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SOLUBILITY ENHANCEMENT AND FTIR COMPATIBILITY CHARACTERIZATION OF A SOLUPLUS-BASED SOLID DISPERSION OF DEXLANSOPRAZOLE

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ABSTRACT

Objective: To prepare dexlansoprazole–Soluplus® solid dispersions by solvent evaporation, compare their saturation solubility at pH 1.2 and pH 6.8 and evaluate drug–polymer compatibility using Fourier-transform infrared (FTIR) spectroscopy.

Methods: Dexlansoprazole–Soluplus® dispersions were prepared at drug-to-polymer ratios of 1:1,1:2 and 1:3 using 95% ethanol. The solvent was removed by rotary evaporation, followed by vacuum drying, pulverization and sieving. Physical appearance, practical yield and drug content were evaluated. Saturation solubility was determined by the shake-flask method at pH 1.2 and pH 6.8 at 37 ± 0.5°C for 48 hours, with spectrophotometric quantification at 285 nm. FTIR spectra of dexlansoprazole, Soluplus®, the physical mixture and the selected dispersion were recorded from 4000–400 cm^{-1}.

Results: All dispersions were homogeneous. Practical yield increased from 94.2 ± 0.8% for ASD-1 to 97.8 ± 0.4% for ASD-3, while drug content ranged from 98.4 ± 0.6% to 100.9 ± 0.5%. At pH 6.8, saturation solubility increased from 82.4 ± 2.1 µg/mL for pure dexlansoprazole to 215.7 ± 4.8, 328.5 ± 5.3, and 465.2 ± 6.8 µg/mL for ASD-1, ASD-2, and ASD-3 respectively. ASD-3 therefore produced a 5.65-fold increase over the pure drug. At pH 1.2, ASD-3 reached 12.7 ± 0.7 µg/mL versus 1.5 ± 0.2 µg/mL for pure drug. FTIR retained the principal characteristic bands without a new major absorption band.

Conclusion: Soluplus® progressively enhanced dexlansoprazole saturation solubility with the 1:3 formulation showing the greatest improvement under the tested conditions. FTIR findings supported drug–polymer compatibility. These findings justify further development of the optimized dispersion using complementary solid-state characterization and stability studies.

KEYWORDS: dexlansoprazole; Soluplus; solid dispersion; solubility enhancement; FTIR; poorly water-soluble drug

INTRODUCTION

Dexlansoprazole is a proton pump inhibitor indicated for treatment of gastro-oesophageal reflux disease and other acid-related disorders. Contemporary evidence continues to support its clinical role. Formulation development remains important because the drug has physico-chemical properties that can constrain dissolution and oral delivery. Recent reviews on proton pump inhibitor dosage forms highlight the need for a compromise between drug protection, dissolution behaviour, manufacturability and patient friendly administration. [1-4]

Poor aqueous solubility is a major challenge in oral formulation development, where dissolution may become the rate limiting step for absorption. The current literature still indicates amorphous solid dispersions (ASDs), polymeric solubilizers, Nanomicelles and other enabling technologies as important approaches to improve apparent solubility and dissolution of poorly water soluble compounds. [5-10]

Soluplus® is an amphiphilic graft copolymer of polyethylene glycol, polyvinyl caprolactam, and polyvinyl acetate segments. Its amphiphilic structure supports drug solubilization and self-assembly in aqueous media. Recent experimental and review studies describe its application in solid dispersions, polymeric nanomicelles, electrosprayed systems and other drug-delivery platforms. [5,6,10,23-25]

The formulation performance of an ASD depends on drug loading, polymer selection, preparation method, drug–polymer miscibility and the ability of the polymer to stabilize super saturation. Recent studies have emphasized that polymer-mediated inhibition of precipitation and maintenance of supersaturation are important determinants of dissolution performance. [11-17, 28-31]

Solvent evaporation is particularly attractive for compounds for which minimizing prolonged thermal exposure is desirable. The drug and polymer are dissolved in a common solvent and the solvent is subsequently removed under reduced pressure. Recent studies have continued to use solvent-based processing and alternative low-temperature approaches to generate ASDs and evaluate their solubility, dissolution and solid-state properties. [10,23,25,26,33,34]

FTIR spectroscopy is routinely used as a complementary tool for evaluating drug–excipient compatibility. Retention of characteristic drug absorption bands and absence of a new major band may support compatibility, although FTIR alone cannot establish complete amorphization. Complementary methods such as differential scanning calorimetry and powder X-ray diffraction are generally required when definitive physical-state characterization is needed. [11,23,29,30,33]

Recent dexlansoprazole research has also demonstrated the continued relevance of formulation optimization. A 2021 formulation study evaluated dexlansoprazole tablets, while a recent Quality-by-Design study developed and optimized dexlansoprazole orodispersible tablets.[3,4] These studies provide a current formulation context, but drug-specific evidence on Soluplus®-based dexlansoprazole solid dispersions remains limited. The Present study aimed to prepare dexlansoprazole–Soluplus® solid dispersions at 1:1, 1:2 and 1:3 drug-to-polymer ratios using solvent evaporation; determine saturation solubility at pH 1.2 and pH 6.8; evaluate practical yield and drug content; and assess drug–polymer compatibility using FTIR spectroscopy.

METHODOLOGY

Materials and reagents

Dexlansoprazole (purity ≥99.0%) was used as the active pharmaceutical ingredient. Soluplus® (BASF SE Germany) was used as the solid-dispersion carrier and 95% ethanol as the processing solvent. Hydrochloric acid medium at pH 1.2 and phosphate buffer at pH 6.8 were used for saturation-solubility testing. All materials and reagents were of analytical grade.

Preparation of dexlansoprazole–Soluplus® solid dispersions

Three drug-to-Soluplus® ratios (1:1, 1:2 and 1:3) were prepared by solvent evaporation. The required quantities of dexlansoprazole and Soluplus® were dissolved in 95% ethanol with continuous stirring at 40 ± 2°C until a uniform solution was obtained. The solvent was removed under reduced pressure using a rotary evaporator maintained at 40–45°C. The recovered solid was vacuum-dried at 40°C for 24 hours, pulverized, passed through ASTM No. 60 sieve and stored in airtight containers until characterization. The formulations were designated ASD-1, ASD-2 and ASD-3 respectively.

Physical characteristics, practical yield and drug content

The prepared dispersions were examined for physical appearance and handling characteristics. Practical yield was calculated from the recovered mass in relation to the theoretical mass. The drug content was determined according to the procedure given in the study and expressed as percentage drug content. Each formulation was assessed using the experimental dataset provided with the manuscript.

Saturation solubility study

Equilibrium saturation solubility was determined using the shake-flask method. Excess pure dexlansoprazole, physical mixture and each solid-dispersion sample were added to the test medium and maintained under continuous agitation until equilibrium was achieved. Testing was performed in hydrochloric acid at pH 1.2 and phosphate buffer at pH 6.8 at 37 ± 0.5°C for 48 hours. Samples were filtered, appropriately diluted and analyzed spectrophotometrically at 285 nm. Measurements were performed in triplicate and expressed as mean ± standard deviation.

Fourier-transform infrared spectroscopy

FTIR spectroscopy was used to investigate possible chemical interactions between dexlansoprazole and Soluplus®. Spectra of pure dexlansoprazole, Soluplus®, the physical mixture and the selected ASD-3 formulation were recorded over 4000–400 cm^{-1}. Characteristic absorption bands were compared between the individual components and formulation. Preservation of the principal drug bands without appearance of a new major band was interpreted as evidence against formation of a new chemical entity.

Data analysis

Results were expressed as mean ± standard deviation. The solubility-enhancement factor at pH 6.8 was calculated as the saturation solubility of each solid dispersion divided by the saturation solubility of pure dexlansoprazole at the same pH. Measured solubility yield, drug-content and FTIR findings were used for descriptive interpretation of the study. No inferential statistical model was used.

RESULTS

Preparation and physical characteristics

All three drug-to-polymer ratios produced homogeneous dispersions without visible phase separation. ASD-1, ASD-2 and ASD-3 showed practical yields of 94.2 ± 0.8%, 96.4 ± 0.6% and 97.8 ± 0.4% respectively. Drug content ranged from 98.4 ± 0.6% to 100.9 ± 0.5%. ASD-3 was described in the supplied dataset as a fine powder with favorable handling characteristics.

Table 1. Composition and preparation design of dexlansoprazole–Soluplus® solid dispersions.

Formulation	Drug:Soluplus® ratio	Physical appearance	Practical yield (%) / Drug content (%)
ASD-1	1:1	Homogeneous, free-flowing powder	94.2 ± 0.8 / 98.4 ± 0.6
ASD-2	1:2	Homogeneous, free-flowing powder	96.4 ± 0.6 / 99.6 ± 0.4
ASD-3	1:3	Homogeneous, fine powder	97.8 ± 0.4 / 100.9 ± 0.5

Saturation solubility

Soluplus® produced a progressive increase in saturation solubility as the polymer proportion increased. At pH 6.8, pure dexlansoprazole showed a saturation solubility of 82.4 ± 2.1 µg/mL. This increased to 215.7 ± 4.8 µg/mL for ASD-1, 328.5 ± 5.3 µg/mL for ASD-2 and 465.2 ± 6.8 µg/mL for ASD-3. Thus, ASD-3 produced a 5.65-fold enhancement compared with pure dexlansoprazole. At pH 1.2, ASD-3 showed 12.7 ± 0.7 µg/mL compared with 1.5 ± 0.2 µg/mL for the pure drug.

Table 2. Saturation solubility of dexlansoprazole and Soluplus® solid dispersions.

Sample	Drug:Polymer ratio	pH 1.2 (µg/mL)	pH 6.8 (µg/mL)	Fold improvement at pH 6.8
Pure dexlansoprazole	—	1.5 ± 0.2	82.4 ± 2.1	1.00
Physical mixture	1:1	2.8 ± 0.3	138.6 ± 3.2	1.68
ASD-1	1:1	4.9 ± 0.4	215.7 ± 4.8	2.62
ASD-2	1:2	8.2 ± 0.5	328.5 ± 5.3	3.99
ASD-3	1:3	12.7 ± 0.7	465.2 ± 6.8	5.65

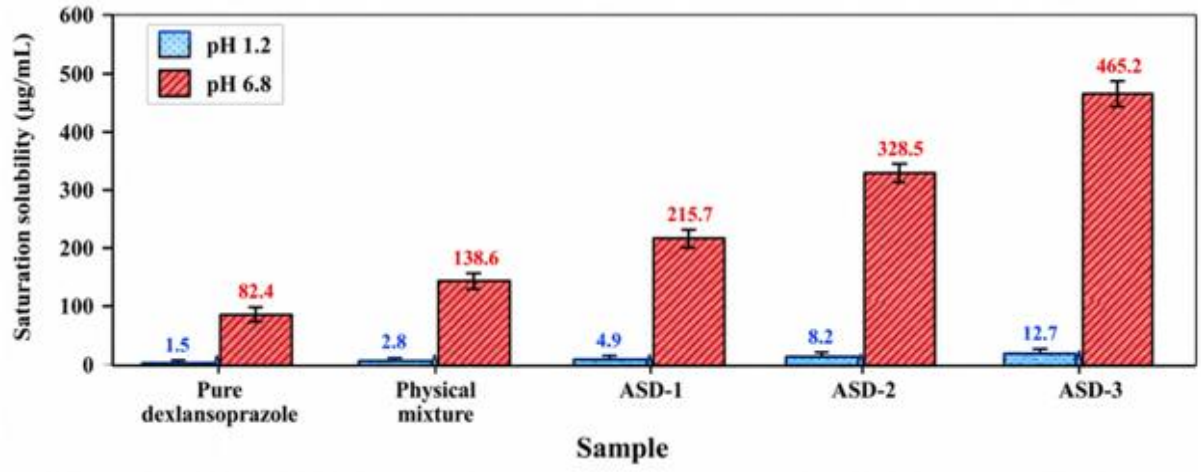


Figure 1. Saturation solubility of pure dexlansoprazole[,] physical mixture[,] and Soluplus® solid dispersions at pH 1.2 and pH 6.8. Values are mean ± SD (n=3).

FTIR characterization

The FTIR spectra of pure dexlansoprazole, the physical mixture and ASD-3 (1:3) showed the same principal characteristic absorption bands at approximately 3448.01, 1637.36, 1466.01, 1358.09 and 1244.01 cm^{-1}. The bands were assigned in the supplied spectrum to N–H stretching, C=N, S=O, C–H and C–N vibrations respectively. The principal bands remained identifiable in ASD-3 and the physical mixture with no additional major absorption band. Minor changes in position or relative intensity were interpreted as possible drug–polymer interactions rather than evidence of a new chemical entity.

Table 3. Principal FTIR bands of dexlansoprazole in the investigated samples

Functional group / vibration	Approx. wavenumber (cm^{-1})	Pure dexlansoprazole	Physical mixture	ASD-3 (1:3)	Interpretation
N–H stretching	**3448.01**	Present	Present	Present	Characteristic band

Functional group / vibration	Approx. wavenumber (cm^{-1})	Pure dexlansoprazole	Physical mixture	ASD-3 (1:3)	Interpretation
					retained
C=N vibration	**1637.36**	Present	Present	Present	Characteristic band retained
S=O vibration	**1466.01**	Present	Present	Present	Characteristic band retained
C–H vibration	**1358.09**	Present	Present	Present	Characteristic band retained
C–N vibration	**1244.01**	Present	Present	Present	Characteristic band retained

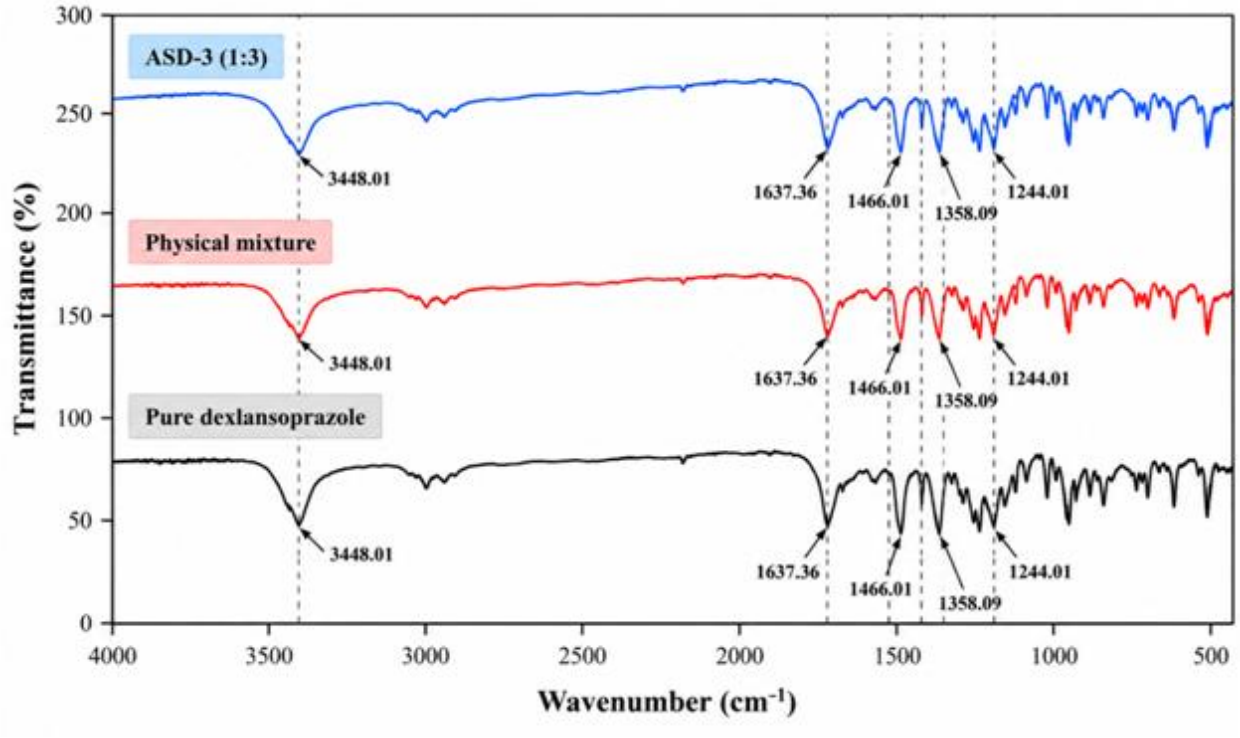


Figure 2. FTIR spectra of pure dexlansoprazole, physical mixture and ASD-3 (1:3). Characteristic bands are labelled at approximately 3448.01, 1637.36, 1466.01, 1358.09 and 1244.01 cm^{-1}.

DISCUSSION

The present study demonstrates a clear, polymer-concentration-dependent increase in dexlansoprazole saturation solubility following incorporation into Soluplus® solid dispersions. The result is consistent with the contemporary literature describing Soluplus® as an amphiphilic carrier capable of improving the apparent solubility and dissolution behavior of poorly water-soluble drugs.[5,6,10,21,22]

At pH 6.8, the 1:3 formulation increased saturation solubility from 82.4 ± 2.1 to 465.2 ± 6.8 µg/mL, equivalent to a 5.65-fold enhancement. The progressive improvement across ASD-1, ASD-2 and ASD-3 suggests that the increased polymer proportion promoted more effective drug dispersion and polymer-mediated solubilization under the experimental conditions. Similar concentration-dependent effects have been reported for Soluplus® systems involving coenzyme Q10, glycyrrhetinic acid, simvastatin and other poorly soluble compounds.[20-23]

Several mechanisms may account for the observed improvement. Soluplus® contains hydrophilic and relatively hydrophobic segments that can interact with both aqueous media and hydrophobic drug molecules. Recent structural studies have demonstrated self-assembly of Soluplus® in aqueous systems, supporting the concept that polymer-mediated molecular and colloidal interactions can contribute to drug solubilization.[24,39] The polymer may also improve wetting[,] reduce the effective lattice-energy barrier associated with the crystalline drug and inhibit precipitation from a supersaturated solution. Contemporary ASD literature emphasizes that these solution-state processes can be as important as solid-state amorphization in determining dissolution performance.[11-17,28-31]

The present results are also consistent with recent experimental studies in which Soluplus® was used with poorly soluble drugs. Simvastatin–Soluplus® solid dispersions showed improved dissolution following supercritical-fluid processing, while Soluplus®-based systems for glycyrrhetinic acid and coenzyme Q10

produced marked solubility and/or bioavailability improvements.[20,21,23] More recent work with bedaquiline fumarate, curcumin, lumefantrine and high-drug-loading celecoxib further demonstrates the versatility of Soluplus® across different processing platforms.[33-36,18]

The solvent-evaporation process used in the present study is particularly appropriate for exploratory formulation development because it provides intimate drug–polymer mixing while limiting prolonged exposure to high processing temperatures. Recent reviews of ASD manufacturing still recognise solvent-based approaches as important options along with spray drying, hot-melt extrusion, electro spraying and other emerging processes.[29,31,33,37]

The practical yields of 94.2–97.8% and drug contents of 98.4–100.9% indicate a relatively low process loss and satisfactory incorporation of dexlansoprazole in the prepared dispersions. An improved recovery of the polymer-rich solid during removal of the solvent could be reflected in the slightly higher yield obtained with increasing polymer proportion. However, the present study used only descriptive analysis, so the numerical differences observed should not be interpreted as statistically significant differences without performing formal inferential tests.

FTIR results provide additional evidence of drug–polymer compatibility. Characteristic dexlansoprazole bands are still detected after preparation of the dispersion and no new major band is observed. This agrees with recent Soluplus® studies where FTIR has been used to show retention of drug functional groups or to explore hydrogen-bonding interactions with no evidence of chemical degradation .[23,33,35,36]

Importantly, FTIR should not be regarded as conclusive evidence of amorphization. FTIR primarily provides information on the functional-group environments and potential molecular interactions. Other solid state techniques such as DSC and powder X-ray diffraction are necessary to give confirmation of the physical state. Recently, the multimodal characterisation in the determination of amorphization, physical stability and resistance to recrystallisation is particularly emphasised in the ASD literature.[11,29,30,33]

The present findings allow therefore a focused conclusion: Soluplus® raises the measured saturation solubility of dexlansoprazole and is compatible with the drug under the preparation conditions applied. The study does not demonstrate long-term physical stability, definitive amorphization, dissolution kinetics or in vivo bioavailability. This distinction is important for rigorous interpretation and provides a clear basis for subsequent development of formulations.

The present work is also drug-specific, which is relevant. Recent research has demonstrated Quality-by-Design optimization of dexlansoprazole orodispersible tablets, emphasizing the continuing interest in patient-friendly and rapidly disintegrating dosage forms.[4] The present Soluplus® dispersion can therefore be considered a potential upstream solubility-enhancement platform for subsequent dosage-form development, although tablet performance was not investigated in the present study.

CONCLUSION

Soluplus®-based solid dispersions enhanced the saturation solubility of dexlansoprazole at both pH 1.2 and pH 6.8 under the experimental conditions. The 1:3 drug-to-polymer formulation, ASD-3 produced the highest solubility, reaching 465.2 ± 6.8 µg/mL at pH 6.8 compared with 82.4 ± 2.1 µg/mL for pure dexlansoprazole, corresponding to a 5.65-fold enhancement. FTIR demonstrated retention of characteristic drug bands and no new major absorption band, supporting drug–polymer compatibility. Further work should include DSC, PXRD, SEM, dissolution profiling, stability testing and dosage-form evaluation before broader formulation or biopharmaceutical conclusions are made.

STUDY LIMITATIONS

The study was limited to laboratory-based saturation-solubility and FTIR compatibility assessment. Thermal, crystalline and morphological characterization were not performed. The study also did not evaluate dissolution kinetics, long-term physical stability, pharmacokinetics, bioavailability or clinical performance. In addition, the data were analyzed descriptively rather than by an inferential statistical model.

ETHICAL APPROVAL

Ethical approval was not applicable to the present in-vitro formulation and analytical study.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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