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SOLUBILITY ENHANCEMENT OF A DRUG BY LIQUISOLID TECHNIQUE

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ABSTRACT

Liquisoild technique is a novel concept for delivery of drugs through oral route. This approach of delivering drugs is suitable mostly for lipophilic drugs and poorly or water insoluble drugs. This approach is suitable for immediate or sustain release formulations. Design and formulation of this approach is prescribed according to new mathematical model given by Spires et al. Increasing the solubility by using a non-volatile solvent which is suitable for drug, their by dissolving the drug in the non volatile solvent and this is termed as liquid medicament . Blending the liquid medicament with mixture of carrier and coating material, liquid medicament can be converted into non adhere, dry looking powder with acceptable flow properties and compression behavior using suitable excipients and tabletting by direct compression method.

KEYWORDS

Liquisolid tablets, Dissolution enhancement, Water insoluble drugs and solvents.

INTRODUCTION

It is prerequisite for active ingredient in solid dosage form must undergo dissolution to get absorb from gastrointestinal tract. The rate limiting step for most of the pharmaceutical formulations is dissolution. Quality control can be ensured for a formulation of different batches by determining in *vitro* dissolution study. Bioequivalence can also be estimated under certain conditions[1], Major rate limiting step for class II and IV is dissolution[2].

The term “water-insoluble drugs” are the drugs which are known as

“Sparingly water-soluble” (1 part solute to 100 parts of water),
“Slightly water-soluble” (1 into 100 to 1000 parts of water) and
“Very slightly water soluble” (1 part solute into 1000 to 10,000 parts of water).[3]

To enhance these properties like absorption, dissolution which are rate limiting step for lipophilic or poorly soluble drugs, different approaches have been designed with required modification such as

- Solid Dispersions[3],
- Inclusion complex using β-cyclodextrins[4],
- Micronization[5],
    - Microwave induced dissolution rate improvement[6],
    - Adsorption onto silica gels[7] and
    - New technique “Liquisolid Technique” developed by Spireas et al.[8, 9],

In past, Liquisolid compacts are derived from “powdered solutions, An past technique based on conversion of a liquid medicament to non-adhere dry appearance powder which adsorb the medicament onto silicas of large specific surfaces.[10,11]These preparations were analyzed by dissolution studies but because they are present in the form of powder-dispersion they could not be compressed into tablets There after studies based on powder solutions, with direct compression enhancers like microcrystalline cellulose were added in solid dispersion to improve compressibility of systems.[12-13]

In these studies more amount of silicas were used, but flow and compression properties were not standardized according to industrial specifications. When these improved powdered solutions were compressed to tablets, they have a nature of “liquid-squeezing-out” phenomena which was not acceptable.

This Liquisolid system which is having acceptable flow and compressibility by using the mathematical model proposed by Spireas et al, The drugs which are water insoluble or liquid lipophilic are dissolved in a suitable selected non-volatile solvent.

This non-volatile solvent with drug dissolved may be existing in solution or else suspension nature known as “liquid medicament”. The liquid medicament is converted into free flowing, non adhere, dry form and readily compressible powders with the help of different compressible carriers like (Starch, cellulose and lactose etc.) and else coating materials like (Collidol silica and Talc etc.).

Because of drug present in the liquid medicament as solubilised or moleulary dispersed state, as the dissolution is enhanced due to increased surface area as well as wetting area. Their by the Liquisolid technique is applied for water insoluble drugs to enhance dissolution rate may also increase bioavailability[10].

METHODOLOGY

Spireas et al proposed the new mathematical model in accordance to retain good flow behavior and compressibility to design the formulation for Liquisolid technique.[8,9]Mandatory requirements

for this technique are suitable drug candidate, suitable non-volatile solvent, carrier and coating materials. The basic properties of powder are proposed according to Spireas et al is "Flowable liquid retention potential" (Φ value) and compressible liquid retention potential"(ψ value). Flowable liquid retentional potential: defined as maximum weight of liquid (solvent) that can be retained per unit weight of powder (excipient) material to produce good flow.

Compressible liquid retention potential: defined as the compression force applied to produce tablets with acceptable strength without squeezing out any liquid during compression.

Excipient ratio (R): defined as Carrier to coating ratio quotated as

R= Q**/q**

Q= Carrier material,

q= Coating material.

Liquid load factor (L_f): defined as weight of liquid medicament (W) to weight of carrier (w).

$L_f = W/Q$

The Φvalue is for calculating excipients quantities. Equation is

$L_f = \Phi + \Phi$ (1/R)

Where, Φ and Φ are values of carrier and coating material.

MATERIALS REQUIRED FOR FORMULATION

Drugs: Which are poorly soluble or else insoluble drugs in water.

Non volatile solvent: They may be hydrophilic or lipophilic in nature based on selection of type of Formulation like immediate or control release. Some of them are

- Polyethylene glycol,
- Propylene glycol,
- Tween 80, 20,
- Span 80,20,
- Liquid Paraffin,
- Cremophore L etc.,

Carrier material: They are preferred to be coarser granular for acceptable flow, Methyl cellulose, Ethyl cellulose, Strach etc (Avicel PH 102, Avivel PH 200, Starch 1500, Ethocel)

Coating material: Nano meter sized silica mostly preferred, like Aerosil, talc.

Disintegrant: Mostly Super Disintegrates like Sodium starch gylcolate and crosspovidone. Etc.,

Pre-formulation studies

Solubility studies- Solubility of the drug by preparing a saturated solutions and drug content in the solvent was assessed by spectrophotometrically, excess drug was made soluble in the suitable solvent by using rotary shaker or by sonicator for 24 hrs and assessed by using spectrophotometrically.

Flow behavior: These flow behavior of the powder is determined by using Hausner ratio and Carr's index.

Dissolution studies

In-Vitro release profiles of drug from the preferred tablets were studied using dissolution apparatus and compared with the formulated Liquisolid tablet. Drug release, % drug dissolved

can be calculated of both the formulation results are estimated.

Differential scanning calorimetry (DSC)

This is prerequisite to know if any possible interaction present between the excipients and d the drug used in the formulation. The characteristic peak in the DSC thermogram belongs to drug is absent that indicates that the drug is present in moleculary dispersed in this system.[14]

X- ray diffraction (XRD)

To get justification that the drug is in the solubilised state or converted into amorphous form because of disappearance of characteristic peaks belongs to drug and their by appearance of peaks which belongs to carrier is absorbed.[15]

Scanning electron microscopy (SEM)

This study confirms that there are any crystals present, or else drug is present in the solubilised form by absence of crystals of drug.[16]

Stability studies

Drug content was determined their after the crystals were charged for accelerated stability studies according to ICH guidelines. Samples were taken and analysed for specified intervals.

CONCLUSION

In This Liquisolid technique gives a design to enhance the absorption as well as dissolution rate their by it may enhance the bio availability of a poorly soluble, insoluble or lipophilic drug and to formulate them into immediate release or else sustain release by selection of suitable solvent and carrier.

In this technique drug is dissolved in a non volatile solvent and their by this liquid medicament is converted to non adherent, dry looking and free flowing by using suitable carrier and coating material. Because of the presence of drug in the state of solubilised or moleculary dispersed state, so solubility of insoluble drug is enhanced.

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