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SIGNIFICANT ROLE OF HYDROTROPES IN EXTRACTION OF PHYTOCONSTITUENTS- A REVIEW

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ABSTRACT

A hydrotrope is an organic substance that increases the solubility of surfactants and water insoluble phyto-constituents such as esters, acids, alcohols, aldehydes, ketones, hydrocarbons, and fats in an aqueous solution. These are amphiphilic substances composed of both a hydrophilic and hydrophobic functional groups. The hydrophobic part of the molecule is benzene substituted polar segment while hydrophilic part; polar segment is an anionic sulfonate group accompanied by a counter ion (i.e., ammonium, calcium, potassium or sodium). Hydrotropes, such as sodium alkyl benzene sulfonates and sodium butyl monoglycol sulfate, were used for the selective extraction of water insoluble phyto-constituents by cell permeabilization. Here disruption of the cellulosic cell wall and disorganization of the phospholipid bilayers by the hydrotrope molecules, then dissolution of the cellular contents, appear to be the mechanism of extraction process.

INTRODUCTION: Extraction of phytoconstituents from the plant material is the first step in the phytochemical process. Extraction of phytoconstituents is dependant on the solubility as well as the surface permeability of the solvent. Many times certain phytoconstituents are not extracted in the normal extraction process due to solubility factor. As a result 100% extraction is not achieved. To counter this problem various techniques have been used time and again. Super critical fluid extraction is one such process which helps to counter many of the problems, but it has certain drawbacks as automation, feasibility and cost factor. A novel approach to overcome all these problems is the use of Hydrotropes.

During the past decades application of hydrotropes became more important in the fields of different pharmaceutical processes, such as phytochemical extraction, distillation, micro-emulsion formulation, and drug formulation [1, 2]. Hydrotrope is an organic substance that increases the solubility of surfactants and other substances in an aqueous solution. These are short chain amphiphilic substances composed of both a hydrophilic (head) and hydrophobic (tail) functional groups. The hydrophobic (non-polar) part of the molecule is benzene substituted while hydrophilic part (polar) is an anionic sulfonate group accompanied by ammonium, calcium, potassium or sodium as a counter ion [3, 4].

These hydrotropes are not surfactants but are used to solubilize complex or insoluble compound in water. Their function is to stabilize solutions, modify viscosity and cloud-point, limit low temperature phase separation and reduce foam [5]. The phenomenon of hydrotropy i.e. increase in the solubility of sparingly soluble compounds in aqueous solution was first reported by Neuberg [6]. Hydrotropes, such as sodium alkyl benzene sulfonates and sodium butyl monoglycol sulfate, were used for the selective extraction of water insoluble or non polar phyto-constituents by cell permeabilization. Some other hydrotropes are sodium benzene sulfonate, sodium toluene sulfonate, sodium xylene sulfonate (SXS), sodium cumene sulfonate, sodium cymene sulfonate.

The self aggregation of the hydrotropes has been considered to be a pre-requisite for a number of applications in various fields such as drug solubilization [7], chemical reactions [8], separation of organic compounds [9], extraction of curcuminoids from turmeric [10] extraction of embelin from *Embelica ribes* [11], Piperine from *Piper nigrum* [12, 13] and Boswellic acids from *Boswellia serrata* resins [14], Diosgenin from *Dioscorea* Rhizomes [15].

Hydrotrope as a true solubilizer [3]: A solubilizer is a surfactant. A solvent insoluble material is solubilized in the surfactant micelle. Factors that cause an increase in either the diameter of the micelle or its aggregation number generally increase solubilization. Some examples of regularly used solubilizers are fatty soaps, polyethoxylated nonionics and quaternary ammonium surfactants. Solubilization greatly increases once the CMC has been reached. Hydrotropes are effective only at high concentrations.

Mechanism of Action:

1. The plant cell wall is made up of phospholipid bilayer. The hydrotrope destroys the phospholipid bilayer and penetrates through the cell wall into the inner structures. The water soaking shows very less effect on cork cells. The cellulose and suberin lamella are the cell wall component of cork cells. The suberin lamella makes the cork cell impermeable to water. But, the hydrotrope solutions break open the water impermeable suberin lamella and then the mature cork cells. The cork cell layers are disturbed by the hydrotrope and the aqueous solution penetrates through the cell wall. When the inner part is exposed to the

hydrotrope solution, the cell swells, and frees the cells from closely bound structures. Hydrotropic solutions precipitated the solutes; out of the solution on dilution with water thus enable the ready recovery of the dissolved solutes [18].

2. Hydrotropic agents can make the O/W and W/O microemulsion and the lamellar liquid crystal destabilized, which results in the 'phase transition' from lamellar liquid crystal phase to bi-continuous structure this is called as Hydrotrope- solubilization action. Vitamin C shows hydrotrope-solubilization action [16, 25].

3. Hydrotropes are known as 'coupling agents'. When hydrotropes are added to a turbid liquid with relatively high water content causes the liquid to become transparent because of 'phase transition'.[17]

Problems with conventional Methods of Extraction:

1. Continuous hot extraction (Soxhlet Extraction): Continuous solvent extraction of raw material results in the extraction of active as well as other components, such as carbohydrates, gums, and oils. As a result, the solvent extraction processes usually gives complex extract. This has to be then purified by multi step techniques such as chromatography or crystallization. Apart from the poor extract quality, difficulties in handling large volumes of inflammable volatile organic solvents and residual solvent traces remaining in the final product limit the use of organic solvents for extraction [18].

2. High-pressure steam treatment and supercritical fluid extraction can also enhance extraction rates by using an osmotic shock and carbon dioxide respectively; however, these techniques can be used only for high-value and low-volume materials due to involvement of high cost [19].

3. Ultrasound treatment ruptures the cell walls through strong dynamic stressing, which results to increase the yield and mass-transfer rate in several solid-liquid extraction processes. The effect of ultrasound is, however, localized, and its application to a large volume of raw material might be inefficient [20].

4. There are two problems to overcome in the extraction from solid plant materials, releasing the essential oil from solid matrix and letting it diffuse out successfully in a manner that can be scaled-up to industrial volumes. Specifically in the essential oil extraction, microwave mediated processes are highly desirable due to their small equipment size (portability) and controllability through mild increments of heating. However, so far the microwave technology has found a purity of 85% of piperine from black pepper [20]. Hydrotropes were used for the selective extraction of piperine by cell permeabilization of *Piper nigrum* fruits. The recovered piperine was approx.90% pure and substantially free from oleoresins [12].

Extraction of Phyto-Constituents with Hydrotropes:

1. Extraction of piperine: Black pepper contains 6-9% piperine by weight. Piperine was extracted using ethanol and the extract was treated with aqueous sodium hydroxide to remove all the fatty material. Other solvents used for extraction are petroleum ether and dichloromethane [19, 22, 23]. The extraction of piperine into these organic solvents is not selective as other compounds like gums, polysaccharides and resins are extracted reducing the purity of piperine. The post extraction processing to purify piperine is time

consuming and uneconomical. Hydrotrope solutions permeabilized the pericarp of *Piper nigrum* fruits and, facilitated the selective extraction of piperine. The hydrotrope molecules probably get adsorbed on the cell wall, disorganize cellulose structure and assisting in disordering the phospholipid bilayer and enable the easy release of piperine. The presence of phosphorus reducing sugars and amino acids in the extract phase suggests the breakdown of cellulose, as well as membrane proteins, to some extent. This leads to a substantial enhancement in extraction and the yield of the product [12, 21].

2. Extraction of Curcumin: Curcuminoids are present in the oleoresin cells, which are present in the cortex. The cork cells covering cortex are composed of inner and outer cellulose layers and a median suberin lamella. The mature cork cell is dead and impermeable to water. In the hydrotropic extraction of turmeric, rhizomes were pulverized to obtain certain mesh size powder. In the process the outer covering of epidermis, hypodermis and cork cells gets disturbed and the oleoresin cells containing curcuminoids can be directly exposed to hydrotrope solution. The hydrotrope action on cork cells need to be monitored by microscopic studies of several sections of rhizomes. The inner part was also exposed directly to aqueous hydrotrope solutions to monitor the hydrotrope effect on the oleoresin cells. Na^+ salt of following hydrotropes have greater ability for extraction of curcuminoids from *Curcuma longa*; Butyl mono glycol sulfate>Salicylate>cumene sulfoante [26].

DISCUSSION: Hydrotropes are promising agents which have the ability to facilitate extraction process. The above cited examples have shown that they can be used in the extraction of various phytoconstituents of varied chemical classes. This technique can be applied in the extraction of such phytomolecules which have low solubility in aqueous medium. Such extracts can be prepared by addition of hydrotropes without affecting the physicochemical properties of the constituents. These hydrotropes can prove efficient in the extraction of various resins as well as certain low permeability agents.

CONCLUSION: Hydrotropic extraction shows tremendous potential to (a) undergo specific interactions with amphiphile, (b) modify mixing behavior of oil and water, (c) self-associate in water (d) enhance aqueous solubility of different solutes and selective extraction of bioactive compounds on a commercial scale. Product yield achieved with the supercritical fluid extraction can be achieved by using the hydrotrope solution in aqueous solutions. Because the solubility enhancement is insignificant at lower hydrotrope concentrations, simple dilution by water provides an easy recovery method, just as does the release of pressure in supercritical fluid extraction. In future hydrotropy will be the promising way to extract polar as well as non polar phyto-constituents without using excess heat and temperature.

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