IN FACT,

WHAT IS AN EXTRACT ?

A plant extract is a substance or an active with desirable properties that is removed from the tissue of a plant, usually by treating it with a solvent, to be used for a particular purpose. Extracts may be used in various sectors of activities : Food and functional properties for foodstuffs (antioxidant, texturizer, etc…), Processing aids, additives – chemical replacers, pharmaceutical for therapeutic properties - preventive and/or curative – cosmetic for functional properties for beauty and well-being, etc…

Some sectors of activities clearly define an extract. For cosmetic uses, for instance, a "cosmetic product" shall mean any substance or preparation intended to be placed in contact with the various external parts of the human body (epidermis, hair system, nails, lips and external genital organs) or with the teeth and the mucous membranes of the oral cavity with a view exclusively or mainly to cleaning them, perfuming them, changing their appearance and/or correcting body odors and/or protecting them or keeping them in good conditions.

An extract may be common to different sectors based on its chemical description, although different sectors mean different technologies (different forms, solubility, stability), different regulation, different claim, different problematic. As representing manufacturers, we feel very concerned by the request of the end-users and may adapt its proposal.

An extract must also respect :

- The quality constraints in terms of irradiation, allergens, toxicity, adulteration, activity, stability, sustainable resources, traceability, etc…
- The chemical and physical request in terms of description (TLC, physical recognition, genotype) as well as heavy metals, nitrates, solvents, residues such as pesticides or residual solvents, additives, foreign bodies, etc…
- The regulation in terms of assay, solvent, environmental components, legal uses, registration or notification (reach, organic grades,…), labeling, claims, certification (GMP, ISO), etc…

Raw Material

It's important to understand that an extract starts from the raw material: the plants. The Identification of a good source includes the description of areas and type of collect, the capacity of collect, the use and not-used area and the impact of our needs for extraction to guarantee a sustainable source. It's so important to analyze the supply chain starting from the collect, including the exporters and the different middle men, which may cause variability on the quality besides the natural variability linked to the weather and the soils. Finally, an overview of the needs of the local citizens and the risk (government, wars, weather, etc…) allows to find the right partners for the long term, and minimize the impact on the nature while checking the return to the people.

Preparation

All equipment may not use the same materials, and the quality of the extraction may vary depending on the preparation of the raw materials. This goes from the cleaning to avoid foreign bodies to the cut or grinding. Dried herbals are more common, with the risk to put out some gaseous components and the benefit that the plant does not start to hydrolyze or produce non needed metabolites. Preparation may also consist in thawing (fruits may be frozen for instance), cooking (to produce aromas for instance), decoating, destemming, or even enzymatic reaction before the extraction.

Solvents

A solvent must comply with the local regulation, be effective and be selective enough (when needed). Most common are Water, Ethanol, Ethyl acetate, CO2, Methanol, Aceton, Acetic acid, Hexane… the choice of the solvent will impact on the yield of extraction (acquaintance with the targeted actives) in the full respect of the request from customers and environmental components (depletion of the ozone layer, life of the solvent in atmosphere, groundwater pollution, air pollution).

On a chemical point of view, the best solvent may be chosen after looking at the dipolar moment : an electric dipole is a separation of positive and negative charges, characterized by their dipolar moment, a vector quantity (Coulomb. meter or Debye), subject to continuous electrostatic attraction and repulsion. Each solvent may be classified based on its dipolar moment (cf. : Ven der Waals Forces).

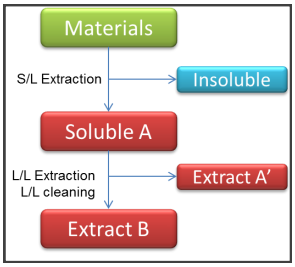
- **Apolar and low polar solvent**, mainly lipophilic characteristic, with a moment from 0 to 1.5 (Hexane, cyclohexane, dimethoxymethane, Chloroform, Ethylic ether, phenol)
- **Polar aprotic** solvent, mainly hydrophilic characteristic

Protic solvent (a protic solvent is a solvent that has a hydrogen atom bound to an oxygen as in a hydroxyl group or a nitrogen as in an amine group). Polar protic solvents are solvents that share ion dissolving power with aprotic solvents but have an acidic hydrogen. These solvents generally have high dielectric constants and high polarity).

Moment of most common solvents : Hexane (0), Ethanol (1.69), Methanol (1.70), Ethyl acetate (1.78), water (1.85), aceton (2.88). Depending on their miscibility, solvents may be used together (combined solvents, or separation from one solvent to another solvent).

Extraction process

The process must generally be simple, fast, economic, in compliance with the local regulation, effective and selective when needed. However, certain steps may require a long time of process.



Pressing : One of the more usual extraction (the morning orange juice), pressing may be used complementary or prior to other process, for instance to prepare the materials, defat it, etc… It causes mechanical perturbation and gives a liquid product.

Distillation and hydro-distillation : By direct heating or steam, this process is mainly used for oils and volatile components. It may cause degradation (oxidation, hydrolysis, enzymatic reaction, ….)

Solid / Liquid extraction : It consist in the extraction or separation of one active or more from solid materials working on the solubility in

Adulteration & Falsification : get the right efficiency

Adulteration means falsification of an extract in terms of origin, assay, extraction, actives, or analysis, mostly in order to improve the price.

- **Method of analysis** :
  - UV versus HPLC : except for very few actives / markers, UV methods always give much higher response than HPLC (when the standard exists of course) without being able to find a correlation. This may be versus HPLC, or can be many others, especially when using internal method.
  - Wave lengths : a different wave length or the use of a different Specific Absorption Coefficient
  - Standard : the use of a different standard for a better response by HPCL.
  - Family of the actives : refer to the global family of the actives instead of the active alone.
  - Reduction of the number of markers, what allows to use addition of chemical origin. The more there are markers in the description, the most difficult it is to falsify them.
- **Plant Extract Ratio** : difficult to be sure to get a 4:1 extract when there's no marker to control.
- **NER / PER** : voluntary misunderstanding between Native extract and Plant extract, sometime even considering the original plant, with the water.
- **Specie** : use of a another bionomial origin, of even a plant close to the original plant (same genus)
- **Part of plant** : use of a different part than the one mentioned or recommended (for instance, leaves instead of roots, even partly)
- **Addition of chemicals** : addition of exogenous origin material, from other plants or from chemical process. They can be added to a colored carrier or sometimes to the plant powder in order to get at least a positive TLC.
- **Solvents** : use of another solvent than the one mentioned for a more selective and efficient extraction.
- **Geographical Origin** : plants may offer a different profile depending on the geographical origin, that you may need specifically. It can be also collected from a non-authorized zone.

Those are the most common noted origins of adulterations.

a liquid to obtain the soluble part and the insoluble part, or fractionation of an homogenous solution. The typical Solid / Liquid extractions are :

- **Maceration** : solid in solvent, room temperature
- **Digestion** : solid in solvent, over room temperature, below ebullition
- **Decoction** (=reflux): solid in solvent, temperature of ebullition
- **infusion** (teas) : solid in liquid at temperature of ebullition, then cooling of the suspension
- **Elution**, **leaching** (Lixiviation) : solvent goes through the solid
- **Lixiviation** : always with cold, fresh and new solvent
- **Percolation** : solvent goes on and through the solid

Concentration

This step consists in the increase of the dry matter content to facilitate the further steps, using for instance evaporation.

Separation / Purification

Different type of separation, based on size, weight, charge, hydrophilic / lipophilic capacity (separation liquid / liquid), solubility, volatility (liquid / steam), etc…

Filter press : the filter press uses increased pressure to maximize the rate of filtration and produce a final filter cake with a low water content.

Membranes, **Ultra filtration**, **Nano filtration** : membrane filtration or cross-flow filtration technology which ranges between ultrafiltration (UF) and reverse osmosis (RO). The fundamental principle of Nanofiltration membrane technology is the use of pressure to separate soluble ions through a semi permeable material.

Liquid / Liquid : Liquid-Liquid Extraction (LLE) is a method used in the recovery of a key component from a multi-component stream using an immiscible solvent. The two steams are contacted and separated. The solvent absorbs the key component stripping it from the original stream.

Crystallization

Crystallization is the (natural or artificial) process of formation of solid crystals precipitating from a solution. Crystallization is also a chemical solid-liquid separation technique, in which mass transfer of a solute from the liquid solution to a pure solid crystalline phase occurs. The crystallization process consists of two major events, nucleation (the solute molecules dispersed in the solvent start to gather into clusters, on the nanometer scale) and crystal growth (subsequent growth of the nuclei that succeed in achieving the critical cluster size). Nucleation and growth continue to occur simultaneously while the supersaturation exists.

- **Single-solvent recrystallization** : "compound A" and "impurity B" are dissolved in the smallest amount of hot solvent to fully dissolve the mixture, thus making a saturated solution. The solution is then allowed to cool => different solubility of compounds in solution drops => compound dropping (recrystallizing) from solution. The slower the rate of cooling, the bigger the crystals formed. The solid crystals are collected by filtration.
- **Multi-solvent recrystallization** : similar to the single-solvent but where two (or more) solvents are used. the proportion of first and second solvents is critical. Possible removal by distillation or by an applied vacuum.
- **Hot filtration-recrystallization** : separate "compound A" from both "impurity B" and some "insoluble matter C".
- **Seeding** : this can be spontaneous or can be done by adding a small amount of the pure compound (a seed crystal)

Chromatography

Chromatography is used for separation of mixtures. A mixture dissolved in a “mobile phase” passes through a stationary phase, which separates the analyte. The ultimate goal of chromatography is to separate different components. The stationary phase or adsorbent in column chromatography is a solid. The most common stationary phase for column chromatography is silica gel, followed by alumina. Also possible are ion exchange chromatography, reversed-phase chromatography (RP), affinity chromatography or expanded bed adsorption (EBA). The mobile phase or eluent is either a pure solvent or a mixture of different solvents. It is chosen so that the retention factor. The Van Deemter equation in chromatography relates the variance per unit length of a separation column to the linear mobile phase velocity by considering physical, kinetic, and thermodynamic properties of a separation

- **Column chromatography** : the stationary bed is within a tube. The particles of the solid stationary phase or the support coated with a liquid stationary phase may fill the whole inside volume of the tube (packed column) or be concentrated on or along the inside tube wall leaving an open, unrestricted path for the mobile phase in the middle part of the tube (open tubular column). Differences in rates of movement through the medium are calculated to different retention times of the sample.
- **Flash column chromatography** : the solvent is driven through the column by applying positive pressure. This allowed most separations to be performed in less than 20 minutes, with improved separations
- **Thin layer chromatography** (TLC) is similar to paper chromatography. However, instead of using a stationary phase of paper, it involves a stationary phase of a thin layer of adsorbent like silica gel, alumina, or cellulose on a flat, inert substrate. Compared to paper, it has the advantage of faster runs, better separations, and the choice between different adsorbents
- **Ion exchange chromatography** uses ion exchange mechanism to separate analytes. It uses a charged stationary phase to separate charged compounds including amino acids, peptides, and proteins. In conventional methods the stationary phase is an ion exchange resin that carries charged functional groups which interact with oppositely charged groups of the compound to be retained. Ion exchange chromatography is commonly used to purify proteins using FPLC (fast protein liquid chromatography)
- **Chiral chromatography** involves the separation of stereoisomers

HPLC

(High Pressure Liquid Chromatography) and LPLC (low pressure). Preparative high performance liquid chromatography is similar to analytical HPLC but features increased injected mass with possibility to “stack” injections automatically. There’s technically no product limitation, but usually expensive.

Semisynthesis

Hemisynthesis or Semisynthesis or partial chemical synthesis is a type of chemical synthesis that uses compounds isolated from natural sources (e.g. plant material) as starting materials. These natural biomolecules are usually large and complex molecules. This is opposed to a total synthesis where large molecules are synthesized from a stepwise combination of small and cheap (petrochemical) building blocks.

It is also possible that the semisynthetic derivative outperforms the original biomolecule itself with respect to potency, stability or safety. Drugs derived from natural sources are usually produced by harvesting the natural source or through semisynthetic methods.

Drying

Drying means putting out the liquid. Dryers may be atmospheric (spray dryer, fluid bed dryer, etc...), or vacuum (belt dryer, tray dryer, etc…).

Spray Dryer

By definition, spray drying is the transformation of feed from a fluid state into a dried form by spraying the feed into a hot drying medium. The process is a one step continuous operation. The feed can be either a solution, suspension or a paste. The spray dried product conforms to powder consisting of single particles or agglomerates, depending upon the physical and chemical properties of the feed and the dryer design and operation

Vacuum dryer

At constant volume, when the pressure decreases, the boiling temperature decreases. Evaporation at a lower temperature makes possible to get a preserved product. In addition the high rate of heat efficiency is said to result in the best drying performance in the world. The drying process is greatly accelerated due to the fact that the loaded material makes contact with the heating panel in the form of a thin layer. Vacuum drying does not cause the emission of any exhaust gases or hazardous smells.

Lyophylization or cryodessication

A lyophilizator needs to cool (for freezing and trapping water), create a vacuum (to sublimate water), generate heat and transfer heat energy to the product.

Others : Rotary Drum Dryer : Wet material is introduced from one end of the dryer, and then stirred evenly by the oar of the inner barrel - Plate Dryer : kind of high-efficiency conductive and continuous drying - Blade Dryer : drying or cooling paste-like, granular, powdery and pulpous material - etc…

Before Packing

Further steps before packing consist in Milling, compacting (to increase the bulk density for instance), grinding (to tune the size reduction in a safe way, especially with fragile particle or components) and then homogenization and standardization : those steps guarantee a optimized repartition and the correct and needed content of actives as mentioned in our CoA (certificate of analysis).