IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

A Review Article Liquid Sol Tablet And It's Advantages For The Poorely Soluble Drug

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Abstract

The solution–liquid–solid (SLS) and related solution-based methods for the synthesis of semiconductor nanowires and nanorods are reviewed. Since its discovery in 1995, the SLS mechanism and its close variants have provided a nearly general strategy for the growth of pseudo-one-dimensional nanocrystals. The various metallic-catalyst nanoparticles employed are summarized, as are the syntheses of III–V, II–VI, IV–VI, group IV, ternary, and other nanorods and nanowires. The formation of axial heterojunctions, core/shell nanowires, and doping are also described. The related supercritical-fluid–liquid–solid (SFLS), electrically controlled SLS, flow-based SLS, and solution–solid–solid (SSS) methods are discussed, and the crystallographic characteristics of the wires and rods grown by these methods are summarized. The presentation of optical and electronic properties emphasizes electronic structures, absorption cross sections, polarization anisotropies, and charge-carrier dynamics, including photoluminescence intermittency (blinking) and photoluminescence modulation by charges and electric fields. Finally, developing applications for the pseudo-one-dimensional nanostructures in field-effect transistors, lithium-ion batteries, photocathodes, photovoltaics, and photodetection are discussed.

Keywords: BCS class, Liquisolid tablets, Powdered drug solutions Powdered drug suspensions Powdered liquid drugs

INTRODUCTION

Oral ingestion is the most suitable and convenient route of drug delivery due to its ease of administration, high patient compliance, cost effectiveness, least sterility constraints, and flexibility in the design of dosage form. Thus, many of the generic drug companies are inclined more to produce bioequivalent oral drug products[1]. Consequently, much effort is focused during drug discovery to identify orally active molecules that will provide reproducible and effective plasma concentrations in vivo. Unfortunately, about the 40% of new active candidates, including several powerful poorly water soluble drugs, are characterized by low aqueous solubility and the oral administration of these drugs are

frequently associated with low bioavailability, and lack of proportional dose-therapeutic effect relationship.[2] The Noyes-Whitney equation (Eq. 1) provides clear suggestion of parameters that can be modified enhance the dissolution rate of poorly soluble drugs:

$$dc/dt = AD (Cs – C) / h \quad (1)$$

Where dc/dt is the dissolution rate, A is the surface area exposed to dissolution medium, D is the diffusion coefficient of the drug in solution, Cs is the solubility of the drug, C is the drug concentration in the dissolution medium at time t, and h is the thickness of diffusion boundary layer. Several parameters in this equation can be adjusted to achieve the enhancement of the dissolution rate. For example, increasing either the surface area or diffusion coefficient can lead to a higher dissolution rate.[3]

The absorption of an active pharmaceutical ingredient (API) released from the oral dosage form depends on two factors, the dissolution of the API in the gastrointestinal tract and its permeability through the mucosa.[4] Based on these two parameters, drugs have been divided in four categories, the so called Biopharmaceutical Classification System (BCS)

CLASS II Low solubility high permeability	**CLASS I** High solubility high permeability
CLASS IV Low solubility Low permeability	**CLASS III** High solubility Low permeability

Figure 1. BCS

Biopharmaceutical classification system.[5] The biopharmaceutical classification system (BCS) is the scientific framework for classifying drug substances based on their aqueous solubilit y and intestinal permeability. It is a drug development tool that allows estimation of the contributions of three major factors, dissolution, solubility and intestinal permeability that affect oral absorption of drugs.[6] BCS class II and IV drugs which have low solubility provide a number of challenges for formulation scientists working on oral delivery of drugs. The enhancement of drug solubility thereby its oral bioavailability remains one of the most challenging aspects of the drug development process especially for oral drug delivery system.[7] There are several methods available and reported in literature to enhance the solubility of lipophilic drugs. The techniques are chosen on the basis of certain aspects such as properties of drug under consideration , nature of excipients to be selected, and the nature of intended dosage form.[8] The poor solubility and low dissolution rate of poorly water soluble drugs in the aqueous gastrointestinal fluids often cause insufficient bioavailability, especially for class II (low solubility and high permeability) substances. According to the BCS, the bioavailability may be enhanced by increasing the solubility thereby increasing the dissolution rate of the drug in the gastrointestinal fluids.[9] As for BCS class II drugs rate limiting step is drug release from the dosage form and solubility in the gastric fluid and not the absorption, so improving the solubility in turn increases the bioavailability for BCS class II drugs.[10]

LIQUISOLID TECHNOLOGY

Among the various techniques available to overcome the solubility issue, several researchers reported that the formulation of liquisolid tablets is one of the most promising techniques for promoting drug dissolution8-13. It is established that soft gelatin capsule preparations containing a solubilised liquid drug show higher and more consistent bioavailability than the conventional oral dosage forms because the active ingredient(s) is already in solution.[11] In fact, liquisolid tablets deliver active ingredient(s) in a similar mechanism as soft gelatin capsule preparation which contains liquid[12] because in liquisolid tablets, non-volatile liquid vehicle was used to dissolve the solid drug, and the preparation does not involve drying and evaporation process; therefore, the drug is held in the solution even though it is in a tabletted or encapsulated dosage form. Consequently, drug dissolution properties and oral bioavailability will be improved.[12] The technique of liquisolid compact has been successfully employed to improve the in vitro release of poorly soluble drugs like indomethacin,[15] piroxicam,[16] griseofulvin, [17] ezetimibe,[18] repaglinide,[19] prednisolone, etc. The liquisolid technology for release enhancement has been successfully applied to low dose poorly soluble drugs. But, the formulation of a high dose poorly soluble drug is one of the limitations of this technology.[13] In order to increase drug loading, the powder must retain high amount of liquid. However, this may lead to poor flow and compression properties of the powder. In order to maintain good flow and compression properties, high amount of carrier and coating material should be used. But, this may result in an increase in tablet weight ultimately leading to an unacceptably large tablet size.[14] The tablet size is a key determinant in the patient compliance. Therefore, a potential approach to load high dose of water insoluble drug is to increase the liquid adsorption capacity by using carrier and coating materials such as Neusilin and Fujicalin with a high specific surface area (SSA) which maintains flow of material, compression properties and reduces tablet weight. Spireas and Bolton have introduced a mathematical model for producing liquisolid compacts with acceptable flowability and compactibility.[15] This model is based on the hypothesis that powder material can only accommodate a specific amount of liquid medicament (co-solvent + drug) in the inner matrix while preserving acceptable flowability and compatibility.[19] Once the proportion of liquid exceeds the certain limit, the flow property and compactibility of the powder material starts to decline. This maximum amount of liquid which a powder material can retain while maintaining acceptable flowability and compatibility is known as flowable liquid-retention.[20]

A Liquisolid structure refers to information shaped by the conversion of fluid medicines, drug suspensions or medication arrangements into unpredictable solvents into dry, non-following, free streaming and compressible powder combinations by mixing the suspension or arrangement with selected transporters and materials covering.[21] The Liquisolid framework is the most encouraging strategy for advancing disintegration Rapid delivery rates are obtained in Liquisolid definitions and can be used effectively for strong water-insoluble drugs or lipophilic fluid drugs or strong water-insoluble drugs broke up in unstable dissolvable and this fluid drug can be converted into free streaming, non-free streaming. On, dry looking, and promptly compressible powders with utilization of transporter and covering materials.[22]

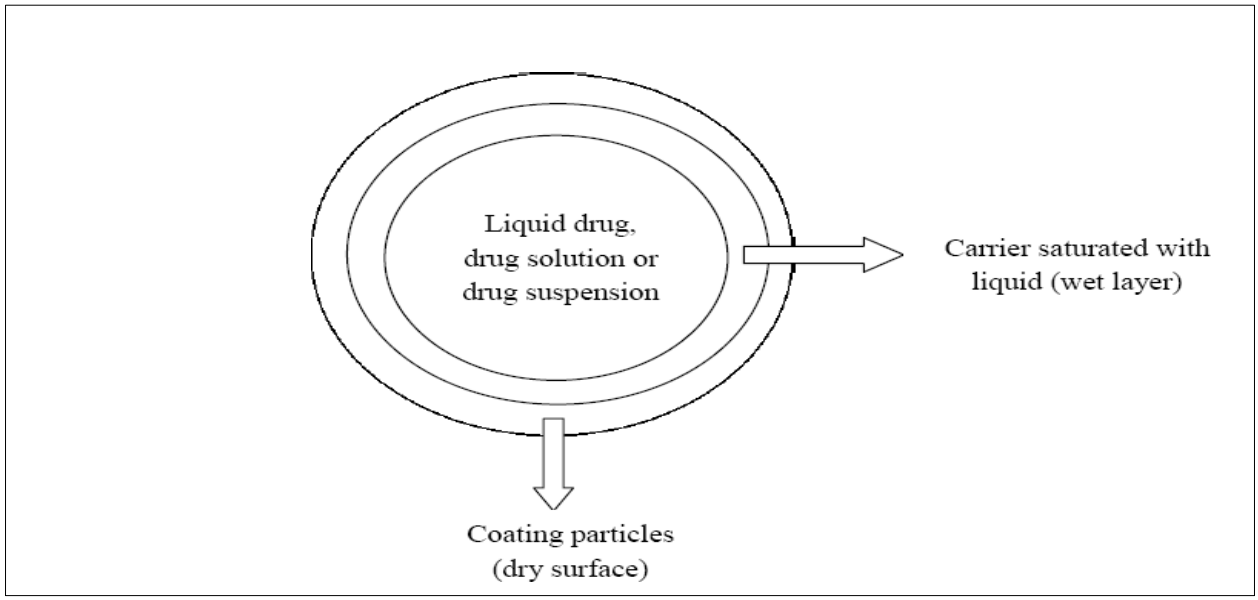

Figure no 2.

Need of Liquisolid technique

The oral route remains the preferred route of drug administration due to its convenience, good patient compliance and low medicine production costs.[23] In order for a drug to be absorbed into the systemic circulation following oral administration, the drug must be dissolved in the gastric fluids. Therefore, low solubility is one of the main obstacles facing drug production today, as an estimated 40 percent of all newly formulated drugs are poorly soluble or insoluble in water. By reducing particle size, decreasing crystallinity, and/or increasing the area of the surface, the dissolution rate of these drugs can be increased. Several studies have been carried out to boost the rate of drug dissolution by rate of drugs by decreasing the particle size, by creating nanoparticles and microparticles.[24] However, the fine drug particles have high tendency to agglomerate due to Vander Waals attraction or hydrophobicity, which both result in a decrease in surface area over time. Another way of increasing the dissolution rate is adsorption of the drug onto a high-surface area carrier. In this technique, the drug is dissolved in an organic solvent followed by soaking of the solution by a high surface area carrier such as silica.[25] Here, agglomeration of the drug particles is prevented due to the binding of drug to the carrier. However, due to the presence of the residual solvent in the drug formulation, it is disadvantageous to use toxic solvents.[26] To overcome the problem, the technique of „Liquisolid compacts" is a new and promising approach towards dissolution enhancement.

Classification of Liquisolid systems

1. Powdered drug solutions

2. Powdered drug suspensions

3. Powdered liquid drugs

The first two may be produced from the conversion of drug solutions or [e.g.prednisolone solution in propylene glycol] or drug suspensions [e. g. gemfibrozil suspension in Polysorbate 80], and the latter from the formulation of liquid drugs [e. g. clofibrate, liquid vitamins, etc.], into Liquisolid systems. Since non-volatile solvents are used to prepare the drug solution or suspension, the liquid vehicle does not evaporate and thus, the drug is carried within the liquid

system which in turn is dispersed throughout the final product. Based on the formulation technique used, Liquisolid systems may be classified into two categories.

1. Liquisolid compacts

2. Liquisolid microsystems.

Liquisolid compacts are prepared for the development of tablets or capsules using the previously described process, while Liquisolid microsystems are based on a modern idea that uses similar technique combined with the addition of an additive, e.g., G., Polyvinylpyrrolidone [PVP], in the liquid drug incorporated in the carrier and coating materials to create an acceptably flowing admixture. The advantage stemming from this new technique is that the resulting unit size of Liquisolid microsystems may be as much as five times less than that of Liquisolid compacts.

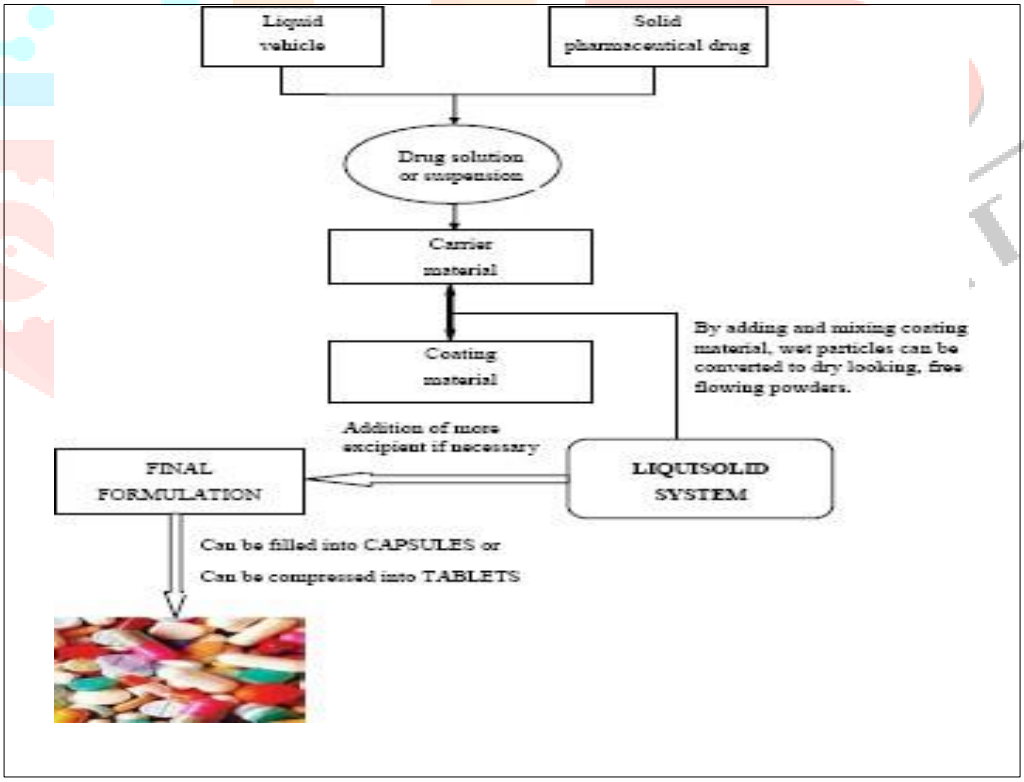

Figure no 3. Liquidcompact conversion of granules and tablet last product Drug release Mechanisms of increased

The three main mechanisms proposed include increased surface area of drug available for release, increased drug aqueous solubility due to the presence of non - volatile vehicle and improved drug particle wettability due to the cosolvent effect of the used vehicle.4,5 Enhanced effectual Surface Area. In the liquid medium whenever the drug, be dissolved within the liquisolid system and it is in a molecularly dispersed condition. Consequently, the drug‟s surface area accessible for release in directly

compressed tablets is more than that of molecules of the drug. Consequently, by improving the solubility of the drug content and thus increasing the portion of the drug that is not dissolved in the liquid vehicle, the release rate decreases., the discharge rates in the liquid formulation may be exposed with many of drugs and to be directly proportional to the portion of the molecularly isolated drug (FM). According to spires FM as the fraction between the drug solubility, (Sd) the real concentration of the drug, (Cd) medium carried by all system.

Method for liquisolid compact

The required amount of the drug and non-volatile co-solvent were added in 20 ml glass beaker and heated gradually until all the drug was solubilized. The resultant warm liquid medication as incorporated into the fixed amount of carrier and coating materials by the following the three steps as suggested by Spireas et al. In the first stage, the powder excipient and liquid medicaments were blended at an estimated mixing rate of one rotation per second for nearly one minute in order to have a uniform distribution of the liquid medication in the powder. In the second stage, the liquid/powder admixture was evenly spread as a uniform layer on the surfaces of a mortar and left standing for approximately 5 min to allow the drug solution to get absorbed in the internal matrix of the powder material. In the third stage, the powder is scraped off from the surface of mortar by using an aluminum spatula and then mixed with the disintegrating agent for another 30 seconds in the same way as described in the first step. The yielded final liquisolid formulation was compressed in tablet form.

Applications of Liquisolid technique in pharmaceutics

1. Liquisolid technique as a tool to enhance drug dissolution Based on the literatures, liquisolid technique has been widely used to improve the dissolution rate of low dose insoluble drugs, such as prednisolone, famotidine, valsartan, ketoprofen, raloxifene hydrochloride, clonazepam, clofibrate, etc.
2. In the case of high dose water insoluble drugs (i.e., carbamazepine), the feasibility of liquisolid technique. It is possible to involve liquisolid technique in the incorporation of high dose water-insoluble drugs into liquisolid systems by adding some additives (such as PVP, HPMC and polyethylene glycol 35000), because these additives have the capability to increase the liquid absorption capacity of carrier and coating materials. have shown another potential approach to load high dose of poorly water-soluble drugs into liquisolid systems, namely by using modern carriers with larger SSA value and higher absorption capacity.

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