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ADVANCEMENT SOLUBILIZATION APPROACHES: A STEP REWARDS BIOAVAILABILITY ENHANCEMENT OF POORLY SOLUBLE DRUGS

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Abstract:

A most important parameter in pharmacy is drug solubility. Solubility affect the efficacy of the drug. Drug solubility has the important role in determining the concentration of a drug a achieve the necessary pharmacological response, all drugs absorbed by the body must be in the form of solution. A difficult challenge in drug development is improving the drug solubility, dissolution rate bioavailability; over 40% of novel chemical entities reported are poorly water-soluble medication. Despite having promising pharmacokinetic properties, a large no of innovative drug's that unable to enter the market because of poor water soluble. The aqueous solubility of a drug also affects the physical, chemical and dose stability; the standard purity, dissolution rate and extent absorption; and achieve the desired concentration of the drug in systematic circulation. Solubility technique such as chemical modification, physical modification and other methods were discussed as they open up new pathway for the production of potent and marketable drug in pharmaceutical industries.

Keywords: absorption, Dissolution, Bioavailability, Dispersion, Solubilization technique.

1. Introduction

A most discussed but a still or not completely resolved issue, solubility or dissolution enhancement technique remains a most challengeable filed for the researchers in the formulation and designed and development process. poorly water-soluble drug can benefit from a range of strategies to improve their solubilization and bioavailability. Solubility and dissolution core concepts of any physical or chemical science including biopharmaceutical and pharmacokinetic consideration in therapy of any medicine. Solid dispersion, co-solvency, micronization, Nanonization, chemical modification, hydrotropy, complexation, micellar solubilization, Ph, adjustment and other method are mostly used for pharmaceutical solubilization. In novel chemical entities screening investigation as well as formulation design and development, the solubilization of purely soluble drugs in a frequent challenge. The ultimate quantity of solute that may be completely dissolve in a volume of the all solvent is known as solubility. It has both quantitive and qualitative characteristics. In qualitative term, it can be describe as spontaneous interaction of two or more substance to form a homogeneous dispersion. Quantitatively it is defined as a concentration of the solute in a saturated solution at a certain temperature.

The solubility is define as maximum amount of solute that can be dissolve in a given amount of solvent. A saturated solution is one in which the solute is in equilibrium with the solvent. The solubility of a drug is represented through various concentration expression such as parts, percentage, molarity, molality, volume function, mole fraction. The solubility of the drug is described in various descriptive term which is based on all the amount of drug dissolve in solvent and discussed in table- 1.

Need of solubility

Drug absorption from the GI tract can be limited by a variety of factors most significant contribution being poor aqueous solubility and poor membrane permeability of the drug molecule. When administered an active agent orally it must first dissolve in gastric and /or intestinal fluids before it can permeate the membranes of the GIT to reach systemic circulation. hence, two areas pharmaceutical research that focus on improving the oral bioavailability of active agents include; enhancing of solubility and dissolution rate of poorly water soluble drugs. The BCS is a scientific framework for classifying a drug substance based on its aqueous solubilty and intestinal permeability.

Table. 1: enhancement of solubility

Descriptive term	**Approximate volume of solvent in milliliters per gram of solute**	**Examples of drug**
Very soluble	<1	Metoprolol, deltiazam
Freely soluble	1-10	Ipratropium bromide
Soluble	10-30	Cyclophosphamide, quinidine, procainamide, propranolol
Sparingly soluble	30-100	Fluorouracil, quinidine sulphate, ramipril
Slightly soluble	100-1000	Fludrabine, atenolol
Very slightly soluble	1000-10000	Busulphan, doxazocine
Insoluble	>10000	Lidocaine, melphalan

Table.2: biopharmaceutical classification system

Class	Solubilty	Permeability	Absorption
I.	High	High	Well absorbed
II.	Low	High	Variable
III.	High	Low	Variable
IV.	Low	Low	Poorly absorbed

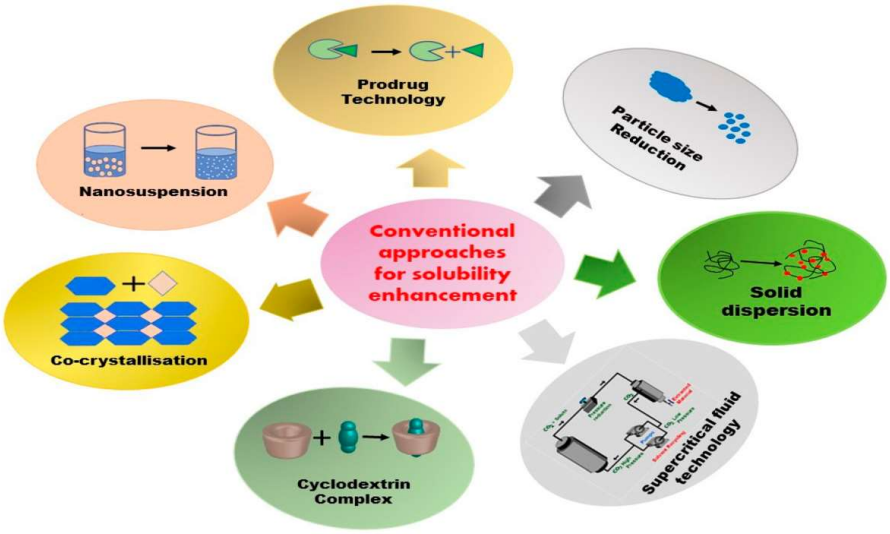
2. Process of solubilization

Step1: it involves the breaking of inter- ionic or intermolecular interactions in the solute, the separation of the interactions between the solvent and the solute molecule or ion.

Step 2 : a solid molecule separates from the bulk

Step 3: it involves integrating the feed of the solid molecule into the hole in the solvent.

Conventional approaches for solubility enhancement:



Conventional approaches have been in use for decades for the enhancement of the aqueous solubility of poorly soluble drug.

1) **Particle size reduction:**
   The primary molecular size of the drug powder has a direct impact on bioavailability of poorly soluble drugs. The reduction in particle size leads to an increase in surface area which further improves the dissolution properties due to the increased contact area with the solvent. Milling techniques, such as jet mills, rotor-stator colloid mills, and other types of reduce the particle size of drug row materials. Micronization techniques can convert particle into size of less than 5μm in diameter and yield uniform particle sizes.

2) **Cyclodextrin inclusion complex:**
   Inclusion complex formed by inserting a non-and polar molecule (guest molecule) cyclodextrin complex are formed when a molecule, called the "guest" is encapsulated within the lipophilic cavity of a cyclodextrin molecule which act as the "host". The inclusion complex cewation approach has been used more accurately than any other solubility enhancement method is increase the aqueous the solubility, dissolution rate, and bioavailability of the drugs.

Here, cyclodextrins (CDs) have been used to most common hole molecule. Poorly soluble therapeutic can have their physiochemical and biological characteristics changed with CDs by having molecule included in the cavity of the disc. CDs can be the lipophilic compound. Rivaroxaban (RIV), an oral anticoagulant, is a poorly soluble drug having a solubility of 0.005 and 0.006 mg/ mL in water and acetate buffer of pH 4.5, respectively. Formulated rivaroxaban-loaded β-cyclodextrin-based inclusion complex. RIV inclusion complex kneading method spry, drying and physical mixing which show the increased solubility in water.

3) **Solid dispersion:**

For oral dosage form, solid dispersion (SD) have been a good technique for enhancing drug solubility, absorption, and therapeutic efficacy. SD is a group solid material with at least two distinct components: a hydrophilic matrix and a hydrophobic drug. The molecular dispersion of one or more hydrophilic matrix and a hydrophobic carrier matrix referred to has solid dispersion. Formulating solid dispersions is a method of choice within pharmaceutical industries for improving drug solubility in the dosage from. Some hydrophilic carriers used to create solid dispersion polyvinylpryrrolidone (povidone, PVP), polyethylene glycols (PEGs), hydroxy propyl methyl cellulose (HPMC).

4) **Prodrug**:

A prodrug is inactive, chemical modified parent drug that has enhanced aqueous solubility and be converted into the active parent drug via rapid biotransformation. The use of prodrug can also enhance pharmaceutical qualities such as odor, test, and chemical stability and alleviate the irritation and pain associated with pharmaceutical problem in the prepration or manufacture of the API. In addition can lead to pharmacokinetic profile optimization and decreses or remove the first-pas effect

Classic prodrug described as carrier-linked prodrugs. Mixed prodrug, as in traditional prodrug, are latent forms in which the carrier has bio precursor properties properties and is linked to a drug. This prodrug form is also known as a CDS (chemical delivery system). Mutual prodrug such as classic prodrug, contain a pharmacologically active carrier, enabling the development of a prodrug.

Some prodrugs do not have an apparent carrier or promoter but instend reemerge out of a molecular change in the actual prodrug, resulting in a novel active molecule. According to US-FDA, among all new drug molecule apperoved,12.4%.

To tackle the poor oral bioavailability of a poorly soluble but highly permeable from the liver or. the intestinal tissues, plasma, simulated gastric fluids and simulated fluid were used in a series of in vitro assays to assess the bioconversion rates of structurally diverse prodrug derivatives. the original medications carboxylic acid component might have been converted to glycolic amide esters. These are solubility in the lipid-based self-emulsifying drug delivery system (SEDDS).

5) **Supercritical fluid technology (SCF):**

Being non-toxic, non-reactive, non-polluting, the implementation of SCF technology has garnered the attention of many researchers. This green technology approach has the potential to make a significant difference in the pharmaceutical industry by overcoming the limitations

of several conventional processes, such as spray drying. The US-FDA recognizers Co2 as a safe supercritical solvent and the most used supercritical solvent in the pharmaceutical manufacturing industry. These are two techniques that use particle generation condition (i.e., solute and solvent) there are the various methods for enhancing the solubility by SCF. For solvent molecule improving solubility developed nanoparticle with SCF using solution-enhanced dispersion method, the dissolution of nanoparticles was amplified approx. similar to this, resveratrol solubility was increased by around 2.8 times and its dissolution rate by about 1.8 times using solution-enhanced dispersion via supercritical fluids micronization.

6) **Nanosuspension:-**
Nanosuspension are submicron colloidal dispersions of drug particles in an aqueous phase, colloidally stabilized with the aid of surfactants. Nanosuspension are employed in the formulation of drug that are insoluble in both water and organic solvent. These are high melting point and high dosage strength are the best candidates to be formulated as nanosuspension. By delivering the nanosuspension orally or intravenously (IV), the rate of saturation of the active component increases and the optimal plasma level is more rapidly achieved. The size distribution of solid particles in nanosuspension range from 200 nm to 600 nm. Enhance the vitro solubility and dissolution rate via a wet milling method. And the result show that at pH = 1.2, the particle size reduction significantly increased the maximum thermodynamic solubility of the drug.

7) **Micelles:**
The combination of a hydrophilic spherical shell composed of polar head or a hydrophobic core composed of a polar tail produces an optimal environment for the solubilization of poorly water-soluble drug. Synthesized griseofulvin loaded core crosslinked micelles, linear dendritic polymers were crosslinked in the study to avoid both it and drug leakage.

3. Conclusion

There are many kinds of solubility enhancement methods for modifying the solubility of poorly water-soluble drugs an important of concept to reach into systemic circulation to show its pharmacological response. Dissolution of the drug is the rate determining step for oral absorption of the poorly water-soluble drugs and solubility is the basic requirement for the absorption of the drug from GIT. This research offer a critical previously reported literature and some newly emerging technology, which include formulation design solid particle technique, prodrug strategies, micronization , solid dispersion particle size reduction technology are poorly water soluble drug.

Result: Bioavailability enhancement of poorly soluble drug was done.

Reference

1. Daugherty AL, Mrsny RJ. Transcellular uptake mechanism of the intestinal epithelial barrier part one. Pharm Sci technol Today 1999;4 :144-51
2. Prentis, R.A, Lis, Y, Walker, S.R. Pharmaceutical innovation by the seven UK- owned pharmaceutical companies. British journal of clinical pharmacology. 1988; 25:387-96.

3. Lipinsk, C.A. Drug-like properties and the causes of poor solubility and poor permeability. Journal of pharmacological & Toxicological Methods. 2000; 44:235-249
4. Kumar S, Singh P. Various techniques for solubility enhancement: An overview. The pharma innovation Jornal.2016, 5(1), 23-28.
5. Singh n. Technique for bioavailability enhancement of BCS class ‖ Drugs Review article. International journal of pharmaceutical and chemical science. 2013,2 (2), 2277
6. Khatri, H., Hussain, M.S. and Tyagi, S., 2022. solubility enhancement technique: An overview
7. Sharma, D.K., 2007. Solubility enhancement Strategies for poorly water -soluble drugs in solid dispersion: A review. Asian Journal of Pharmaceutics (AJP), 1(1).
8. Khan, A.D., Tabish, M., Kaushik, R.; Saxena, V.: Kheshrwari, P.: Gupta, S.; Alam, M.N.; Sharma, v. hydrotropy: Recent advancements in enhancement of drug solubility and formulation development.int. J drug deliv. technol. 2021
9. Gupta, J.; A solubility enhancement techniques for poorly soluble pharmaceutical: a review. Indian J. pharma. Biol. Res. 2019,7,09-16
10. Ghumre, P.B.; Bote, S.S.; Korde, A.B Bhosale, B.S.; chaudhari, R.B solubility enhancement technique- overview Ward J. pharma. Res. 2021, 10, 571-589.
11. Kumar, a.; sahoo, S.K.; kochar, P.S.; sathpathy, A., pathak, N.J.P.G. review on solubility enhancement techniques for hydrophobic drugs. Int. J. Compr. Pharm. 201, 3,001-007.
12. Vandana, K.; Raju, Y.P.; Chowdary, V.H.; Sushma, M.; Kumar, N.V An overview on in situ micronization technique – An emerging novel concept in advanced drug delivery. compr. Pharm 2011, 3, 001-007.
13. Argade, P.; Magar, D.; saudagar, R.B. solid dispersion: Solubility enhancement technique for poorly water-soluble drug. J. Adv. Pharm. EDU. Res. 2013, 3, 427-439.
14. Cid, A.G.; simonazzi, A.; Palma, S.D.; Bermudez, J.M solid dispersion technology as a strategy to improve the bioavailability of poorly soluble drugs. Ther. Deliv.2019.10,363-382.
15. Ita, K. Chapter7- prodrugs. In transdermal drug delivery, Ita, K., Ed.; academic press: Cambridge, MA, USA,2020; pp. 123-141.
16. Kanala, R.K.; Zhang, Y.S.; Wang, S.B.; Lee, C.H.; Chen, A.Z. Supercritical fluid Technology: An Emphasis on Drug delivery and Related Biomedical applications. Adv. Health Master. 2017, 6, 1700433
17. Deshpande, P.B.; Kumar, A.R.; Shavi, G.V.; Karthik, A.; Reddy, M.S.; Udupa, N. Supercritical fluid technology: Concepts and pharmaceutical application. PDA J. pharm. Sci. Technol. 2011, 65,333-344
18. Jacob, S.; Nair, A.B.; Shah, J. Emerging role of nanosuspensions in drug delivery system. Biomater. Res. 2020, 24,3.
19. Bhakay, A.; Rahman, M.; Dave, R.N.; Bilgili, E. Bioavailability enhancement of poorly water-soluble Drugs Via Nanocomposites: Formulation(-)processing Aspects and Challenges. Pharmaceutics 2018, 10, 86.
20. Saddam, H.; Abdul Baque, A.; Jiban, D. Nanosuspension: A promising drug delivery system for poorly water soluble drug and enhanced bioavailability. Int. J. Pharm. Sci. Res. 2020, 10,4822-4832.
21. Aghrbi, I.; Fulop, V.; Jakab, G.; Kallai-Szabo, N.; Balogh, E,; Antal , I. Nanosuspension with improved saturated solubility and dissolution rate of cilostazol and effect of solidification on stability. J. Drug Deliv. Sci. Technol. 2021, 61,102165.