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Journal DOI: <https://doi.org/10.7439/ijap>Journal home page: <http://ssjournals.com/index.php/ijap>**Review Article****Liquisolid Compacts: A Review****Urvashi B. Patel^{*1}, Dikshit C. Modi² and Dhiren P. Shah³**¹M. Pharm, Department of Pharmaceutics, Shree Naranjibhai Lalbhai Patel College of Pharmacy, Umrah - 394 345, Gujarat, India²Assistant Professor, Shree Naranjibhai Lalbhai Patel College of Pharmacy, Umrah - 394 345, Gujarat, India³Principal, Shree Naranjibhai Lalbhai Patel College of Pharmacy, Umrah - 394 345, Gujarat, India**QR Code*****Correspondence Info:**Urvashi B. Patel
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Umrah - 394 345, Gujarat, India***Article History:****Received:** 28/03/2017**Revised:** 09/04/2017**Accepted:** 10/04/2017**DOI:** <https://doi.org/10.7439/ijap.v6i7.4056>**Abstract**

Solubility is a major problem for nearly one third drugs in their development phase. Liquisolid technique is a most promising technique for promoting dissolution by increase in solubility. Liquisolid compact technology is a novel concept for oral drug delivery. Liquisolid compact technology was first described by Spireas *et al* (1998). According to the new formulation method of liqui-solid compacts, liquid medications such as solutions or suspensions of water insoluble drugs in suitable nonvolatile liquid vehicles can be converted into acceptably flowing and compressible powders by blending with selected powder excipients.

Keywords: Solubility enhancement, Liquisolid Compact.**1. Introduction**

Solubility of drugs is a major factor in the design of pharmaceutical formulations lead to variable oral bioavailability. Dissolution is an important factor for absorption of drugs especially in case of water insoluble or poorly soluble drugs.

The new developed technique by Spireas liqui-solid system improves the dissolution properties of water insoluble or poorly soluble drugs. The term “liqui-solid systems” (LS) is a powdered form of liquid drug formulated by converting liquid lipophilic drug or drug suspension or solution of water-insoluble solid drug in suitable non-volatile solvent systems, into dry looking, non-adherent, free-flowing and readily compressible powdered mixtures by blending with selected carrier and coating materials. [1,2]

1.1 Theory of liquid solid systems [3-4]

A powder can retain only limited amounts of liquid while maintaining acceptable flow and compression properties. To calculate the required

amounts of powder excipients (carrier and coating materials) a mathematical approach for the formulation of liqui-solid systems has been developed by Spireas. This approach is based on the flowable (Φ - value) and compressible (Ψ -number) liquid retention potential introducing constants for each powder/liquid combination.

1.2 Concept of liquisolid technology [5]

When the drug dissolved in the liquid vehicle is incorporated into a carrier material which has a porous surface and closely matted fiber in its interior such as cellulose, both absorption and adsorption take place. The liquid initially absorbed into the interior of the particle is captured by its internal surface. After saturation, adsorption of the liquid onto the internal and external surface of the porous carrier particle occurs. Then, coating material provides the desirable flow property to the liquisolid system due to its high adsorptive properties and large surface area.

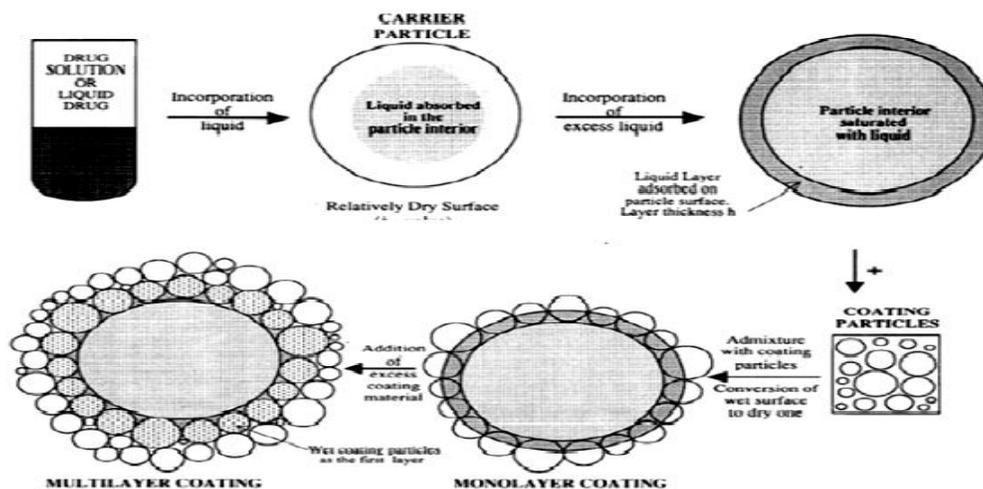


Figure 1: Concept of liquisolid compacts

2. Method of preparation [6-7]

Calculated quantities of drug are added to the non-volatile solvent, and then it is heated to dissolve the drug. This liquid drug solution is added to the carrier and coating materials and then it is mixed properly. The mixing process is carried out in three steps as described by Spireas et al.

- The system is blended at a rate of one rotation per second for approximately one minute in order to distribute the drug evenly in liquid.
- This admixture is evenly spread over the motor surface and left standing for 5min. to absorb the drug into the powder particle.
- Then powder is scraped off and then blended with other excipients for another 30 sec. similar to first step. This gives the final formulation of liquisolid tablets.

3. Mechanism of action [8-9]

3.1 Increased in surface area

The drug within the liqui-solid system is in molecularly dispersed state. So, the surface area of drug available for release is much greater than that of drug particles within directly compressed tablets.

3.2 Increased in wettability

Due to the fact that the liquid vehicle can either act as surface active agent or has a low surface tension, wetting of the liqui-solid primary particles is improved. Wettability of these systems has been demonstrated by measurement of contact angles and water rising times.

3.3 Increased in aqueous solubility of drug

The relatively small amount of liquid vehicle in a liqui-solid compact is not sufficient to increase the overall solubility of the drug in the aqueous dissolution medium. However, at the solid/liquid interface between an individual liqui-solid primary particle and the release medium it is possible that in this microenvironment the amount of liquid

vehicle diffusing out of a single liqui-solid particle together with the drug molecules might be sufficient to increase the aqueous solubility of the drug if the liquid vehicle acts as a cosolvent.

4. Classification of liqui-solid systems [10-11]

- 1) Powdered drug solutions
- 2) Powdered drug suspensions
- 3) Powdered liquid drugs
- 4) Powdered drug emulsion

5. Formulation components [5-8]

The major formulation components of liqui-solid compacts are:

5.1 Drug :

It should be of bcs class II and IV. It should be lipophilic in nature.

5.2 Non volatile solvents :

They decreased the interfacial tension between the drug and dissolution medium.

5.3 Carrier Material

Relatively large, preferably porous particles possessing a sufficient absorption property which contributes in liquid absorption. e.g. various grades of cellulose, starch²², lactose²⁵, sorbitol etc.

5.4 Coating Material

These are flow-enhancing, very fine (10 nm to 5,000 nm in diameter), highly adsorptive coating particles. e.g., silica of various grades like Cab-O-Sil M5, Aerosil 200, Syloid 244FP etc.) Inert, high boiling point, preferably water-miscible and not.

5.5 Disintegrants

Most commonly used disintegrant is sodium starch glycolate (Explotab¹³, Pumogel, etc.)

6. Evaluations parameters [1-6]

6.1 Pre-formulation studies:

6.1.1 Solubility study:

Solubility study is done by preparing a saturated solution of the drug in non-volatile solvents & analyzing them by using a spectrophotometer. Saturated solutions are prepared by adding excess amount of drug to vehicles and let it stay to achieve the equilibrium state (e.g., by shaking, stirring) for a specific time of period. Solvents with greater ability to solubilize the drug are selected for the formulation of liquisolid system for enhanced release.

6.1.2 Determination of angle of slide (θ):

Angle of the slide is determined to evaluate the flow property of powder excipients. The required amount of carrier is weighed and placed on one side of a metal plate with polished surface. The end is gradually raised till the plate become angular to the horizontal at which powder is about to slide. This angle is known as the angle of the slide. The angle of slide of 330 is regarded as an optimum flow behavior for compressing in to tablet or filling in capsules.

6.2 Pre-compression studies:

6.2.1 Flow property:

The angles of repose, compressibility index, Hauser's ratio are determined for evaluation of flow property of resulting final liquisolid powder.

6.2.2 Differential Scanning Calorimetry (DSC):

It is used to determine any possible interaction between excipients used in the formulation. There is an indication that the drug is in the form of solution in liquisolid formulation if the characteristic peak of the drug is absent in the DSC thermogram.

6.2.3 X-ray diffraction (XRD) and Scanning Electron Microscopy (SEM):

XRD & SEM studies are recommended to control the crystallinity of the drug. Disappearance of characteristic peak or crystals of the drug generally indicates that the drug is converted into the amorphous form or is solubilized in the liquisolid formulation.

6.3 Post compression studies

6.3.1. Thickness and Hardness test:

The thickness of the tablets was determined using a digital caliper; reading shown was noted. The hardness was tested by using Monsanto tester.

6.3.2 Friability test

The friability of the tablets was determined using Roche friabilator.

The % friability was then calculated using the formula:

$$\% \text{ friability} = \frac{\text{Initial Weight} - \text{Final Weight}}{\text{Initial Weight}} * 100$$

6.3.3 Weight variation test:

The test was performed as per USB by weighing 20 tablets individually on electronic balance, calculating the average weight, and comparing the individual tablet weights to the average.

6.3.4 *In-vitro* dispersion time:

In-vitro dispersion time was measured by following procedure. The tablet was then carefully positioned in the center of the petri dish containing 6 ml of water and the time required for the tablet to completely disintegrate into fine particles was noted. Three tablets from each formulation were randomly selected and *In-vitro* dispersion time was measured.

6.3.5 *In-vitro* disintegration test:

The test was carried out on 6 tablet using a tablet disintegration tester. Water at 37 ± 2 °C was used as a disintegration medium and the time taken for the complete disintegration of the tablet was noted with no palpable mass remaining in the apparatus was measured.

6.3.6 *In-vitro* release studies:

The dissolution rate of formulations was measured in dissolution test apparatus using USB type II. Dissolution studies were carried out using 900 ml of Phosphate buffer pH 7.4 at 37 ± 0.5 °C at 50 RPM. 5 ml samples were withdrawn at various time intervals and placed by 5 ml fresh phosphate buffer pH 7.4 to maintain sink condition. The solutions were immediately filtered through filter paper, diluted and the concentration of the drug was determined spectrophotometrically.

6.3.7 Wetting time:

A piece of tissue paper was folded and placed twice and placed in a small petri dish containing sufficient water. A tablet was kept on the paper and the time for complete wetting of the tablet was measured.

6.3.8 Water absorption ratio (R):

The weight of the tablet prior to placement in the petri dish was noted (Wb). The wetted tablet was removed and weighed (Wa). Water absorption ratio, R, was then determined according to the following equation.

$$R = 100 \times (W_a - W_b) / W_b$$

Where, Wb and Wa are tablet weights before and after water absorption, respectively

6.3.9 Stability studies:

Whenever a new formulation is developed, it is very essential to establish that the therapeutic activity of the drug has not undergone any change. To confirm this, the selected formulations were subjected to stability studies. Accelerated stability testing studies were performed for 6 months as per ICH guidelines. The optimized formulations were kept at 40 ± 2 °C and $75 \pm 5\%$ RH. Tablets were evaluated for physical appearance, hardness, *In-vitro* dispersion time, % drug content and % drug release.

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