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Formulation and optimization: Liquisolid of domperidone for solubility enhancement

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ABSTRACT

In the present study, liquisolid formulations of domperidone were prepared using Tween 80, microcrystalline cellulose, Aerosil 200 as solvent, carrier, and coating material, respectively. 2-factors, 3-level central composite experimental design was employed to examine the effect of independent variables (excipient ratio and load factor) on dependent variables (solubility and drug content). Differential scanning calorimetry (DSC), Fourier transform infrared (FTIR), X-ray powder diffraction (XRD) and scanning electron microscopy (SEM) studies were utilized to characterize the optimized formulation. The results of solubility studies of different batches of liquisolid formulations revealed an improvement in solubility ranging from 17.02-58.10 µg/mL as compared to pure drug domperidone (7.47 µg/mL). The *in-vitro* dissolution profile of optimized batch of liquisolid formulation depicted higher rate of drug release (93.63%) when compared with conventional marketed tablets (Dompy®, 81.98%) following non fickian diffusion ($n<0.5$) as mechanism of drug release from the matrix.

Keywords: liquisolid, domperidone, solubility enhancement, optimization

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INTRODUCTION

Domperidone (Domperidonum), 5-chloro-1-[1-[3-(2,3-dihydro-2-oxo-1H-ben zimidazol-1-yl) propyl]-4-piperidinyl]-1,3-dihydro-2H-benzimidazole-2-one, having molecular formula of $C_{22}H_{24}ClN_5O_2$ belongs to biopharmaceutical classification system (BCS) class II drug. It is a selective D_2 and D_3 dopamine receptor antagonist with a peripheral effect. It reduces the nausea by blocking dopamine receptor. It has poor bioavailability (13-17%) because of extensive presystemic metabolism (83-87%) with short biological half-life. Moreover, domperidone is insoluble in water, resulting in poor absorption from the Gastrointestinal tract (GIT)[1]. The poor bioavailability of domperidone has influenced a number of researchers to develop novel techniques like solid dispersion of domperidone[2-4], nanoparticles[5], nanocrystals[6], nanostructured lipid carrier[7], solid lipid nanoparticles[8], microemulsion nasal spray[9], emulgel alginate based beads[10,11], microcrystals[12] and also liquisolid compacts of domperidone[13-15] indicating a considerable increase in solubility and dissolution rate of domperidone. The above approaches have some limitations such as instability during storage, agglomeration, sticky product and need innovative expensive tools. Out of these, liquisolid strategy is particularly interesting and attractive because of manufacturing process simplicity, low production costs and ease of scale-up to industrial tablet production.

Spireas and Sadu first presented the liquisolid formulation in 1998 which incorporated water-insoluble drugs into rapid-release solid dosage forms[16]. The liquisolid system (LS) refers to "formulations comprised of water-insoluble drugs (liquid drugs, drug suspensions or drug solution) dissolved or dispersed in a suitable water-miscible nonvolatile solvent system later transformed into dry, non-adherent, free-flowing and compressible mixtures by blending the suspension or solution with selected carrier and coating materials". Carrier materials are compression-enhancing, relatively massive, ideally porous particles with adequate absorption properties that aid in liquid absorption examples includes starch lactose, eudragit RL and RS, sorbitol, microcrystalline cellulose, Neusilin® and Fujicalin®. Coating materials are flow enhancing, very tiny (10 nm-5,000 nm in diameter), strongly adsorptive coating particles (e.g. Aerosil 200, Cab-O-Sil M5, Syloid 244FP, etc.) that support to cover the wet carrier particles and exhibiting a dry looking powder by adsorbing extra liquid[17]. Non-volatile solvents are "Organic solvent systems that are inert, have a high boiling point, are usually water-miscible, and are not viscous". Several non-volatile solvents are employed in the formulation of liquisolid systems[18]. Examples includes propylene glycol, polysorbate 20 and 80, polyethylene gly-

col 200 and 400, Cremphor® EL, capryol 90, glycerine and transcutol HP. The non-volatile solvent functions as wetting agent in the liquisolid system thereby helps to enhance the dissolution rate by lowering the interfacial tension between the dissolution medium and the surface of particles. Besides formulating liquisolid, the solubility of poorly soluble drugs is increased because the high porous surface area improves molecular dispersion and wetting properties, ultimately boosting its dissolution and solubility. Pre-compression tests[18] of the Liquisolid powder systems were recommended by Lu et al.[18]. In the literature, liquisolid has effectively exhibited enhancement in the *in-vitro* release of poorly soluble drugs like risperidone[19], iloperidone[20], progesterone[21], simvastatin[22,23], carvacrol[24,25], propranolol hydrochloride[26,27], tadalafil[28-30], naproxen[31,32], felodipine[33,34], furosemide[35-37], silymarin[38], efavirenz[39] hydrochlorothiazide[40] and chlorpromazine[41] etc. The primary goal of the current study is to use an optimization technique for systematic medicinal product development in order to achieve good performance, greater efficiency and high quality. The Design Expert® is regarded as a vital tool that gives maximum knowledge with least experimental work. In the current research work, liquisolid of domperidone were performed by using tween-80 as solvent medium, microcrystalline cellulose (MCC) as a carrier material and aerosil-200 as a coating material employing Design Expert® Software (11.0) and followed by characterization using DSC, FTIR, XRD and SEM examinations. In 1999, Spireas and Bolton suggested a mathematical model for the successful fabrication of a free-flowing and compressible liquisolid formulation, which was further used to calculate the optimum quantities of carrier and coating ingredients. The liquid load factor (Lf) is the weight ratio of the liquid drug (W) and carrier material (Q). The excipient ratio is the weight proportion of the carrier (Q) and coating material (q)[42].

METHODOLOGY

Materials

Domperidone, Microcrystalline cellulose (MCC), glycerin, sodium starch glycolate (SSG) were supplied by Hi-media Laboratories Pvt. Ltd., Mumbai, India. Aerosil-200 was supplied by Central Drug House Pvt. Ltd., New Delhi, India. Cremophor EL (Sigma-Aldrich, USA). PEG-600, propylene glycol (PG), and empty hard gelatin capsule shells (Patco Pharmaceuticals, India) were supplied by Loba Chemie Pvt. Ltd. All other chemicals and reagents used in the study were of analytical grade and used as received without further processing.

Selection of non-volatile solvent

Domperidone solubility was determined in distilled water and five other non-volatile solvents like PEG 400, tween 80, glycerin, cremophor-EL and propylene glycol. Saturated solution was made by mixing excess quantity of domperidone in 10 mL solvent vehicles. Above samples were set on a shaker incubator for 48 hours at room temperature. The samples were then filtered through a 0.45 µm whatman filter paper, diluted with methanol and analyzed by UV spectrophotometer at λ_{max} 284 nm for its drug content (n=3). Solvent showing highest solubility of domperidone was selected[43].

Preparation of liquisolid formulation

Liquisolid formulations were made by dispersing an appropriate quantity of drug (domperidone) and non-volatile solvent (Tween 80) by solvent evaporation method (heated at 60-80°C with continuous stirring) and the solution was sonicated for 15 minutes. The liquid drug solution was blended with the binary mixture of carrier (MCC) and coating (Aerosil-200) material into mortar and pestle uniformly followed by addition of sodium starch glycolate to the above mixture with continuous stirring for about 10 to 15 min. The resultant mixture was finally filled into empty capsule shell size 1 for further studies[44]. The final composition of different batches was shown in the results section.

Experimental design

Liquisolid formulation was optimized using 2-factor, 3-level central composite design (CCD). The excipient ratio (X_1) was varied from 5 to 15 and liquid load factor (X_2) 1.1 to 1.5 designed as independent variables whereas the solubility (Y_1) and drug content (Y_2) were selected as dependent variables (3). Each independent variable was taken at three levels (-1, 0 and +1) as given in Table 1.

Table 1. Optimization of domperidone LS via CCD at different variables and their respective levels

Independent variables	Level		
	-1	0	+1
X_1 (liquid load factor)	1.1	1.3	1.5
X_2 (Excipient ratio)	5	10	15
Dependent variables	Goal		
Y_1 (Solubility)	Maximum		
Y_2 (Drug content)	Maximum		

Solubility studies of liquisolid formulation

Liquisolid formulations (F_1 to F_{13}) containing domperidone equivalent to 10 mg were dispersed in 10 mL distilled water, separately and were kept on continuous shaking for 48 h at room temperature to determine the solubility of drug. The obtained solution was filtered by 0.45 μm whatman filter paper and the domperidone content was observed by taking absorbance at 284nm using UV-VIS spectrophotometer (n=3). The amount of drug was calculated using calibration curve in distilled water[45].

Determination of drug content

Liquisolid formulations (F_1 to F_{13}) containing domperidone equivalent to 10 mg were dissolved in 20 mL of phosphate buffer (pH 6.8), separately. All the samples were sonicated separately for 15 minutes and then filtered through 0.45 μm whatman filter paper[46]. The samples were diluted accurately and analyzed taking absorbance at 284 nm using UV-VIS spectrophotometer (n=3).

FTIR spectroscopy

The drug, MCC, Aerosil-200, and optimized batch of liquisolid formulation were exposed to FT-IR spectroscopy (Perkin Elmer Spectrum, BX II spectrophotometer) and the spectrum was documented in the wavelength region of 4000cm^{-1} to 400 cm^{-1} using KBr pellet method. The method involves dispersing of sample in potassium bromide (KBr) and compressing into disc by applying a pressure of 50 kg/cm^2 in hydraulic press[47].

Differential scanning calorimetry (DSC)

Thermal behavior of domperidone, MCC, Aerosil-200 and optimized batch of domperidone liquisolid formulation was studied using DSC (Q-10, TA instruments waters) by heating the samples within the temperature range of 10–400°C with a scanning rate of 10°C/min in aluminum pans under nitrogen flow at a rate of 50 mL/min[48].

X-ray powder diffraction

The domperidone, MCC, Aerosil-200 and optimized batch of domperidone liquisolid formulation powder samples were examined using an X-ray diffractometer (Miniflex 2, Rigaku, Japan) with Cu-Kα from 10° to 80° diffraction angle (2θ)[49].

Scanning electron microscopy (SEM)

The surface morphology of optimized batch of domperidone liquisolid formulation was examined using SEM (JSM-6100 scanning microscopy, Japan). The sample (optimized batch) after coated with gold was mounted on aluminum stub containing double-adhesive carbon tape. The photographs were observed at acceleration voltage of 10kV[50].

Flow properties of liquisolid formulation

The flow properties of powder were determined by angle of repose (θ) using fixed funnel method. Powders that had previously been sieved were allowed to pass through the funnel until the tip of the conical pile of powder just touched the tip of the funnel. The mean radius (R) and height (H) of powder base were measured, and the tangent of the angle of repose was calculated by $\tan\theta = H/R$. Powder compressibility was determined by calculating the bulk density, tapped density, Carr's index and Hausner ratio as per the method given in United State Pharmacopeia (USP). Carr's index (% CI) [% CI = 100(1-bulk density/tapped density)] and Hausner ratio (HR) [HR = tapped density/bulk density] values reflect the flow properties of a powder; the higher the value of the Hausner ratio, the worse the flow of the powder[25,52].

Weight variation

The weight variation test was performed by the method given in Indian Pharmacopeia (IP)[53].

In-vitro drug release study

In-vitro dissolution studies of pure domperidone, optimized batch of drug loaded LS and marketed domperidone tablets (Dompy® that was crushed and filled in empty capsule shells) equivalent to 20 mg, was carried out in USP type-II apparatus. The dissolution study was conducted in 900 mL phosphate buffer (pH 6.8) at a temperature 37 ± 0.5 °C and the paddle speed was set at 50 rpm. The samples of around 5 mL were taken at fixed time periods of 5, 15, 30, 45, 60, 90 and 120 min. and replaced with an equivalent volume of fresh dissolution medium to maintain the sink condition[23]. The samples were filtered using 0.45 μm Millipore filters and were examined using a uv-vis spectrophotometer at λ_{max} 284nm after appropriate dilution (n=3). To find out the mechanism of drug release, the release data were put in various models like Zero-order, First-order, Higuchi and Korsmeyer-Peppas.

Stability studies

The stability studies were carried out on optimized batch of liquisolid for 3 months in a stability chamber maintaining the temperature of 40 ± 2°C at 75% relative humidity. The samples were stored in hermetically sealed vials containing rubber plugs and aluminum bung. Following a three-month interval, samples were withdrawn and tested for drug content, solubility, and *in-vitro* drug release studies and also for any physical changes[54].

RESULTS and DISCUSSION

Selection of non-volatile solvent

The domperidone exhibited varying proportions of solubility in a variety of non-volatile solvents like Tween-80 (57.13 ± 0.60 µg/mL), PEG 600 (32.52 ± 0.42 µg/mL), Cremophor EL (23.11 ± 0.51 µg/mL), glycerine (3.11 ± 0.73 µg/mL) and Propylene glycol (2.08 ± 0.92 µg/mL). The solubility of domperidone was found to be highest in Tween-80 and hence, Tween-80 was selected as solvent vehicle.

Optimization studies

Domperidone liquisolid formulation was produced and optimization was performed using two-factor, three-level CCD and evaluated for designated responses that are given as below.

Solubility studies of liquisolid formulation

Table 2 shows the solubility (Y_1) and drug content (Y_2) of the domperidone liquisolid produced according to the Design Expert Software, version 11.0. The generated responses were fitted into several polynomial models. The response, solubility (Y_1) was fitted best into the linear response surface model with no data processing. Domperidone liquisolid solubility values range from 17.02 - 59.10 µg/mL in various batches whereas pure domperidone displayed a solubility of 7.478µg/mL. The liner regression fitted for solubility (Y_1) has a good correlation (R^2) of 0.921 is shown in equation (1).

$$Y_1 = 36.21 + 14.87\ X_1 + 5.16\ X_2 \quad (1)$$

Table 2. Formulation parameters and responses for experimental design

St. No.	Conc. of drug (mg)	Tween-80 (mg)	Liquid load factor (X_1)	Excipient ratio (X_2)	MCC (mg)	Aerosil-200 (mg)	SSG	Total (mg)	Solubility in Distilled water (Y_1) (µg/mL)	Drug content (Y_2) (%)	Weight Variation (mg)
F_1	25	100	1.1	15	90	6	19	240	28.01 ± 0.0043	93.82 ± 0.63	205.21 ± 0.45
F_2	25	100	1.1	5	90	18	7	240	17.02 ± 0.0054	90.65 ± 0.23	227.41 ± 0.52
F_3	25	100	1.1	10	90	9	16	240	22.01 ± 0.0036	91.06 ± 0.49	215.38 ± 0.38
F_4	25	100	1.5	10	66	6.6	43	240	51.06 ± 0.0055	98.98 ± 0.96	267.26 ± 0.59
F_5	25	100	1.3	10	75	7.5	33	240	34.02 ± 0.0056	95.18 ± 0.36	257.61 ± 0.65
F_6	25	100	1.3	10	75	7.5	33	240	34.11 ± 0.0045	95.81 ± 0.63	255.92 ± 0.70
F_7	25	100	1.3	10	75	7.5	33	240	35.08 ± 0.0049	96.21 ± 0.23	251.75 ± 0.62
F_8	25	100	1.3	15	75	5	35	240	39.03 ± 0.0051	97.05 ± 0.36	240.85 ± 0.82
F_9	25	100	1.3	5	75	15	25	240	32.04 ± 0.0054	93.26 ± 0.27	311.72 ± 0.72
F_{10}	25	100	1.3	10	90	18	7	240	37.08 ± 0.0045	96.21 ± 0.99	230.11 ± 0.48
F_{11}	25	100	1.3	10	75	7.5	33	240	36.03 ± 0.0044	96.62 ± 0.61	260.54 ± 0.57
F_{12}	25	100	1.5	15	66	4.4	45	240	59.10 ± 0.0058	98.99 ± 0.21	243.08 ± 0.48
F_{13}	25	100	1.5	5	66	13	36	240	46.11 ± 0.0037	97.58 ± 0.31	320.31 ± 0.77
Drug									7.478 ± 0.0032		

R: Excipient ratio (carrier: coating material), Q: Carrier material (microcrystalline cellulose), q: Coating material (Aerosil 200). All values are expressed as mean ± S.D., n=3

The results of the ANOVA test on the solubility and drug content response surface model, revealing that the model was deemed significant with lack of fit as non-significant. Adequate precision of solubility was found to be 48.66 and indicated a requisite signal. It is preferable to have an adequate precision measurement signal to noise ratio (higher than 4). The combined effect of liquid load factor (L_f) and excipients ratio (R) on solubility and drug content was shown in Figure 1. The plot indicates that independent and dependent variables have a curvilinear correspondence. The plot also shows that with increasing value of liquid load factor and excipient ratio the solubility also increases.

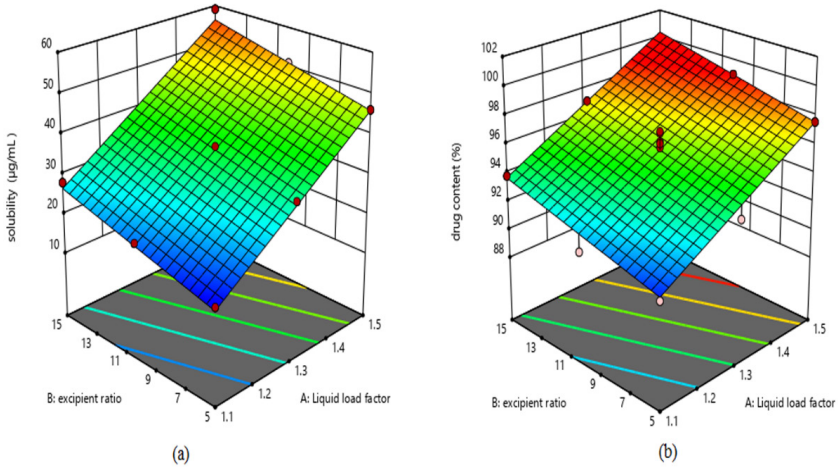


Figure 1. Response surface plots displaying effect of Load factor and excipients ratio on solubility (a) and drug content (b)

Desirability function for the selection of optimized batch

The different set of solutions was provided by the optimization tool in the software. The software combines all the response factors so that the final optimized batch has the optimal balance of all the required attributes. A desirability value of 0 indicates an inappropriate value for the responses while a value of 1 indicates the most desirable. The software assessed desirability ability to each response and calculated a composite desirability value for each batch through considering the geometric mean of all the responses desirability. The desirability index value was estimated to be 1 as shown in Figure 2.

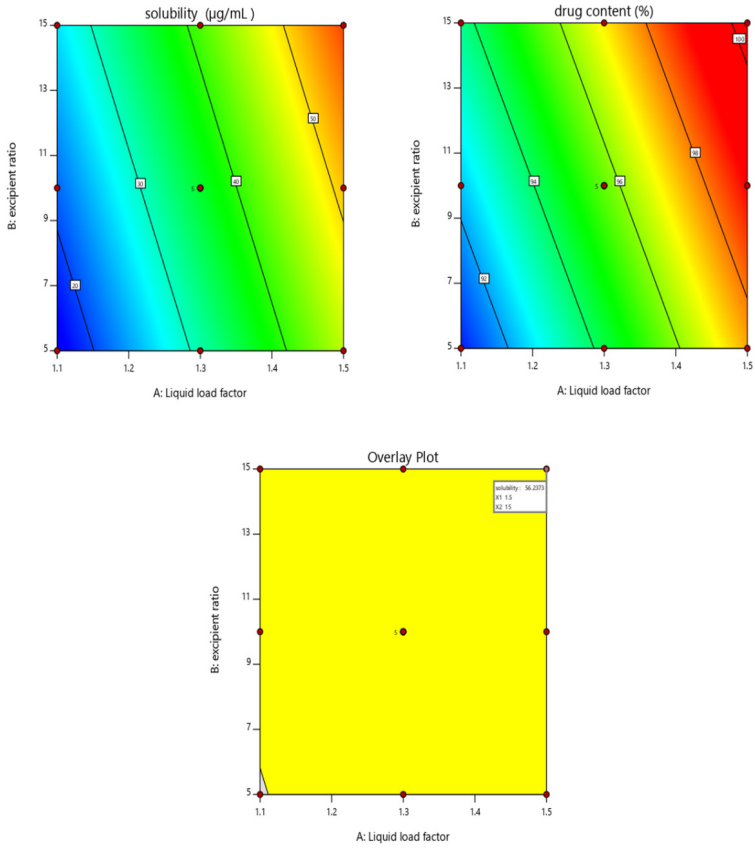


Figure 2. Desirability index of optimized formulation (F_{12})

Drug content

The response, drug content (Y_2) was fitted best into the linear response surface model with no data processing as shown in equation (2). Drug content values range from 90.65 to 98.99% in various batches. The linear regression fitted for drug content (Y_2) has a good correlation (R^2) of 0.9069.

$$Y_2 = 95.63 + 3.34\,X_1 + 1.39\,X_2$$

Adequate precision of drug content was found to be 21.94 (higher than 4) indicated a requisite signal.

The optimization Eqs. (1) and (2), relating the responses and independent factors, were acquired based on a quadratic and linear model. To the responses i.e. solubility and drug content the desirability function was applied with con-

straints to obtain the higher magnitude of both the factors. In this manner, the formulation having liquid load factor (1.5) and excipient ratio (15) established the maximum desirability, was organized, and evaluated. The optimization of independent variables was done with constraints of maximum solubility and maximum drug content. The parameters suggested by the design were liquid load factor (1.5) & ratio of excipients (15) that provided liquisolid with solubility of 56.00 μg/mL (predicted value 56.24 μg/mL) and drug content 98.77% (predicted value 100.0%). The closer concordance between observed and predicted values discerned high predictive ability of the model. Based on solubility and drug content data, batch F_{12} (optimized batch suggested by design expert) containing Lf (1.5) and R (15) was selected for further examination[23,55].

Characterization

Fourier Transform Infrared (FTIR) spectroscopy

Fourier transform infrared spectroscopy (FT-IR characterization) was performed to examine the possible interactions between drug and excipients, the FTIR absorption spectra for the drug, MCC, Aerosil-200 and LS formulation (F_{12}) represented in Fig. 3a. The FTIR spectra of domperidone showed characteristic absorption band at 3354 cm^{-1} to 3706 cm^{-1} (-N-H stretching) and the peak appearing at 1728 cm^{-1} (-C=O stretching), 3028 cm^{-1} to 3139 cm^{-1} (=C-H stretching), 2865 cm^{-1} to 3028 cm^{-1} (Sp_3–C-H stretching) and 1493 cm^{-1} to 1605 cm^{-1} (-C=C stretching). The FTIR spectra of MCC showed the characteristic absorption band at 1406 cm^{-1} (-N-H stretching), 1648 cm^{-1} (-C=O stretching), 1236 cm^{-1} (-C=C stretching), 1430 cm^{-1} to 1374 cm^{-1} (–CH_2 stretching), 2902 cm^{-1} (-C-H stretching) and 3352 cm^{-1} to 3802 cm^{-1} (-OH stretching). The FTIR spectra of Aerosil-200 showed characteristic absorption band at 1648 cm^{-1} (-OH stretching), 1670 cm^{-1} (-C=O stretching), 1108 cm^{-1} (Si-O-Si stretching) and 2896 cm^{-1} to 2958 cm^{-1} (-C-H stretching). The FTIR spectra of LS formulation showed peak at 1112 cm^{-1} to 1374 cm^{-1} (-OH stretching), 1488 cm^{-1} (-C=C stretching), 1694 cm^{-1} (-C=O stretching), 3014 cm^{-1} (-N-H stretching) and 3885 cm^{-1} (-C-H stretching). The intensity of the absorption bands of domperidone was found to be diminished in the LS formulation, which could be explained to the hydrogen bonding interaction between the carboxylic group of domperidone[56].

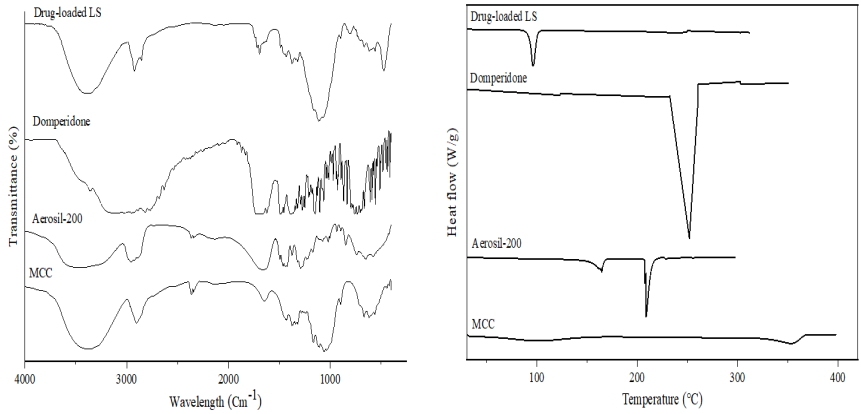


Figure 3. (a) FTIR and (b) DSC Spectra of MCC, Aerosil-200, Domperidone and LS formulation (F_{12})

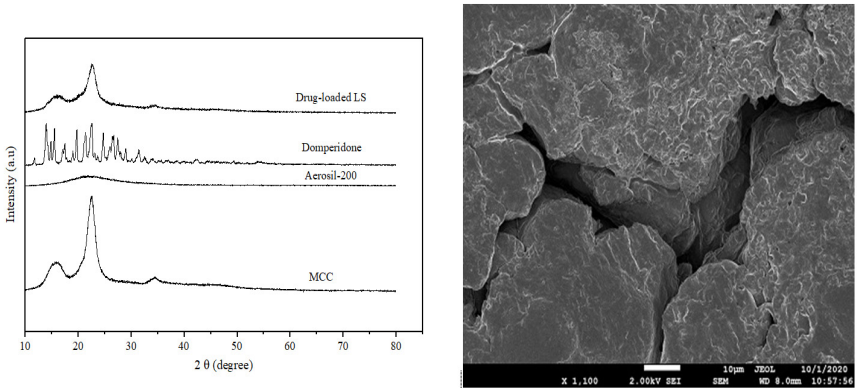
Differential scanning calorimetry (DSC)

The DSC thermograms for the drug, MCC, Aerosil-200 and LS formulation (F_{12}) are shown in Fig. 3b. Domperidone exhibited a sharp peak at 251.8°C that corresponds to its melting point with a fusion enthalpy (ΔH) of -14.08W/g. MCC and Aerosil-200 exhibited a sharp peak at 103.029°C and 208.77°C corresponds to the melting point of MCC and Aerosil-200. However, LS formulation (F_{12}) exhibited a strong peak at 96.15°C. The thermogram of the liquisolid system showed the disappearance of the domperidone endothermic peak, which corresponds with the establishment of drug solution in the LS formulation (i.e. the drug was molecularly disseminated inside the liquisolid matrix). Such disappearance of the drug peaks during formation of the liquisolid system was in accordance with Brittain and Mccauley[13]. The thermogram of LS also indicated that the constituents' crystalline habit was disrupted, which might be explained to physical interactions between the constitutional components during processing.

Powder x-ray diffraction analysis (P-XRD)

Fig. 4a shows the x-ray diffraction spectra of drug, MCC, Aerosil-200 and LS formulation (F_{12}). The x-ray diffraction spectra of domperidone exhibited different characteristic peaks at 11.77°, 13.96°, 15.54°, 17.5°, 19.76°, 21.42°, 24.8°, 26.46°, 27.48°, 29° and 31.46° that indicate the crystalline nature of domperidone. The diffraction spectra of MCC exhibited characteristic peaks at 14.6°, 22.02°, 34.62° indicates the crystalline nature of MCC. On other hand aero-

sil-200 has no characteristic peak because it is amorphous in nature. The diffraction spectra of LS formulation (F_{12}) exhibited characteristic peak at 13.24°, 16°, 18.66° and 25.32°. The reduction in the intensity and the disappearance of many peaks of domperidone in the LS formulation suggest that the molecule was dissolved molecularly in the LS formulation. The drug may become solubilized in a liquid vehicle, which could explain this behavior. This also implies that domperidone was in an amorphous form in the LS formulation[57].



(a) **(b)**

Figure 4. (a) XRD and (b) SEM images of MCC, Aerosil-200, Domperidone and LS formulation (F_{12}) flow properties and weight variation of Liquisolid formulation

Scanning Electron Microscope (SEM)

The SEM image of optimized domperidone liquisolid (F_{12}) was shown in Fig. 4b. Liquisolid had an uneven form and a dimension of around 10 μm. The disappearance of domperidone crystals in the liquisolid system was reported to be associated with drug solvation in non-volatile solvent. The surface of liquisolid seems to be uneven and porous and this porosity, makes it more soluble[58].

The angle of repose, bulk densities, Carr's index, tapped densities and Hausner's ratio were determined to evaluate the flow parameters of the prepared LS powder. Powders with an angle of repose value of less than 45° are deemed to have acceptable flow characteristics, according to the USP. The liquisolid optimized batch has bulk density (0.34), tapped density (0.38), Carr's index (10.5), Hausner's ratio (1.11) and angle of repose (34.06°) shows the good flow. The average weight of liquisolid capsules ranged between 205.21 mg and 320.31 mg was found to be in acceptable limits.

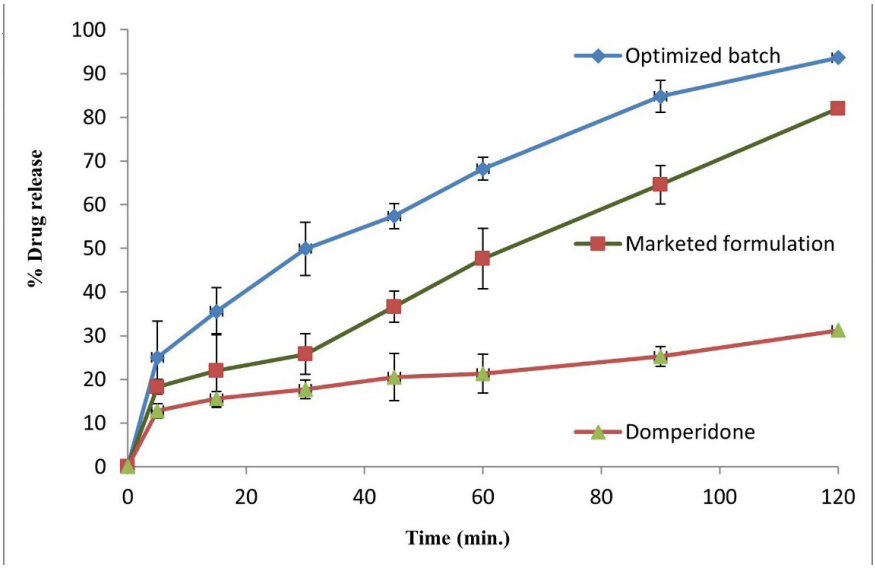


Figure 5. Graph showing comparison between drug release kinetics of pure domperidone, liquisolid optimized batch (F_{12}) and marketed formulation (Dompy ®)

Stability studies

After the stability period of 3 months, there was no discernible change in the physiochemical characteristics of optimized LS formulation (F_{12}). The solubility and drug content differed slightly, but all were confirmed to be within acceptable limits[61,62]. There was no discernible influence on the dissolution profile also as shown in Table 3.

Table 3. Stability studies of optimized LS formulation

Parameter	Before	After 3 months
Solubility (µg/mL)	58.10 ± 0.0058	56.04 ± 0.0047
Drug content (%)	98.77 ± 0.21	96.61 ± 0.68
% drug release at 120 min.	93.63 ± 3.68	90.93 ± 2.81

Domperidone has a high permeability across biological membranes, but its absorption is limited following oral administration due to its low dissolution rate and poorly water solubility. The liquisolid-capsule strategy could be a good way to speed up the dissolution of water-insoluble drugs like domperidone. In the liquisolid formulation, the liquid vehicle aids in increasing the dissolution characteristics of an aqueous insoluble drug. To improve the domperidone liquisolid formulation, a 3^2 Central Composite Design was used. Aerosil-200,

MCC, Tween-80 and sodium starch glycolate are selected as coating material, carrier material, solvent and disintegrant respectively, in the liquisoild formulation. The results of solubility studies of different batches of liquisolid formulations revealed an improvement in solubility ranging from 17.02-58.10 μg/mL as compared to pure drug domperidone (7.47 μg/mL). There was no interaction between the drug and the additives, as per FTIR and DSC investigations and XRD revealed the absence of the drug characteristic peaks in the optimized liquisolid formulation, implying that the pure medication had been partially transformed into an amorphous or solubilized form. The disapperance of crystallinity of drug in liquisolid formulation, which is then, adsorbed onto the coating and carrier materials. Pure drugs that have been amorphous or soluble may have a fast rate of dissolution. Further the SEM study conform the drug is in amorphous form and solubilized into the liquisolid formulation. The data on drug release at 120 min. was found to be 93.63% further it is mathematically analyzed and fitted into zero-order release kinetics. A stability analysis of optimized batch for solubility, drug content and drug release were done which revealed that there was no significant change seen after three months of storage. This novel approach to the formulation may be helpful in improving solubility of poorly soluble drug domperidone.

STATEMENT OF ETHICS

This study does not require any ethical permission.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflict of interests that could have appeared to influence the work reported in this paper.

AUTHOR CONTRIBUTIONS

Meenakshi Bhatia- Conceptualization, Supervision; Geeta Rani- Writing – Original Draft Preparation; Sunita Devi - Review & Editing, Software; Kavita Bahmani- Review & Editing, Data Curation.

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