International Journal of Trend in Scientific Research and Development (IJTSRD)
Volume 6 Issue 4, May-June 2022 Available Online: www.ijtsrd.com e-ISSN: 2456 – 6470

A Review on Solid Dispersion

Dhiresh Yennuwar, Snehal Jadhav, Mr. Sujit Kakade, Dr. Ravindra Patil, Dr. Ashok Bhosale

Shankarrao Ursal College of Pharmaceutical Science and Research Centre, Kharadi, Pune, Maharashtra, India

ABSTRACT
Oral route of drug administration is the most preferred and convenient method of drug administration, but due to the poor solubility of drug is the major drawback for the dissolution and bioavailability of that drug. Absorption, distribution, metabolism and excretion of the drug depends on the solubility of the drug molecule. Solid dispersion is defined as dispersion of one or more active pharmaceutical ingredient in water soluble carriers at solid state to increase the dissolution of poorly water-soluble drugs. Solid dispersion technique improves the dissolution rate of highly lipophilic drugs by enhancing bioavailability by means of decreasing particle size of drug, improving its wettability and forming amorphous particles of crystalline drugs. For preparation of solid dispersion carriers such as hydrophilic and hydrophobic are used. Nowadays the use of natural carriers is prepared over the synthetic carriers. Solid dispersion techniques are very effective and promising than conventional dosage forms. In this review we have mainly focused on historical background, introduction to solid dispersion, advantages and disadvantages, characterization of solid dispersion, method of preparation, applications, types of solid dispersion, carriers used in solid dispersion.

KEYWORDS: *Solid Dispersion, Solubility, Dissolution, Bioavailability, Surfactant, Stability, Poorly soluble drug, Carriers, Solubility enhancement*

How to cite this paper: Dhiresh Yennuwar | Snehal Jadhav | Mr. Sujit Kakade | Dr. Ravindra Patil | Dr. Ashok Bhosale "A Review on Solid Dispersion" Published in International Journal of Trend in Scientific Research and Development (ijtsrd), ISSN: 2456-6470, Volume-6 | Issue-4, June 2022, pp.507-513, URL: www.ijtsrd.com/papers/ijtsrd50101.pdf

IJTSRD50101

Copyright © 2022 by author(s) and International Journal of Trend in Scientific Research and Development Journal. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0) (http://creativecommons.org/licenses/by/4.0)

INTRODUCTION
Oral route is very convenient route and it has more patient compliance than the other routes of drug administration but, due to some reasons oral route has several drawbacks such as limited absorption of poorly water-soluble drugs and hence it affects the bioavailability of drug. Many drugs are lipophilic in nature and hence they are poorly absorbed. Absorption of drugs is altered due to solubility. To reduce the effect of low solubility of drugs various methods such as use of surfactants is used to increase the solubility. Solid dispersion consists of solid products which have two different molecules, 'hydrophobic drug 'and 'hydrophilic carrier'. the carrier may be crystalline or amorphous. When the solid dispersion comes in contact with any aqueous media the carrier is dissolved and the drug is released as fine particles which enhance the solubility and dissolution rate of drug.

Advantages of solid dispersion
1. Solid dispersion after particles size reduction shows significant dissolution of the drug in dissolution medium. This can be achieved by mixing water soluble drugs and highly soluble carriers.
2. The solubility of the drug depends on its wettability. Using carriers such as urea, colic acid, bile salts increases the wettability of the drug. They act as co-solvents.
3. Particles in solid dispersion have high degree of porosity. The increase in porosity depends on the carries. Linear polymers have high dissolution rate.
4. Poorly water-soluble crystalline drugs, when in the amorphous state tend to have higher solubility. The enhancement of drug release can usually be achieved using the drug in its amorphous state, because no energy is required to break up the crystal lattice during the dissolution process.

Disadvantages of solid dispersion

1. Due to solid dispersion the amorphous state may undergo crystallization in commercial products due to stress and storage conditions.
2. When solid dispersion formulation comes in contact with moisture it tends to decrease its storage stability thus promoting crystallization.
3. It is found that wen solid dispersion comes in contact with the moisture it absorbs the moisture and causes phase separation of solid dispersion, eventually decrease it solubility and effects on pharmacokinetic properties.

Classification of solid dispersion

Solid dispersion can be classified based on their molecular arrangement as follows;

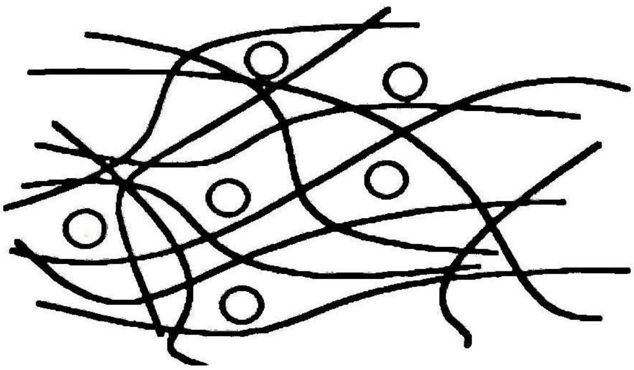
1. Eutectic mixture
2. Amorphous Precipitation In crystalline matrix
3. Solid solution
   a. Continues solid solution
   b. Discontinuous solid solution
   c. Substitutional solid solution
   d. Interfacial solid solution
4. Glass solution and suspension

1. Eutectic mixture: -

This mixture consists of two compound's which are soluble in the liquid state but has limited extent in the solid state. This mixture is prepared by solidification of fused melt of two compounds that are completely miscible but negligible in solid solution.

2. Amorphous Precipitation In crystalline matrix: -

This method is same as eutectic mixture, but the drug is precipitated out in amorphous form.



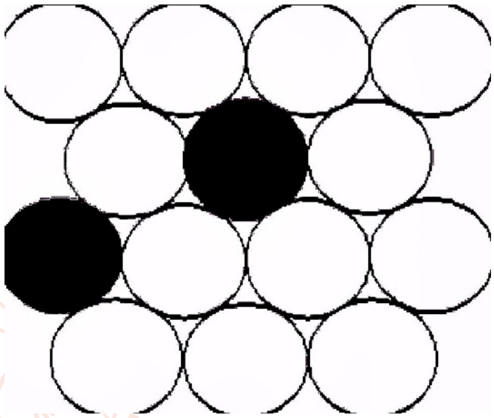
3. Solid Solution: -

Solid solution is same as liquid solution, it consists of only one phase without considering the number of component's present in it. In solid solution the particle size is reduced and hence it increases the surface area. Solid solutions are further classified depending on the solubility.

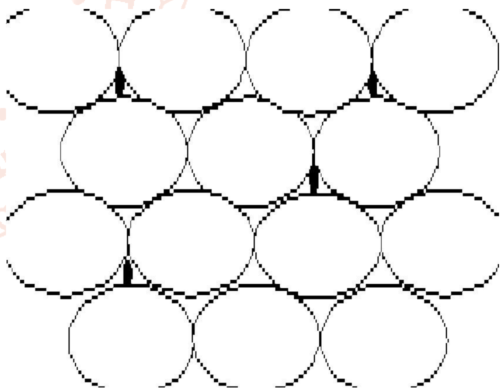
A. Continuous solid solution - In continuous solid solution the components are soluble completely. The strength between two components is stronger than the strength between the molecule.

B. Discontinuous solid solution - In discontinuous solid solution the miscibility of either of component is low.

C. Substitutional solid solution - This is only possible when the size of the molecule is less than 15 percent then the solvent molecule. Solid solution has crystalline structure in which the solute molecule can fit into the crystal lattice of the solvent molecule.



D. Interstitial solid solution - The molecules fit in to the interstitial species Within the solvent molecule. In this, solute molecule should be 0.95 times less in diameter then that of solvent molecular diameter.



4. Glass solution and suspension.

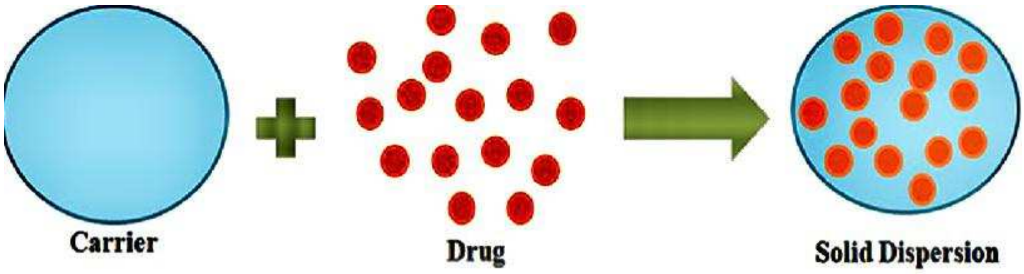
Glass solution are homogenous in nature that has glassy system in which the solute dissolves in glass carriers. Glass suspension consist of particle that are precipitated and are suspended in glass solvent. The lattice energy is less in suspension and glass suspension.

Selection of carriers for solid dispersion

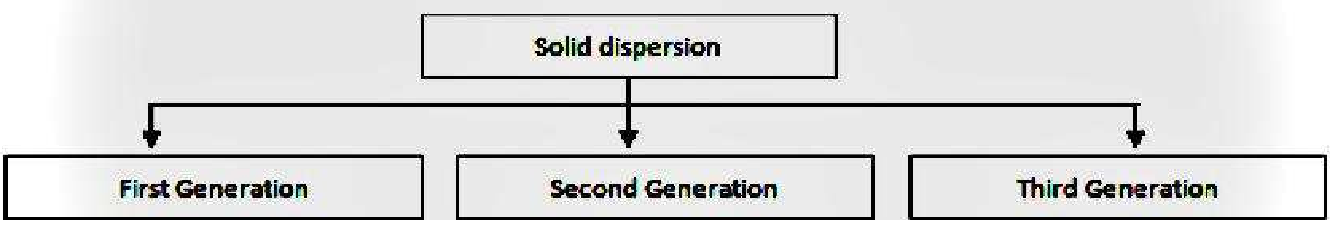
The dissolution rate of drug can be enhanced by incorporating of carriers during preparation of solid dispersion. A carrier should have followed criteria.

1. Freely water soluble, increased dissolution properties.
2. It must be non-toxic inert

3. Thermally stable with a low melting point it must be miscible with solvents during solvent evaporation method
4. It must be able to enhance the dissolution of drug in aqueous media.
5. It must be compatible with the drug and should not form complex



Types of carriers



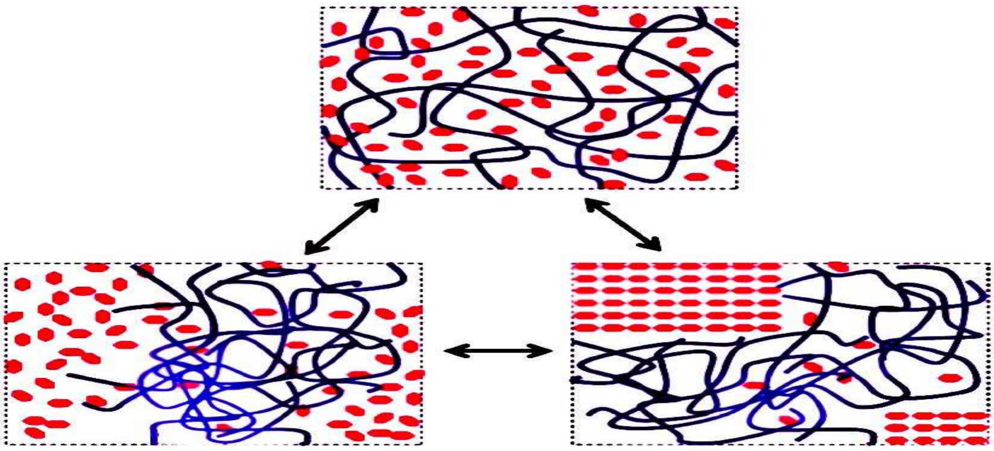
A. First generation carriers (crystalline carrier) – Urea sugar and organic acids.

B. Second generation carriers (polymeric carrier)- PEG, HPMC, PVP.

C. Third generation (surfactant or polymers)- Poloxamer 408, Tween 80, SLS.

Polymers-

1. Polyethylene glycols (PEG)- Polyethylene glycols are derivatives of ethylene oxide and have molecular weight of 200 to 300000. PEG which has mol. wt. of 1500 to 20000are used in production of solid dispersion usage of polyethylene glycols in solid dispersion enhances solubility in organic solvents. Addition of peg also increases compound wettability. Drawbacks associated with Peg there are few toxicity issues related to peg associated with excipients. PEG is low molecular weighs shows high chances of toxicity than that of high molecular Polyethylene glycols. Polyethylene glycols does not have confirm stability issues during hot melt method.



2. Polyvinyl pyrrolidine when vinyl pyrrolidone undergoes polymerization process Polyvinyl pyrrolidine is synthesized. It has molecular weigh about 2500 to 300000. Temperature of Polyvinyl pyrrolidine depends on two paraments, its

3. Molecular weight and moisture contents. Polyvinyl pyrrolidine has high glass transition temperature and hence has only limited application of production of solid dispersion by hot melt method. As Polyvinyl pyrrolidine have high solubility in various organic solvent there mostly used in solvent method as the increasing concentration of Polyvinyl pyrrolidine not only decreases aqueous solubility but also increases it viscosity due to high molecular weight.

Cellulose derivatives-

1. Hydroxy propyl methyl cellulose - Hydroxy propyl methyl cellulose (HPMC) is combination of ethyl cellulose; in that around 16.5 to 30 percent; of hydroxyl group are methylated and about 4 percent to 32 percent; are derivatized by use of hydroxy propyl group. HPMC molecular weight of around 10000 to 1500000. HPMC are miscible in water and with ethanol with dichloromethane methanol with dichloromethane poorly soluble acids such as nilvadipine shows quick release by use of HPMC in solid dispersion
2. Hydroxy propyl Cellulose - Hydroxy propyl Cellulose (HPC) has good solubility in various solvent for eq. water, chloroform, methanol the molecular wight of Hydroxy propyl Cellulose is around 37000 to 11. 5000.using low molecular weight Hydroxy propyl Cellulose as carrier in preparation of solid dispersion thus increasing the releases rate.
3. Carboxymethyl ethyl cellulose – Carboxymethyl ethyl cellulose (CMEC) this belongs to the class of cellulose ether, but under gastric condition its dissolution rate is hampered Carboxymethyl ethyl cellulose are readily soluble in acetone mixture of ethanol and dichloromethane.
4. Hydroxypropyl methyl cellulose phthalate (HPMCP) - They are commonly used as enteric coating polymer Hydroxypropyl methyl cellulose phthalate molecular weight ranges from 20000 to 2000000. There are various grades are available and they dissolve at Ph of 5 or 5.5. By using co-evaporate of HPMCP by incorporating in Griseofulvin at Ph 6.8 it is seen that the dissolution rate is increased.
5. Polyacrylates and polymethacrylates - These are formed by method of polymerization of acrylic and methacrylic acid, and also the derivatives of nitriles and ester amides. In the field of pharmaceutical, they are commonly used as coating polymers to restrict the release of drug. Like eudragit e is commonly used because it enhances the release rate and is soluble in buffer.
6. Urea- Urea is produced as end product of protein metabolism in human it is nontoxic. It shows high solubility in water and also organic solvents. When urea was used with phenytoin the release ate f drug is enhanced by twice over, but using PEG 6000 in this technique gives more efficient results.
7. Sugar- Sugars, polyols and polymers- sugars shows high solubility in water, but there are less harmful issues. And hence they are not commonly used as carriers. As the melting point of sugars is more hot melt method may cause issues during preparations. Sugars are less soluble in organic solvents and so it is difficult to produce co-evaporates. mannitol has melting point of 165^0 C; 168^0 C and hence it is used to prepare solid dispersion by hot melt technique as it degrades at a temperature above 250^0C.

Method of preparation of solid dispersion-

There is main two process of preparing solod dispersion melting and solvent evaporation

1. Melting method
2. Melt agglomeration method
3. Solvent evaporation method
4. Hot melt extrusion method
5. Fusion method
6. Spray drying
7. Supercritical fluid method
8. Freeze drying
9. Co precipitation method
10. Dropping method

1. Melting method – In melting method the drug is added in a suitable liquid solvent. This solution is then mixed with melted polyethylene glycol which is obtained below 70^0 C. by using this method 5 to 10 percent of the liquid sample must be added to polyethylene glycol 6000. This method is done by preparing a mixture of drug and water-soluble carrier with help of heating until its melt. Then the solid mass which is obtained is crushed and sieved.
2. Melt agglomeration method – In this method a conventional high shear mixture is used which allows preparation of solid dispersion by melt agglomeration in this the drug is added to molten carrier along with heated excipient. the mixture of drug, carrier and excipient low heated to temperature more than the melting point of carrier. This technique is used where the binder act as carrier the melt in procedure gives a homogenous distribution of the drug.
3. Solvent evaporation method – In this technique the drug and carrier are solubilize in a volatile solvent by using this technique the decomposition of drugs and carrier by heat can be prevented, because most of the organic solvent evaporate at low temperature. In this the drug and carrier are mixed and dissolved in solvent such as ethanol or chloroform.
4. Hot melt extrusion method- In this process the component is mixed with the help of extruder with intense pressure. An extruder consists of barrel, hopper, Screw for kneading, Heating jacket and die. The drug and ca solid dispersion

can also be processed continuously so that large scale production is possible due to various shape the product can be convenient to handle. In solubility of drug and carrier creates an issue. The extruder generates heats during the production and hence the thermos labile component can be degraded.

5. Fusion method- This method is one of the oldest methods for the production of solid dispersion. Previously the solid dispersion used in the field of pharmaceutical were produced by this method. When the starting material are in the crystalline state it is called as melt method.
6. Spray drying method - This technique Is most commonly used for solid dispersion. This procedure involves solvent evaporation. In this method the drug is suspended in the carrier and sprayed in to the heated air flow which evaporates the solvent. Due to lesser particle size, the surface area is increased due to which the solvent is evaporated and the solid dispersion ins produced
7. Supercritical fluid extraction method - This Supercritical fluid extraction (SCF) method uses co_2 as a supercritical fluid this method is also called as micritization method. Application of co_2 removes the polymeric component from the process. SCF are also used to decreases the temperature during the melt dispersion procedure.
8. Freeze drying method - In this process drug and matrix are incorporated in liquid nitrogen and is frozen completely. This frozen solution is then lyophilized. In freeze drying the drug is not degraded due to heat. The major benefit of freeze-drying process is phase separation solid dispersion is not possible.
9. Co-precipitation method - Co-precipitation technique is most promising method for the drugs which less solubility and thus solubility and bioavailability in this technique non solvent is incorporated in drug and carrier solution by addition of non-solvent the drug and carrier are further precipitated which has less particle size finally this suspension is then filtered and dried.
10. Drooping method- This technique has major application then other various methods in this method spherical particle are generated from fused solid dispersion. Generally fused drug carrier complex Is pipetted out and solidified into spherical particle various factor influence on shape and size of particle.

Characterization techniques are used to distinguish between Solid solution, physical mixtures of drug and carriers. Analytical methods that are used to characterize solid dispersion are as follow

A. Fourier Infrared spectroscopy
B. Differential scanning spectroscopy
C. Powder x ray diffraction
D. UV-vis spectrophotometry

A. Fourier transform infrared spectroscopy

Fourier transform infrared spectroscopy (FTIR) is a technique is carried out for identification of functional group and identification of unknown compounds I in various field. FTIR Shows a infrared spectra of compound and it is used for estimation of functional group in the sample compound or mixture of compound like solid, liquid and gases. FTIR consist of a infrared source, fixed mirror, beam splitter, moving mirror, laser diode, gas ample cell and detector. FTIR is commonly used in pharmaceutical filed, research field, forensic investigation, food research and biochemical and biomedical research industry.

B. UV-vis Spectrophotometry

UV-vis spectrophotometry is a quantitative technique which is used in the field of biochemistry. It is used to determine species and to study the biochemical process. This method helps us to detect micro-molar concentration in the sample. The absorption of UV or visible light by chemicals compound gives us a distinct spectrum. When a compound absorbs a v radiation transition of electrons Whitin the molecule occurs from ground state (low electronic level) to excited state (high electronic energy level). The components of UV visible spectrophotometer are source, filter or monochromator, sample holders and detector. UV spectroscopy is used to detect impurities in the sample, identification of sample, it is also used for structural elucidation of organic compounds. Quantitative determination of compounds which absorbs UV radiation. It also has wide range of application in the field of inorganic species, organic compounds and proteins.

C. X-ray Diffraction

X ray diffraction technique is mainly used for identification of nature of compounds whether present in crystalline or amorphous form. X-ray Diffraction is also used for structural analysis of compounds like crystal nature, crystal habit, strain and size. X-ray Diffraction works on Braggs equation. X rays were introduced by W.C. roentgen in 1895. X-ray Diffraction technique is used for determination and identification of crystal habit and structure of compounds. It is also used in determination of crystallite size. This technique for both crystallin and non-crystalline material. in general, X-ray Diffraction is an equipment used for study of crystalline materials. X-ray Diffraction consist of x ray source calorimeter and photographic film it is also used for study of qualitative and quantitate parameter's. X-ray Diffraction technique is widely used in pharmaceutical industry, paint industry, Geology and minerology.

D. Differential Scanning Calorimetry

Differential Scanning Calorimetry (DSC) it is a thermal analysis technique in which sample is introduced to a controlled temperature program. DSC is commonly used for indentation of compound, compatibility of drug compounds with excipients and carriers. In DSC sample and reference are heated simultaneously and temperature is increased or decreased linearly. DSC has wide application in various fields such as identification, purity determination of compounds, stability-compatibility of compounds, detection of polymorphism, detection of isomorphism and pharmaceutical industry.

Application of solid dispersion

1. To increase the bioavailability, dissolution rate, solubility of poorly soluble drugs.
2. To sustain instability by hydrolysis, oxidation, recrimination, isomerization, photo oxidation and other decomposition procedures.
3. To reduce side effect of certain drugs.
4. To mask unpleasant taste and smell of drugs.
5. To enhance drug release from formulations such as, ointments, creams and gels.
6. To reduce incompatibilities.
7. To gain equal distribution of a small amount of drug in solid state.
8. To produce rapid release dose in a sustained release dosage form.
9. To prepare sustained release formulation of drugs by using poorly soluble carriers.
10. To decrease inactivation of drug that occurs pre systemically.

REFERENCE

[1] Gurunath S, Kumar SP, Basavaraj NK, Patil PA. Amorphous solid dispersion method for improving oral bioavailability of poorly water-soluble drugs. journal of pharmacy research. 2013 Apr 1;6(4):476-80.

[2] Giri TK, Kumar K, Alexander A, Badwaik H, Tripathi DK. A novel and alternative approach to controlled release drug delivery system based on solid dispersion technique. Bulletin of Faculty of Pharmacy, Cairo University. 2012 Dec 1;50(2):147-59.

[3] Huang Y, Dai WG. Fundamental aspects of solid dispersion technology for poorly soluble drugs. Acta Pharmaceutica Sinica B. 2014 Feb 1;4(1):18-25.

[4] Bhujbal SV, Mitra B, Jain U, Gong Y, Agrawal A, Karki S, Taylor LS, Kumar S, Zhou QT. Pharmaceutical amorphous solid dispersion: A review of manufacturing strategies. Acta Pharmaceutica Sinica B. 2021 Aug 1;11(8):2505-36.

[5] Dispersions: a review on drug delivery system and solubility enhancement. ChemInform. Allawadi D, Singh N, Singh S, Arora S. Solid 2014 May 6;45(18): 2094-2105.

[6] Aggarwal S, Gupta GD, Chaudhary S. Solid dispersion as an eminent strategic approach in solubility enhancement of poorly soluble drugs. International journal of pharmaceutical sciences and research. 2010;1(8):1-3.

[7] Singh MC, Sayyad AB, Sawant SD. Review on various techniques of solubility enhancement of poorly soluble drugs with special emphasis on solid dispersion. J Pharm Res. 2010 Oct;3(10):249-50.

[8] Kamalakkannan V, Puratchikody A, Masilamani K, Senthilnathan B. Solubility enhancement of poorly soluble drugs by solid dispersion technique–A review. J. Pharm. Res. 2010 Sep;3(9):2314-21.

[9] Sharma A, Jain CP. Solid dispersion: A promising technique to enhance solubility of poorly water soluble drug. International Journal of Drug Delivery. 2011 Apr 1;3(2):149.

[10] Patil RM, Maniyar AH, Kale MT, Akarte AM, Baviskar DT. Solid dispersion: strategy to enhance solubility. Cheminform. 2012 Jun 5;43(23): 66-73.

[11] Singh S, Baghel RS, Yadav L. A review on solid dispersion. International journal of pharmacy & life sciences. 2011 Sep 1;2(9).

[12] Saffoon N, Uddin R, Huda NH, Sutradhar KB. Enhancement of oral bioavailability and solid dispersion: a review. Journal of Applied Pharmaceutical Science. 1930 Jan 11(Issue):13-20.

[13] Singh J, Walia M, Harikumar SL. Solubility enhancement by solid dispersion method: a review. Journal of drug delivery and Therapeutics. 2013 Sep 14;3(5):148-55.

[14] Nikghalb LA, Singh G, Singh G, Kahkeshan KF. Solid Dispersion: Methods and Polymers to increase the solubility of poorly soluble drugs. Journal of Applied Pharmaceutical Science. 1930 Jan 11;2(10):170-5.

[15] Mehta S, Joseph NM, Feleke F, Palani S. Improving solubility of BCS class II drugs using solid dispersion: a review. Journal of drug delivery and therapeutics. 2014 May 15;4(3):7-13.

[16] Bhasin N. Current trends in solid dispersion: a review. Journal of Drug Delivery and Therapeutics. 2014 May 15;4(3):80-6.

[17] Bhirud YD, Phalak HM. Advances in solid dispersion technology and its applications in the development of solid dosage forms. Journal of Drug Delivery and Therapeutics. 2016 Nov 15;6(6):40-7.

[18] Mankar SD, Rach PR. Solubility enhancement of poor water soluble drugs by solid dispersion: A review. Journal of drug delivery and therapeutics. 2018 Sep 6;8(5):44-9.

[19] Das PS, Verma S, Saha P. Fast dissolving tablet using solid dispersion technique: a review. Int J Curr Pharm Res. 2017;9(6):1-4.

[20] Tekade AR, Yadav JN. A review on solid dispersion and carriers used therein for solubility enhancement of poorly water soluble drugs. Advanced pharmaceutical bulletin. 2020 Jul;10(3):359

[21] Sanklecha VM. A Systematic Review on Solid Dispersion: Enhancing the Solubility of Poorly Soluble Drug. drugs.;6:7.

[22] Kadam SV, Shinkar DM, Saudagar RB. Review on solubility enhancement techniques. IJPBS. 2013;3(3):462-75.

[23] Kumar A, Kumar J. Solid Dispersion Techniques: A Review. International Journal of Research in Engineering, Science and Management. 2021 Jun 13;4(6):104-11

[24] Serajuddin AT. Solid dispersion of poorly water-soluble drugs: Early promises, subsequent problems, and recent breakthroughs. Journal of pharmaceutical sciences. 1999 Oct;88(10):1058-66.

[25] Nair AR, Lakshman YD, Anand VS, Sree KS, Bhat K, Dengale SJ. Overview of extensively employed polymeric carriers in solid dispersion technology. AAPS Pharm SciTech. 2020 Nov;21(8):1-20.

[26] Tran P, Pyo YC, Kim DH, Lee SE, Kim JK, Park JS. Overview of the manufacturing methods of solid dispersion technology for improving the solubility of poorly water-soluble drugs and application to anticancer drugs. Pharmaceutics. 2019 Mar;11(3):132.

[27] Kaushik R, Budhwar V, Kaushik D. An overview on recent patents and technologies on solid dispersion. Recent Patents on Drug Delivery & Formulation. 2020 Mar 1;14(1):63-74.

[28] Nikam VK, Shete SK, Khapare JP. Most promising solid dispersion technique of oral dispersible tablet. Beni-Suef University Journal of Basic and Applied Sciences. 2020 Dec;9(1):1-6.

[29] Jatwani S, Rana AC, Singh G, Aggarwal G. An overview on solubility enhancement techniques for poorly soluble drugs and solid dispersion as an eminent strategic approach. International journal of pharmaceutical Sciences and Research. 2012 Apr 1;3(4):942.

[30] Kumar B. Solid dispersion-a review. Pharma Tutor. 2017 Feb 1;5(2):24-9.

[31] Sridhar I, Doshi A, Joshi B, Wankhede V, Doshi J. Solid dispersions: an approach to enhance solubility of poorly water soluble drug. J Sci Innov Res. 2013;2(3):685-94.

[32] Chaudhari SP, Dugar RP. Application of surfactants in solid dispersion technology for improving solubility of poorly water soluble drugs. Journal of drug delivery science and technology. 2017 Oct 1;41:68-77.

[33] Tiwari R, Tiwari G, Srivastava B, Rai AK. Solid dispersions: an overview to modify bioavailability of poorly water soluble drugs. International Journal of PharmTech Research. 2009 Oct 1;1(4):1338-49.

[34] Bhatnagar P, Dhote V, Chandra Mahajan S, Kumar Mishra P, Kumar Mishra D. Solid dispersion in pharmaceutical drug development: from basics to clinical applications. Current drug delivery. 2014 Apr 1;11(2):155-71.

[35] Singh N, Mk S. Solid dispersion-a novel approach for enhancement of bioavailability of poorly soluble drugs in oral drug delivery system. Global Journal of Pharmacy & Pharmaceutical Sciences. 2017;3(2):30-7.

[36] Chiou WL, Riegelman S. Pharmaceutical applications of solid dispersion systems. Journal of pharmaceutical sciences. 1971 Sep 1;60(9):1281-302.