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A REVIEW ON HYDROTROPHIC SOLUBILIZATION METHOD

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ABSTRACT

A significant problem in both formulation research and screening tests of novel chemical entities has been the solubilization of poorly water-soluble pharmaceuticals. Hydrotropic solubilization is one of the methods used to improve the aqueous solubility of weakly water-soluble medications. A substance that dissolves hydrophobic substances in aqueous solution is known as a hydrotrope. Aqueous solubility of poorly water soluble drugs and insoluble drugs can be increased by the phenomenon called hydrotropic solubilization. The emulsification issue, which is typically discovered in hydrotrope solutions are not present in normal surfactant solutions. This approach is the most efficient one, especially when used to industrial settings, due to the simplicity of recovering the dissolved solute and the potential for reusing hydrotrope solutions. Furthermore, this method is better than others due to its advantages, which include the solvent's pH-independent character, good selectivity, non-flammability, and inexpensive and convenient availability of hydrotropes. Hydrotropic agents include, sodium salicylate, sodium benzoate, urea, nicotinamide, sodium citrate and sodium acetate.

KEYWORDS: Hydrotrophic solubilisation.

INTRODUCTION

It can be described qualitatively as the spontaneous interaction of two or more substances to form a homogenous molecular dispersion, or quantitatively as the concentration of the solute in a saturated solution at a specific temperature.

Sir Neuberg first proposed the idea of a hydrotropic agent (HDA) in 1916 to describe the capacity of anionic organic salts to improve the solubility of poorly soluble solutes at high concentrations.

It has been demonstrated that hydrotropes like urea, sodium citrate, and sodium benzoate are useful in increasing the solubility of poorly soluble medications. Compared to other solubility enhancement methods, this approach has a number of benefits, such as being environmentally friendly, affordable, and not requiring the use of organic solvents or chemical modification of hydrophobic medications.

These days, hydrotropic agents are being used to improve the therapeutic effectiveness and bioavailability of poorly water-soluble drugs by creating a variety of dosage forms, such as injections, mouth-dissolving tablets, and solid dispersions. An overview of techniques for hydrotropic solubilization will be given in this review paper.

HYDROTROPHY

In a process known as hydrotrophy, the first solute's fluid solvency expands as a result of the hydrotropic operator's large-scale expansion of the second solute.

Ionic organic salts are mentioned as hydrotropic agents. The term "salt in" refers to an additive or salt that makes a solute more soluble in a particular solvent, whereas the term "salt out" refers to a salt that makes the solute less soluble.

MECHANISM OF HYRDOTROPIC AGENTS

When using hydrotropy, chemists and analysts have always been interested in the fundamental principles underlying increases in the solubility of medicinal medicines in water in the analysis of pharmaceuticals. The investigations that supposedly explain the plausible mechanistic causes for solubilization lag behind in their application of hydrotropy principles. Regardless of the underlying causes, understanding the mechanism helps confirm its applicability for the intended objective. The extensive literature study revealed nearly all of the HDAs' potential methods of solubilization. To contribute to the promising uses of hydrotropes, we are going to address the mechanisms that may underlie hydrotropic solubilization.

These can be divided conveniently as

1. The self-aggregation potential

2. Formation of the micelles

3. The structure breakers and the structure maker

1. SELF-AGGREGATION POTENTIAL

The self-aggregation potential, or minimum hydro-tropic concentration (MHC), is the critical concentration at which hydrotrope molecules begin to aggregate. The self-aggregation potential of hydrotropic agents determines their solubility power. This potential is dependent on the solute molecule's makeup and their amphiphilic characteristics. The volume-fraction-dependent solubilization potential is primarily displayed by them.

2. FORMATION OF THE MICELLES

This process is predicated on hydrotropes joining forces with solutes to form a micellar arrangement. With a solute molecule, they create stable mixed micelles that lessen the electrostatic repulsion between the head groups. Alkyl-benzene sulfonates, lower alkanoates, and alkyl sulphates are examples of hydrotropic agents that self-associate with solutes to produce micelles.

Through a self-association process, aromatic anionic hydrotropic compounds such as Nicotinamide increase the solubility of riboflavin.

3. STRUCTURE-BREAKER AND STRUCTURE-MAKER

The donor-acceptor molecule's electrostatic force is crucial to the hydrotropic solubilization process. function; as a result, they are often referred to as structure-makers and -breakers. Solutes with the ability to both receive and donate hydrogen contribute to increased solubility. Hydrotropic substances, like urea, cause a solvent's nature to change, which in turn affects the solvent's capacity to participate in structure formation or to do so through intermolecular hydrogen bonding, which is how they achieve their solubilizing action.

Hydrotropes that break structures are referred to as chapotropes, whereas those that create structures are referred to as kosmotropes.

Kosmotropes lower the cloud point by enhancing the hydrophobic interaction, which lowers the critical micelle concentration (CMC).

HYDROTROPIC AGENTS

1. Organic acids and their metal salts-Citric acid, benzoic acid, sodium salicylate, sodium benzoate, sodium citrate, sodium acetate, sodium ascorbate, potassium citrate
2. Urea and its derivatives-Urea, N, N-dimethyl urea
3. Alkaloids -Caffeine, nicotinamide, N,N-diethyl nicotinamide, N,N dimethyl benzamide
4. Phenolic derivatives-Resorcinol, pyrogallol, catechol, a,b-napthols
5. Surfactants- Sodium dodecyl sulphate
6. Aromatic cations-Procaine hydrochloride, para amino benzoic acid rug Hydrotropic agent Key finding

Zaltoprofen Urea, sodium benzoate Improved in solubility more than 600 fold Aceclofenac Urea, sodium citrate Improved in solubility more than 250 folds.

Aceclofenac Sodium citrate, nicotinamide, urea Improved in solubility more than 200 folds.

Riboflavin Caffeine, nicotinamide Two hydrotropic agents lead to increase in the solubility of vitamin in three components Etodolac Sodium benzoate, sodium acetate 15% sodium benzoate and 25% sodium acetate were found to be more stable.

Nimesulide Piperazine, sodium benzoate Improved in solubility using piperazine as hydrotrope was developed.

Indomethacin Arginine Aqueous formulation using arginine as hydrotrope was developed.

Ofloxacin Sodium citrate, sodium benzoate, urea Aqueous injection of drug was prepared for antimicrobial effectiveness and stability.

Halofantrine Caffeine, nicotinamide Solubility is increased to a greater extent in the presence of caffe.

Rub M, Azum N etal studied that the some parentral formulation such as the drug Zaltoprofen, by using the hydrotrophic agent Urea & sodium benzoate is Improved the solubility more than 600 fold.

Also Aceclofenac by using hydrotrphic agent Urea, sodium citrate & nicotinamide is Improved the solubility more than 250 folds & 200 folds respectively.

Maheshwari RK etal studied that the spectrophotometric of hydrochlorothiazide in tablets using mixed hydrotropic solubilisation technique the drug Hydrochloric thiazide, by using the hydotropic agent 40% niacinamide, sodium acetate is increase the solubility 25-folds.

Kumar S etal studied that the Association model of hydrotropy for theeffect of hydrotropes on solubility and mass transfer co-efficient of acetylsalicylic acid the drug Paracetamol, by using hydrotrophic agents 5M urea is increase the solubility 22-folds.

Hydrotropic agent Key finding Zaltoprofen Urea, sodium benzoate Improved in solubility more than 600 fold Aceclofenac Urea, sodium citrate Improved in solubility more than 250 folds Aceclofenac Sodium citrate, nicotinamide, urea Improved in solubility more than 200 folds Riboflavin Caffeine, nicotinamide Two hydrotropic agents lead to increase in the solubility of vitamin in three components Etodolac Sodium benzoate, sodium acetate 15% sodium benzoate and 25% sodium acetate were found to be more stable Nimesulide Piperazine, sodium benzoate Improved in solubility using piperazine as hydrotrope was developed Indomethacin Arginine Aqueous formulation using arginine as hydrotrope was developed Ofloxacin Sodium citrate, sodium benzoate, urea Aqueous injection of drug was prepared for antimicrobial effectiveness and stability Halofantrine Caffeine, nicotinamide Solubility is increased to a greater extent in the presence of caffe.

REFERENCES

1. Behera AL, Sahoo SK, Patil SV. Enhancement of solubility: a pharmaceutical overview. Der pharmacia letter, 2010; 2(2): 310-318.
2. Mangesh R. Patil, Saurabh B. Ganorkar, Amod S. Patil, Atul A. Shirkhedkar & Sanjay. J. Surana Hydrotropic Solubilization in Pharmaceutical Analysis: Origin, Evolution, Cumulative Trend and Precise Applications, Critical Reviews in Analytical Chemistry, DOI:10.1080/10408347.2020.1718484, 2020.
3. India Pharmacopoeia. Govt. of India Vol-I. Ghaziabad: Ministry of Health and Family Welfare, 4th edition. Published by The Indian Pharmacopoeia Commission, 2014; 174.
4. Jain P, G oal A, Sharma S, Parmar M., Solubility enhancement techniques with special emphasis on hydrotropy, International Journal of Pharma Professional's Research, 2010; 1(1): 34-35.
5. Neuberg C. Hydrotropy. Biochemistry Z., 1916; 76: 107-109.
6. Martin A, Bustamante P, Chun Ahc. Physical Pharmacy, New Delhi, b.i. Wavely pvt. Ltd, 1994; 4: 223.

7. Dhapte V, Mehta P. Advances in Hydrotropic Solutions: An Updated Review, Petersburg Polytechnical University Journal: Physics and Mathematics, 2015; 1: 424–435.
8. Masthannamma SK, Sravani K, Ananta sridhar T, Siva Sankar Naik B. UV Spectrophotometric Determination of Metronidazole in Bulk and Pharmaceutical Dosage Form Using Hydrotropic Solubilization Technique. Journal of global trends in pharmaceutical sciences, 2015; 6(1): 2365 – 2371.
9. Vimalson DC, Parimalakrishnan S, Jeganathan NS and Anbazhagan S: Techniques to enhance the solubility ofhydrophobic drugs: An overview. Asian Jour of Pharmaceutics, 2016; 10: 67-75.
10. Kansara H, Panola R and Mishra A: Techniques used to enhance bioavailability of BCS Class II drugs: A review International Journal of Drug Development and Research, 2015; 7: 82-93.
11. Singh G, Kaur I, Gupta GD and Sharma S: Enhancement of the solubility of poorly water-soluble drugs through solid dispersion: A comprehensive review. Indian Journal of Pharmaceutical Sciences, 2017; 79: 674-687.
12. Manogna K, Nagaveni P and Thyagaraju K: Enhancement of solubility of poorly soluble drugs by solid dispersion:An overview. Ind Jour of Pharmaceutical and Biological Research, 2017; 5: 17-23.
13. Martin A: Solubility and distribution phenomena. Physical pharmacy, Lippincott William & Wilkins, Edition 4th, 2003; 213.
14. Osol A: Remington‟s pharmaceutical sciences, Eastern Pensylvania, Mack Publishing Company, 1990; 18: 203.