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The Role of Excipients in Liquisolid Technology

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Abstract: **This article gives criteria for choosing excipients in liquisolid technology. Liquisolid technology is applicable for non polar drugs by converting drug solution into dry free flowing powder. Patient compliance is more in oral route of administration .Numerous techniques like solid dispersion, micronisation, lyophilisation co-grinding, co-precipitation,complexation and nanotechnology are used to increase aqueous solubility Solid dispersion having stability issues while micronization and complexation can cause agglomeration. In Nanotechnology, high cost involved in sophicticated instruments. Liquisolid technology is considered to be one of the best technique to to overcome solubility,dissolution and bioavailability. It convert drug solution into dry free flowing powder. This technique is simple manufacturing process with low production cost. In vitro release is enhanced by using this technology. There is significant role of excipients in this novel technique to get effective release of drug. Associated problems of BCS class II and IV is mostly solved in respect to solubility. Especially carrier with high specific surface area gives good results in overcoming all challenges. Carriers such as Lactose, Starch, Avicel pH101,Fujacilin, Neusilin ,each having specific properties in release of drug. Among all mostly used carriers are Avicel, Fujacilin and Neusilin as with highest Specific Surface Area (SSA) than others. PVP and SSG is considered best disintegrating agent as having good swelling property and flow property as Polyvinypyrrolidine can be used in high dose drugs. With large SSA and high adsorptive property Neusilin, Aerosil , PVP as carrier, coating material and disintegrating agent are considered perfect excipients in liquisolid technology**

***Indexed Terms*- Solubility, Non volatile solvent, Carrier, Coating materials**

I. INTRODUCTION

Liquisolid compact technique can be defined as the formulation that is formed by conversion of drug suspension into compressible non sticky and dry 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 layer on the carrier material which decrease the inter-particulate friction.Hence, they should be very fine and highly absorptive silica powders.[1] Sodium Starch Glycolate(SSG) and , Polyvinylpyrrolidine are good disintegrants with swelling properties and good flowability..Many drugs belong to BCS Class II and IV. This Novel technology helps to solve their challenges. 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.[2]

A. Mechanism of action

i) 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 enoughtoincrease aqueous solubility.[3,4]Mechanism is shown in Figure 1

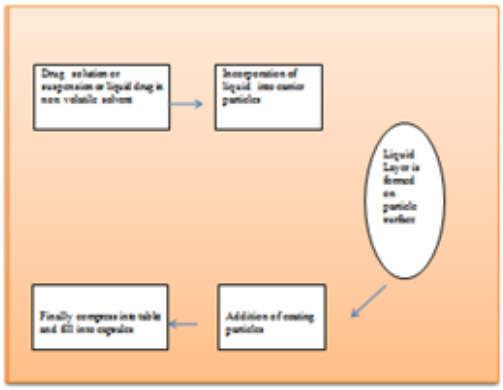

Figure1. Mechanism of Liquisolid Technology

B. Method of Preparation including steps are:

1. Drug solution or suspension is prepared with help of non volatile solvent
2. By using suitable carrier liquid is incorporated into drug
3. Liquid layer is formed on surface of particles due to saturation of carrier with liquid
4. With addition of coating particles wet turns into dry surface.
5. Disintegrant are essential to add if silicates are used.

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 33º [5]˚The major advantages of Liquisolid technology is its low cost and simple manufacturing process and having great potential in industrial application. While limitation is that it works only in low dose lipophyllicdrugs .Excipients play vital role in pre and postcompression properties. As in

NebivololHydochlorideFujacilin have great impact on In Vitro Release[6]Compatability of excipients between each other and with drug is very necessary in each novel formulation. Type of excipients shown in Figure 2.

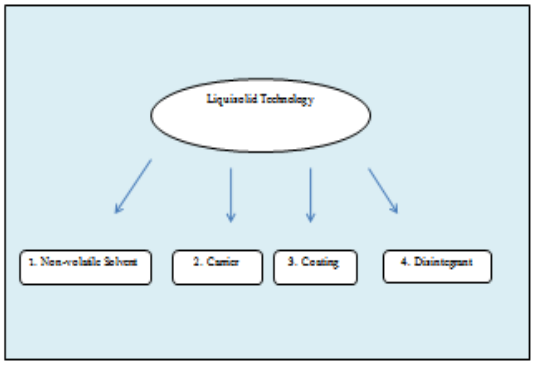

Figure 2. Type of excipients shown

There should be maximum solubility of drug in non volatile solvent.[7] Higher amounts of excipients needed in high dose drugs which ultimately increase tablet weight is major limitation.[8]

C. Excipients Selection

Non-volatile Solvent

1) Non-toxic
2) High boiling point,
3) Good solubilization power
4) Good binding ability.[9]

Maximum solubility of drug in solvent decrease the tablet weight. Enhanced dissolution rate in molecularly diffused drug.[10] Stability of API depends on appropriate selection of vehicle.[11] Excipients are a different gathering of materials with a wide reach in their properties. They are utilized in various items to give various functionalities, contingent over certain applications.[12]

Glycols : Polyethylene Glycol, Propylene glycol (PG), Oils : Olive oil, Castor oil, Soyabean oil, Liquid Paraffin, Glycerin,

Polysorbate : Tween 20 and 80 are most used solvents from this class.

Carrier Material include :

Avicel pH 101

Fujicalin (Dibasic Calcium Phosphate)

Neusilin (Magnesium aluminometa silicate),

Eudragit RL and RS,

Lactose,

Xanthamgum,ethyl cellulose

Methyl cellulose.

Carrier is selected mainly on basis of specific surface area as in order Neusilin (300m^2/g) > Calcium Silicate (290 m^2/g) >Fujacilin (40 m^2/g) >Avicel(1.18 m^2/g) >Lactose (0.35 m^2/g)Flowability and compressibility parameteris are evaluated after liquisolid powder is formed.

Liquid Loading Factor (L_f) is refers to the fraction of weight of non-volatile solvent to carrier material

$$L_f = W/Q \quad (1)$$

W: weight of non-volatile Solvent

Q: weight ofcarrier material

Flow Properties such as Angle of slide Angle of Repose Bulk density Tapped density Carr's index and Hausner'sratioshould be evaluated The standard values are tabulated in Table 1

TABLE 1. OPTIMUM FLOW PARAMETERS VALUES

S. No	Parameters	Values
1	Angle of Slide	33˚
2	Angle of Repose	25˚-30˚
3	Carr's Index	5 -15%
4	Hausner's ratio	1.25

FourierTransform Infrared spectroscopy It is used to check compatibility of drug with excipients X-Ray Diffraction (XRD) and Scanning Electron Microscopy (SEM)are considered for crystallinity of the drug. X-raydiffractometer is used to check nature of particle.

Most Commonly Used Carrier Materials are

Lactose, Microcrystalline Cellulose Dibasic Calcium Phosphate(Fujicalin):

Silicates:Calcium Silicate (Fluorite):Magnesium Alumino-metasilicate (Neusilin):

Bioavailability and stability is enhanced by using these carriers.[13-19]Mainly carriers used are tabulated in Table 2

TABLE 2. GENERAL PROPERTIES OF THESE CARRIERS

S. No	Carriers	SSA m^2/g
1	Lactose	0.35
2	Avicel pH 101	1.18
3	Fujicalin	40
4	Neusilin US2	300
5	Calcium Silica	290

Coating Material

It helps to make a layer on the carrier material l which tends to decrease the inter-particulate friction

Coating materials are:
Colloidal Silica (Aerosil200),
HPMC-E4M, Silicon dioxide,
Neusilin(Magnesium Aluminum meta silicate)
Specific Surface Area of coating materials are tabulated in Table 3

TABLE 3. MAJOR COATING MATERIAL WITH THEIR SPECIFIC SURFACE AREA

S. No	Coating Material	Specific Surface Area m^2/g
1	Aerosil 200 (Hydrophilic Fumed Silica)	220
2	Neusilin (Amorphous Alumino-metasilicate)	44-250
3.	Syloid (Amorphous Silicon dioxide	220
4.	Can–o-sil (Untreated fumed silica)	312

Disintegrants
They include
Explotab,
Croscarmellose Sodium,
Pregelatinized Starch
Polyvinyl Pyrrolidone(PVP)
Sodium Starch Glycolate (SSG)

They have property of good flowability and strong swelling Excipients play important role in increasing drug solubility as well as feasible alternative to conventional dosage forms.[20]All excipients can be used in liquisolid technology are tabulated in Table .4

TABLE 4. LIST OF DRUGS FORMING LIQUISOLID COMPACTS WITH VARIOUS EXCIPIENTS

Drug	Carrier	Coating	Non Volatile solvent
Efavirenz[21]	Neusilin + Corn Starch	Aerosil 200	Transcutol -HP
Glyburide[221	Neusilin US 2	Aerosil	2-Pyrolidine
Albendazole[23]	Neusilin	Aerosil	PEG 400
Ritonavir[24]	MCC pH 102	Crosspovidone	PEG 400
Chlorpromazine[25]	Avicel pH 200	Neusilin US2	PEG 400
Olanzapine[26]	Avicel PH 102	Aerosil 200	Tween 80 , PG
Acyclovir[27]	MCC pH 102	Syloid XDP	Tween 60
Carbamazepine [28]	Fujicalin,Neucilin, Avicel pH 102	Neusilin ,Aerosil 200	PEG 200
Atorvastatin [29]	PEG 400	Avicel pH 101,102 Neusilin	Aerosil

II. CONCLUSION

Liquisolid technology benefits attained by using exact suitable excipients.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 article proves excipient plays important role in overcoming all challenges.

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