[**EXTRACTION OF HERBAL DRUGS BY USING HYDROTROPY SOLUBLIZATION PHENOMENON**](https://www.researchgate.net/publication/267484060_EXTRACTION_OF_HERBAL_DRUGS_BY_USING_HYDROTROPY_SOLUBLIZATION_PHENOMENON?enrichId=rgreq-c6bc004ba36f74730aacd28796cb84ce-XXX&enrichSource=Y292ZXJQYWdlOzI2NzQ4NDA2MDtBUzoxNTc1NTg5MjA3MjAzODRAMTQxNDU3NjM4MjM4OA%3D%3D&el=1_x_3&_esc=publicationCoverPdf)

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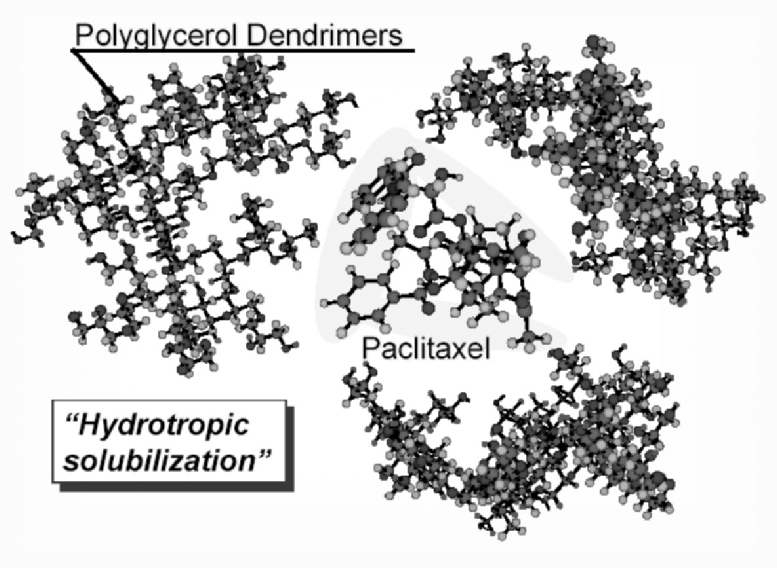
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**Graphical Background**

The extraction of natural medications has long been a difficult task for researchers. The purpose of this paper is to provide an overview of the extraction of herbal medications using the hydrotropy solubilization phenomena. A hydrotrope is an organic molecule that improves the solubility of surfactants and water-insoluble phyto-constituents of herbal medications in an aqueous solution, such as esters, acids, alcohols, aldehydes, ketones, hydrocarbons, and lipids. By cell permeabilization, hydrotropes such as sodium alkyl benzene sulfonates and sodium butyl monoglycol sulphate were employed to selectively extract water insoluble phyto-constituents.



**INTRODUCTION**

Plant-derived compounds have recently gained popularity due to their numerous applications. Medicinal plants are the richest bio-resource of medications from ancient medical systems, modern medicines, nutraceuticals, food supplements, folk remedies, pharmaceutical intermediates, and chemical entities for synthetic drugs [1]. The separation of medicinally active sections of plant (and animal) tissues using selective solvents and established processes is known as extraction. The plant products obtained in this manner are relatively complicated combinations of metabolites in liquid or semisolid form, or (after removal of the solvent) in dry powder form, and are designed for oral or external application. Decoctions, infusions, fluid extracts, tinctures, pilular (semisolid) extracts, and powdered extracts are examples of these preparations. Popular names for such preparations. Such preparations have been popularly called galenicals, named after Galen, the second century Greek physician [2]. The first step in the phytochemical process is the extraction of phytoconstituents from plant material. The extraction of phytoconstituents is dependent on the solvent's solubility as well as its surface permeability. Because of the solubility factor, certain phytoconstituents are frequently not recovered in the standard extraction method. As a result, complete extraction is not possible. Various strategies have been used to address this issue on numerous occasions. Supercritical fluid extraction is one such procedure that helps to solve numerous difficulties, but it has some downsides in terms of automation, feasibility, and expense. The usage of Hydrotropes [3] is an innovative technique to overcoming all of these issuesNeuberg (1916) used the term hydrotropic agent to describe anionic organic salts that, at high concentrations, significantly improve the water solubility of poorly soluble solutes [4]. However, the word has been used in the literature to refer to nonmicelleforming chemicals that can solubilize insoluble compounds, whether liquids or solids, organic or inorganic. Rather than a particular complexation event or a process dominated by a medium effect, such as cosolvency or salting-in, the hydrotropic solubilization process involves cooperative intermolecular interaction with numerous balancing molecular forces. Hydrotropic compounds have been shown to improve the aqueous solubility of medications that are weakly water soluble [5-24]. By cell permeabilization, hydrotropes such as sodium alkyl benzene sulfonates and sodium butyl monoglycol sulphate were employed to selectively extract water insoluble or non-polar phyto-constituents. Sodium benzene sulfonate, sodium toluene sulfonate, sodium xylene sulfonate (SXS), sodium cumene sulfonate, and sodium cymene sulfonate are some more hydrotropes. The self-aggregation of hydrotropes has been considered a prerequisite for a variety of applications in various fields such as drug solubilization [25], chemical reactions [26], separation of organic compounds [27], extraction of curcuminoids from turmeric [28], extraction of embelin from Embelica ribes [30, 31], Boswellic acids from Boswellia serrata resins [32], Diosgenin from Dioscorea Rhizomes [33].

**Mechanism of Action**

1. Plant cell walls are composed of phospholipid bilayers. The hydrotrope degrades the phospholipid bilayer and enters the cell wall through the inner structures. Water soaking has virtually little effect on cork cells. Cork cells' cell walls are composed of cellulose and suberin lamella. The suberin lamella renders the cork cell watertight. The hydrotrope solutions, on the other hand, dissolve the water-impermeable suberin lamella and then the mature cork cells. The hydrotrope disturbs the cork cell layers, allowing the water solution to permeate through the cell wall. When the interior section of the cell is exposed to the hydrotrope solution, it swells and releases the cells from tightly linked structures.. Hydrotropic solutions precipitated the solutes; out of the solution on dilution with water thus enable the ready recovery of the dissolved solutes [34].

2. Hydrotropic substances can destabilise the O/W and W/O microemulsions and the lamellar liquid crystal, resulting in a "phase transition" from the lamellar liquid crystal phase to the bi-continuous structure. This is referred to as the hydrotrope-solubilization action. Vitamin C has hydrotrope solubilizing properties [35, 36].

3. Hydrotropes are referred to as 'coupling agents'. When hydrotropes are added to a turbid liquid with a high water content, the liquid transparentifies due to phase transition"[37].

**Choice of solvents for conventional Methods**

The type of solvent employed in the extraction technique has a considerable impact on the success of determining physiologically active chemicals from plant material. Low toxicity, ease of evaporation at low heat, promotion of quick physiologic absorption of the extract, preservation action, and inability to cause the extract to complex or dissociate are all characteristics of a good solvent in plant extractions. The quantity of phyto-chemicals to be extracted, the rate of extraction, the diversity of different compounds extracted, the diversity of inhibitory compounds extracted, the ease of subsequent handling of the extracts, the toxicity of the solvent in the bioassay process, and the potential health hazard of the extractants are all factors that influence the solvent choice [38]. The intended use of the extract influences the solvent selection. Because traces of residual solvent will be present in the final result, the solvent should be non-toxic and should not interfere with the bioassay. The decision will also be influenced by the molecules to be extracted [39].

**The various solvents that are used in the extraction procedures are :**

The various solvents that are used in the extraction procedures are as follow

1. Water

2. Acetone

3. Alcohol

4. Chloroform

5. Ether

6. Dichloromethanol [40].

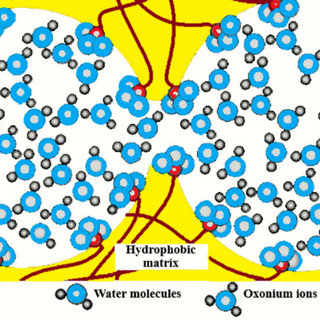
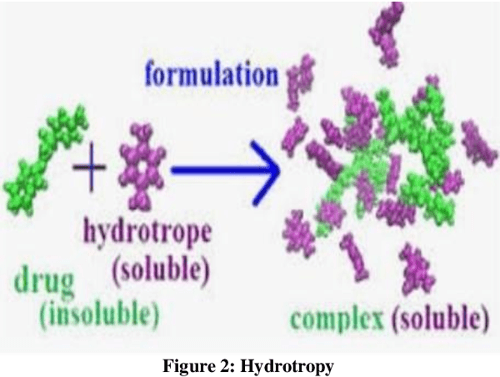
**Problems associated with conventional Methods of Extraction:**

**1. Continuous hot extraction (Soxhlet Extraction**): The extraction of active as well as other components, such as carbohydrates, gums, and oils, results from continuous solvent extraction of raw material. As a result, solvent extraction procedures typically produce complicated extracts. This must then be purified using multi-step procedures like chromatography or crystallisation. Aside from poor extract quality, the problems in handling large volumes of flammable volatile organic solvents and residual solvent traces in the finished product limit the use of organic solvents for extraction.

**2. High-pressure steam treatment and supercritical fluid extraction**: It can also improve extraction rates by applying an osmotic shock and carbon dioxide, respectively; however, due to the high cost involved, these procedures can only be utilised for high-value and low-volume materials [41].

**3. Ultrasound treatment**: It can shatter cell walls by severe dynamic straining, increasing yield and mass-transfer rate in a variety of solid-liquid extraction procedures. However, the action of ultrasound is localised, and applying it to a wide volume of raw material may be inefficient [42].

**4. Problems in extraction of solid plant material:** There are two challenges in extracting essential oils from solid plant materials: freeing the essential oil from the solid matrix and successfully allowing it to diffuse out in a way that can be scaled up to industrial proportions. Microwave-mediated techniques, in particular, are extremely desired in essential oil extraction due to their small equipment size (portability) and controllability via mild increments of heating. So far, microwave technology has discovered a purity of 85% piperine from black pepper. Piperine was extracted selectively by cell permeabilization of Piper nigrum fruits using hydrotropes. The recovered piperine was approximately 90% pure and devoid of oleoresins.



**Figure 1: Hydrotropic matrix Formation**

**Figure 2: Hydrotropic Solubilization mechanism**

**Application of Hydrotropic agent for extraction of herbal drugs**

1. **Extraction of Embelin from Embelia ribes by Hydrotropes:** The study presents an alternative extraction approach for embelin (2,5dihydroxy3undecylpbenzoquinone) from Embelia ribes. Aromatic hydrotropes such as sodium n butyl benzene sulfonate (NaNBBS) and sodium cumene sulfonate (NaCS) were discovered to be effective for the selective extraction of embelin, with a recovery of 95% embelin from high purity aqueous solutions of hydrotropes. The technique was further optimised in terms of hydrotrope concentration and extraction temperature [43].
2. **Extraction of Piperine from Piper nigrum (Black Pepper) by Hydrotropic Solubilization:** Piperine was selectively extracted from Piper nigrumfruits using hydrotropes such as sodium alkyl benzene sulfonates and sodium butyl monoglycol sulphate. The increased extraction rates of aqueous hydrotrope solutions were attributed to the penetration of hydrotrope molecules into cellular structures and subsequent cell permeabilization. After adsorption on a cell wall, hydrotrope molecules disrupt its structure and the bilayered cell membrane, allowing piperine to be extracted quickly. The hydrotrope solution extracted piperine from black pepper in a selective and fast manner. The recovered piperine was 90% pure and nearly oleoresin-free. The hydrotrope type and nature, hydrotrope concentration, temperature, and particle size all had a major impact on the extraction process[44].
3. **Extraction of dioscin from dioscorea rhizomes by Hydrotropes:** Cell permeabilization and dioscin extraction from dioscorea rhizomes were examined using aqueous solutions of aromatic hydrotropes. Unlike the traditional technique, the recovered dioscin was hydrolyzed to diosgenin in the same hydrotropic solutions without considerable degradation to 3,5-diene. The parameters influencing dioscin extraction, such as the nature and concentration of the hydrotrope, temperature, and particle size, were optimised. At 353 K, sodium cumene sulfonate was the most efficient hydrotrope for dioscin extraction and hydrolysis to diosgenin. Diosgenin precipitates with >95% purity from aqueous NaCS solutions at 293 K due to its poor solubility in aqueous solutions [45].
4. **Extraction of Curcumin by Hydrotropes:** Cell permeabilization and dioscin extraction from dioscorea rhizomes were examined using aqueous solutions of aromatic hydrotropes. Unlike the traditional technique, the recovered dioscin was hydrolyzed to diosgenin in the same hydrotropic solutions without considerable degradation to 3,5-diene. The parameters influencing dioscin extraction, such as the nature and concentration of the hydrotrope, temperature, and particle size, were optimised. At 353 K, sodium cumene sulfonate was the most efficient hydrotrope for dioscin extraction and hydrolysis to diosgenin. Diosgenin precipitates with >95% purity from aqueous NaCS solutions at 293 K due to its poor solubility in aqueous solutions [45].
5. **Extraction of bioactive limonoid aglycones and glucoside from Citrus aurantium L. using hydrotropy:** Citrus limonoids have been shown to have potential biological actions in lowering the risk of certain diseases. Citrus fruits contain limonoids in the form of aglycones and glucosides. Currently, limonoid aglycones and glucosides are extracted in many processes using various solvents. It may be advantageous to isolate and purify these chemicals using environmentally friendly procedures in order to better understand their potential bioactivity. A hydrotrope polystyrene adsorbent resin was used to develop a new method of extracting and purifying limonoids. Using an aqueous solution of sodium cumene sulphonate (Na-CuS), aglycones and glucosides were extracted in a single step. Sour orange (Citrus aurantium L.) seed powder was extracted for 6 hours with a 2 M Na-CuS solution at 45° C. The structures of the isolated compounds were confirmed by NMR spectroscopy as deacetyl nomilinic acid glucoside (DNAG), deacetyl nomilin (DAN) and limonin (LIM) [46].
6. **Hydrotropic Extraction Process for Recovery of Forskolin from Coleus Forskohlii Roots:** Citrus limonoids have been demonstrated to have biological activities that may reduce the risk of certain diseases. Limonoids are found in citrus fruits in the form of aglycones and glucosides. Currently, limonoid aglycones and glucosides are extracted using a variety of solvents in a variety of procedures. To further understand their potential bioactivity, it may be helpful to isolate and purify these compounds utilising environmentally safe processes. To create a new method of extracting and purifying limonoids, a hydrotrope polystyrene adsorbent resin was used. Aglycones and glucosides were extracted in a single step using an aqueous solution of sodium cumene sulphonate (Na-CuS). At 45° C, a 2 M Na-CuS solution was used to extract sour orange (Citrus aurantium L.) seed powder for 6 hours.
7. **Hydrotropic extraction of bioactive limonin from sour orange (Citrusaurantium L.) seeds:** Limonoids are bioactive chemicals found only in citrus fruits and vegetables. Using aqueous hydrotropic solutions, a new method for extracting limonoid aglycones from sour orange (Citrus aurantium L.) seeds was studied. The extraction efficiency was affected by hydrotrope concentration, extraction temperature, and raw material loading percentage. The Box-Behnken experiment design was used to study two hydrotropes, sodium salicylate (Na-Sal) and sodium cumene sulphonate (Na-CuS). Data was subjected to response surface analysis (RSA) to investigate the effect of factors on extraction efficiency. Limonin, a prominent limonoid aglycone, was isolated and measured for process optimisation. Both hydrotropes had the highest limonin yield at 2 M concentration, 45 °C extraction temperature, and 10% solid loading. Na-CuS produced the highest limonin output of 0.65 mg/g seeds, while Na-Sal produced just 0.46 mg/g seeds. Using this method, the usage of organic solvents can be drastically decreased, making the extraction of bioactive substances more environmentally friendly [46].

**DISCUSSION**

Herbal medicines are a superior choice to current synthetic treatments because they have little or no negative effects. Herbal preparations, in general, imply the use of fresh or dried plant parts. The precise knowledge about such raw pharmaceuticals is a critical feature in the creation, safety, and efficacy of herbal therapies. Extraction procedures involve utilising particular solvents to separate medicinally active elements of plant organisms from inert components. Maceration, infusion, percolation, digestion, decoction, hot continuous extraction, aqueous-alcoholic extraction through fermentation, counter-current extraction, microwave-assisted extraction, ultrasound extraction (sonication), supercritical fluid extraction, photonic extraction, and hydrotrophic solubilization technique are examples of standard medicinal plant extraction strategies. The type of solvent used in the extraction technique has a substantial impact on the systematic study of plant species for the purpose of discovering new bioactive components and the effective evaluation of biologically active substances from plant parts. Non-standardized extraction methods can also result in the destruction of phytochemicals found in plants. Efforts must be taken to develop batches that are as consistent as possible and adhere to the nice extraction strategies.

The hydrotrophic solubilization process is a common method of extracting medicinal plants. Hydrotropes are potential compounds that can aid in the extraction process by increasing solubility. The examples given above demonstrate that they can be employed in the extraction of numerous herbal medications. This technique can be used to extract herbal medications that have a low solubility in aqueous solution. Such extracts can be made by adding hydrotropes without changing the ingredients' physicochemical properties. These hydrotropes can be used to extract a variety of resins as well as low permeability agents. This review focuses on the use of hydrotropic agents in herbal medicine extraction technologies and their implications for pharmaceutical research and development. The primary goal of this review is to investigate the feasibility of using a novel affordable hydrotropic agent to replace the use of an organic solvent.

**CONCLUSION**

Hydrotropic extraction has the ability to (a) undergo particular interactions with amphiphiles, (b) affect the mixing behaviour of oil and water, (c) self-associate in water, (d) increase the aqueous solubility of various solutes, and (e) selectively extract bioactive chemicals on a commercial scale. The hydrotrope solution in aqueous solutions can be used to attain the product yield obtained with supercritical fluid extraction. Because the solubility improvement is modest at lower hydrotrope concentrations, simple dilution by water, like pressure release in supercritical fluid extraction, provides a straightforward recovery approach. In the future, hydrotropy will be a potential method of extracting herbal drugs without the use of excessive heat and temperature.

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