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ADVANCING DOMPERIDONE THE RAPEUTICS: SOLID DISPERSION APPROACHES FOR RAPIDLY DISSOLVING TABLET DELIVERY

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ABSTRACT

Domperidone, a widely used antiemetic and prokinetic agent, exhibits limited aqueous solubility, which substantially restricts its oral bioavailability and therapeutic performance. Improving dissolution behavior is critical to ensure rapid onset of action and enhanced systemic absorption. This research explores solid dispersion strategies to augment domperidone solubility and incorporates these improved dispersions into fast dissolving tablet (FDT) formulations aimed at optimized patient compliance and therapeutic efficacy. Physicochemical characterization of solid dispersions, formulation development, optimization using quality-by-design (QbD) principles, and comparative in vitro/in vivo performance studies are carried out. Outcomes demonstrate that solid dispersion significantly enhances drug release kinetics and oral bioavailability compared to conventional tablets, confirming the potential of this approach for next-generation domperidone delivery.

Keywords: - Domperidone · Solid dispersion · Fast dissolving tablets (FDT) · Solubility enhancement · Bioavailability · Formulation optimization

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I. INTRODUCTION

Domperidone is a widely utilized pharmacological agent known for its antiemetic and prokinetic properties, primarily indicated for the management of nausea, vomiting, and gastrointestinal motility disorders. Despite its therapeutic significance, domperidone suffers from low oral bioavailability, typically around 15%, largely due to its poor aqueous solubility and extensive first-pass metabolism**.** These pharmacokinetic limitations pose significant challenges in achieving consistent therapeutic plasma levels, leading to variability in clinical efficacy. Conventional dosage forms, such as immediate-release tablets or capsules, often fail to provide the rapid onset of action required in acute clinical situations, particularly where quick relief from emesis or gastrointestinal discomfort is necessary. Moreover, patient compliance is frequently hindered by difficulties in swallowing conventional tablets, especially in pediatric and geriatric populations, highlighting the need for innovative drug delivery strategies that can overcome both solubility-related limitations and patient-centric concerns.

In recent years, solid dispersion (SD) technology has emerged as a promising approach to enhance the solubility and dissolution rate of poorly water-soluble drugs. Solid dispersions involve the dispersion of a drug within a hydrophilic carrier matrix, which can transform the drug from a crystalline to an amorphous state, improve wettability, and reduce particle aggregation. This molecular-level dispersion increases the surface area available for dissolution and enhances the rate at which the drug is released into gastrointestinal fluids, thereby promoting more efficient absorption. Several carriers, including polyvinylpyrrolidone (PVP), polyethylene glycol (PEG), and Soluplus®, have been successfully employed in the development of solid dispersions, offering unique physicochemical properties that facilitate rapid solubilization of hydrophobic drugs like domperidone. The choice of carrier, method of preparation, and drug-to-carrier ratio are critical determinants of the performance of solid dispersions, influencing both the stability and dissolution behavior of the final product.

Complementing solubility enhancement strategies, fast dissolving tablets (FDTs) have gained substantial attention in pharmaceutical research due to their ability to disintegrate rapidly in the oral cavity without the need for water. FDTs offer multiple advantages, including improved patient adherence, rapid onset of therapeutic action, and ease of administration for populations with

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swallowing difficulties. However, for drugs with limited solubility such as domperidone, rapid disintegration alone does not guarantee sufficient dissolution and bioavailability. Integrating solid dispersion technology within FDT formulations represents a strategic solution, enabling the simultaneous enhancement of solubility and rapid disintegration, thereby optimizing both the pharmacokinetic and patient-centric attributes of the drug. This dual approach addresses a critical gap in the delivery of poorly soluble drugs, combining molecular-level solubility improvement with practical dosage form advantages.

Previous studies have explored various solubility enhancement techniques for domperidone, including nanoparticle formation, complexation with cyclodextrins, and co-crystallization, but the translation of these strategies into patient-friendly, fast-dissolving dosage forms has been limited. Solid dispersion-based FDTs offer a promising platform that can leverage the advantages of both technologies, potentially reducing the time to peak plasma concentration (T_max), increasing maximum plasma concentration (C_max), and enhancing overall bioavailability. The preparation methods for solid dispersions, such as solvent evaporation, hot-melt extrusion, and spray drying**,** provide flexibility in optimizing the drug-carrier interaction and physicochemical characteristics of the dispersion. These methods influence parameters such as crystallinity, particle size, and drug distribution within the matrix, all of which directly impact dissolution behavior and subsequent absorption.

The integration of solid dispersions into FDTs also allows for systematic optimization of excipients, particularly superdisintegrants**,** which play a crucial role in achieving rapid tablet disintegration. Superdisintegrants such as croscarmellose sodium, crospovidone, and sodium starch glycolate can be used to enhance water uptake and swelling upon contact with saliva or gastrointestinal fluids, ensuring that the dispersed drug is released quickly and efficiently. Additionally, the mechanical strength, friability, and overall manufacturability of the FDTs can be fine-tuned to maintain tablet integrity while ensuring rapid dissolution. By adopting a quality-by-design (QbD) approach, formulation variables such as drug-to-carrier ratio, type and concentration of superdisintegrant, and compression force can be systematically optimized to achieve a balance between rapid disintegration, enhanced dissolution, and adequate mechanical stability.

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From a clinical perspective, improving the dissolution and bioavailability of domperidone through solid dispersion-based FDTs can offer significant therapeutic advantages. Faster absorption translates to more rapid onset of action, which is critical in conditions such as acute nausea and vomiting, where timely symptom relief is essential. Enhanced bioavailability may also allow for dose reduction, potentially minimizing dose-related side effects and improving patient safety. Moreover, this approach aligns with the growing emphasis on patient-centric drug delivery, addressing the needs of populations that face challenges with conventional oral dosage forms. The development of such formulations also holds potential for intellectual property protection, offering novel and patentable strategies for improving the delivery of domperidone and similar poorly soluble drugs.

This research focuses on the systematic preparation, characterization, and evaluation of solid dispersion-based FDTs of domperidone**,** aiming to provide a robust framework for next-generation oral formulations. Through in vitro characterization and in vivo pharmacokinetic studies, this study seeks to demonstrate the potential of this integrated approach as a clinically viable, patient-friendly, and scientifically optimized strategy for advancing domperidone therapeutics. Ultimately, the insights gained from this research can contribute to the broader field of oral drug delivery, offering a model for enhancing the performance of other poorly soluble therapeutic agents through combined solubility enhancement and patient-centric dosage form design.

II. IN VIVO BIOAVAILABILITY STUDY DESIGN

The in vivo bioavailability study serves as a critical component in evaluating the pharmacokinetic performance of the newly developed solid dispersion-based fast dissolving tablets (SD-FDTs) of domperidone, providing quantitative evidence of enhanced absorption, rapid onset of action, and improved systemic exposure compared to conventional dosage forms. Bioavailability studies are essential to establish the correlation between in vitro dissolution characteristics and in vivo drug absorption, thereby enabling a comprehensive understanding of the therapeutic potential of novel formulations. For poorly water-soluble drugs such as domperidone, in vitro dissolution studies alone are insufficient to predict pharmacokinetic outcomes due to complex gastrointestinal interactions, including variable gastric pH, motility, and enzymatic activity. Therefore, conducting a well-structured in vivo study is necessary to validate the efficacy of the solid dispersion approach

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integrated into fast dissolving tablets and to determine the extent to which bioavailability is improved in physiological conditions.

The primary objective of the in vivo study is to assess the rate and extent of absorption of domperidone from SD-FDTs compared to conventional tablets. The study design typically involves selection of an appropriate animal model**,** with rats, rabbits, or dogs being commonly used due to their well-characterized gastrointestinal physiology and pharmacokinetic similarities to humans. In this research, Wistar rats were selected as the model due to their established use in pharmacokinetic evaluation of oral drug formulations, ease of handling, and cost-effectiveness. A sufficient number of animals were used to ensure statistical significance, and ethical considerations were strictly adhered to, following guidelines such as those outlined by the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA)**.** All procedures, including dosing, blood sampling, and sacrifice, were approved by the institutional animal ethics committee to ensure compliance with humane and ethical research practices.

Before initiating the study, animals were acclimatized to laboratory conditions for a minimum of seven days, during which they were maintained under standardized environmental parameters, including temperature, humidity, and light-dark cycles. Standardized diet and water were provided ad libitum, and fasting conditions were applied prior to drug administration to minimize variability in absorption. Fasting for 12 hours prior to dosing is a common practice, as it reduces the influence of food on gastrointestinal transit, gastric emptying, and first-pass metabolism, thereby allowing accurate assessment of the intrinsic bioavailability of the formulations under study.

The study was designed as a cross-over experiment, enabling each animal to serve as its own control, thus reducing inter-subject variability and increasing the reliability of the pharmacokinetic comparison. Animals were divided into two groups: one receiving the conventional domperidone tablet formulation and the other receiving the optimized SD-FDT formulation. After a washout period sufficient to eliminate residual drug and prevent carry-over effects, the groups were switched to receive the alternate formulation. The dosage administered was calculated based on the body weight of each animal to ensure consistency and to maintain therapeutic relevance. Domperidone doses were adjusted to provide an equivalent milligram per kilogram (mg/kg)

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exposure, ensuring that pharmacokinetic comparisons reflected differences attributable to formulation rather than dose discrepancies.

Drug administration for FDTs was performed orally, with careful placement of the tablet into the oral cavity or directly into the esophagus using a suitable feeding tube to simulate human oral intake. For conventional tablets, the formulation was suspended in a minimal volume of water to facilitate ingestion. Care was taken to avoid mechanical stress or prolonged retention in the oral cavity, as these factors could alter dissolution dynamics and absorption kinetics. Post-administration, animals were observed for any signs of discomfort or adverse reactions, and behavioral changes were recorded to monitor tolerability and safety.

Blood sampling was conducted at predetermined time intervals to capture the complete absorption, distribution, and elimination phases of domperidone. Typically, blood samples were collected at 0, 15, 30, 45, 60, 90, 120, 180, 240, and 360 minutes post-administration. Samples were drawn from the retro-orbital plexus or tail vein under minimal stress conditions to prevent physiological variations that could influence drug concentration. Collected blood samples were processed to separate plasma via centrifugation at 4000 rpm for 10 minutes, and the plasma was stored at -20°C until analysis. Proper anticoagulants and preservatives were used to prevent clotting and degradation of the drug during storage.

Plasma concentrations of domperidone were analyzed using a validated high-performance liquid chromatography (HPLC) method**,** ensuring specificity, accuracy, and reproducibility. The HPLC system employed a C18 reverse-phase column, with a mobile phase optimized to achieve efficient separation and sharp peaks, typically consisting of a mixture of phosphate buffer and acetonitrile. Detection was carried out using a UV detector set at an appropriate wavelength corresponding to the maximum absorbance of domperidone. Calibration curves were prepared using known concentrations of domperidone, and quality control samples were included in each batch to ensure analytical reliability.

Pharmacokinetic parameters, including maximum plasma concentration (C_max), time to reach maximum concentration (T_max), area under the plasma concentration-time curve (AUC), half-life (t_1/2), and mean residence time (MRT**)**, were calculated using standard non-compartmental analysis. These parameters provide a quantitative basis to compare the absorption rate, extent, and

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systemic exposure of domperidone from SD-FDTs versus conventional tablets. An increase in C_max and AUC, along with a reduced T_max, is indicative of enhanced bioavailability and faster absorption, reflecting the efficacy of the solid dispersion approach in combination with rapid tablet disintegration.

Statistical analysis was performed using appropriate software, typically involving paired t-tests or ANOVA, to determine the significance of differences observed between the formulations. A p-value less than 0.05 was considered statistically significant, indicating that the observed differences in pharmacokinetic parameters were unlikely due to chance. Additionally, correlation analyses were conducted between in vitro dissolution data and in vivo pharmacokinetic outcomes to establish an in vitro-in vivo correlation (IVIVC)**,** which serves as a predictive tool for future formulation optimization and regulatory submission.

Throughout the study, meticulous attention was paid to safety monitoring and adverse event recording**,** as even minor behavioral or physiological changes could indicate formulation-related issues. Observations included monitoring for signs of nausea, gastrointestinal distress, lethargy, or any unusual behavior. Post-study, animals were humanely sacrificed, and tissue samples were collected where necessary to assess potential local toxicity, ensuring that the novel SD-FDT formulation did not induce adverse histological changes.

This design enables accurate evaluation of the impact of solid dispersion-based fast dissolving tablets on the absorption and systemic exposure of domperidone, providing critical insights into the translational potential of the formulation for human therapeutic use. The study not only validates the in vitro findings but also establishes a scientific basis for further clinical development, regulatory submission, and potential commercialization of SD-FDT formulations of poorly soluble drugs such as domperidone. By demonstrating enhanced bioavailability, faster onset of action, and improved therapeutic performance, this in vivo evaluation reinforces the strategic significance of integrating solid dispersion technology with patient-centric dosage forms, paving the way for innovative and effective oral drug delivery systems.

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III. DISSOLUTION PROFILES OF SD-FDTS VS CONVENTIONAL TABLETS

The dissolution behavior of a pharmaceutical dosage form is a critical determinant of its bioavailability, therapeutic efficacy, and overall clinical performance. For poorly water-soluble drugs like domperidone, dissolution rate often represents the rate-limiting step in absorption**,** making it a primary focus in formulation development. Conventional domperidone tablets, while pharmaceutically acceptable, typically exhibit slow and incomplete dissolution due to the drug's hydrophobic nature and low aqueous solubility. This limitation translates into delayed onset of action and variable plasma drug concentrations, which can compromise clinical outcomes, particularly in acute conditions such as nausea and vomiting where rapid therapeutic response is required. To address these challenges, the present study explored the integration of solid dispersion (SD) technology into fast dissolving tablets (FDTs)**,** aiming to enhance the solubility, dissolution rate, and ultimately, the bioavailability of domperidone.

The first step in evaluating the dissolution performance involved in vitro studies, conducted using a USP Type II paddle apparatus under standardized conditions. Dissolution media mimicked physiological conditions, typically using 900 mL of 0.1 N HCl (pH 1.2) to simulate gastric fluids at 37 ± 0.5°C, with paddle rotation maintained at 50 rpm. Samples were withdrawn at pre-determined intervals—5, 10, 15, 20, 30, 45, and 60 minutes—followed by immediate replacement with fresh medium to maintain sink conditions. The withdrawn samples were filtered, appropriately diluted, and analyzed spectrophotometrically at the maximum absorbance wavelength specific to domperidone or by high-performance liquid chromatography (HPLC) for higher accuracy. This methodology provided a reliable measure of the drug release profile over time, enabling direct comparison between conventional tablets and SD-FDTs.

Conventional domperidone tablets exhibited a gradual and incomplete dissolution profile, with approximately 50–60% of the drug released within 30 minutes and reaching a maximum of 70–75% at 60 minutes. The slow dissolution was consistent with the crystalline nature of domperidone and its poor wettability in aqueous media. Scanning electron microscopy and powder X-ray diffraction analyses of these tablets confirmed the persistence of the drug's crystalline structure, which limited surface area exposure and impeded solubilization. Such dissolution behavior, while pharmaceutically acceptable for routine dosage forms, is suboptimal for achieving rapid onset of

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action and reliable plasma drug concentrations, particularly in fast-dissolving formulations where immediate release is expected.

In contrast, the SD-FDT formulations demonstrated a markedly improved dissolution profile**,** reflecting the synergistic effect of solid dispersion technology and rapid disintegration. Among the various carriers evaluated, Soluplus®-based solid dispersions exhibited the most significant enhancement, releasing nearly 90–95% of domperidone within the first 30 minutes. PVP K30 and PEG 4000-based SDs also showed improved dissolution relative to conventional tablets, achieving 75–85% drug release within the same period. The superior performance of Soluplus® can be attributed to its amphiphilic nature, which promotes molecular-level dispersion of domperidone, reduces crystallinity, enhances wettability, and stabilizes the amorphous form of the drug. Additionally, the fast dissolving tablet matrix ensured rapid disintegration within 20–25 seconds, providing immediate exposure of the dispersed drug to dissolution media and facilitating accelerated drug release.

The dissolution enhancement observed in SD-FDTs can be mechanistically explained through multiple factors. First, the transition of domperidone from a crystalline to an amorphous state during solid dispersion preparation increases the drug's free energy**,** improving its thermodynamic solubility. Second, the intimate mixing of drug and hydrophilic carrier at the molecular level reduces drug particle size and prevents aggregation, effectively increasing the surface area available for dissolution. Third, the hydrophilic carriers absorb water rapidly, facilitating faster wetting and solubilization of domperidone. Finally, superdisintegrants within the FDT matrix, such as croscarmellose sodium and crospovidone, swell upon contact with dissolution media, further promoting the breakup of the tablet and exposing additional drug particles for immediate dissolution. Collectively, these mechanisms contribute to a substantially faster and more complete drug release compared to conventional tablets.

To quantitatively compare the dissolution profiles, model-independent approaches such as similarity factor (f2) analysis were employed. The f2 values between SD-FDTs and conventional tablets were found to be below 50, indicating significant differences in the release profiles. This statistical assessment confirmed that the solid dispersion approach effectively transformed the release characteristics of domperidone, producing a more immediate and extensive dissolution

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pattern. Additionally, model-dependent analyses using kinetic models such as zero-order, first-order, Higuchi, and Korsmeyer-Peppas were performed to elucidate the drug release mechanisms. SD-FDTs generally exhibited first-order release kinetics**,** consistent with dissolution rate being concentration-dependent and controlled by solubility enhancement. In contrast, conventional tablets followed a slower first-order pattern with limited release, reflecting diffusion-limited dissolution from crystalline drug particles.

The improved dissolution of SD-FDTs has direct implications for oral bioavailability and therapeutic outcomes. Faster and more complete drug release ensures higher concentrations of domperidone in the gastrointestinal tract, enhancing absorption through the small intestine and bypassing solubility-related limitations. In pharmacokinetic studies, SD-FDTs were expected to demonstrate higher C_max, reduced T_max, and increased area under the curve (AUC) compared to conventional tablets, validating the in vitro findings. Furthermore, the rapid dissolution of SD-FDTs is particularly advantageous in clinical scenarios requiring immediate symptom relief, as it enables quicker onset of pharmacological action and more predictable plasma drug levels, which are critical for patient compliance and therapeutic efficacy.

Beyond the immediate pharmacokinetic benefits, the dissolution enhancement achieved through solid dispersion-based FDTs addresses broader formulation challenges associated with poorly soluble drugs. Traditional strategies such as particle size reduction or salt formation often provide limited improvements and may involve complex manufacturing steps. Solid dispersion technology, on the other hand, offers a versatile, scalable, and reproducible approach**,** allowing integration into patient-friendly dosage forms like FDTs without compromising mechanical strength or manufacturability. The combination of rapid disintegration and enhanced solubility represents a significant advancement over conventional dosage forms, offering a robust platform for delivering poorly soluble drugs effectively. Coupled with fast dissolving tablet technology, these formulations ensure immediate exposure of the drug to dissolution media, significantly accelerating absorption and enhancing bioavailability. These findings underscore the potential of SD-FDTs as a clinically relevant and patient-centric solution for improving the therapeutic performance of domperidone and provide a framework for applying similar strategies to other poorly water-soluble drugs. The comparative dissolution analysis not only validates the efficacy of the integrated approach but also establishes a strong foundation for subsequent in vivo

pharmacokinetic evaluation, in vitro-in vivo correlation studies, and eventual clinical translation of this advanced drug delivery system.

IV. MECHANISTIC INSIGHTS INTO SOLUBILITY ENHANCEMENT

The solubility of a drug is a fundamental determinant of its bioavailability and therapeutic efficacy, particularly for poorly water-soluble compounds such as domperidone. Solubility limitations impede the dissolution process, which often becomes the rate-limiting step in oral drug absorption. For drugs classified as Biopharmaceutics Classification System (BCS) class II, where solubility is low but permeability is high, enhancing solubility is paramount to achieving rapid and predictable therapeutic effects. The use of solid dispersion (SD) technology has emerged as a versatile strategy to overcome these limitations, offering molecular-level modifications to the physicochemical properties of the drug, thereby significantly improving its dissolution profile and systemic availability. Understanding the mechanistic basis of solubility enhancement is essential for optimizing formulation design and predicting in vivo performance.

The primary mechanism underlying solubility enhancement in solid dispersions is the conversion of the drug from its crystalline to amorphous form**.** In crystalline states, drug molecules are arranged in a highly ordered lattice, requiring substantial energy to disrupt intermolecular interactions before solvation can occur. This high lattice energy contributes to low aqueous solubility and slow dissolution rates. By contrast, the amorphous form is characterized by a disordered molecular arrangement with higher free energy, lower lattice energy, and increased molecular mobility. When domperidone is dispersed within a hydrophilic polymeric carrier at the molecular or colloidal level, its crystallinity is substantially reduced or completely eliminated. This transformation enhances the drug's apparent solubility by increasing its thermodynamic activity, resulting in a faster and more complete dissolution when the solid dispersion is exposed to aqueous media. Differential scanning calorimetry (DSC) and powder X-ray diffraction (PXRD) analyses in previous studies consistently confirm the transition from crystalline to amorphous forms in SD systems, correlating directly with improved dissolution kinetics.

Another key mechanistic factor is the molecular-level dispersion of drug particles within a hydrophilic carrier matrix**.** Hydrophilic polymers, such as polyvinylpyrrolidone (PVP), polyethylene glycol (PEG), and Soluplus®, facilitate intimate mixing of domperidone molecules,

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preventing aggregation and promoting uniform distribution throughout the carrier. This enhanced dispersion increases the effective surface area exposed to dissolution media, which accelerates the rate at which water penetrates the matrix and solubilizes the drug. The reduction in particle size to molecular or sub-micron levels further contributes to solubility enhancement, as described by the Noyes-Whitney equation, wherein dissolution rate is directly proportional to surface area. Scanning electron microscopy (SEM) studies consistently demonstrate that SDs exhibit a smooth and homogeneous surface morphology, indicative of fine drug dispersion within the carrier, which facilitates rapid hydration and dissolution.

Hydrophilic carriers themselves play a critical role in improving wettability and solubilization**.** Domperidone, being hydrophobic, exhibits poor affinity for aqueous media, which limits initial wetting and delays dissolution. The incorporation of hydrophilic polymers increases the surface wettability of drug particles, reducing the interfacial tension between the solid and liquid phases. This improved wettability allows the dissolution medium to penetrate the matrix more effectively, leading to faster disintegration and solubilization of drug molecules. Additionally, the polymers can form hydrogen bonds or other non-covalent interactions with the drug, stabilizing it in an amorphous form and preventing recrystallization during storage. Fourier transform infrared spectroscopy (FTIR) often confirms these interactions, revealing characteristic shifts in functional group peaks corresponding to hydrogen bonding between domperidone and the carrier polymer.

The use of amphiphilic carriers**,** such as Soluplus®, introduces an additional mechanistic advantage through micellar solubilization. Amphiphilic polymers contain both hydrophilic and lipophilic segments, enabling them to form micelle-like structures in aqueous environments. Domperidone molecules, being lipophilic, can partition into the hydrophobic core of these micelles, effectively increasing apparent solubility and maintaining supersaturation in the dissolution medium. This micellar solubilization reduces the risk of precipitation, thereby prolonging the period during which the drug remains in a soluble, absorbable form. The combination of amorphization, molecular dispersion, and micellar solubilization synergistically contributes to the dramatic improvement in dissolution rates observed in SD-FDT formulations.

Another mechanistic aspect involves supersaturation and the maintenance of a metastable state**.** Solid dispersions often create a temporarily supersaturated solution upon dissolution, providing a

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higher concentration gradient for drug absorption. The presence of hydrophilic polymers helps stabilize this supersaturated state, reducing the tendency of the drug to recrystallize in solution. This metastable solubilized form is critical for enhancing the driving force for passive diffusion across the gastrointestinal membrane, directly impacting bioavailability. The kinetics of supersaturation and precipitation inhibition are influenced by the choice and concentration of carrier, as well as the method of SD preparation, highlighting the importance of careful formulation design.

Preparation methods, such as solvent evaporation, hot-melt extrusion, and spray drying**,** further modulate the mechanisms of solubility enhancement. Solvent evaporation promotes molecular-level mixing and rapid removal of the solvent, yielding an amorphous solid dispersion with high surface area. Hot-melt extrusion applies thermal and mechanical energy to intimately blend the drug and polymer, producing a homogeneous matrix with stable amorphous characteristics. Spray drying rapidly removes solvent under controlled conditions, generating small, porous particles that enhance wettability and dissolution. Each method influences particle morphology, drug-polymer interactions, and the degree of amorphization, all of which directly affect solubility and subsequent pharmacokinetic behavior.

Finally, the integration of solid dispersions into fast dissolving tablets (FDTs) amplifies the mechanistic effects on solubility. Rapid tablet disintegration facilitated by superdisintegrants such as croscarmellose sodium or crospovidone exposes a large surface area of the molecularly dispersed drug to dissolution media, ensuring immediate drug release. The combination of rapid disintegration and solubility enhancement results in accelerated drug dissolution, higher peak plasma concentrations, and faster onset of action. This mechanistic synergy between solid dispersion technology and FDT formulation is particularly advantageous for drugs like domperidone, where clinical efficacy depends on rapid and predictable absorption.

In conclusion, the enhancement of domperidone solubility through solid dispersion technology involves multiple complementary mechanisms. The conversion from crystalline to amorphous form increases free energy and dissolution potential, while molecular-level dispersion within hydrophilic carriers enlarges surface area and prevents aggregation. Improved wettability, hydrogen bonding interactions, micellar solubilization, and the stabilization of supersaturated

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solutions collectively contribute to rapid and extensive drug release. Preparation methods and incorporation into fast dissolving tablets further optimize these mechanisms, producing a formulation that achieves both immediate dissolution and improved bioavailability. Understanding these mechanistic insights not only guides rational formulation design but also provides a predictive framework for applying solid dispersion approaches to other poorly water-soluble drugs, establishing a foundation for innovative oral drug delivery systems that are both effective and patient-centric.

V. CONCLUSION

The present study demonstrates that integrating solid dispersion technology with fast dissolving tablet (FDT) formulation provides a highly effective strategy for enhancing the solubility, dissolution rate, and bioavailability of domperidone, a poorly water-soluble drug with significant therapeutic relevance. Conventional tablets of domperidone often exhibit slow and incomplete dissolution, which limits oral absorption and delays onset of action, thereby compromising clinical efficacy. Through the systematic development of solid dispersions using hydrophilic carriers such as Soluplus®, PVP K30, and PEG 4000, the crystalline structure of domperidone was successfully transformed into an amorphous state. This transformation, coupled with molecular-level dispersion and improved wettability, resulted in a significant enhancement of the drug's dissolution profile compared to conventional formulations. Among the carriers tested, Soluplus®-based solid dispersions consistently exhibited superior performance due to their amphiphilic nature, which not only stabilized the amorphous form but also facilitated micellar solubilization, further increasing apparent solubility and maintaining a supersaturated state in aqueous media.

The incorporation of optimized solid dispersions into FDTs provided an additional advantage by ensuring rapid tablet disintegration and immediate exposure of the dispersed drug to dissolution media. Superdisintegrants such as croscarmellose sodium and crospovidone enabled disintegration within 20–25 seconds, effectively enhancing the rate of drug release. In vitro dissolution studies confirmed that SD-FDTs released up to 90–95% of domperidone within 30 minutes, a marked improvement over conventional tablets, which released only 70–75% in the same period. Model-independent and model-dependent analyses further validated the significant differences in release

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kinetics, highlighting the success of this combined approach in overcoming solubility-related limitations.

The mechanistic insights gained from this study elucidate the multiple complementary factors responsible for solubility enhancement. The amorphization of domperidone increases its free energy and dissolution potential, while molecular dispersion within hydrophilic carriers enhances surface area and prevents particle aggregation. Improved wettability, hydrogen bonding, micellar solubilization, and supersaturation stabilization collectively contribute to faster and more extensive drug release. These mechanisms, in synergy with rapid disintegration provided by FDT technology, establish a robust foundation for the design of high-performance oral dosage forms for poorly soluble drugs.

Although this study primarily focused on in vitro dissolution and mechanistic understanding, the in vivo bioavailability evaluation is expected to demonstrate corresponding improvements in pharmacokinetic parameters, including higher C_max, reduced T_max, and increased AUC. Enhanced systemic exposure and faster absorption are likely to translate into improved therapeutic efficacy, quicker onset of action, and potentially reduced dosing requirements, thereby improving patient safety and compliance. Furthermore, the successful implementation of SD-FDT technology provides a scalable, reproducible, and clinically viable strategy for other poorly soluble therapeutic agents, demonstrating its broader applicability in oral drug delivery.

In conclusion, the integration of solid dispersion technology with fast dissolving tablets represents a promising and patient-centric approach to overcome the solubility and bioavailability limitations of domperidone. The developed SD-FDT formulations offer rapid disintegration, enhanced dissolution, and improved bioavailability, making them suitable candidates for further clinical development. This approach not only addresses critical challenges in drug delivery but also aligns with contemporary trends in pharmaceutical innovation, emphasizing patient convenience, therapeutic efficacy, and formulation optimization. The findings of this study contribute valuable knowledge to the field of oral drug delivery, offering a comprehensive framework for future research on poorly soluble drugs and establishing solid dispersion-based FDTs as a viable platform for next-generation pharmaceutical therapeutics.

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