Journal of Pharmacological Reviews and Reports

Extended Abstract
Vol.2, Iss. 3
2019

Pharma Sci-An Updated Review on The Utilization of Various Carriers and Methods to Prepare Solid Dispersions of BCS Classified Drugs- Izza Tariq- Lahore University of Management Sciences

Izza Tariq

Department of Computer Science, Lahore University of Management Sciences, Lahore, Pakistan

Introduction

Among the drug administration methods, oral route is the most suitable and preferable method for drug delivery, owing to its easy ingestion and convenience. Taking drug orally is more compliant then other routes of administration, but this route of administration presents serious problems regarding the mode of delivery for a significant number of reasons. Poor bioavailability is the major issue. Multiple techniques including: co-solvent-solubilization method, particle size reduction, complex formation using cyclodextrin, salt formation and many others were used to combat these issues, but all had some limitations.

Solid dispersion, in comparison to all other approaches proved to be the best suitable technique. Sekiguchi and obi were the first, who came with the idea of preparing solid dispersion to overcome the issue of poor bioavailability and for sustained release of drug. A dispersion containing a minimum of two components in inert matrix (one hydrophilic and other hydrophobic), in order to increase the dissolution rate and permeability of poorly water-soluble drugs, is known as solid dispersion. The carriers used in the preparation of solid dispersion vary in grades and nature (crystalline or amorphous). However, various grades of PEGs, PVPs, urea and sugar, are the among the most used carriers in the preparation of solid dispersions.

The literature review indicates that the use of solid dispersion has been for decades. Moreover, the main aim of this review is to provide a background on solid dispersion, its various methods of preparation, the selection of carrier owing to the drug characteristics. However, the main emphasis is on the carriers and type of methods used to prepare solid dispersion over the past few decades, along with the comparison that which method and carriers were found most suitable for its preparation.

Methods of Preparation of Solid Dispersion

Various methods of preparation are suggested for the preparation of solid dispersions and researchers have utilized them accordingly.

Fusion (melting) Method

In this process, a physical mixture containing drug and carrier is prepared and melted until a liquid state is achieved. This liquid mixture is later cooled to form dry mass. Sekiguchi and obi used this method for the preparation of sulfathiazole. However, this method is not preferable for thermolabile drugs owing to its immiscibility between the drug and carrier.

Solvent Evaporation Method

This process involves the dissolution of drug and carrier in a same solvent at the same time. The resultant solution is then subjected to evaporation, using various techniques such as: vacuum or slow evaporation methods, heating, spray drying, or freeze drying. The substances which has its limitations in fusion method could use this technique.

Spray Drying

This is a sophisticated technique, where after the preparation of physical mixture of drug and

This work is partly presented at World Congress on Advances in Pharmaceutical Sciences

carrier, the solution is evaporated in chamber. The solution is sprayed under specified conditions in the chamber and later separated after drying.

Melting Solvent Method

This process is the amalgamation of melting and solvent evaporation method, that's why known as melting solvent method. This technique involves the dissolution of drug in specified solvent and later in carrier. The final solution is then cooled until a dry mass is achieved. This method is most suitable for thermolabile drugs and carriers.

Lyophilization

Lyophilization also known as freeze drying, is a method in which the drug-carrier solution containing solvent is initially subjected to freezing followed by drying at less pressure. However, this is a time taking process yet giving less yield.

Kneading Method

In this technique, a paste is produced using suitable carrier and water as a solvent. The drug is then incorporated and kneaded for drying. Moisture sensitive drugs have its limitations in this method.

Co-grinding Method

The blender containing the drug and carrier is blended at a specified speed to form a powder, which is later transferred to a vibrating ball mill. The resultant mixture is pulverized and gathered for future use.

Co-precipitation Method

In this process, the carrier is primarily mixed with a suitable solvent to form a solution. The drug is later added to this solution and subjected to agitation under magnetic stirrer. The final precipitates formed are collected via vacuum filtration, and later dried.

Super Critical Fluid Technique

This is an advanced technique, where the physical mixture of drug and carrier is dissolved in a suitable solvent. The final solution is sprayed in a chamber using atomizer, where particles are formed. The chamber, which is occupied with super critical fluids (mainly CO_2) captures the solvent as soon as the drug carrier solution enters the chamber, leading to the formation of solid dispersed particles. These particles are later collected from the walls of chamber.

Carriers Used in the Preparation of Solid Dispersion

Polyethylene glycol (PEG)

PEG (molecular weight: 200-300000), are polymers of ethylene oxide. The molecular weight (MW) plays a vital role in the preparation of solid dispersion, as the molecular weight and viscosity are directly proportional to each other (greater the MW, greater will be the viscosity). However, MW ranging from 1500-20000 is desired for the preparation of solid dispersion.

They are soluble in water, also improves the wettability of compound which gives it the advantage in enhancing the dissolution rate of drug.

Polyvinylpyrrolidone (PVP)

PVP, a polymer of vinylpyrrolidone, has a molecular weight falling between 2500-3000000. Moisture content and MW are responsible for the maintenance of PVP's temperature. It is used in various methods of solid dispersions such as: solvent evaporation method owing to its increase solubility. It is also used in hot melt extrusion method due to its high melting point.

Cellulose Derivatives

Hydroxypropylmethylcellulose (HPMC), molecular weight (10000-1500000), are unsymmetrical ethers of cellulose. Due to its excellent solubility in water, HPMCs are widely used in the formation of solid dispersion . Researchers have seen enhanced solubility of nilvadipine (poorly water-soluble drug), when used with HPMC.

Hydroxypropylcellulose (HPC), a derivative of cellulose has a MW of 37000-1150000. The solubility of HPC in solvents is high and varies to a wide range of solvents (ethanol, chloroform, water).

Carboxymethylethylcellulose (CMEC), is a class of cellulose with mixed ethers. In comparison to other cellulose derivatives, the dissolution rate of CMEC is altered in stomach due to acidic pH. Its dissolution in many solvents like ethanol, acetone and isopropanol is excellent and quick. However, its dissolution is rapid at pH above 6.

Hydroxypropylmethylcellulose phthalate (HPMCP), esters of cellulose, have a MW between 20000-20000. Their pH of dissolution falls between 5-5.5. however, their solubility in different solvents depends on the type of HPMCP used.

Polyacrylates and Polymethacrylates

These are the type of polymers which owing to their transparency are known as plastics. Methacrylate and acrylic acid undergo process of polymerization to produce these polymers. In market, they appear by the name of Eudragit (varying in grades). Some of the eudragit grades like eudragit L prevents the release of drug in gastric pH. However, other grades like eudragit E, due to its high solubility, increases the drug release. They are mainly used to coat the drugs, in order to control their release.

Urea

Urea, which is produced in the final step of metabolism of human protein, is considered to be sparingly soluble in water and many solvents. Due to their non-toxic effect in human body, they are also used as carrier for the preparation of solid dispersion by many researchers

Conclusion

The poor dissolution and bioavailability of orally administered drugs had been a concern. With many solubility enhancing techniques, solid dispersions have proved to be the most suitable method to overcome this issue. The review demonstrates that the researchers have mostly utilized drugs mentioned in BCS class II for enhancing the solubility of orally administered, poorly water-soluble drugs. However, very few works have been done on drugs with high solubility and low permeability (BCS class III). Moreover, multiple methods explained in this review are utilized for the preparation of solid dispersion but among all the preparation techniques and carriers, solvent evaporation and co-precipitation technique has found to be widely used technique. Among carriers, different grades of PVP and PEGs are being mostly employed. However, the recent advancement includes the use of different classes of alkyl cellulose ω-carboxyesters, for the preparation of amorphous solid dispersion.

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Biography

Department of Computer Science, Lahore University of Management Sciences, Lahore, Pakistan

izzatariq57@hotmail.com