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A REVIEW ON PHARMACEUTICAL APPLICATIONS OF LIQUISOLID TECHNIQUE

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ABSTRACT

The term “liquisolid medication” implies oily liquid drugs and solutions or suspensions of water insoluble drugs carried in suitable non-volatile solvent systems. Liquisolid compacts demonstrated a considerably higher drug dissolution rates than those of conventionally made capsules and directly compressed tablets. This was due to the increased wetting properties and surface of drug available for dissolution. This review paper highlights the application of liquisolid technique to enhance the solubility and dissolution of water insoluble drugs. This technique is appropriate for poorly or water insoluble drugs and also for immediate or sustained release formulations. This review also depicts the various formulation parameters that must be optimized before formulation the liquisolid compacts.

Keywords: Liquisolid technique; Solubility; Dissolution; Poorly; Water insoluble drugs

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INTRODUCTION

The liquisolid technique as described by Spireas¹ a novel concept where a liquid may be transformed into a free flowing, readily compressible and apparently dry powder by simple physical blending with selected carrier and coating material. The liquid portion, which can be a liquid drug, a drug suspension or a drug solution in suitable non-volatile liquid vehicles, is incorporated into the porous carrier material. Inert, preferably water-miscible organic solvent systems with high boiling point such as propylene glycol, liquid polyethylene glycols, or glycerine are best suitable as liquid vehicles. Once the carrier is saturated with liquid, a liquid layer is formed on the particle surface which is instantly adsorbed by the fine coating particles². Thus, an apparently dry, free flowing, and compressible powder is obtained. Microcrystalline cellulose is used as carrier material and amorphous silicon dioxide (colloidal silica) as coating material usually.

Various excipients such as lubricants and disintegrants (immediate release) or matrix forming materials (sustained release) may be added to the liquisolid system to produce Liquisolid compacts (Figure 1).

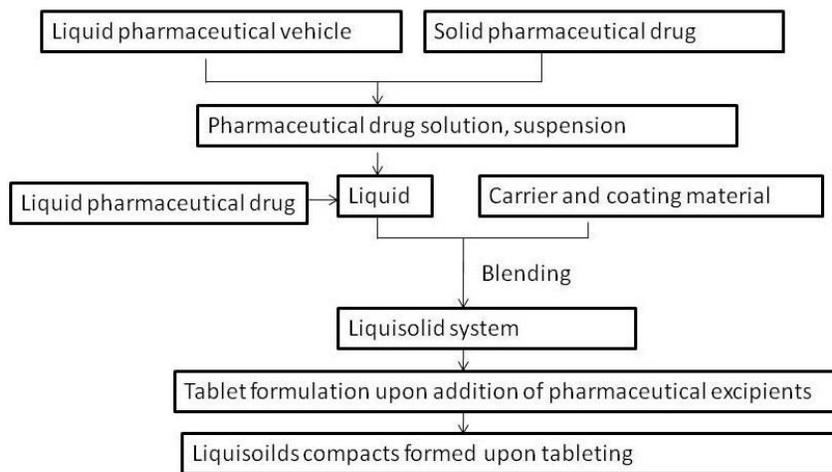


Figure 1: Schematic outline of the steps involved in the preparation of liquisolid compacts

Liquisolid compacts of poorly water soluble drugs containing a drug solution or drug suspension in a solubilising vehicle illustrate enhanced drug release due to an increased surface area of drug available for release, an increased aqueous solubility of the drug, and an improved wettability of the drug particles^{3,4}. Therefore, this enhanced drug release may result in a higher drug absorption in the gastrointestinal tract and thus, an improved oral bioavailability^{5,6}.

The Liquisolid Technique is also used to postponement of the drug release^{1,4,7,8}. Sustained release oral dosage forms are advantageous with regard to patient compliance because of the

reduced dosing frequency. Superlatively, a sustained release dosage form leads to therapeutic plasma levels, which are maintained throughout the dosing interval. It has been pragmatic that by using the hydrophobic carriers such as Eudragit® RL and RS in place of hydrophilic carriers, sustained release systems may be obtained⁸. Sustained release from lquisolid compacts with the conventional carrier and coating materials may also be obtained after addition of a matrix forming material such as hydroxypropyl methylcellulose¹.

FORMULATION DESIGN OF LIQUISOLID SYSTEMS

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 lquisolid systems has been developed by Spireas^{1,9}. This approach is based on the flowable (Φ -value) and compressible (Ψ -number) liquid retention potential introducing constants for each powder/liquid combination. The Φ -value of a powder is defined as the maximum amount of a given non-volatile liquid that can be retained inside its bulk [w/w] while maintaining an acceptable flowability. The flowability may be determined from the powder flow or by measurement of the angle of repose. The Ψ -number of a powder is defined as the maximum amount of liquid the powder can retain inside its bulk [w/w] while maintaining acceptable compactability¹⁰. The terms “acceptable flow and compression properties” imply the desired and thus preselected flow and compaction properties which must be met by the final lquisolid formulation. Depending on the excipient ratio (R) of the powder substrate an acceptably flowing and compressible lquisolid system can be obtained only if a maximum liquid load on the carrier material is not exceeded. This “liquid load factor (L_f)” [w/w] is defined as the weight ratio of the liquid formulation (W) and the carrier material (Q) in the system:

$$L_f = W / Q$$

R represents the ratio between the weights of the carrier (Q) and the coating (q) material present in the formulation:

$$R = Q/q$$

The liquid load factor that ensures acceptable flowability ($^{\Phi}L_f$) and for production of lquisolid systems with acceptable compactability ($^{\Psi}L_f$) can be determined by:

$$^{\Phi}L_f = \Phi + (1/R); \quad ^{\Psi}L_f = \Psi + \psi \cdot (1/R)$$

where Φ and ϕ are the Φ -values of the carrier and coating material, respectively and Ψ and ψ are the Ψ -numbers of the carrier and coating material, respectively. As soon as the optimum liquid

load factor is determined, the appropriate quantities of carrier (Q_o) and coating (q_o) material required to convert a given amount of liquid formulation (W) into an acceptably flowing and compressible liquisolid system may be calculated as: $Q_o=W/L$; $q_o=Q/R$

LIQUISOLID FORMULATIONS FOR ENHANCED DRUG RELEASE

Many poorly water soluble drugs have been formulated as liquisolid systems showing enhanced drug release. Different liquid vehicles, carrier and coating materials were used to formulate these drug delivery systems as shown in Table 2.

Table 2: Formulations of liquisolid systems with enhanced drug release and sustained drug release

S.No.	Dug	Liquid vehicle	Carrier and Coating material
1.	Aceclofenac	PEG 400	MCC and Colloidal silica ¹¹
2.	Bromhexine HCL	PG	MCC and Colloidal silica ¹²
3.	Carbamazepine	PEG 200	MCC and Colloidal silica ¹³
4.	Famotidine	PG	MCC and Colloidal silica ¹⁴
5.	Glibenclamide	PEG 400	MCC and Colloidal silica ¹⁵
6.	Griseofulvin	PEG 400	MCC and Colloidal silica ¹⁶
7.	Hydrocortisone	PG	MCC and Colloidal silica ¹⁷
8	Nifedipine	PEG 400	MCC and Colloidal silica with HPMC ¹⁸
9	Propranolol HCL	Polyysorbate 80	Eudragit RS or RL and Colloidal silica with HPMC ¹⁹
10	Theophylline	Polyysorbate 80	Eudragit RS or RL and Colloidal silica with HPMC ²⁰
11	Tramadol HCL	PG	MCC and Colloidal silica with HPMC ²¹

Mechanisms of enhanced drug release from liquisolid systems

The three recommended mechanisms include an increased surface area of drug available for release, an increased aqueous solubility of the drug, and an improved wettability of the drug particles.

a. Increased drug surface area

When the drug within the liquisolid system is absolutely dissolved in the liquid vehicle it is positioned in the powder substrate in a solubilized, molecularly dispersed state. Therefore, the surface area of drug available for release is much greater than that of drug particles within directly compressed tablets.

Consequently, with increasing drug content beyond the solubility limit and thus, increasing fraction of undissolved drug in the liquid vehicle the release rate decreases. It has been pragmatic with various drugs that the release rates are directly proportional to the fraction of the

molecularly dispersed drug (F_M) in the liquid formulation^{3, 9, 17, 22}. F_M is defined by Spireas as the ratio between the drug's solubility (S_d) in the liquid vehicle and the actual drug concentration (C_d) in this vehicle carried by each system¹⁷.

Therefore

$$F_M = S_d / C_d$$

$$\text{Where } F_M = 1 \text{ if } S_d \geq C_d$$

b. Increased aqueous solubility of the drug

In addition to the first mechanism of drug release enhancement it is expected that C_s , the solubility of the drug, might be increased with liquisolid systems. In fact, the relatively small amount of liquid vehicle in a liquisolid 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 liquisolid primary particle and the release medium it is possible that in this microenvironment the amount of liquid vehicle diffusing out of a single liquisolid particle together with the drug molecules might be sufficient to increase the aqueous solubility of the drug if the liquid vehicle acts as a co solvent^{3, 9, 17}. The overall increase in the solubility of drugs caused by liquisolid systems was confirmed by Yadav et al^{11, 16, 23, 24}.

c. Improved wetting properties

Due to the fact that the liquid vehicle can either act as surface active agent or has a low surface tension, wetting of the liquisolid primary particles is improved. Wettability of these systems has been confirmed by measurement of contact angles²⁵ and water rising times^{6, 16, 23}.

Optimization of Liquisolid Formulations with Enhanced Drug Release

The Liquisolid Technique has been successfully useful to low dose, poorly water soluble drugs. The formulation of a high dose, poorly soluble drug is one of the limitations of the Liquisolid Technique. As the release rates are directly proportional to the fraction of molecularly dispersed drug (F_M) in the liquid formulation a higher drug dose requires higher liquid amounts for a desired release profile. Therefore, to obtain liquisolid systems with acceptable flowability and compactability high levels of carrier and coating materials are required. However, this results in an increase in tablet weight ultimately leading to tablet sizes which are difficult to swallow. Therefore, to overcome this and various other problems of the Liquisolid Technique several formulation parameters may be optimized as shown in Table 3.

Table 3: Optimization of formulation parameters for liquisolid systems with immediate drug release

S. No	Formulation parameters	Optimization	Effect
1.	Liquid vehicle	High drug solubility in vehicle	Increased fraction of the molecularly dispersed drug (F_M)
2.	Carrier and Coating material	High specific surface area	Increased Liquid load factor (L_f)
3.	Addition of excipient	Polyvinyl pyrrolidone (PVP) Superdisintegrant	Increased liquid load factor (L_f), Increased viscosity of liquid vehicle, Inhibition of precipitation
4.	Excipient ratio (R)	High R-value	Fast disintegration Inhibition of precipitation

In various studies the effect of different types of non-volatile liquid vehicles has been investigated. The results reveals that the selection of a liquid vehicle with a high solubilizing capacity for the drug and thus, an increased F_M , leads to enhanced release profiles^{9, 12, 22, 26, 27}. It means that by selection of a liquid vehicle with optimum solubilizing properties the amount of liquid and thus, the weight and size of the liquisolid compacts can be reduced. However, in addition to the drug solubility in the liquid vehicle other physicochemical characteristics of the liquid vehicles such as polarity, viscosity, molecular weight, chemical structure, and lipophilicity may also have an effect on drug release⁹.

A further approach to minimize tablet weight is to increase the liquid load factor by addition of carrier and coating materials with a high specific surface area or by adding PVP to the liquid formulation. It was found that the higher the specific surface area of an excipient the higher the liquid load factor². For instance, the liquid adsorption capacity of microcrystalline cellulose (1.18 m²/g) is higher than that of lactose (0.35 m²/g), starch (0.6 m²/g), and sorbitol (0.37 m²/g)²⁵. Fujicalin® (30 m²/g), a spherically granulated dicalcium phosphate anhydrous, and Neusilin® US2 (300 m²/g), a magnesium aluminometasilicate, turned out to be very effective excipients for liquid adsorption while maintaining acceptable flow and compaction properties^{28, 29}.

Khaled³⁰ observed precipitation and consequently retention of the drug in the cavities of porous excipients upon contact of the liquid formulation with the release medium. This retention could be minimized by using either a diluted drug solution or PVP as crystallization inhibitor^{13, 30}. However, PVP may also act as binder during compaction leading to an increase of the liquid load factor¹³.

The release rate of a drug from a dosage form is dependent on its disintegration and the dissolution rate of the drug. Therefore, it is very important for liquisolid systems with enhanced

drug release to ensure that disintegration is not the rate-limiting step and drug dissolution is not hindered by a slow disintegration of the dosage form. It was found that the release rate increases by addition of superdisintegrants such as sodium starch glycolate or croscarmellose sodium to the liquisolid formulation^{11, 16, 23}.

Another formulation parameter that may be optimized is the ratio of carrier to coating material (*R*). An increase in the *R*-value results in an enhanced release rate if microcrystalline cellulose and colloidal silica are used as carrier and coating materials, respectively. Liquisolid compacts with high *R*-values contain high amounts of microcrystalline cellulose, low quantities of colloidal silica, and low liquid/powder ratios. This is associated with enhanced wicking, disintegration and thus, enhanced drug release. In contrast, if high amounts of colloidal silica are used, which means that the *R*-value is low, the liquisolid compact is overloaded with liquid formulation due to a high liquid load factor. In such cases, even though drug diffusion out of the primary particles may be rapid, oversaturation might occur resulting in local precipitation/recrystallization of the drug and thus decreased release rates^{13, 31}. Moreover, as colloidal silica is a hydrophobic material high amounts of it can cause retardation of drug release. Therefore, Spireas *et al.* recommend a minimum *R*-value of 20³¹. In the case of liquisolid sustained release compacts lower *R*-values may be used^{28, 29}.

LIQUISOLID FORMULATIONS FOR SUSTAINED DRUG RELEASE

Various methods have been established to produce sustained release formulations, among which the Liquisolid Technique is a quite new and promising technique resulting in a sustained release pattern with zero order kinetics^{4, 7}. However, only few drugs have been formulated as liquisolid systems with prolonged drug release as shown in Table 2.

Mechanisms of sustained drug release from liquisolid systems

Liquisolid formulations with sustained drug release may contain hydrophobic carriers such as Eudragit® RL or RS instead of hydrophilic carriers, the latter being used for fast release liquisolid formulations^{19, 20}. Hydrophobic carriers may lead to poor wetting properties of the compacts resulting in slow disintegration and thus, prolonged drug release. Furthermore, the liquid vehicle may affect drug release. A comparison of drug release from conventional matrix tablets (direct compression) and liquisolid compacts, both containing Eudragit® RS or RL as matrix forming material, showed that the retardation effect of liquisolid compacts with polysorbate 80 as liquid vehicle is much more pronounced than that of conventional matrix tablets^{19, 20}. This confirms the important role of the liquid vehicle in sustaining drug release from

liquisolid matrix systems. It was shown that the liquid vehicle polysorbate 80 may act as a plasticizer³² and thus, decreases the glass transition temperature of the polymer Eudragit® RS.

Accordingly, with liquisolid compacts the coalescence of the polymer particles occurs at lower temperatures than with conventional matrix tablets. This more pronounced coalescence of polymer particles of liquisolid compacts leads to a matrix with lower porosity and higher tortuosity. Consequently, the drug is surrounded by a fine network of the hydrophobic polymer resulting in a sustained release of the drug^{33,34}.

Moreover, it has been observed that the addition of hydroxypropyl methylcellulose (HPMC) increases the retardation effect of liquisolid compacts^{1,8}. Depending on its molecular weight the polymer either swells in contact with water or forms a hydrated matrix layer through which the drug has to diffuse or erodes resulting in a zero order drug release kinetic³⁵. In the case of HPMC it was also found that a stronger retardation effect was observed with liquisolid compacts as compared to directly compressed tablets (conventional formulation)²⁸.

Optimization of Liquisolid formulations with sustained drug release

Sustained drug release liquisolid formulations may be optimized by selection of low *R*-values, suspensions with a high percentage of undissolved drug and by avoidance of disintegrants. If the *R*-value is low, which means that the applied amount of silica is high, the liquisolid compacts are overloaded with liquid formulation due to a high liquid load factor. In such cases oversaturation might occur resulting in local precipitation of the drug and thus, decreased release rates^{13,31}. Furthermore, the higher the percentages of undissolved drug in the liquid formulation the slower the release rate. This is principally important for poorly soluble drugs, as the dissolution rate of these drugs is low. In addition, as drug release from a tablet is dependent on the disintegration of the tablet and the subsequent dissolution of the drug, the absence of disintegrants, which prevents disintegration, will slow down drug release.

Furthermore, it was pragmatic with liquisolid compacts that the higher the HPMC concentration and the higher the amount of Eudragit® RS / RL, respectively, the more marked the decrease in drug release^{19,20}.

ADVANTAGES OF LIQUISOLID SYSTEMS³⁶

Liquisolid tablets have many advantages. These include:

- Liquisolid systems are low cost formulations than soft gelatin capsules.
- Production of them is similar to that of conventional tablets.
- Drug release can be modified using suitable formulation ingredients.

- Drug can be molecularly dispersed in the formulation.
- Capability of industrial production is also possible.
- Enhanced bioavailability can be obtained as compared to conventional tablets.

Many Researchers have been found them suitable to enhance the dissolution and prolong the drug release of various poorly or water insoluble drugs by applications of Liquisolid Technique as described in Table 4.

Table 4: Applications of Lquisolid technique to enhance and sustain the drug release of various formulations

Study	Vehicle used	Carrier material	Coating material	Result
Enhancement of prednisolone dissolution properties using liquisolid compacts	Propylene glycol	Microcrystalline cellulose (Avicel PH 200)	Colloidal silica (cab-o-sil)	Liquisolid compacts demonstrated significantly higher drug release rates, in different dissolution media and volumes, compared to tablets prepared by the direct compression method. It was also observed that the drug dissolution rate from liquisolid tablets was independent of the volume of dissolution medium, in contrast to the plain tablets which exhibited declining drug release patterns with decreasing dissolution volumes ⁹
In vivo evaluation of hydrochlorothiazide liquisolid tablets in beagle dogs	PEG 200	Avicel PH 101, Avicel PH 102	Colloidal silica (aerosil)	Results of the oral administration revealed statistically significant differences between the liquisolid and the commercial tablets in the area under the plasma concentration–time curve, the peak plasma concentration, and the absolute bioavailability. The absolute bioavailability of the drug from the liquisolid tablets was 15% higher than that from the commercial one. The parametric 90% confidence intervals for the different parameters were higher than the commonly expected intervals for bioequivalency, indicating greater bioavailability of the liquisolid tablets ⁶
The effect of type and concentration of vehicles on the dissolution rate of poorly soluble drug (indomethacin) from liquisolid compacts	Propylene glycol, PEG 400, Tween 80	Microcrystalline cellulose	Amorphous silica	Results showed that liquisolid compacts demonstrated considerably higher drug dissolution rates than those of conventionally made capsule and directly compressed tablets containing indomethacin. Also it has been shown that the fraction of molecularly dispersed drug (F_M) in the liquid medication of liquisolid systems was directly proportional to their indomethacin dissolution rates (D_r) ²²
To improve the dissolution properties of the practically	Propylene glycol	Avicel PH 102	Aerosil 200	Reported liquid load factors, and excipient ratios were used to calculate the required amounts of excipients necessary to prepare the compacts or tablets according to

insoluble antiepileptic drug, Carbamazepine (CBZ) by adopting the liquisolid compaction technique				a mathematical model. Avicel PH 102, and Aerosil 200 were used as the carrier and the coating materials, respectively, and explotab was used as disintegrant to prepare four tablet formulae, out of which formula 1 was successfully compressed into tablets. The dissolution patterns of liquisolid CBZ tablets, carried out according to the USP, were comparable to those of Tegretol. It was observed that Liquisolid CBZ tablets show enhanced drug release as compare to Tegretol ³⁷
Liquisolid technique for dissolution rate enhancement of a high dose water-insoluble drug(Carbamazepine)	PEG 200	Microcrystalline cellulose	Colloidal silica	Liquisolid formulations containing PVP as additive, exhibited significantly higher drug dissolution rates compared to the compacts prepared by the direct compression technique. The results showed that the dissolution rate of liquisolid tablets was not significantly affected by storing the tablets at 25 °C/75% relative humidity for a period of 6 months ¹³
Enhancement of Famotidine dissolution rate through liquisolid tablets formulation: In vitro and in vivo evaluation	Propylene glycol	Avicel PH 102	Aerosil 200	All the tested liquisolid tablet formulations showed higher drug dissolution rates (DR) than the conventional, directly compressed tables. In addition, the selected optimal formula released 78.36% of its content during the first 10 min which is 39% higher than that of the directly compressed tablets. Further, the bioavailability study indicated that the prepared optimal liquisolid formula did not differ significantly from the marketed Famotidine tablets concerning C_{max} , t_{max} , and AUC (0–8) at $P < 0.05$ ¹⁴ .
Liquisolid technique as a new approach to sustain propranolol hydrochloride release from tablet matrices	Polysorbate 80	Eudragit RL or RS	Colloidal silica	The release rate of propranolol HCl from liquisolid compacts was compared to the release of propranolol HCl from conventional tablets. The results also showed that wet granulation had remarkable impact on release rate of propranolol HCl from liquisolid compacts, reducing the release rate of drug from liquisolid compacts. The results showed that aging (liquisolid

				tablets were kept at 25 °C/75% relative humidity for 6 months) had no effect on hardness and dissolution profile of drug. The kinetics studies revealed that most of the liquisolid formulations followed the zero-order release pattern ¹⁹ .
Improvement of Solubility and Dissolution of Indomethacin by Liquisolid and Compaction Granulation Technique	PEG 400	Microcrystalline cellulose (Avicel PH 102), dicalcium phosphate	Hydroxy propyl methyl cellulose	The obtained granules from liquisolid compact system display enhanced solubility and <i>in vitro</i> release profiles due to the increased wetting properties and surface of drug available for dissolution compared to granules obtained from compaction technique and physical mixture. It was also observed that the drug release rate, water solubility and wettability of liquisolid granules containing super disintegrants were on higher side compared to liquisolid granules without superdisintegrants ²³ .
Effects of liquisolid formulations on dissolution of naproxen	Polyoxyl 35 castor oil, Poloxamer 181, polyoxyethylenepolyoxypropylene co-polymer, PEG 400	Avicel PH 102	Colloidal silica	It was found that liquisolid tablets formulated with Cremophor EL at drug concentration of 20%w/w produced high dissolution profile with acceptable tablet properties. The stability studies showed that the dissolution profiles of liquisolid tablets prepared with Cremophor EL were not affected by ageing significantly ³⁸ .
Evaluation of in vitro dissolution profile comparison methods of sustained release Tramadol hydrochloride liquisolid compact formulations with marketed sustained release tablets	Propylene glycol	Avicel PH 102 HPMC K4M	Aerosil 200	Liquisolid sustained release formulations were prepared by using HPMC K4M as adjuvant for sustaining release. Comparison of dissolution profiles was carried out by using model independent, model dependent and statistical approach. The prepared liquisolid compacts are new dosage forms showing more sustained release behaviour as compared to marketed sustained formulations ²¹ .
Dissolution Rate	Propylene glycol	Avicel PH 102	Aerosil 200	Enhanced drug release profiles due to increased wetting

Enhancement of Fenofibrate using Lquisolid Tablet Technique				properties and surface of drug available for dissolution was obtained in case of lquisolid tablets ³⁹ .
Formulation and characterization of atorvastatin calcium lquisolid compacts	PEG 400, propylene glycol	Avicel PH 102	Aerosil 200	The prepared lquisolid system showed acceptable micromeritic properties. The tableting properties of the lquisolid compacts were within the acceptable limits. The release rates of lquisolid compacts were markedly higher compared with directly compressed tablets, due to increasing wetting properties and surface area of the drug. From the obtained pharmacokinetic parameters, such as the AUC, tmax and Cmax, the lquisolid compacts demonstrated better bioavailability compared with their conventional formulation. This study shows that the lquisolid technique is a promising alternative for improvement of the dissolution and oral bioavailability of water insoluble drugs a confirmed by estimating the pharmacokinetic parameters <i>in vivo</i> in rabbits ⁴⁰ .
Bioavailability and biological activity of lquisolid compact formula of repaglinide and its effect on glucose tolerance in rabbits	Polysorbate 80	Avicel PH 101	Calcium silicate	The results of the glucose tolerance test showed that the blood glucose level was decreased significantly after the commercial drug (percent change, 18.1%) while in groups treated with the new formulation the decrease was highly significant ($p < 0.01$) with a percent change of 29.98%. The change in area under the curve for blood glucose was significantly higher in the commercial drug plus glucose load than in the new formulation plus glucose load group ($p < 0.05$) in the periods of 30-45 min and 45-60 min. Furthermore, the new repaglinide formulation significantly decreased blood glucose levels more than the commercial formula ⁵ .

Liquisolid Systems to Improve the Dissolution of Furosemide	Polyoxyethylene polyoxypropylene polyoxyethylene block copolymer, 1,2,3-propanetriol, homopolymer, 9- octadeceno- ate PEG 400	Avicel PH 101	Fumed silica	The results showed that all formulations exhibited higher percentage of drug dissolved in water (pH 6.4–6.6) compared to that at acidic medium (pH 1.2). Liquisolid compacts containing Synperonic® PE/L 81 demonstrated higher release rate at the different pH values. Formulations with PEG 400 displayed lower drug release rate, compared to conventional and liquisolid tablets. Caprol® PGE-860, as a liquid vehicle, failed to produce furosemide liquisolid compacts ²⁶ .
Formulation and evaluation of rofecoxib liquisolid tablets	PEG 600	Avicel 101	Fumed silica	Rofecoxib liquisolid tablets showed higher dissolution profiles than the three studied commercial tablet. The powder excipient ratio was directly proportional to the in vitro release of Rofecoxib from their formulations ⁴¹ .
Liquisolid Technique for Enhancement of Dissolution Properties of Bromhexine Hydrochloride	Propylene glycol, PEG 400	Avicel PH 102	Aerosil 200	The drug release rates of LS compacts were distinctly higher as compared to directly compressed tablets, which show significant benefit of LS in increasing wetting properties and surface area of drug available for dissolution. The LS-1 of LS powder system showed acceptable flowability, Carr's compressibility index and Hausner's ratio ¹² .
Formulation and Evaluation of Orodispersible Liquisolid Compacts of Aceclofenac	Propylene glycol, PEG 400, Tween 80	Microcrystalline cellulose	-----	The combination of superdisintegrants enables us to study the effect of combined disintegrating action on drug release. Among this, compacts with Sodium starch glycolate added intragranularly and Crosspovidone extra granularly showed highest dissolution rate. Orodispersible liquisolid compacts prepared with Tween 80 enhance the dissolution rate of Aceclofenac to a greater extent ⁴² .

CONCLUSION

The present review paper showed that the liquisolid compact technique can be effectively used to prepare sustained release matrices of drugs such as Tramadol hydrochloride, Theophylline, Propranolol HCl, Nifedipine as well as enhanced drug release such as Bromhexine HCl, Carbamazepine, Famotidine, Griseofulvin, Hydrocortisone etc. using desired liquid vehicle. Rapid disintegration rates are observed compared to conventional tablets and therefore, they show improved release rates and hence greater bioavailability. Modification of formulation by use of some excipients cause sustained release of drugs from the liquisolid tablets.

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