986) separated the human growth hormone (hGH) from recombinant *E. coli*[13,19].

THE PURIFICATION OF ANTIBIOTICS

Most applications of aqueous two phase are in the separation of macromolecules. With the development of researches, it was found that some small molecules have also the uneven distribution in the aqueous two phase systems, so aqueous two-phase systems found their application in the purification of small molecules[20].

β Lactam Antibiotics

Different from the original organic solvent extraction, Guan *et al*. (1996) studied the application of aqueous two phase system in the recovery of penicillin. The volume of fermentation broth processed was 1 000 mL, the mass of penicillin crystal obtained was 7.228 g with an average purity of 84.15%, the overall recovery ratio of aqueous two-phase partitioning technology was 76.56% (Table No.2). Lee *et al*. (1998) investigated the partitioning behavior of phenylacetic acid (PAA) and 6aminopenicillanic acid (6APA) in the nonionic surfactant *N* decyltetra(ethylene oxide) ($C_{10}E_4$) based, temperature induced aqueous two-phase system. PAA shows a high affinity toward the surfactant rich top phase. The partition coefficient of PAA is much greater than unity and strongly affected by pH. 6APA, on the other hand, has a partition coefficient smaller than unity. It stays preferably in the surfactant lean bottom phase. A high degree of separation of PAA from 6APA is achieved when penicillin hydrolysate is subjected to cloud point extraction. Hernandez Justiz*et al*.(1998) evaluated the partitioning of cephalexin in different aqueous two-phase systems. The largest partition coefficient for cephalexin (K=23) was found in 100% PEG600 - 3M ammonium sulfate system where cephalexin was extracted to the PEG phase. Preincubating penicillin G acylase, covalently immobilized inside porous supports, in ammonium sulfate and further suspension with 100% PEG600, it could be obtained a 90% synthetic yield of cephalexin from 150 mMphenylglycine methyl ester and 100 mM 7aminodesacetoxycephalosporanic acid (7ADCA)[18].

THE PRODUCTION AND PARTITIONING OF LACTIC ACID

A typical biotechnological process is characterized by rather low productivity in comparison to chemical synthetic reactions. Integration of bioconversion and downstream processing can increase productivity of bioprocesses due to a number of reasons. For example, during fermentation lactic acid inhibits growth of the organisms and product formation. This can be avoided by extracting lactic acid from the broth. Further, productivity can be improved by increasing the catalyst density in the reactor. To meet all these requirements and to avoid detrimental effects of conventional extraction media on bioconversion aqueous two-phase systems are a possible alternative. With PEG/Dextran system, Katzbauer *et al*. (1995) carried out the batch and continuous aqueous two-phase.

THE PURIFICATION OF OTHER PHARMACEUTICALS

The Purification of Pharmaceuticals from Plants Ecdysone and 20 hydroxyecdysone, hormones that regulate molting cycles of anthropods, are of commercial interest as insecticides and indicators of helminth and nematod parasitism and other medical disorders in humans. Both molecules are steroids, but soluble in water (Baswaid*et al*., 1990; Gharib *et al*., 1991). Alred *et al*. (1993) studied the partitioning behaviour of ecdysone and 20 hydroxy ecdysone in aqueous two-phase systems. The ecdysteroids were first partitioned in a two-phase system with a UCON

50HB500 rich top phase and a dextran rich bottom phase. After the phases had separated, the top phase was subjected to temperature induced phase separation. Ecdysteroids partitioned mainly to the final top water phase in this new two-phase system. Therefore, temperature induced phase separation could be utilized to recover UCON polymer and obtain ecdysteroids in a water buffer solution. See application in Table No.3. The partitioning behaviour was manipulated by adding ethanol, sodium chloride or sodium sulphate to the primary two-phase systems. The recovery of ecdysteroids increased when ethanol was added to the system. In a two-phase system with an ethanol concentration of 20%, recovery was 73.6% for ecdysone and 85.6% for 20 hydroxyecdysone. With the UCON 50HB5100/hydroxypropyl starch (Reppal PES 200) system, they successfully extracted ecdysone and 20hydroxyecdysone from the common spinach plant, *Spinaciaoleracea* (Modlin*et al*., 1994). With 20% ethanol in the primary system recovery was 88.7% for ecdysone and 91.2% for 20hydroxyecdysone. Results indicated that aqueous two-phase partitioning coupled with temperature induced phase separation is a quick, easy and inexpensive bench top technique for extracting and purifying ecdysteroids from raw material. This technique could also be readily up scaled for commercial use (Table No.4)[14].

Table No.1: Parameters

Agitated Columns	Static Columns
KARR® Column SCHEIBEL® Column Rotating Disc Contactor (RDC) Pulsed Column	Sieve Trays Random Packing Structured (SMVP) Packing

Table No.2: Some aqueous two-phase systems

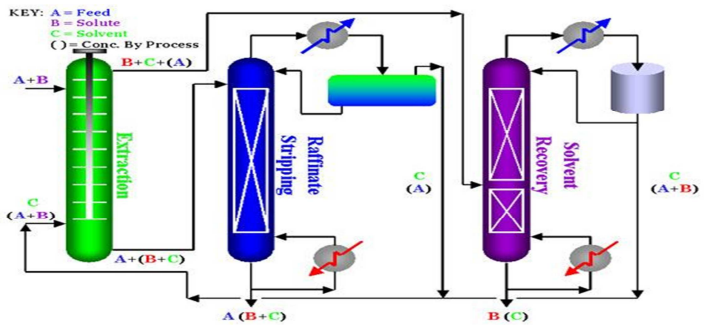
S.No	Component 1	Component 2	References
1	Polymer/polymer	Systems	-
2	Polyethylene glycol	Dextran	Albertsson, 1958
		Ficoll	Albertsson, 1958
		Polyvinyl pyrrolidone	Albertsson, 1958
		Polyvinyl alcohol	Albertsson, 1958
		Hydroxypropyl starch	Tjernel*det al*., 1986
3	Polypropylene glycol	Dextran	Albertsson, 1958
		Hydroxypropyl dextran	Albertsson, 1958
		Polyvinyl pyrrolidone	Albertsson, 1958
4	Polyvinyl alcohol	Dextran	Albertsson, 1958
		Hydroxypropyl dextran	Albertsson, 1958
5	Polyvinyl pyrrolidone	Dextran	Albertsson, 1958
		Maltodextrin	Giuliano, 1991
6	Methyl cellulose	Dextran	Albertsson, 195
		Hydroxypropyl dextran	Albertsson, 1958
7	Ethylhydroxyethyl cellulose	Dextran	Albertsson, 1958
8	Polymer/salt	Systems	---
9	Polyethylene glycol	Potassium phosphate	Albertsson, 1956
		Sodium sulphate	Eitemane*t al*., 1989
		Magnesium sulphate	Eitemane*t al*., 1989
		Ammonium sulphate	Albertsson, 1958
		Sodium citrate	Vernaue*t al*., 1990
10	Polypropylene glycol	Potassium phosphate	Albertsson, 1958
11	Methoxypolyethylene glycol	Potassium phosphate	Albertsson, 1958
12	Polyvinyl pyrrolidone	Potassium phosphate	Albertsson, 1958

Table No.3: Pharmaceuticals purified in ATPS

S.No	Pharmaceuticals	Recovery (%)	Purification factors	References
1	Human insulinlike	---	---	Hart *et al*., 1994
2	Growth factor 1	70	-	
3	(IGF1)	---	---	---
4	Human recombinant			Guan *et al*., 1996
5	Interferon α1	76	25	
6	(rhIFNα1)	---	---	---
7	Tumor necrosis	75	6	Wang *et al*., 1999
8	Factor (TNF)	---	---	---
9	α_1Antitrypsin	91	---	Harriset*et al*., 1997
10	(AAT)	---	---	---
11	Apolipoprotein A1	80	4.5	Perssonet *al*., 1999a
12	Milano variant of	85	7.2	Perssonet *al*., 1999b
13	Apolipoprotein A1	---	---	---
14	Protein A	80	26	Kamihirae*t al*., 1992
15	IgG	---	5.9	Andrews *et al*., 1996
16	Penicillin	76	---	Guan *et al*., 1996

Table No.4: Applications of extraction process in various Industries and medical sciences

Nuclear Industry Purification of uranium	**Inorganic Chemicals** Purification of phosphoric acid	**Metals Industry** Recovery of cobalt and nickel Recovery of rare earth elements	**Food Industry** Decaffeination of coffee and tea Separation of essential oils (flavors and fragrances)
Petrochemicals Separation of olefins/parafins Separation of structural isomers	**Polymer Processing** Recovery of caprolactam for nylon manufacture Separation of catalyst from reaction products	**Petroleum** Lube oil quality improvement Separation of aromatics/aliphatics (BTX)	**Effluent Treatment** Recovery of phenol, DMF, DMAC Recovery of acetic acid from dilute solutions
Pharmaceuticals Recovery of active materials from fermentation broths Purification of vitamin products	**Biotechnology** Recovery of carboxylic acids from biomass such as fermentation broths Recovery of oil from algae broths	**Chemical** Washing of acids/bases, polar compounds from organics Recovery of acrylic acid	-----



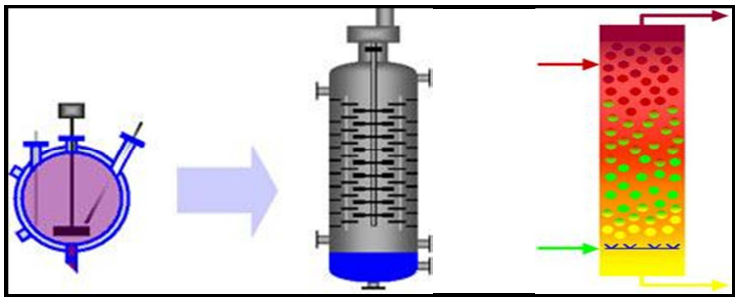


Figure No.1: General representation of extraction process

CONCLUSION

Extraction in pharmaceutical sciences and biotechnology (e.g for the production of antibiotics), in the herbal drug industry, in the food, essential oil and flavor industries, and in the production of other pharmacologically active products. In particular, it is used in the production of top quality pharmaceutical grade extracts, pharmacologically active intermediates, antibiotic extracts and phyto pharmaceuticals. However, the fact that it is used in all these areas in no way prevents its use in other areas. The technique is being used in the extraction of high quality essential oils, oleoresins, natural food colors, flavors and aromatic oils from all manner of plant materials.

ACKNOWLEDGMENT

The author is gratefully acknowledged the Management of Department of Pharmacy, Manav Bharti University, Solan, Himachal Pradesh, India for providing the facility.

CONFLICT OF INTEREST

We declare that we have no conflict of interest.

BIBLIOGRAPHY

1. Akama E, Tong A J, Ito M, Tanaka S. The study of the partitioning mechanism of methyl orange in an aqueous two-phase system, *Talanta, Oxford*, 48, 1999, 1133-1137.
2. Akama E, Tong A J, Ito M, Tanaka S. The study of the partitioning mechanism of methyl orange in an aqueous two-phase system, *Talanta, Oxford*, 48, 1999, 1133-1137.
3. Alred P A, Kozlowski A, Harris J M, Tjerneld F. Application of temperature induced phase partitioning at ambient temperature for enzyme purification, *J. Chromatogr. A, amsterdam*, 659, 1994, 289-298.
4. Andrews A T, Harris D P, Wright G, Pyle D L, Asenjo J A. Affinity gel electrophoresis as a pre dictive technique in the fractionation of transgenic sheep milk proteins by affinity aqueous two-phase partitioning, *Biotechnol. Lett., dordrecht*, 22, 2000, 1349-13-53.
5. Andersson K, Wingren C, Hansson U B. Liquidliquid partition chromatography as a method to ex amine surface properties of antibodies and antigenanti body complexes, *Scand. J. Immunol., oxford*, 38, 1993, 95-101.
6. Albertsson P A. Chromatography and partition of cells and cell fragments, *nature, london*, 177, 1956, 771-774.
7. Bailey R B, Wood word A. Isolation and characterization of a pleiotropic glucose repression resistant mutant of *saccharomyces cerevisiae, Mol. Gen. Genet., New York*, 193, 1984, 507-512.
8. Doss M O, Curtius H CH, Roth M. Clinical bio chemistry principles and methods, *New york: de gruyter*, 2, 1974, 13-23.
9. Bodhankar S S, Harihar V, Gaikar V G. Partitioning of amino acids in aqueous two-phase system of polyethylene glycol sodium sulfate in presence of surface active additives, *Bioseparation, dordrecht*, 6, 1996, 47-54.
10. Gharib B, Baswaid S, Quilici M, Dereggi M. Ecdysteroidlike compounds in human urinethey can occur in the absence of any

parasitic infection, *Clin.chim.acta, amsterdam,* 199, 1991, 159-166.
11. Baswaid S, Gharib B, Doumbo O, Quilici M, Dereggi M. Ecdysteroids in urine of African patients infected with helminthes, *Acta trop., amsterdam*, 47, 1990, 197-204.
12. Cheng I, Joelsson M, Johansson G. Combination of polymer bound charged groups and affinity ligands for extraction of enzymes by partitioning in aqueous two-phase systems, *J. Chromatog., amsterdam*, 523, 1990, 119-30.
13. Den hollander J L, Stribos B I, Van buel M J, Luyben K C A M, Van der wielen A M. Centrifugal partition chromatographic reaction for the production of chiral amino acids, *J. Chromatogr. B, amsterdam*, 711, 1998, 223-235.
14. Datar R, Rosen C G. Studies on the removal of escherichiacoli cell debris by aqueous two-phase polymer extraction, *J. Biotechnol., amsterdam*, 3, 1986, 207-219.
15. Bhide A A, Patel R M, Joshi J B, Pangarkar V G. Affinity partitioning of enzymes using unbound triazine dyes in peg/phosphate system, *Sep. Sci. Technol., new york*, 30, 1995, 2989-3000.
16. Gaikar V G, Bodhankar S S, Latha V. The effect of surface active additives on the partitioning of proteins and enzymes in aqueous two-phase systems, *J. Chem. Technol. Biotechnol., sussex*, 67, 1996, 329-332.
17. Albertsson P A. Particle fractionation in liquid two phase systems the composition of some phase systems and the behavior of some model particles in them, application to the isolation of cell walls from microorganisms, *Biochim. Biophys. Acta, amsterdam*, 27, 1985, 378-395.
18. Eiteman M A, Gainer J L. Peptide hydrophobicity and partitioning in poly(ethylene glycol) magnesium sulfate aqueous two-phase systems, *iotechnol.progr., washington*, 6, 1990, 479-484.
19. Den hollander J L, Wang Y W, Luyben K C A M, Van der wielen A M. Non separating effects in a centrifugal partition chromatographic reactor for the enzymatic production of lamino acids, *Chem. Eng. Sci., oxford*, 54, 1992, 201-18.
20. Bisson F, Fraenkel D G. Involvement of kinases in glucose and fructose uptake by saccharomyces cerevisiae, *Proc. Nat. Acad. Sci. United states amer. Biol. Sci., washington*, 80, 1983, 1730-1734.
21. Cohen M, Eiteman M A, Gainer J L. A model to predict the partition coefficients of aminoacids in peg salt aqueous two-phase systems, *Sep. Sci. Technol., new york*, 30, 1995, 225-237.

Please cite this article in press as: Sunil Kumar. Design and Development of Extraction Process in the Isolation of Phytopharmaceuticals from Plant Sources, *International Journal of Medicine and Health Profession Research,* 1(1), 2014, 28 - 38.