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Application of Liquisolid Technology in Antidiabetics

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Abstract: **In this paper we have surveyed about formulation and evaluation of Liquisolid formulations and its work in antidiabetics . Mostly poorly water soluble drugs are in research category despite of less dissolution rate and poor bioavailability. Solubility is a vital parameter to develop new formulation as industries faced serious issue regarding the poor aqueous solubility of the drugs. Various methods for solubility enhancement include modifications of the drug, involvement of co-solvents, complexation, salt formation, size reduction. A propitious technique to solve major challenges like solubility, dissolution rate and their bioavailability. This technique can be defined as the conversion of poorly soluble liquid medications into non-adherent, dry, compressible and free flowing powder mixtures with help of excipients. Many anti-diabetic drugs are belonging to BCS Class-II facing challenges like solubility and bioavailability.**

***Indexed Terms*- excipients, compact, antidiabetic.(Keywords)**

I. INTRODUCTION

Oral route is one of the best acceptable route of administration. Bioavailability is key factor to determine the therapeutic efficacy of the drug. Poor water-soluble drugs have low solubility which ultimately lead to their declined dissolution, absorption and bioavailability. Hence, nowadays the drawback of hydrophobic drugs can be improved by rising drug's surface area, reducing the particle size, co-solvents or by formulating the drug in the solution form. However, the fine drug particles have the property of agglomeration due to Vander Waal forces of attraction and hydrophobicity which may lead to decrease in surface area over the period of time.

There is an alternative method of using high surface area carriers (e.g., Silica). This method involves the use of organic solvents in which the drug is dissolved. Agglomeration can be reduced due to binding of drug with the carrier. Toxicity can occur by residual solvent.[1]Various other methods for improving solubility are micronisation, solid dispersions, lyophilisation co-grinding, co-precipitation, formulation of inclusion complexes and Liquisolid compact technology.[2]Micronisation can create agglomeration ,stability problems can occur by solid dispersion. While Liquisolid technology is promising technique to overcome challenges such as solubility , dissolution and bioavailability.

Spireas *et al* developed a new technique namely, liquisolid compacts, which involved the dissolution of drug into non-volatile solvent.[3]Liquisolid compact technique can be defined as the formulation that is formed by conversion of free flowing, non-adherent and compressible powder mixtures. Spireas *et al*. proposed that porous particles have high absorption properties which can be used as coating materials like starch, cellulose. That is used to make a film on the carrier material which tends to decrease the inter-particulate friction.Hence, they should be very fine and highly absorptive silica powders.[4] Sodium Starch Glycolate(SSG) and , Polyvinylpyrrolidine are good disintegrants with swelling properties and good flowability.

Diabetes Mellitus is associated with deficiency of Insulin by beta cell destruction .Many drugs belong to BCS Class II and IV. This Novel technology helps to solve their challenges.

A. Concept of Liquisolid Technology

The drug is being dissolved in non volatile solvent then binary mixture of carrier and coating material in different ratio added in liquid mixture till angle of slide comes 33 ˚Large SSA and high adsorptive propertie delivers good flow properties.[5]

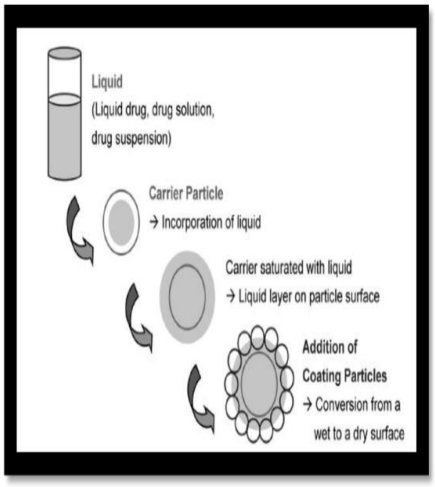

Fig 1: Brief Representation of Novel Technology

B. Preparation of Liquisolid Compact

Spireas *et al.* describes the mixing process in three steps that are: -

- The system is blended at a rate of one rotation per second for approximately one minute.
- This admixture is evenly spread over a motor surface and left still for 5 minutes.
- Then the powder is scraped off and then blended with other excipients for another 30 seconds.[6,7]

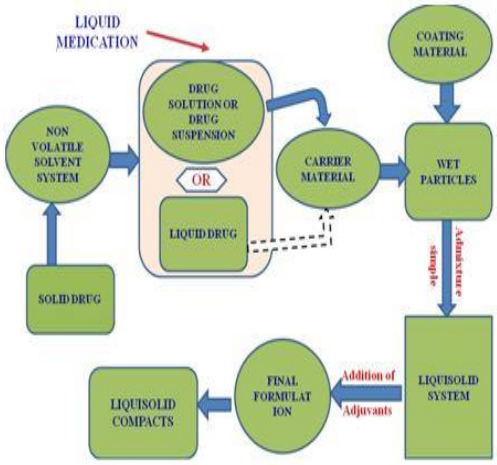

Fig 2: Method of preparation of liquisolid tablet

C. Mechanism of action

a) Increasing wettability: Wettability of liquid solid particles can be improved by the liquid vehicle which act as surfactant.The wettability of such systems has been demonstrated by measuring their water rising times and contact angles.

b) Increasing surface area : Drug's surface area is more (as drug in molecular dispersed state) than the drug particles in the direct compressible tablets.

c) Increasing drug's aqueous solubility: At the solid – liquid interface the concentration of liquid carrier could be enough to enhance the water solubility of the drug.[8,9]

D. Formulation components for liquisolid compacts [10]

The major formulation components required for liquisolid compact techniques are discussed below:

Drug: The drug should belong to BCS Class II and Class IV

Non - volatile Solvents: They are inert, mostly water-miscible and less viscous organic solvents.For example, N, N-dimethylacetamide, propylene glycol, polysorbates, etc.

a) Carrier Materials:They are relatively large, compression-enhancing, porous particles that possess sufficient absorption ability to favour liquid absorption.
   For example Starch,MCC etc.

b) Coating Materials:They are very fine (10nm-5,000nm in diameter), flow enhancers, and have high adsorption properties that covers the wet carrier particles.
   For example, various grades of Silica, Aerosil 200, etc.

c) Lubricants:They wil low down the friction between particles in mutual contact.
   For example, magnesium stearate, talc, sodium stearate, etc.

d) Disintegrants:It enhances disintegration when comes in contact with the aqueous medium.
   For example, Sodium Starch Glycolate

II. LITERATURE REVIEW

Antidiabetic drugs are used to lower down the blood glucose levels in the body and primarily used in the treatment of Diabetes Mellitus. These are also known as Hypoglycaemic Drugs.[11]Mostly antidiabetic drugs facing solubility problems and thus effects their bioavailability. Liquisolid formulations on Antidiabetics are tabulated in Table 1.

Table 1. Liquisolid formulations of Anti-Diabetics

Sulfonylureas (Generations)	Meglitinide	Thiazolidi-nediones
Glibenclamide Glipizide Gliclazide Glyburide Glimipride	Nateglinide Repaglinide	Pioglitazone

Various antidiabetic drugs are difficult to formulate because of their low solubility, poor dissolution and bioavailability. Liquisolid Technology is novel technology to overcome these problems. Such drugs belong to BCS Class-II and Class-IV. Many Liquisolid compacts of Antidiabetic drugs are formulated using novel carriers. Excipients play vital role in increasing drug solubility as well as feasible alternative to conventional dosage forms.[12]Different excipients involved in liquisolid formulations tabulated in Table 2

Table 2:Excipients used in Antidiabetic Liquisolid formulations

Drug	**Non volatile solvent**	**Carrier**	**Coating**	**Ref.**
Glibenclamide	PEG 400	Avicel	Aerosil 200	[13]
Glipizide	PEG 400	Avicel pH 102	Aerosil 200	[14]
Gliclazide	Castor Oil	Avicel pH102 , Neusilin	Aerosil 200	[15]
Glimipride	PG	MCC	Silica	[16]
Nateglinide	PG,Tween 80,PEG	MCC	Aerosil	[17]
Repaglinide	PEG 400	Avicel pH 102	Aerosil 200	[18]
Pioglitazone	PG	Avicel pH 102	Aerosil 200	[19]

Numerous non volatile solvents can be used like Glycols, Tween 80, Span 80, and Castor Oil rely on its solubility. Carrier And Coating Material can be choosen on basics of Specific Surface Area(SSA). As high SSA proved good flowability. Many herbals having property of antidiabetic as Curcumin,Quercetin act as antidiabetic Crystalline state of drug is changed to amorphous state in Curcumin Liquisolid tablets exhibited improvement in dissolution rates as well as apparent solubility was obtained [20]

III EVALUATION

A. Preformulation Studies:

Solubility and Angle of Slide are critical parameter for selecting non volatile solvent and optimum flow behaviour

B Pre-Compression Studies:

Flow Properties such as Angle of Repose ,Bulk Density ,Tapped Density[12]Compressibility Index ,Hausner's Ratio are all involved for its characterization of its flow behaviour.

Fourier Transform Infrared spectroscopy It is used to check compatibility of drug with excipients X-Ray Diffraction (XRD) and Scanning Electron Microscopy (SEM)-They are considered for crystallinity of the drug. Thermal behavior is examined and in X-Ray Diffraction Studies the machine usually serves at an angle 5 to 70° and counting rate of 0.45/step, use a 30mA current and a copper target of voltage 40KV.

C Post-Compression Studies [21,22]

Weight Variation, Thickness, Hardness ,Friability and *In-vitro* Disintegration Test are all parameters which should be in acceptable limits. .

D. In-vitro Release Studies –

In vitro Drug Release Studies which involves USP dissolution apparatus type II,900 ml 0.1N HCl at constant temperature of 37 °C±2 and at speed of 50 to 200 rmp

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E. Advantages

Liquisolid compacts possess number of advantages. Some of them are: -.

- They possess lower cost of production
- Improves dissolution rate.
- Increased bioavailability[23]

F. Disadvantages

It is not suitable for the formulation of high dose, water insoluble drugs.By increasing quantity of excipients weight of tablet is increased that create problem in swallowing[24]

G. Applications

The various applications of the liquisolid system are as follows: -

- By using Liquisolid formulations, rapid release rates of drug are obtained.
- Act as weapon to enhance the bioavailability of hydrophobic drugs..
- They are used in probiotics.
- They possess good flowability and compressibility.

IV CONCLUSION

Anti-Diabetic drugs, particularly belongs to BCS Class II and IV tends to have low aqueous solubility, Hence, they are formulated as liquisolid compacts so as to improve their solubility and ultimately improves their bioavailability. This novel technology helps in development of formulation of lipophyllic drugs.

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