

Review Article

## A novel method: Phytonics

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### ABSTRACT

Plants are the most abundant source of crude drugs and many phyto-constituents have been proved to be very potent in the prevention, mitigation and treatment of various ailments. Extract is a substance isolated from plant tissues mostly by treating with a solvent and contains desired constituents but sometimes may have some residue of solvent. A solvent is expected to leach out the desired constituent but to be safe as well as automation and eco-friendly. Mostly organic solvents are used which may affect the health of the patient as well as the environment adversely. Phytonics has served as an ideal process for small as well as large scale extraction based on the use of non-chlorofluoro carbons as solvent and found to be very effective with very few limitations.

### 1. INTRODUCTION

Natural products are all chemical substances produced by living organisms and some of them are bioactive compounds which are used to cure and prevent diseases from so many years. Primary metabolites are directly linked to the normal growth, development or reproduction of an organism like, chlorophyll, starch, alurone grains, calcium oxalate crystals and amino acids. With the help of these primary metabolites, secondary metabolites are biosynthesized. These are biologically active compounds which give competitive advantage like survivability, fecundity etc. Plants contain many active compounds such as alkaloids, steroids, tannins, glycosides, volatile oils, fixed oils, resins, phenols and flavonoids which are deposited in their specific parts such as leaves, flowers, bark, seeds, fruits, root, etc. These are therapeutically active and some are very potent in action which is investigated by phyto-chemical investigation [1,2]

Extraction is the first step of phyto-chemical investigation followed by separation, purification and identification. Extraction, as the term is used pharmaceutically, involves the separation of medicinally active portions of plant or animal

tissues from the inactive or inert components by using selective solvents in standard extraction procedures. Extraction mostly is based on a physical transfer from the original plant material into another phase may be a liquid or gas. The products so obtained from plants are relatively impure liquids, semisolids or powders intended only for oral or external use [3]. Five basic steps of plant extraction are size reduction, extraction, filtration, concentration and further isolation and purification if required.

Quantity and nature of drug, degree of comminution, moisture content, nature and volume of solvent, mixing ratio, process of solution from disintegrated cells, process of solution from intact cells, imbibition of drugs, speed of establishment of equilibrium, temperature, pH of extracting solvent, interaction between dissolved constituents, lipophilicity of the solvent mixture and operation governing separation are the factors which affects the extraction of herbal drugs. Solvents or extraction agents must be suitable for dissolving the important therapeutic drug constituents and thus for separating them from the substances containing the drug which are to be extracted. Water, pure organic liquids and their mixtures are used as extraction solvents. Most of the organic liquids are hydrocarbons and their derivatives such as

halogenated hydrocarbons, alcohol, esters, ketones, ethers and oils etc. Selection of suitable solvent is governed by its selectivity towards constituents, ease of handling, economy, protection of the environment, and safety [4].

Due to increased attention and awareness towards the protection of the environment and safety attempts are being made to design efficient extraction processes using optimum number and quantity of safe liquids. Organic solvents are very important as liquid medium for reactions to take place. The majority of solvents are organic chemicals with hazardous and toxic properties, costly and part of the large waste by products of the chemical industry causing environmental problems. Although most of their toxic potential is known and there are safety rules for their use, prolonged and high concentration exposures can cause occupational diseases. Some solvents were replaced or severely restricted due to their high toxicity or carcinogenicity. Many epidemiological studies with chemists and laboratory technicians in analytical, chemical and biochemical laboratories showed that solvent exposure can cause adverse health effects. Various occupational solvents like benzene and atmospheric polluted air are absorbed into the human body either through the respiratory tract or via epidermal contact. These may cause primary respiratory symptoms and impaired pulmonary and dermatological functions. The haematopoietic system, as the cells recycle continually, is highly sensitive to most of the air pollutants, which are reaching the blood very fast without being bio-transformed. The solvents and air pollutants may interfere in the process of red blood cells proliferation. These changes are reflected in the synthesis of heme and the life expectancy of RBCs. Toxic material from air leads to significant damage to red blood cells causing a plastic anemia [5].

Another considerable factor is residual solvent which should be physiologically harmless if present in the end product. Residual solvents in pharmaceuticals are defined by the ICH as organic volatile chemicals that are used or produced in the manufacture of drug substances, excipients, or in the preparation of drug products. In general, solvents are not completely removed by practical manufacturing techniques. Solvents provide no therapeutic benefit, therefore all residual solvents should be removed to the extent possible to meet product specifications, good manufacturing practices, or other quality-based requirements. Appropriate selection of solvent for processing of a drug substance may enhance the yield, allow isolation of a preferred crystal form, improve purity, or enhance solubility. Given the presence of solvents in most pharmaceutical processing steps, the content of solvents in pharmaceutical products should be evaluated.

Drug products should contain no higher levels of residual solvents than can be supported by safety data. Commonly used solvents have been grouped by toxicity under the ICH Q3C guidance. The most toxic solvents- Class 1, should be avoided in the production of drug substances, excipients, or drug products unless their use can be strongly justified in a risk-benefit assessment. Some solvents associated with less severe toxicity (Class 2) should be limited in order to protect patients

from potential adverse effects. Ideally, less toxic solvents (Class 3) should be used where practical.

Several of the residual solvents frequently used in the production of pharmaceuticals are also listed as toxic chemicals in Environmental Health Criteria (EHC) monographs and the Integrated Risk Information System (IRIS). The objectives of such groups as the International Programme on Chemical Safety (IPCS), the United States Environmental Protection Agency (USEPA), and the United States Food and Drug Administration (USFDA) include the determination of acceptable exposure levels. The aim is protection of human health and maintenance of environmental integrity against the possible deleterious effects of chemicals resulting from long-term environmental exposure [6].

## 2. PHYTONICS EXTRACTION

Advanced Phytonics Limited (Manchester, UK) has developed this novel patented technology termed “Phytonics Process” or “Florasol Extraction” and the extracts thus obtained are referred as Phytols. Phytols describes a group of chemicals that are derived from non-chlorinated fluoro-hydrocarbons. The products mostly extracted by this process are fragrant components of essential oils, biological or phytopharmacological extracts which can be used directly without further physical or chemical treatment [7].

## 3. SOLVENT

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 hydrofluorocarbon-134a (HFC-134a) or Florasol (R134a) which was developed as a refrigerant, replacement for chlorofluorocarbons (Freon). The boiling point of this solvent is  $-25^{\circ}\text{C}$ . 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.

The process is advantageous in that the solvents can be customized: by using modified solvents with HFC-134a, 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.

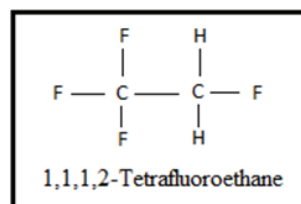


Fig. 1. Structure of 1,1,1,2-Tetrafluoroethane

1,1,1,2-Tetrafluoroethane (Fig.1) (CAS no. 811-97-2;  $\text{C}_2\text{H}_2\text{F}_4$ ; 1,2,2,2-tetrafluoroethane, HFC 134a, HFA 134a, HCFC 134a) is a colourless, non- inflammable gaseous fluorocarbon with a faint ether like odour. It is soluble in alcohols, esters, and

chlorinated solvents, but it is only slightly soluble in water. It has a boiling point of 26°C and a vapour pressure of 630 kPa at 25°C. It is manufactured by the reaction of hydrogen fluoride with trichloroethylene in a closed system and available as a liquefied gas, supplied in a variety of pressurized containers. 1,1,1,2- Tetrafluoroethane is used primarily as a refrigerant for “high-temperature” refrigeration, such as domestic refrigerators and automobile air conditioners. Other potential uses include application in plastic foam blowing, as a solvent, as an aerosol propellant for medical inhalers, and as a fire extinguishant in place of halons. It’s global warming potential over a 100- year time horizon (relative to carbon dioxide) has been estimated at 1300, compared with 3800 for CFC-11 and 8100 for CFC-12, for which 1,1,1,2-tetrafluoroethane is the main substitute [8].

#### 4. INSTRUMENTATION AND METHOD



Fig. 2. Phytosol extraction unit [7]

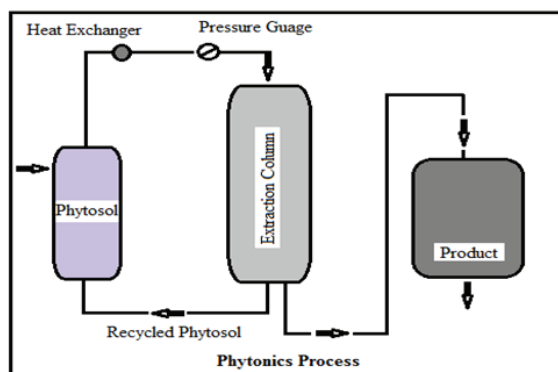


Fig. 3. Phytosol process

For solid-liquid extraction using phytosols a stirred extraction vessel or an extraction column, evaporation/collection vessel,

gas compressor and heat exchanger is required. Phytosol is evaporated with the aid of a gas compressor, re-liquefied and passed through the medium, which can be either a stirred batch or a packed column. Phytosol rich in product (or contaminant) passes through an inline filter into the evaporation vessel. By carrying out this operation continuously, only a small inventory of phytosol is required. At the end of the extraction, phytosol flow is redirected into a storage cylinder and the extracted material is recovered from the evaporator. The AP process using phytosols has been used for extraction of essential oils and biologically active compounds from solid botanical materials and claimed to show enhanced biological activity compared with conventional extracts [7].

Phytosols work similarly for liquid-liquid continuous extraction. Components include an extraction column, treated aqueous collection vessel, evaporation/isolation vessel, gas compressor and a heat exchanger. Phytosol is continuously evaporated, re-liquefied and recycled through the column in a down-flow mode. When steady state is attained, rich aqueous stream is introduced through the column in a counter current fashion. The now rich Phytosol continues to be fed into the evaporation vessel, evaporated (distilled) and re-liquefied. A multi-vessel design enables the process to be run in a continuous fashion. Alternatively, efficient extraction can be achieved using a centrifugal mixer/ separator. Podbielniak equipment has been successfully used in a variety of applications. This has proved extremely useful in cases where the morphology of the aqueous stream may inhibit efficient phase separation [9].

#### 5. ADVANTAGES

- (a) 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.
- (b) The processing plant is totally sealed so that the solvents are continually recycled and fully recovered at the end of each production cycle. 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 “ecofriendly” to handle.
- (c) The process is cool and gentle and its products are never damaged by exposure to temperatures in excess of ambient.
- (d) No vacuum stripping is needed which, in other processes, leads to the loss of precious volatiles.
- (e) The process is carried out entirely at neutral pH and, in the absence of oxygen, the products never suffer acid hydrolysis damage or oxidation.
- (f) The technique is highly selective, offering a choice of operating conditions and hence a choice of end products.
- (g) It is less threatening to the environment.
- (h) It requires a minimum amount of electrical energy.

- (i) It releases no harmful emissions into the atmosphere and the resultant waste products (spent biomass) are innocuous and pose no effluent disposal problems.
- (j) The solvents used in the technique are not flammable, toxic or ozone depleting.
- (k) The solvents are completely recycled within the system.
- (l) The solvents are neither acidic nor basic, so there is minimal potential reaction with botanicals.
- (m) Unlike, supercritical carbon dioxide (SCCO<sub>2</sub>) equipment costs is low, since high pressure equipment is not required.
- (n) Unlike CO<sub>2</sub>, phytosols do not form acids when exposed to water.
- (o) The other principal benefit is a much lower working pressures for liquification. Low working pressures also translate into lower operating costs.

## 6. LIMITATIONS

- (a) The only limitation is need of electricity, however consumption is very low.
- (b) Theoretically this is a poor solvent.
- (c) The solvent is not miscible with mineral oils or triglycerides, and
- (d) The solvent does not dissolve plant wastes [10,11].

## 7. APPLICATIONS

The phytonics process can be used for extraction in 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 phytopharmaceuticals. 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. The technique is also used in refining crude products obtained from other extraction processes. It provides extraction without waxes or other contaminants. It helps remove many biocides from contaminated biomass [13-15].

### Industrial User

Wilde and Company, U.K. (Florasols developed by Dr. Peter F. Wilde) [12].

## 8. CONCLUSION

In search of a suitable and safe solvent various processes have been proposed, some of them are found suitable for small scale extraction, while some for large scale extraction and although theoretically excellent sometimes feasibility limits their use. Compliance of international rules and guidelines in this regard is today's basic need, if the products are expected to be used worldwide. The study summarizes the basic principle, the process and the instrumentation of phytonics extraction and finds that the

method is useful in isolation of desired phyto-constituents, serves the solution for toxic solvents while having no adverse effect on environment. However there are some limitations out of which some could be worked out by proper scale up techniques while some by further research.

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