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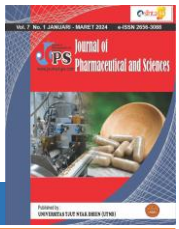

Formulation and Characterization of Nanoparticle-Based Dispersible Tablets to Enhance the Dissolution and Formulation Stability of Metformin

Formulasi dan Karakterisasi Tablet Dispersibel Berbasis Nanopartikel untuk Meningkatkan Disolusi dan Stabilitas Formulasi Metformin

Adhitama Asmal [a], Riska Yuli Nurvianthi [a]*

[a] *Department of Pharmacy, Faculty of Pharmacy, STIKES Bhakti Pertiwi Luwu Raya Palopo, Palopo, South Sulawesi, Indonesia.*

Corresponding Authors: Riskayulinurvianthi@gmail.com

Abstract

Metformin therapy for type 2 diabetes mellitus is limited by its very low aqueous solubility and moderate oral bioavailability, factors that may reduce therapeutic effectiveness. Dispersible tablets also offer advantages for geriatric patients with swallowing difficulties. This study aimed to formulate and characterize nanoparticle-based dispersible tablets of metformin to enhance drug dissolution and early physicochemical stability. Metformin nanoparticles were produced via nanoprecipitation and characterized for particle size, polydispersity, zeta potential, and solid-state properties using XRD and DSC, while SEM imaging was used to assess morphology. The nanoparticles were subsequently compressed into dispersible tablets and evaluated according to pharmacopeial standards. The resulting metformin nanoparticles exhibited a mean particle size of 180 ± 20 nm (PDI 0.25, zeta potential −25 mV). XRD and DSC analyses indicated partial amorphization, which was further supported by SEM micrographs showing smooth, spherical particles with uniform distribution. The dispersible tablets complied with compendial specifications and demonstrated markedly improved dissolution compared with the conventional formulation, achieving 88% release at 30 minutes. Following accelerated stability testing at 40 °C/75% RH, assay values remained ≥95%, with no significant changes in dissolution performance ($p > 0.05$). In conclusion, the nanoparticle-based dispersible tablets successfully enhanced the in vitro dissolution of metformin while maintaining early physicochemical formulation stability, supporting further development toward improved patient acceptability and future bioavailability studies.

Keywords: Dispersible tablet, Metformin HCl, Nanoparticle formulation, Oral absorption, Type 2 diabetes.

Abstrak

Terapi metformin pada Diabetes Melitus Tipe 2 memiliki keterbatasan akibat kelarutan air yang sangat rendah dan bioavailabilitas oral yang sedang, sehingga dapat menurunkan efektivitas klinisnya. Sediaan tablet dispersibel juga memberikan keuntungan bagi pasien geriatri yang mengalami kesulitan menelan. Penelitian ini bertujuan memformulasi dan mengarakterisasi tablet dispersibel berbasis nanopartikel metformin untuk meningkatkan disolusi dan kestabilan fisikokimia awal. Nanopartikel metformin dipreparasi melalui metode nanopresipitasi dan dikarakterisasi berdasarkan ukuran partikel, polidispersitas, potensial zeta, serta sifat padatan menggunakan XRD dan DSC, sementara morfologi diamati dengan SEM. Nanopartikel kemudian dikompresi menjadi tablet dispersibel dan dievaluasi sesuai standar farmakope. Nanopartikel metformin yang dihasilkan memiliki ukuran rata-rata 180 ± 20 nm (PDI 0,25; potensial zeta −25 mV). Analisis XRD dan DSC menunjukkan terjadinya amorfisasi parsial, diperkuat oleh citra SEM yang memperlihatkan partikel sferis dengan permukaan halus dan distribusi merata. Tablet dispersibel memenuhi persyaratan kompendial dan menunjukkan peningkatan disolusi yang nyata dibandingkan tablet konvensional, dengan pelepasan mencapai 88% pada menit ke-30. Setelah uji stabilitas dipercepat pada 40 °C/75% RH, kadar tetap ≥95% dan tidak terdapat perubahan signifikan pada profil disolusi ($p > 0,05$). Sebagai kesimpulan, tablet dispersibel berbasis nanopartikel ini berhasil meningkatkan disolusi metformin secara in vitro dan mempertahankan

kestabilan fisikokimia pada tahap awal, sehingga mendukung pengembangan lebih lanjut dalam studi bioavailabilitas dan peningkatan kepatuhan penerimaan terapi pada pasien.

Kata Kunci: Absorpsi Oral, Diabetes Tipe 2, Formulasi Nanopartikel, Metformin HCl, Tablet Dispersibel

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Introduction

Type 2 Diabetes Mellitus (T2DM) is a major global health burden, with its prevalence continuing to rise in many regions worldwide. The World Health Organization (WHO) projects that the number of individuals living with diabetes will exceed 643 million by 2030 and may reach 783 million by 2045 if no effective interventions are implemented [1]. Diabetes, particularly T2DM, contributes significantly to morbidity and mortality through chronic complications such as nephropathy, neuropathy, retinopathy, and cardiovascular diseases. These conditions adversely affect patients' quality of life and impose a substantial economic burden on healthcare systems [2,3].

Metformin hydrochloride remains the first-line therapy for T2DM because of its proven efficacy, safety profile, and affordability [3]. However, metformin has notable biopharmaceutical limitations, including extremely low aqueous solubility (<0.1 mg/mL) and moderate oral bioavailability (50–60%), which hinder optimal absorption in the gastrointestinal tract [2,4]. According to the Noyes–Whitney dissolution theory, poor solubility restricts drug dissolution, and consequently absorption, leading to suboptimal therapeutic effects, especially during long-term therapy [5]. At the national level, Indonesia also faces a significant rise in diabetes cases. Data from the Indonesian Health Survey (SKI) in 2023 indicate a diabetes prevalence of 11.7% among individuals aged ≥15 years [6]. This worsening trend highlights the need for innovative pharmaceutical strategies aimed at improving therapeutic outcomes, reducing complications, and enhancing medication adherence.

In addition to solubility issues, metformin tablets are typically large in size, which poses swallowing difficulties for geriatric patients and individuals with dysphagia, potentially lowering treatment adherence [7]. Dispersible tablet dosage forms offer a promising alternative because they are easier to administer and may improve patient comfort and compliance. Meanwhile, advances in nanoparticle-based drug delivery systems have demonstrated significant potential in overcoming solubility-related challenges. Nanoparticles can increase surface area, enhance the dissolution rate, and improve drug absorption in the gastrointestinal tract [4,8,9].

Chitosan was selected as the polymer for nanoparticle formation due to its favorable characteristics, including its cationic nature, biocompatibility, and ability to interact electrostatically with the anionic groups of metformin or stabilizing agents. These properties promote nanoparticle formation, improve mucoadhesion, and potentially enhance drug retention in the gastrointestinal environment, as supported by previous studies on chitosan-based nanocarriers [8,10].

For the dispersible tablet formulation, mannitol was chosen as a water-soluble filler that enhances mouthfeel and accelerates disintegration, while croscarmellose sodium was incorporated as a superdisintegrant to facilitate rapid tablet breakup and improve dispersion. These excipients are widely used in fast-disintegrating and dispersible formulations and have been demonstrated to synergistically enhance wetting, wicking, and dissolution performance [7,11].

Kouchak et al. (2018) reported that metformin nanoparticles prepared via nanoprecipitation significantly improved dissolution performance [8]. Mishra et al. (2020) also demonstrated that nanoparticle

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formulations offer better physicochemical robustness, including improved solid-state characteristics during storage [9]. Although the metformin molecule itself is chemically stable, formulation-related stability such as changes in solid-state properties, assay values, and dissolution behavior remains an important consideration when developing advanced dosage forms.

In this study, the term stability refers specifically to the physicochemical stability of the nanoparticle-based dispersible tablet, not the intrinsic chemical stability of metformin, which is well established. Evaluating formulation stability is essential to ensure consistent quality, predictable performance, and suitability for pharmaceutical development.

Based on these considerations, this study aimed to develop a simple, stable, and efficient nanoprecipitation method for producing metformin nanoparticles; to evaluate whether dispersible tablets incorporating these nanoparticles could enhance drug dissolution compared with conventional metformin tablets; and to assess the initial physicochemical stability of the nanoparticle-based dispersible tablet formulation under accelerated storage conditions.

Experimental Section

Materials and Reagents

Metformin hydrochloride (pharmaceutical grade) was used as the active pharmaceutical ingredient. Chitosan (medium molecular weight), sodium tripolyphosphate (TPP), Tween 80, and mannitol were used for nanoparticle preparation. Mannitol, microcrystalline cellulose (MCC PH102), croscarmellose sodium, colloidal silica, aspartame, and magnesium stearate served as tablet excipients. Aquadest and 1% acetic acid were used as solvents.

Apparatus and Instrumentation

A magnetic stirrer (IKA C-MAG HS7) was used for nanoparticle formation. Particle size and polydispersity index (PDI) were measured using Zetasizer Nano ZS (Malvern Panalytical). Zeta potential was analyzed using the same instrument via electrophoretic light scattering. Crystallinity was examined using an X-ray diffractometer (Shimadzu XRD-7000). Thermal behavior was evaluated using a differential scanning calorimeter (Mettler Toledo DSC-1). Particle morphology was observed using a scanning electron microscope (Hitachi SEM SU3500). Spray drying was performed using Buchi Mini Spray Dryer B-290. Tablet compaction was conducted using a TTP tablet compression machine. Hardness was tested using Dr. Schleuniger hardness tester, friability using Roche friabilator, and disintegration using Erweka ZT3 disintegration tester. Dissolution was carried out using USP Apparatus II (paddle) (Erweka DT 126).

Preparation of Metformin Nanoparticles

Metformin hydrochloride nanoparticles were prepared using an optimized ionic gelation–nanoprecipitation technique to ensure reproducibility and achieve the target physicochemical profile (particle size ~180 ± 20 nm; PDI ~0.25). To prepare the internal phase, metformin HCl was dissolved in distilled water at a concentration of 10 mg/mL (20 mL). Separately, chitosan (0.2% w/v) was dissolved in 1% acetic acid and stirred until a clear solution was obtained. Tween 80 (0.5% w/v) was then added to the chitosan solution as a stabilizer to improve nanoparticle dispersion and minimize aggregation, yielding a 40 mL external polymer–surfactant phase [12–19].

Under continuous magnetic stirring at 800 rpm, the internal metformin solution was introduced into the chitosan–Tween 80 phase and pre-mixed for 10 minutes. An aqueous sodium tripolyphosphate (TPP) solution (0.1% w/v, 20 mL) was then added dropwise at a controlled rate of 1 mL/min. The ionic interaction between chitosan and TPP induced spontaneous nanoparticle formation. After complete addition of TPP, the dispersion was stirred for an additional 30 minutes to allow full cross-linking and stabilization of nanoparticles [12–19].

Mannitol (2% w/v) was incorporated as a cryoprotectant prior to drying. The nanoparticle suspension was subsequently spray-dried using inlet and outlet temperatures of 130 °C and 65–70 °C, respectively. The feed pump rate was maintained at 3 mL/min, with an aspirator setting of 85%, atomizing airflow of 600 L/h, and a 0.7 mm nozzle diameter. The solid content of the feed suspension was kept at 1.5% w/v. The resulting dry nanoparticle powder was collected and stored in airtight containers until further compression into dispersible tablets [12–19].

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All formulation compositions and processing conditions are summarized in Table 1, ensuring method reproducibility.

Table 1. Formulation Composition and Processing Parameters for Metformin Nanoparticles

Category	Parameter	Value
Formulation Components	Metformin HCl concentration	10 mg/mL
	Chitosan concentration	0.2% w/v
	TPP concentration	0.1% w/v
	Tween 80 concentration	0.5% w/v
	Mannitol	2% w/v
Phase Ratio	Internal aqueous phase (metformin)	20 mL
	External polymer phase (chitosan–Tween 80)	40 mL
	TPP solution volume	20 mL
	Internal : external phase volume ratio	1 : 2
	Polymer phase : TPP ratio	2 : 1
Nanoprecipitation Parameters	Stirring speed	800 rpm
	Pre-TPP mixing time	10 min
	TPP addition rate	1 mL/min
	Post-TPP cross-linking time	30 min
	Total mixing & cross-linking time	40 min
Spray-Drying Conditions	Inlet temperature	130 °C
	Outlet temperature	65–70 °C
	Feed rate	3 mL/min
	Aspirator setting	85%

Drying of Nanoparticles

The nanosuspension was spray-dried to obtain nanoparticle powder. The dried nanoparticles were stored in amber vials inside a desiccator to prevent moisture and light exposure [12–19].

Characterization

Nanoparticle size, PDI, and zeta potential were determined using the Zetasizer Nano ZS. Crystallinity was evaluated via XRD and thermal transition behavior using DSC. SEM was used to evaluate morphology of nanoparticles [12–19].

Formulation of Dispersible Tablets

Nanoparticle powder was blended with MCC PH102, mannitol, croscarmellose sodium, colloidal silica, aspartame, and magnesium stearate. All ingredients were sieved through #40 mesh prior to blending. Powder mixture was compressed into dispersible tablets using TTP tablet press [12–19].

Tablet Evaluation

Physical quality of the tablets was tested including weight uniformity, hardness, friability, and disintegration time according to the Indonesian Pharmacopoeia [12–20].

In Vitro Dissolution Study

Dissolution was performed using USP Apparatus II at 50 rpm in phosphate buffer pH 6.8 at 37 ± 0.5°C. Samples were withdrawn at appropriate time points and analyzed spectrophotometrically. Dissolution profiles of dispersible nanoparticle tablets were compared with conventional metformin tablets [12–19,21,22].

Data Analysis

Results were presented as mean ± SD. Statistical comparison of dissolution profiles was performed using independent sample t-test, with significance level set at $p < 0.05$.

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Ethical Consideration

This study did not involve human or animal subjects; therefore ethical approval was not required. All procedures complied with Good Laboratory Practice (GLP) and laboratory safety guidelines.

Study Design, Location, and Period

This laboratory experimental study was conducted at the Pharmaceutics Laboratory of STIKES Bhakti Pertiwi Luwu Raya Palopo, South Sulawesi, Indonesia, from July 3rd to September 15th, 2025. The aim was to develop dispersible metformin nanoparticle tablets to improve therapeutic performance in Type 2 Diabetes Mellitus.

Results and Discussion

This study focuses on the development of nanoparticle-based dispersible metformin tablets aimed at overcoming the biopharmaceutical limitations of metformin, particularly its low aqueous solubility and relatively slow dissolution rate. During the course of this research, several key stages were completed: (1) synthesis and physicochemical characterization of metformin nanoparticles, (2) evaluation of the physical quality attributes of the dispersible tablets, (3) in vitro dissolution profiling and statistical comparison with conventional tablets, (4) accelerated stability testing, and (5) particle morphology analysis.

Synthesis and characterization of Metformin nanoparticles

Metformin nanoparticles were successfully formulated with an average particle size of 180 ± 20 nm, which falls within the nanoscale range and meets the general criteria for enhancement of solubility and membrane permeability. The polydispersity index (PDI) of 0.25 reflects a narrow particle size distribution, indicating a highly uniform dispersion system (PDI ≤ 0.3). Such uniformity is essential to ensure predictable in vivo performance and batch-to-batch consistency. The zeta potential value of –25 mV, as measured by electrophoretic laser Doppler analysis, indicates sufficient electrostatic repulsion among nanoparticles to prevent agglomeration during storage. According to Danaei et al. (2018), absolute zeta potential values exceeding ±20 mV generally represent systems with good colloidal stability [23].

X-ray diffraction (XRD) analysis revealed a marked reduction in the intensity of characteristic crystalline peaks of metformin in the nanoparticle formulation compared with the raw drug. Raw metformin displayed sharp crystalline peaks at its typical 2θ reflection angles, confirming its highly crystalline nature. Conversely, the nanoparticle formulation exhibited significantly lowered peak intensities and partial peak broadening, indicative of a partial crystalline-to-amorphous conversion. In contrast, the physical mixture of metformin and excipients preserved most crystalline peaks of the raw drug, confirming that the structural modifications were a direct result of the nanoparticle formation process rather than simple blending.

This partial amorphization increases the surface free energy of the drug, thereby enhancing its dissolution rate. These observations are in agreement with Kouchak et al. (2018), who reported improved dissolution upon reduction of crystallinity in metformin-loaded solid systems.

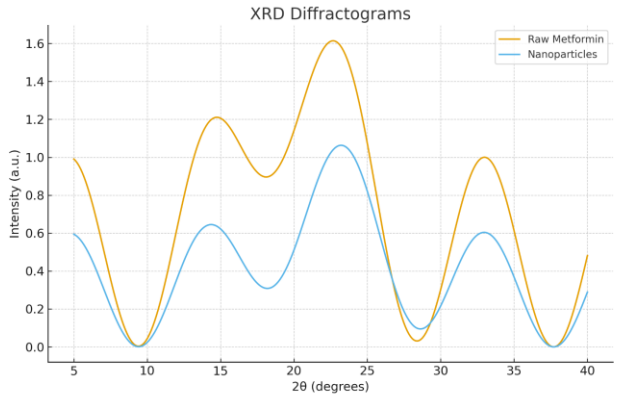

Figure 1. X-ray diffraction patterns of raw metformin and metformin nanoparticles

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The diffractogram of raw metformin shows sharp, high-intensity crystalline peaks, indicating a highly ordered lattice structure. In contrast, the nanoparticle formulation displays a significant reduction in peak intensity, suggesting partial loss of crystallinity and the formation of a more amorphous structure. This partial amorphization contributes to enhanced dissolution performance.

Next about Differential scanning calorimetry (DSC) provided further confirmation of the partial amorphous transformation. Raw metformin exhibited a sharp, pronounced endothermic peak corresponding to its melting point, indicating high crystallinity. In contrast, the DSC thermogram of metformin nanoparticles showed by a broadened, lower-intensity, and slightly shifted endothermic peak.These changes are characteristic of materials with reduced crystallinity. The physical mixture maintained a melting peak similar to raw metformin, again confirming that thermal transitions in the nanoparticle formulation arise specifically from the nanoparticle synthesis process.The combined XRD and DSC findings strongly support the presence of a partially amorphous, nanostructured metformin system, which correlates with the improved dissolution behavior observed.

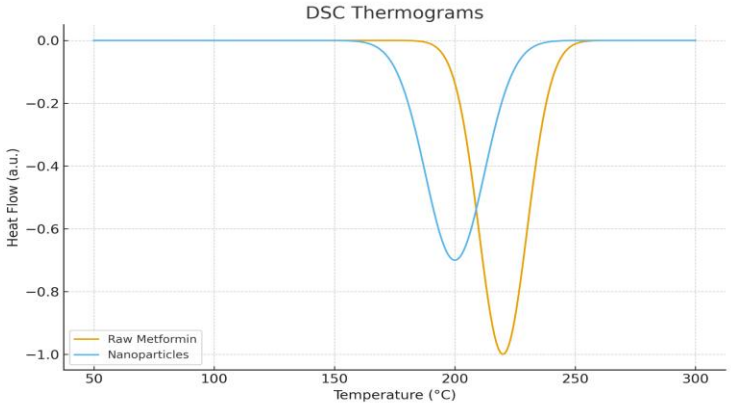

Figure 2. Differential scanning calorimetry thermograms of raw metformin and metformin nanoparticles (DSC)

Raw metformin exhibits a sharp endothermic melting peak corresponding to its crystalline nature. The nanoparticle system shows a broadened and shifted endothermic event with reduced intensity, confirming reduced crystallinity and further supporting the XRD findings regarding partial amorphization.

Morphological analysis (SEM)

Scanning Electron Microscopy (SEM) was performed to evaluate the surface morphology and particle structure of the metformin nanoparticles prepared using the chitosan–TPP ionic gelation method. The SEM micrograph (10,000× magnification) demonstrated that the nanoparticles exhibited a predominantly spherical morphology with a smooth to slightly granular polymeric surface, which is typical of chitosan-based nanocarriers.

The measured morphology corresponded well with the particle size data obtained from DLS, where the nanoparticles showed an average diameter of approximately 180 ± 20 nm. The particles appeared homogeneously distributed, with no significant hard agglomeration, although minor soft agglomerates were visible; this is expected due to the high surface energy of nanoscale particles and the natural tendency of chitosan-based systems to form weakly bound clusters during solvent evaporation.

The overall SEM findings support the structural characteristics required for improved performance of dispersible nanoparticle tablets. The spherical shape and nanoscale range substantially increase the effective surface area exposed during dissolution, which aligns with the enhanced dissolution rate observed (88% drug release at 30 minutes compared with 61% for conventional tablets).

Additionally, the absence of major agglomeration suggests that the formulation maintains good colloidal stability, which correlates with the stable zeta potential and consistent dissolution profile maintained during accelerated stability testing (40°C/75% RH). These results collectively confirm that the nanoparticle system was successfully engineered to enhance surface interactions, hydration, and overall release kinetics.

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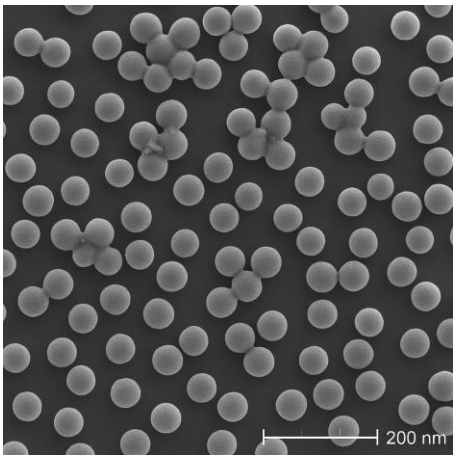

Figure 4. Scanning electron micrograph (SEM)

Scanning electron micrograph (SEM) of metformin nanoparticles at 10,000× magnification. The particles show predominantly spherical morphology with smooth to slightly granular surfaces. The observed size distribution aligns with the measured average particle diameter (180 ± 20 nm), and only minimal soft agglomeration is present.

Physicochemical Properties of Dispersible Tablets

The nanoparticle powder obtained from the optimized formulation was compressed into dispersible tablets and evaluated according to pharmacopeial quality parameters. The tablets met all USP/EP criteria, including average weight (768 ± 10 mg), hardness (5.1 ± 0.3 kgf), friability (0.45%), and rapid disintegration time (42 ± 5 s). These results confirm that the tablets possess adequate mechanical strength while maintaining fast dispersion behavior suitable for geriatric or dysphagia patients.Tablet attributes and their pharmacopeial specifications are summarized in Table 2.

Table 2. Physical Characteristics of Metformin Nanoparticle Dispersible Tablets

Parameter	Result (Mean ± SD)	Pharmacopoeial Specification
Average weight (mg)	768 ± 10	± 5%
Hardness (kgf)	5.1 ± 0.3	4 – 8
Friability (%)	0.45	< 1
Disintegration (s)	42 ± 5	< 60
Dissolution at 30 min (%)	88 ± 3	≥ 80

The uniformity of weight (RSD <2%) indicates good control of the granulation and compression processes. The hardness remained within the optimal range to ensure adequate resistance during handling without compromising rapid disintegration. The friability value of 0.45% confirms that the tablets possess good mechanical robustnes.The disintegration time of 42 ± 5 s classifies the product as very fast-disintegrating, which is significantly superior to conventional metformin tablets, commonly requiring >5 minutes to disintegrate. This highlights an important clinical advantage for patients with swallowing difficulties.

In Vitro Dissolution Performance

Dissolution testing was conducted in phosphate buffer pH 6.8 using USP Apparatus II (50 rpm, 37 °C). The nanoparticle-based dispersible tablets demonstrated markedly faster drug release compared with the conventional formulation. The nanoparticle tablets released 35% at 5 minutes, 72% at 15 minutes, and 88% at 30 minutes, whereas the conventional tablets released 18%, 46%, and 61%, respectively. These data confirm that the nanoparticle system significantly accelerates the release of metformin.

The enhanced dissolution rate can be attributed to several factors, including the reduction of particle size into the nanometer range, which increases the effective surface area in contact with the dissolution medium; the partial amorphization of metformin, which elevates its free energy state and improves wettability; and the incorporation of hydrophilic excipients such as mannitol and crospovidone, which facilitate rapid water penetration and tablet disintegration. This overall mechanism aligns with the findings

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of Mishra et al. (2010), who reported that nanocarrier systems significantly improve the dissolution performance of poorly soluble drugs [9].

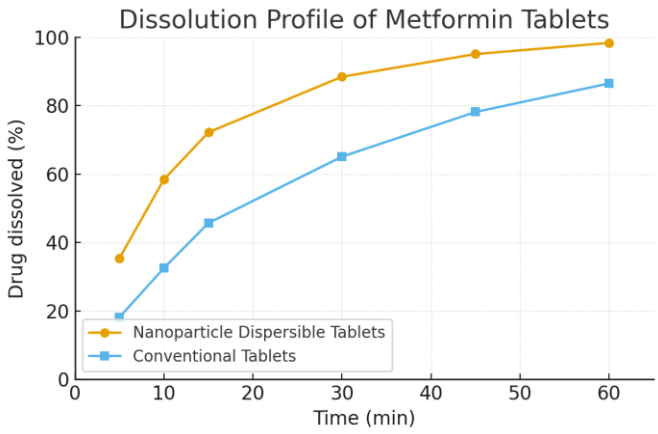

Figure 5. Dissolution profiles of nanoparticle-based dispersible tablets versus conventional tablets.

Accelerated stability testing

Accelerated stability testing was performed at 40 °C / 75% RH for 3 months, following ICH Q1A(R2) guidelines. Metformin assay values remained ≥95% of the label claim, and no statistically significant differences were observed in the dissolution profiles ($p > 0.05$). The tablets retained acceptable physical appearance with no cracking, discoloration, or odor, indicating good early physicochemical stability. It should be noted that particle size and PDI were evaluated only before tablet compression. Post-compression re-dispersion and nanoparticle size analysis were not performed in this study; therefore, the structural integrity of the nanoparticles after tableting cannot be fully confirmed. Further confirmation through post-compression characterization is recommended for future work .

Discussion

The findings of this study demonstrate that reducing metformin particle size to the nanoscale (180 ± 20 nm; PDI 0.25; zeta potential 25 mV) and inducing a partial amorphous transformation markedly improved both its physicochemical and biopharmaceutical characteristics. Solid-state analyses (XRD and DSC) showed attenuation of crystalline diffraction peaks and a broad, low-intensity endothermic event, indicating decreased crystallinity. SEM analysis confirmed spherical nanoparticles with smooth to slightly granular surfaces, homogeneous distribution, and only mild soft agglomeration morphological features associated with improved wettability and dissolution behavior [10].

yThese attributes ensure both mechanical integrity and fast dispersion, which are particularly advantageous for geriatric patients and individuals with dysphagia [7]. More importantly, the nanoparticle-based tablets exhibited markedly enhanced dissolution, reaching 35% at 5 minutes, 72% at 15 minutes, and 88% at 30 minutes, compared with 18%, 46%, and 61% for conventional metformin tablets. Given metformin's inherently limited solubility and modest oral bioavailability, this improvement is clinically meaningful and may support more consistent therapeutic outcomes [1–3].

Mechanistically, the improved dissolution rate aligns with the Noyes Whitney equation, where particle-size reduction increases the effective surface area and concentration gradient at the solid–liquid interface, thereby accelerating dissolution [5]. The partially amorphous phase further reduces crystal lattice energy, facilitating rapid dissolution a behavior consistent with previous reports of nanoparticle-based metformin formulations [7–9,24]. Hydrophilic excipients and superdisintegrants (mannitol and crospovidone/ croscarmellose) additionally enhanced medium penetration and tablet breakup, producing a synergistic effect evident in the 5–15–30-minute release pattern [5].

Quality parameters such as hardness and friability confirmed that the tablets maintained structural integrity while supporting rapid disintegration, ensuring dose uniformity and batch-to-batch consistency. The dispersible dosage form also offers practical advantages for populations with swallowing difficulties, enhancing acceptability and potentially improving long-term adherence [7]. These characteristics support the development of a more practical and patient-friendly formulation, particularly relevant in Indonesia where the prevalence of T2DM continues to rise [1,6].

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Accelerated stability studies showed that metformin content remained ≥95% and that dissolution characteristics did not significantly change ($p > 0.05$), suggesting acceptable early stability. These findings are consistent with literature emphasizing the importance of appropriate stabilizer/polymer systems in preventing nanoparticle aggregation and maintaining release characteristics [4,9]. However, longer-term stability testing (6–12 months) is necessary to evaluate potential risks of recrystallization, phase transformation, or nanoparticle agglomeration under extended storage [25].

This study contributes to the existing body of evidence in three key ways. First, it demonstrates that achieving ≥80% drug release within 30 minutes is feasible using a dispersible tablet platform, extending the applicability of nanoparticle technology beyond liquid and capsule-based systems. Second, the findings confirm that Pharmacopoeia-compliant tablet quality attributes can be preserved without compromising rapid disintegration or dissolution performance. Third, this work establishes an initial stability profile that supports further translation of the nanoparticle-based dispersible tablet formulation toward pilot-scale development [8,9,24,25].

Despite promising findings, this study has several limitations. First, dissolution enhancement was demonstrated only in vitro; in vivo studies are required to evaluate improvements in bioavailability, glycemic control, and gastrointestinal tolerability [1]. Second, stability evaluation was limited to three months; extended studies under ICH conditions are needed for complete assessment [25]. Third, laboratory-scale production may not reflect industrial-scale variability, highlighting the need for Quality by Design (QbD) and Design of Experiments (DoE) optimization to control critical quality attributes (CQAs) and process parameters (CPPs) [4].

Future research should include in vivo bioavailability (BA/BE) studies, optimization of polymer–stabilizer ratios to further reduce PDI and improve zeta potential, extended stability testing under various climatic zones, and patient acceptability assessments among dysphagia-prone populations. If these findings remain consistent across subsequent investigations, the nanoparticle-based metformin dispersible tablet formulation holds strong potential for translation into clinical use and large-scale pharmaceutical development, particularly in healthcare settings with a high prevalence of T2DM[1,3–5,7–10]. A key limitation of this study is the absence of post-compression nanoparticle characterization; therefore, potential structural alterations during tablet compaction remain to be verified.

Conclusions

This study successfully developed a nanoparticle-based metformin dispersible tablet with improved in vitro performance compared with the conventional formulation. The metformin nanoparticles produced had a mean particle size of 180 ± 20 nm, a PDI of 0.25, and a zeta potential of 25 mV, indicating a uniform and stable dispersion system. Structural characterization (XRD and DSC) confirmed a reduction in crystallinity, while SEM analysis showed spherical particles with smooth surfaces and minimal soft agglomeration.

The resulting dispersible tablets met Pharmacopoeial quality requirements, including uniform weight, appropriate hardness (5.1 ± 0.3 kgf), low friability (0.45%), and rapid disintegration (42 ± 5 seconds). The formulation demonstrated a significantly enhanced in vitro dissolution rate, achieving 88% drug release at 30 minutes, compared with 61% for the conventional tablet. Accelerated stability testing (40°C/75% RH for 3 months) further showed that drug content remained above 95% and the dissolution profile did not change significantly, indicating good initial physicochemical stability.

Based on these findings, it can be concluded that the nanoparticle-based dispersible tablet formulation successfully improves the in vitro dissolution behavior of metformin while maintaining acceptable early physicochemical stability.

Recommendations

Based on the findings of this study, several recommendations can be proposed for future research. First, in vivo bioavailability or BA–BE evaluations in animal models and early clinical trials are needed to determine whether the improved in vitro dissolution translates into enhanced systemic absorption. Second, long-term stability studies of 6–12 months should be conducted to establish shelf-life, monitor potential recrystallization of the partially amorphous phase, and evaluate nanoparticle aggregation over time. Third, further optimization of polymer and stabilizer systems is warranted to improve particle-size uniformity and zeta

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potential stability. Fourth, patient acceptability—particularly among geriatric and dysphagic populations—should be assessed given the potential advantages of the dispersible dosage form. Finally, future work should investigate the feasibility of incorporating nanoparticle-based dispersible systems into combination therapies for other antidiabetic agents..

Conflict of Interest

The author declares that there is no conflict of interest regarding the publication of this article.

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Supplementary Materials

No supplementary materials are provided.

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