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ADVANCING POORLY SOLUBLE DRUGS: A COMPREHENSIVE REVIEW OF QUALITY BY DESIGN SOLID DISPERSION TECHNIQUES AND PAST INNOVATIONS

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ABSTRACT

This study undertakes a meticulous examination of past endeavors on solid dispersions using the Quality by Design (QbD) approach, offering in-depth insights into their types and methods of preparation. Through a comprehensive review of peer-reviewed literature, the research elucidates the effectiveness of solid dispersion techniques in addressing the inherent solubility limitations of poorly soluble drugs. Noteworthy among these findings is the emergence of the QbD approach as a transformative methodology in experimental design, providing a structured framework for the systematic optimization of drug formulations. By synthesizing past research and illuminating key insights, this review aims to serve as an invaluable resource for aspiring researchers, equipping them with a nuanced understanding of solid dispersions by QbD and facilitating expedited access to pertinent information for future investigations in this dynamic field.

Keywords: Bioavailability, Quality by design, Release, Solid dispersions, Solubility

INTRODUCTION

The drug's bioavailability and the rate and volume of its absorption are largely determined by the drug's solubility and its gastrointestinal permeability. The solubility of medicines in water is a crucial element in absorption following oral drug delivery. The recent increase in poorly soluble pharmaceuticals, with low aqueous solubility present in 70% of innovative prescriptions, poses significant challenges for drug innovation and development. Drugs with low solubility convey a higher risk of failure due to their impact on pharmacokinetics, pharmacodynamics, and other factors like drug distribution, protein binding, and absorption. Low solubility often leads to limited dissolution in the gastrointestinal tract, hindering absorption and potentially resulting in inconsistent or insufficient drug levels in the body, affecting treatment outcomes. Additionally, it can impede drug distribution to target tissues and organs, contributing to variability in drug response among patients. Moreover, drugs with low solubility may exhibit higher levels of protein binding, altering their pharmacokinetic profile and increasing the risk of drug interactions or toxic effects. Overcoming these challenges requires innovative formulation strategies and interdisciplinary collaborations to improve solubility and bioavailability while ensuring stability and safety, ultimately enhancing the success rate of drug development and optimizing therapeutic outcomes **[1]**.

According to their solubility, permeability, and dissolution, the medicines are categorized in BCS. The biopharmaceutics Classification System (BCS) divides pharmacological compounds into four groups based on permeability and solubility. Medications with high permeability and high solubility are classified as class I. These substances are readily absorbed, and their rate of absorption typically exceeds that of excretion. For instance, metoprolol with paracetamol. Drugs in Class II have limited solubility and high permeability. Their solvation rate restricts such compounds' bioavailability. For instance, glibenclamide and bicalutamide. Class III drugs are those with high solubility and poor permeability **[2]**. The drug solvates quickly, but the absorption is restricted by the penetration rate. Cimetidine is one example. Drugs of Class IV have low solubility and low permeability. These substances are not very bioavailable. They typically diffuse poorly through the digestive mucosa, therefore significant heterogeneity is to be expected. Bifonazole, for instance **[3]**.

Enhancing drug solubility in formulations addresses a critical user need within the realm of pharmaceuticals. Many drugs, particularly those classified as poorly

soluble, face challenges in achieving adequate dissolution rates and bioavailability upon administration. This limitation often translates to suboptimal therapeutic outcomes, necessitating the development of innovative formulation strategies. By enhancing drug solubility, formulations can facilitate more efficient drug absorption, thereby improving the onset of action, efficacy, and overall patient experience. Addressing this user need not only enhances the effectiveness of pharmaceutical interventions but also contributes to the advancement of patient-centered care by optimizing treatment outcomes and promoting medication adherence **[4]**.

Poorly soluble drugs have the highest attrition rates while being the majority of therapeutic candidates under development; this is typically due to their low bioavailability. When a medication is accessible in an amorphous form, amorphous solid dispersion can ultimately increase the drug's bioavailability. Amorphous solid dispersions (ASDs) are one potential solution for drug distribution, and choosing an appropriate polymer carrier can help optimize the drug's solubility, rate of dissolution, and solid-state physical stability. The increased interest in ASD research over the past few decades is demonstrated by a new literature review and patent analysis, which show an exponential increase in papers and patents in both academia and industry **[5]**.

Solid dispersions play a pivotal role in enhancing the solubility of poorly soluble drugs, thus addressing a significant challenge in pharmaceutical formulation. By dispersing drug molecules within a solid matrix, typically a polymer carrier, solid dispersions increase the surface area available for dissolution upon administration. This facilitates the dissolution of the drug in biological fluids, thereby improving its bioavailability and therapeutic efficacy. Furthermore, solid dispersions can alter the physicochemical properties of the drug, such as crystallinity and particle size, leading to enhanced solubility and dissolution kinetics. The versatility of solid dispersion techniques allows for precise control over the formulation parameters, enabling tailored solutions for a wide range of drug compounds with varying solubility profiles. Consequently, solid dispersions offer a versatile and effective approach to overcoming solubility challenges, ultimately contributing to the development of more efficacious pharmaceutical formulations **[6, 7]**.

Solid dispersion is defined as the dispersion of one or more active ingredients (hydrophobic) in an inert carrier (hydrophilic) at a solid state prepared by various methods as per **Figure 1**.

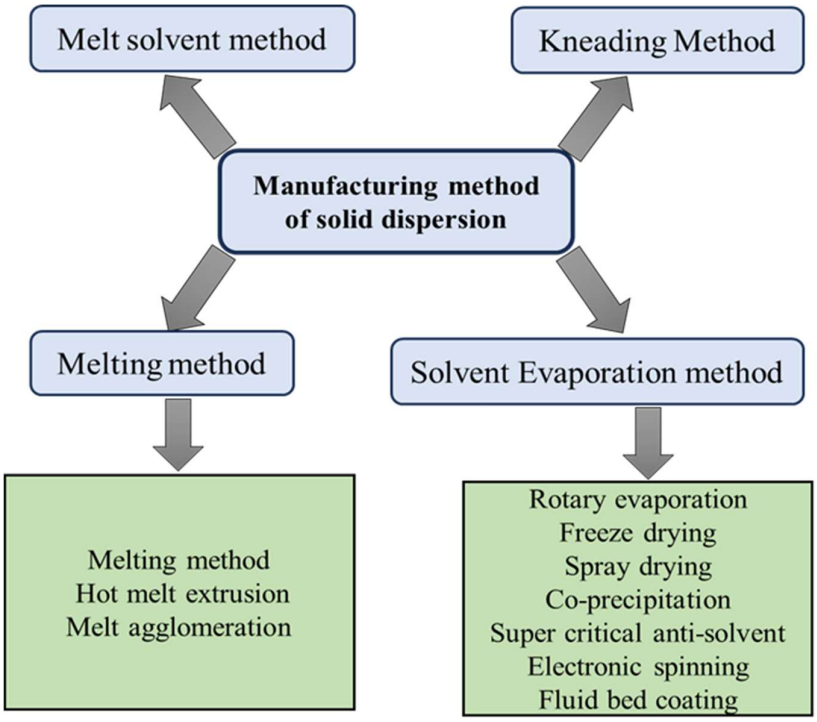

Figure 1: Various approaches for making solid dispersions

Melt solvent method

To prepare solid dispersions, the medication needs to dissolve initially in a suitable liquid solvent. This solution is subsequently mixed with the molten polyethylene glycol and left to evaporate until a transparent film, free from solvent, remains. Following this, the film is dried until it reaches a uniform weight **[8]**.

Kneading method

Initially, the drug and carrier are weighed individually, then blended and ground using a mortar and pestle to reduce their size. Subsequently, a water-methanol mixture in a ratio of 3:1 is introduced to the blend. Following extensive mixing, the resulting slurry undergoes filtration to gather the solid, which is then subjected to drying in a hot-air oven at 50°C for 2 hours. The dried material is further desiccated for 12 hours. Lastly, the solid dispersion is sieved through mesh size # 80 to ensure uniform particle size **[9]**.

Melting method

The melting or fusion method involves blending a drug with a water-soluble carrier and heating the mixture until it liquefies. The molten blend is then rapidly solidified in an ice bath while vigorously stirring. The resulting solid mass is crushed, ground, and sieved. This process has been refined over time, with variations such as pouring the homogeneous melt onto a ferrite or stainless-steel plate and cooling it with air or water. Furthermore, by rapidly cooling the melt from a high temperature, it's possible to achieve a supersaturation of the drug in the system. This rapid solidification process

traps the drug molecules within the solvent matrix. The quenching technique produces a finer dispersion of crystallites, especially when applied to simple eutectic mixtures **[10]**.

Solvent evaporation method

In this approach, the drug and carrier are combined into a physical mixture and dissolved in a shared solvent. This solvent is then evaporated until only a clear, solvent-free film remains. The film is subsequently dried until it reaches a constant weight. A key benefit of the solvent evaporation method is that it helps prevent the thermal decomposition of drugs or carriers, as the relatively low temperatures needed for organic solvent evaporation reduce the risk **[11]**.

Classification of solid dispersion

First-generation solid dispersion is made up using carriers such as urea or sugars which are crystalline. The product formed is thermodynamically stable with good drug-release properties. Second-generation solid dispersion makes use of carriers such as PVP and PEG, it has been proven to be better than first-generation solid dispersion in terms of stability. Carriers having emulsifying or surfactant properties are used for the preparation of third-generation solid dispersion. Excellent dissolution property has been shown by the third-generation class. The demerits such as recrystallization, precipitation, and stability problems can be rectified by these carriers. The most commonly used carriers in this class are inulin, poloxamer, etc. We might refer fourth fourth-generation solid dispersion as controlled release solid dispersions (CRSD). The dual objectives of CRSD are controlled medication release and solubility augmentation. Eudragit RS, Eudragit RL, HPC, and ethyl cellulose are examples of water-soluble carriers utilized in CRSD **(Figure 2) [12]**.

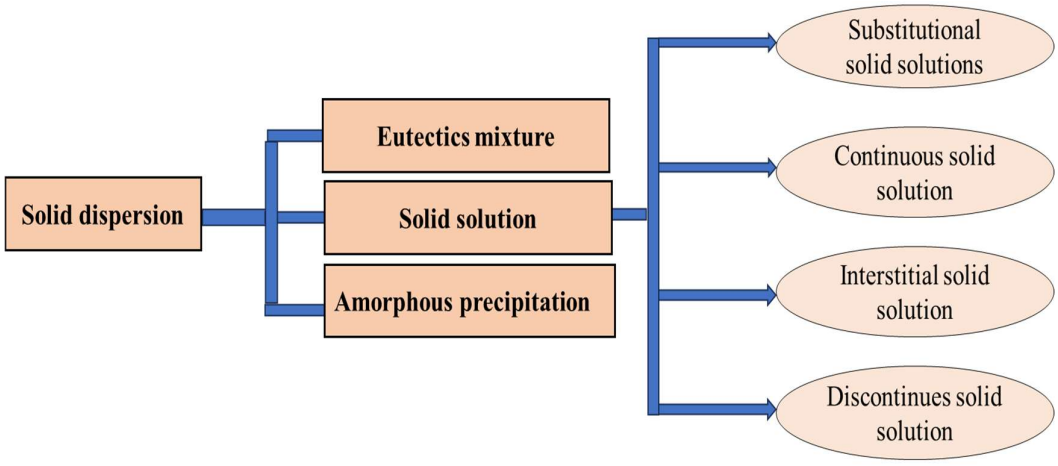

Figure 2: Types of solid dispersion

Purpose of solid dispersion

The purpose of solid dispersion is as follows **[13]**:

- Provides a promising way to increase the dissolution rate of poorly water-soluble drugs
- Reduces pre-systemic metabolism, due to saturation of enzymes responsible for biotransformation of drugs
- Provides easy transformation of the liquid form of the drug into a solid form, avoiding polymorphic changes and thereby bioavailability problems
- Protects certain drugs against decomposition by saliva to allow buccal absorption. E.g. Cardiac glycosides by PEG.
- This technique can be valuable for drug discovery and development when the solubility of the compound is one of the key factors.
- It enhances the absorption of drugs.
- To obtain a homogeneous distribution of a small amount of drug in solid state.
- It stabilizes unstable drugs and protects against decomposition by processes such as hydrolysis, oxidation, racemization, photo-oxidation, etc.
- It dispenses liquid or gaseous compounds.
- To formulate a fast-release priming dose in a sustained-release dosage form.
- To formulate sustained release preparation of soluble drugs by dispersing the drug in poorly soluble or insoluble carriers.
- It reduces side effects the binding ability of drugs for example to the erythrocyte membrane is decreased by making its inclusion complex.
- It masks unpleasant taste and smell e.g., the very unpleasant taste of anti-depressant famoxetine hindered the development of oral liquid formulations.

Quality by design (QbD)

Quality by Design (QbD) is a systematic approach revolutionizing the development of pharmaceutical dosage forms. Rooted in the philosophy that quality should be built into products from the outset, QbD emphasizes a proactive, science-based methodology to ensure the consistent delivery of safe and effective medicines to patients **[14]**.

In the context of pharmaceutical dosage forms, QbD entails a comprehensive understanding of the formulation and manufacturing processes, to achieve predefined quality objectives. This involves identifying critical quality attributes (CQAs) that directly impact the safety, efficacy, and

performance of the dosage form. By defining these CQAs early in the development process, formulators can focus on optimizing critical formulation and process parameters to ensure desired product quality **[15]**.

A key aspect of QbD is the utilization of risk-based approaches to identify and mitigate potential sources of variability that could affect product quality. Through quality risk management (QRM) techniques, such as failure mode effects analysis (FMEA) and design of experiments (DoE), formulators can systematically evaluate and prioritize risks, allowing for informed decision-making to enhance product robustness and reliability.

Furthermore, QbD promotes the integration of advanced analytical techniques and in-depth characterization studies to better understand the relationship between formulation components, manufacturing processes, and product performance. This knowledge-driven approach enables formulators to design robust formulations and manufacturing processes that are more resistant to variations in raw materials, equipment, and operating conditions **[16]**.

By implementing QbD principles, pharmaceutical companies can streamline development timelines, reduce manufacturing costs, and ultimately improve patient outcomes by ensuring the consistent delivery of high-quality dosage forms. Moreover, QbD aligns with regulatory expectations, as agencies like the FDA increasingly encourage the adoption of QbD principles to enhance pharmaceutical development and manufacturing practices.

Objectives of QbD

The objectives of QbD are as described below **[17]**:

- The foremost objective of QbD is to attain high-quality products consistently throughout their lifecycle.
- QbD aims to achieve positive performance testing by systematically designing and controlling critical attributes of the product.
- It ensures product quality through the implementation of an effective control strategy that encompasses the entire manufacturing process.
- QbD facilitates the integration of process knowledge acquired during development stages, enabling a deeper understanding of the relationship between formulation variables, process parameters, and product quality attributes.
- By leveraging this knowledge and data, QbD allows for the construction of robust process measurements and desired product attributes, leading to more reliable and predictable outcomes.

The past successful attempts made on solid dispersions using QbD are illustrated in **Table 1**.

Table 1: The previous effective tactics in solid dispersions employing the QbD approach

Drug	Method	Design	Independent variables	Depended variables	Reference
Meloxicam (MLX)	Fusion method (FM)	3^3 full factorial design(FFD)	Drug loading (X_1), carrier ratio (X_2), and method of preparation (X_3)	Percentage (%) of drug dissolved Q_{10} (Y_1) and Q_{30} (Y_2)	[18]
Lurasidone HCl	FM	3^2FFD	Poloxamer188 (X_1) and Florite SD(X_2)	% dissolution efficiency(Y_1), t_{50} (Y_2) and Q_{30}(Y_3)	[19]
Lamotrigine	Kneading method (KM)	3^2FFD	Crospovidone (X_1) and sodium starch glycolate(X_2)	Disintegration time (DT), percent friability (%F), and wetting time (WT)	[20]
MLX	FM	3^3FFD	Camphor (X_1), Croscarmellose sodium (X_2), and PEG (X_3)	Dissolution rate (Y_1) and DT(Y_2)	[21]
Rofecoxib	Solvent evaporation method (SE)	3^2FFD	Camphor (X_1) and Crospovidone (X_2)	DT(Y_1) and %F (Y_2)	[22]
Hippophae rhamnoides	SE	3^2FFD	Solvent (X_1) and drug: polymer ratio (X_2)	Q_{10} (Y_1)	[23]
Celecoxib	SE	3^2FFD	Croscarmellose sodium (X_1) and pearlitol (X_2)	DT (Y_1), % F (Y_2), WT (Y_3), and % DR after 20 min (Q_{20}) (Y_4)	[24]
Aceclofenac	KM	3^2 Box Behnken Design (BBD)	Avicel 200 (X_1), HPMC E-5 (X_2), and drug: polymer mixture (X_3)	Angle of repose (Y_1) and % DR at 5 min (Q5)(Y_2)	[25]
Valsartan	Freeze drying	3^2FFD	Valsartan (X_1) and mannitol (X_2)	Solubility (Y_1) and particle size (Y_2)	[26]
MLX	Melting method	3^2FFD	Drug: polymer ratio (X_1) and cooling temperature (X_2)	% DR at 30 min (Y_1), % DR at 60 min (Y_2), % DR at 120 min (Y_3), and % yield of the SD (Y_4)	
Furosemide	SE	3^2FFD	Anhydrous lactose (X_1) and colloidal silicon dioxide (X_2)	Dissolution efficiency(Y_1)	[27]
Curcumin	FM	3^2FFD	Cu-Pol 407 ratio(X_1) and spheronization speed (X_2)	Geometric mean diameter of pellets(Y_1), and % DR after 2 h (Y_2)	[28]
Clopidogrel	FM and SE	3^2FFD	PEG 6000 (X_1) and Clopidogrel (X_2)	%DR (Y_1)	[29]
Aprepitant	SE	3^2FFD	Drug:Carrier ratio (X_1) and solvent (X_2)	%DR at 60 min (Y_1)	[30]
Glimepiride	FM	3^3FFD	Drug (X_1), PEG 6000 (X_2) and PVP K25 (X_3)	% DR 30 min (Y_1)	[31]
Fenofibrate	FD	3^2FFD	Poloxamer (X_1) and Lyophilization Temperature(X_2)	Angle of repose (Y_1)	[32]
Rofecoxib	FM	3^2FFD	Temperature to which the melt-drug mixture cooled (X_1) and the Drug: Polymer ratio (X_2)	Time required for 90% DR (Y_1)	[33]
Diclofenac sodium	Co-evaporation method	3^2FFD	Total polymer payloads in the solid dispersion	Percentage drug incorporation (Y_1), drug release at the	[34]

			(X_1) and the proportion of Eudragit RL 100 in the total polymer (X_2)	**end of 12 h (Y_2), and drug released at the end of 3h (Y_3)**	
Aceclofenac	**SE**	**3^3FFD**	**crospovidone (X_1), tri-ethanolamine (X_2) and ethanol (X_3)**	**Drug permeated at 10h (Y_1) and permeation flux (Y_2)**	**[35]**
MLX	**SE, FM, and melting solvent method**	**3^3FFD**	**Tween 80(X_1), methylcellulose (X_2) and sodium citrate(X_3)**	**Viscosity(Y_1) and Sedimentation volume(Y_2)**	**[36]**

CONCLUSION

In conclusion, this study provides a meticulous examination of past efforts in solid dispersions using the Quality by Design (QbD) approach, shedding light on their various types and preparation methods. Through a thorough review of peer-reviewed literature, the research underscores the efficacy of solid dispersion techniques in overcoming the solubility challenges associated with poorly soluble drugs. Particularly noteworthy is the ascendancy of the QbD approach as a transformative methodology in experimental design, offering a structured framework for the systematic optimization of drug formulations. By synthesizing previous research and elucidating key insights, this review serves as a valuable resource for aspiring researchers, imparting a nuanced understanding of solid dispersions by QbD and facilitating access to pertinent information for future investigations in this dynamic field.

REFERENCES

[1] Zuccari G, Russo E, Villa C, Zorzoli A, Marimpietri D, Marchitto L, *et al*. Preparation and Characterization of Amorphous Solid Dispersions for the Solubilization of Fenretinide. Pharmaceuticals 2023;16:388.

[2] Patel K, Kevlani V, Shah S. A novel Posaconazole oral formulation using spray dried solid dispersion technology: in-vitro and in-vivo study. Drug Delivery and Translational Research 2024;14:1253-76.

[3] Hermans A, Milsmann J, Li H, Jede C, Moir A, Hens B, *et al*. Challenges and strategies for solubility measurements and dissolution method development for amorphous solid dispersion formulations. The AAPS Journal 2022;25:11.

[4] Bikiaris DN. Solid dispersions, part I: recent evolutions and future opportunities in manufacturing methods for dissolution rate enhancement of poorly water-

soluble drugs. Expert opinion on drug delivery 2011;8:1501-19.

[5] Telange DR, Bhaktani NM, Hemke AT, Pethe AM, Agrawal SS, Rarokar NR, *et al*. Development and characterization of pentaerythritol-eudragitrs100 Co-processed excipients as solid dispersion carriers for enhanced aqueous solubility, in vitro dissolution, and ex vivo permeation of atorvastatin. ACS omega 2023;8:25195-208.

[6] Cid AG, Simonazzi A, Palma SD, Bermúdez JM. Solid dispersion technology as a strategy to improve the bioavailability of poorly soluble drugs. Therapeutic delivery 2019;10:363-82.

[7] Annepogu H, Ahad HA, Nayakanti D. Determining the best poloxamer carrier for thiocolchicoside solid dispersions. Turkish Journal of Pharmaceutical Sciences 2020;17:372.

[8] Ahad HA, Chinthaginjala H, Reddy G, Ganthala AK, Siddhartha TT. Optimized Rapid Disintegrating Tablets produced through Central Composite Design. Current Issues in Pharmacy and Medical Sciences 2022;35:152-5.

[9] Annepogu H, Ahad HA. Unique Solid Dispersions by Microwave Fusion Technique with Etoricoxib and Thiocolchicoside: In vivo Evaluation and Comparison with Marketed Formulation. Adv Pharmacol Pharm 2022;10:104-13.

[10] Chinthaginjala H, Ahad HA, Samhitharao B, Yasaswini VS, Madana G, Varam NJ, *et al*. Formulation and In Vitro Evaluation of Fast Disintegrating Tablets of an Anti-Inflammatory Drug using Natural Super Disintegrating Agents.(2). Int J Life Sci Pharma Res 2021;2:9-18.

[11] Jwalapuram R, Ahad HA, Haranath C, Thadipatri R, Varshitha C, Kumar YB. A desktop reference to the solubility enhancement of drugs with the aid of surfactants.(2020). Int J Life Sci Pharma Res;11:P11-6.

[12] Malkawi R, Malkawi WI, Al-Mahmoud Y, Tawalbeh J. Current trends on solid dispersions: past, present, and future. Advances in Pharmacological and Pharmaceutical Sciences 2022;2022.

[13] Deac A, Qi Q, Indulkar AS, Purohit HS, Gao Y, Zhang GG, *et al*. Dissolution mechanisms of amorphous solid dispersions: role of drug load and molecular interactions. Molecular Pharmaceutics 2022;20:722-37.

[14] Kumar LS, Ahad HA. Quality by Design based Quercetin Hydrate Nanoemulsions for Enhanced Solubility by Reducing Particle Size. Ind J Pharm Edu Res 2023;57:965-70.

[15] Yadiki MN, Suggala VS, Puchalapalli DSR, Ahad HA. Temperature and Exposure Time Impact on the Extraction of Opuntia ficus-indica and Opuntia dillenii Cladodes on% Yield as a Response: Screening using Design Expert Software. Global Journal of Medical, Pharmaceutical, and Biomedical Update 2022;17.

[16] Eltahir AKAE, Ahad HA, Haranath C, Meharajunnisa B, Dheeraj S, Sai BN. Novel Phytosomes as Drug Delivery Systems and its Past Decade Trials. 2023.

[17] Babu GN, Muthukaruppan M, Ahad HA. Impact of Azadirachta indica Fruit Mucilage on particle size and swelling index in Central Composite Designed Acyclovir mucoadhesive microspheres. Baghdad Science Journal 2023;20:0425-.

[18] Issa AA, Marchidan D, Cojocaru V, Anuța V. Preparation and evaluation of meloxicam solid dispersion by melting method. Farmacia 2013;61:1216-32.

[19] Mahajan A, Surti N, Koladiya P. Solid dispersion adsorbate technique for improved dissolution and flow properties of lurasidone hydrochloride: characterization using 32 factorial design. Drug development and industrial pharmacy 2018;44:463-71.

[20] Singh J, Garg R, Gupta GD. Enhancement of solubility of lamotrigine by solid dispersion and development of orally disintegrating tablets using 32 full factorial design. Journal of pharmaceutics 2015;2015.

[21] Aboelwafa AA, Fahmy RH. A pilot human pharmacokinetic study and influence of formulation factors on orodispersible tablet incorporating meloxicam solid dispersion using factorial design. Pharmaceutical Development and Technology 2012;17:1-14.

[22] Sammour OA, Hammad MA, Megrab NA, Zidan AS. Formulation and optimization of mouth dissolve tablets containing rofecoxib solid dispersion. AAPS PharmSciTech 2006;7:E167-E75.

[23] Xie Y, Li G, Yuan X, Cai Z, Rong R. Preparation and in vitro evaluation of solid dispersions of total flavones of Hippophae

rhamnoides L. Aaps Pharmscitech 2009;10:631-40.

[24] Pandya VM, Patel DJ, Patel JK, Patel RP. Formulation, characterization, and optimization of fast-dissolve tablets containing celecoxib solid dispersion. Dissolution Technol 2009;16:22-7.

[25] A Maulvi F, T Thakkar V, G Soni T, R Gandhi T. Optimization of aceclofenac solid dispersion using Box-Behnken design: in-vitro and in-vivo evaluation. Current drug delivery 2014;11:380-91.

[26] Shirsath NR, Goswami AK. Design and development of solid dispersion of valsartan by a lyophilization technique: A 32 factorial design approach. Micro and Nanosystems 2021;13:90-102.

[27] Hardikar SR, Mulla SS. Optimization of formulation of solid dispersion of furosemide by factorial design. Int J Pharm Pharm Sci 2020;12:43-8.

[28] Deshkar S, Satpute A. Formulation and optimization of curcumin solid dispersion pellets for improved solubility. Int J Appl Pharm 2020;12:36-46.

[29] Singh SK, Som S, Shankhwar U. Formulation and optimization of solid dispersion of Clopidogrel with PEG 6000. Journal of applied pharmaceutical science 2011:217-26.

[30] Dhillon R, Ojha R, Bedi N. Preparation, characterization and optimization of poloxamer solid dispersions of a poorly water soluble drug aprepitant. British Journal of Pharmaceutical Research 2014;4:2436-54.

[31] Rajpurohit VS, Rakha P, Goyal S, Dureja H, Arorac G, Nagpal M. Formulation and Characterization of Solid Dispersions of Glimepiride through Factorial Design: Formulation and characterization of glimepiride. Iranian Journal of Pharmaceutical Sciences 2011;7:7-16.

[32] Tejas P, Patel L, Adeshara S, Timir P, Sunil M, Tushar P. Dissolution enhancement of fenofibrate by solid dispersion technique. Journal of Current Pharma Research 2011;1:127.

[33] Shah TJ, Amin AF, Parikh JR, Parikh RH. Process optimization and characterization of poloxamer solid dispersions of a poorly water-soluble drug. Aaps Pharmscitech 2007;8:E18-E24.

[34] Shivakumar H, Desai B, Deshmukh G. Design and optimization of diclofenac sodium controlled release solid dispersions

by response surface methodology. Indian journal of pharmaceutical sciences 2008;70:22.

[35] Jana S, Ali SA, Nayak AK, Sen KK, Basu SK. Development of topical gel containing aceclofenac-crospovidone solid dispersion by "Quality by Design (QbD)" approach. Chemical Engineering Research and Design 2014;92:2095-105.

[36] Pathak D, Dahiya S, Pathak K. Solid dispersion of meloxicam: Factorially designed dosage form for geriatric population. Acta pharmaceutica 2008;58:99-110.