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Comparative Study of Hydrophilic Polymer-Based Solid Dispersions of Griseofulvin Incorporating HPMC E6, PVP K30, and Soluplus

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Abstract:

Solid dispersion approach with hydrophilic carriers is one of the most effective methods for improving the solubility, dissolution profile, and ultimately the oral bioavailability of poorly water-soluble drugs. In this study, Griseofulvin (GF), a BCS class II drug with poor solubility and a strong tendency to recrystallize, was formulated using hydrophilic polymers (HPMC E6, Polyvinylpyrrolidone K30 (PVP), and Soluplus) at drug to polymer ratios of 1:2, 1:3, and 1:4 using the solvent evaporation method.
An experimental polymer-selection approach was employed to determine the optimal carrier type and ratio, wherein drug–polymer compatibility studies (FTIR), solid-state characterization (PXRD), saturated solubility studies, and dissolution behavior were systematically evaluated. The 1:3 HPMC formula demonstrated the most favorable performance, showing superior saturated solubility, enhanced dissolution rate, and good stability at harsh conditions across 90 days. This formulation represents a promising approach for improving the biopharmaceutical properties of Griseofulvin.

Keywords: Amorphous, crystalline, Griseofulvin, Hydrophilic polymers, Solid dispersion.

تصميم وتقييم المبعثرات الصلبة المعتمدة على البوليمرات المحبة للماء لدواء غريزيوفولفين

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الخلاصة:

تُعد تقنية التشتت الصلب باستخدام الحوامل المحبة للماء واحدة من أكثر الاستراتيجيات فاعلية لتحسين الذوبانية ومعدل الانحلال، وبالتالي تعزيز التوافر الحيوي الفموي للأدوية ضعيفة الذوبان في الماء. في هذه الدراسة، تم استخدام الغريزيوفولفين وهو دواء من الفئة الثانية حسب نظام التصنيف الحيوي الدوائي ويتميز بضعف الذوبانية وقابلية عالية لإعادة التبلور، حيث جرى تحضيره على هيئة تشتتات صلبة باستخدام ثلاثة بوليمرات محبة للماء هي هيدروكسي بروبل مثيل سيليلوز وبولي فينيل بيرولدين وسولوبلس وبنسب دواء إلى بوليمر بلغت 1:2، و1:3، و1:4، وذلك باستخدام طريقة تبخير المذيب.
تم اعتماد نهج تجريبي لاختيار البوليمر الأنسب ونسبته المثلى، حيث جرى التقييم المنهجي لتوافق الدواء مع البوليمر باستخدام مطيافية الأشعة تحت الحمراء ودراسة الحالة الصلبة باستخدام حيود الأشعة السينية بالإضافة إلى دراسات الذوبانية المشبعة وسلوك الانحلال. أظهرت صيغة التشتت الصلب المحضّرة باستخدام بوليمر هيدروكسي بروبل مثيل سيليلوز بنسبة 1:3 أفضل أداء، إذ حققت

ذوبانية مشبعة أعلى، ومعدل انحلال محسّن، ومحتوى مرتفعًا من الطور غير المتبلور. وتمثل هذه الصيغة نهجًا واعدًا لتحسين الخصائص الحيوية الدوائية للغريزيوفولفين .

الكلمات المفتاحية: غير متبلور، متبلور، غريزيوفولفين، التشتت الصلب، البوليمرات المحبة للماء

Introduction

Over the past few decades, a significant proportion of new chemical entities (NCEs) emerging from pharmaceutical research have exhibited poor aqueous solubility, posing significant challenges in developing effective oral dosage forms (1). The Biopharmaceutics Classification System (BCS) offers a useful scientific framework for understanding solubility–permeability limitations and guiding formulation choices for poorly water-soluble compounds (2). Griseofulvin (GF),is a BCS class II antifungal agent with poor water solubility and variable oral absorption, which can fluctuate with food intake. (3).It is non-ionizable drug that is characterized by pH independence and tends to rapidly recrystallize in the solid form(4, 5). Although it is considered a first-line treatment in tinea capitis fungal infections, its poor water solubility impairs its oral drug absorption could lead to high plasmatic fluctuations according to patient food intake (3). Numerous formulation strategies have been explored to improve its dissolution rate. Among these , solid dispersion (SD) has gained prominence due to its various processing and excipient alternatives, enabling greater flexibility in formulating oral delivery systems (5-8). Chiou and Riegelman stated that SD is “the solid-state dispersion of one or more active substances in an inert carrier or matrix generated by the fusion, solvent evaporation, or melting-solvent process” (9). The carrier (matrix) enhances wetting, increases dissolution rate, and facilitates the uniform dispersion of drug molecules within the carrier matrix. The selection of an appropriate carrier is therefore one of the most decisive factors in successful formulation design, as its properties (including hydrophilicity, molecular weight, viscosity, glass transition temperature, and intermolecular interaction) potentially influence drug solubility, dissolution behavior, and physical stability (10).

In this study, the effect of polymer amount and type on the dissolution rate and maintaining the supersaturated state in the GI-tract to have adequate driving force for absorption.

Material and methods

Griseofulvin was obtained from Shanghai UCHEM Inc., China. PVP-K30 and Soluplus® were sourced from BASF (Germany). HPMC- E6 was purchased from Macklin (China). Methanol and acetone were obtained from Himedia (India), while ethanol was supplied by Honeywell (Germany).

Solid dispersion preparation

GF solid dispersion prepared by the solvent evaporation method using three different polymers which are HPMC E6, PVP k30, and Soluplus, each at varying drug to polymer ratios 1:2, 1:3, and 1:4 as shown in Table 1. The drug and polymer dissolve in organic solvents or cosolvents, selected based on drug and polymer solubility. See Table 1. The solution was evaporated by Buchi Rotavapor Interface (I-300 Pro, Germany) under reduced pressure at 40- 70°C. The dried material was crushed and kept in an oven at 40°C for two hours to remove any trace solvent, then sieved using a stainless-steel laboratory sieve (250 µm) to achieve a uniform particle size. The SD formulations were stored in desiccators for characterization (11).

Table (1): SD formulas composition

Formula	HPMC (mg)	PVP (mg)	Soluplus (mg)	Solvent type	Drug :Polymer ratio
SD.H2	250	---	---	60% ethanol	1:2
SD.P2	---	250	---	Methanol	1:2
SD.S2	---	---	250	Acetone	1:2
SD.H3	375	---	---	60% ethanol	1:3
SD.P3	---	375	---	Methanol	1:3
SD.S3	---	---	375	Acetone	1:3
SD.H4	500	---	---	60% ethanol	1:4
SD.P4	---	500	---	Methanol	1:4
SD.S4	---	---	500	Acetone	1:4

All formulations contain 125mg of Griseofulvin

Preparation of the physical mixture: when needed, the physical mixture (PM) was created by mixing the proper proportions of drug and polymers by vortex mixer (3).

Evaluation of GF solid dispersion

Fourier Transforms Infrared spectroscopy (FTIR): The drug, PM, and SD formulations from Table 1 all undergo FTIR analysis. The materials were combined with KBr and pressed into thin disc before being analyzed. The scans were taken by (Shimadzu, Japan) between the 4000–400 cm−1 range (12).

Powder X-ray diffraction (PXRD) : The crystallinity GF, and SD formulations was studied using a Cu radiation-equipped PXRD system (Shimadzu, Japan) (=1.54060 A°) with 40 Kv and 30 mA setting. Samples were analyzed in the range (2-60) at a scanning speed of (5°/min) and (2θ) degree (13).

Selecting the dissolution media for preformulation study: The dissolution media were selected based on experimentation by studying the dissolution profile of GF in water containing SLS (0-0.54%w/v).

In vitro dissolution tests were conducted using USP apparatus 2 with a rotational speed of 50 rpm and a temperature at 37 °C and 1000 ml of the selected dissolution medium (14).

Saturated solubility: using the phase solubility method, the saturated solubility of pure GF and SD formulations was determined in two media, which were water at 25 °C and the above-selected media at 37 °C. The drug was put in an excess amount in 10 ml of the media and stirred for 72 h at 200 rpm. After that, the mixtures were centrifuged using a Hettich (Germany) centrifuge at 5,000 RPM for 30 min, filtered through a 0.22µm filter syringe, and then drug concentration was measured using a UV spectrophotometer at 292 nm (15).

***In vitro* dissolution study:** The same dissolution apparatus described above in was used with the selected dissolution media. (125 mg) of pure drug and equivalent amounts of the solid dispersion formulas, Table 1, were added. An aliquot of 5 ml was withdrawn through 22-µm filter discs at accurately determined time of 15 ,30, 45, 60 and 120 minutes. At each withdrawal, the same volume of dissolution media was compensated for to maintain the sink condition. GF concentration measured using UV visible spectrophotometer (16). Each test was performed in triplicate. Similarity factor (f2) was calculated utilizing Moore and Flanner approach to compare the formulations dissolution profile

$f2 = 50 \log \{[1 +(1/n) \Sigma_{t=1}{}^{n}(Rt - Tt)^{2}]^{-0.5}100\}$

Rt and Tt are the cumulative % dissolved reference and test product, respectively, at each of the selected (n) time points (17).

Further evaluation of the optimum formula

a. **Field emission-scanning electron microscopy (FESEM):** The surface morphology of the pure GF and optimum formula were investigated at different resolutions using a FESEM (Carl Zeiss Evo Ma10, UK). The samples were gold coated and examined (18)

b. **Stability study:** stability study was conducted on the optimum formula by storing it for 90 days under accelerated temperature and humidity conditions (40 °C and 75% RH) using an incubator–desiccator system. The 75% relative humidity was generated using a desiccator containing saturated sodium chloride solution (19). The evaluation of the formulations was studied using PXRD and DSC.

c. **Differential scanning calorimetry (DSC):** The optimum formula that was stored at harsh conditions, SD at zero time and pure GF were subjected to thermodynamic analysis using Shimadzu (Japan). 10 mg powder samples were placed in an aluminum-sealed pan and scanned at 5 °C/min heat rate from 30 °C to 250 °C in nitrogen atmosphere (12).

Statistical analysis

Statistical analysis was performed using GraphPad Prism version 13. Statistical significance was assessed using one and two-way analysis of variance (ANOVA), with a $p\text{-value} < 0.05$ considered statistically significant. The data were reported as mean ± standard deviation (SD).

Results and discussion

Drug -polymer compatibility study.

To study possible GF-polymers interactions, FTIR was applied (Figure 1 and Table 1). Pure Griseofulvin displays two characteristic peaks at 1705 and 1656 cm1, which are referred to the carbonyl group of benzofuran and cyclohexanone stretching, respectively, present in its structure (20). These are quite sensitive to hydrogen bond interaction between GF and stabilizers (21). The spectrum of the pure GF powder was comparable to that of the physical mixture, and 1:2 SD formulas as both exhibited the same characteristic peaks with slightly reduced intensity and without the appearance of additional peaks.

For the 1:3 and 1:4 drug-polymer ratio groups, the spectra of both PMs and pure GF did not differ significantly from one another. For the SD formulations, the characteristic peaks of griseofulvin (C=O at ~1705 cm^{-1} and 1656 cm^{-1}) showed a marked reduction in intensity along with significant broadening and minimal shift. This peak broadening, attenuation, and shifting suggest a structural rearrangement, reduced drug crystallinity, and are likely due to intermolecular interaction, such as hydrogen bonding in the case of HPMC and Soluplus-based formulations (22) or van der Waals in the case of PVP-based formulations (23).

No new functional group observed, which indicates that there was no chemical interaction between GF and polymers in SD formulations at all ratios. This result was anticipated, since the preparation of the solid dispersion was not to produce a new substance but to modify the physicochemical properties(24).

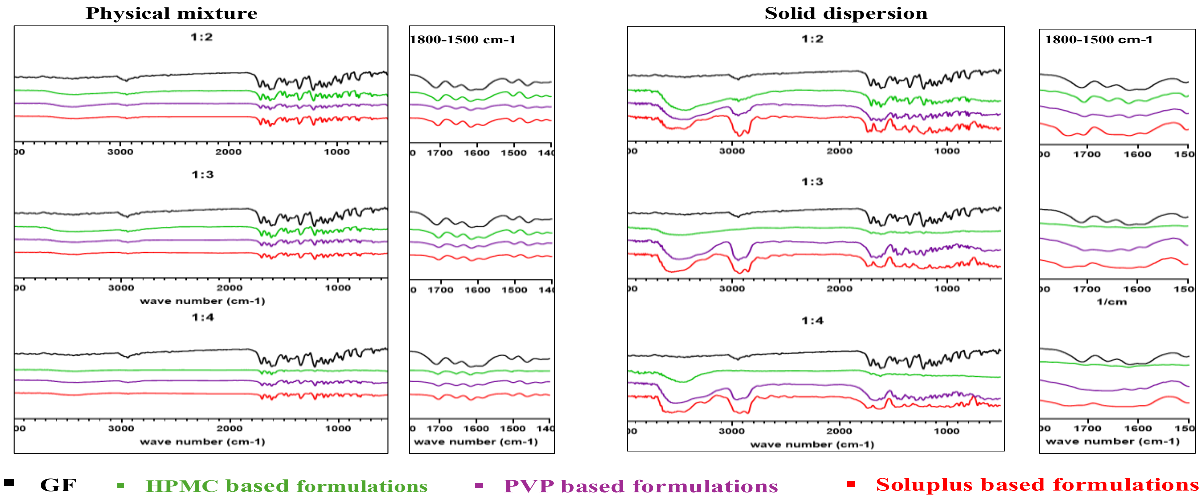


Figure (1): FTIR spectra of GF, PM (containing drug and polymer at the same ratio relative SD formulations), and the solid dispersion formulas with HPMC, PVP, and Soluplus in 1:2, 1:3, and 1:4 ratios

Table (2): the main observation of FTIR analysis of GF, and the solid dispersion formulations with HPMC, PVP, and Soluplus in 1:2, 1:3 and 1:4 ratios

Polymer	**Original GF C=O stretch; benzofuranone ring carbonyl**	**Observed Position**	**Original GF C=O stretch; cyclohexanone carbonyl**	**Observed Position**	**Original GF C=C stretch, aromatic and cyclic unsaturation**	**Observed Position**
HPMC 1:2	~1705 Strong and sharp	1707 Medium and sharp	1656 strong	Same	1616 Strong	1618 Medium
HPMC 1:3	~1708 Strong and sharp	1707 Medium and broadened	1656 strong	1658 Very small and barely there	1616 Strong	1616 Broad and weak
HPMC 1:4	~1708 Strong and sharp	1703 Weak	1656 strong	1651 and very weak	1616 Strong	1618 Broad and weak
PVP 1:2	~1708 Strong and sharp	1705 medium and broad	1656 strong	1656 medium and broad	1616 Strong	1616 medium
PVP 1:3	~1708 Strong and sharp	1710 medium and broad	1656 strong	Merged with 1616	1616 Strong	1614 medium and broad
PVP 1:4	~1708 Strong and sharp	Merged with 1656	1656 strong	1658 very broad	1616 Strong	1612 medium and broad

Soluplus 1:2	~1708 Strong and sharp	~1707 medium	1656 strong	1641 medium and broad	1616 Strong	1616 medium
Soluplus 1:3	~1708 Strong and sharp	~1703 broad	1656 strong	1656 broad	1616 Strong	1616 medium
Soluplus 1:4	~1708 Strong and sharp	Disappeared	1656 strong	Merged with 1616	1616 Strong	1618 medium and broad

Physical state study by powder X-ray diffraction

Powder X-ray diffraction was utilized to assess the physical state of Griseofulvin in the prepared solid dispersion. As illustrated in Figure 2, the pure drug exhibits intense and sharp diffraction peaks at 10.6°,13.8°,14.4°,16.4°,23.7°,26.5°and 28.4°, confirming its highly crystalline nature and validating its purity and integrity by aligning with the reported data (25). For Soluplus-based formulations, the analysis showed a linear, concentration-dependent decline in crystallinity with increasing polymer ratios, culminating in the complete disappearance of Bragg peaks at the 1:4 ratio, and the appearance of a halo pattern indicating full amorphization. This is probably due to Soluplus's amphiphilic nature, which forms H- bonds with GF. In the case of HPMC, the amorphization trend was non-linear.

The 1:3 HPMC formulation displayed a semi-amorphous profile due to moderate interaction potential with GF. Whereas the 1:4 formulation exhibited partial crystallization, as evidenced by the reappearance of diffraction peaks. This is attributed not to the polymer's insufficiency (as in 1:2) but rather to the preparation method. Using solvent evaporation, the formulation was prepared using a solvent mixture containing 60% ethanol. During the drying process, ethanol (more volatile) evaporates faster than water, which led to a sudden change in solvent composition, causing the system to enter a miscibility gap that led to liquid–liquid phase separation between the drug and polymer. As the drug concentration exceeded the solubility limit in the polymer-rich, predominantly aqueous phase, the excess drug crystallized rather than remaining dispersed (26). On the other hand, PVP also exhibited a concentration-dependent decrease in Griseofulvin crystallinity; however, complete amorphization was not achieved even at the 1:4 drug-to-polymer ratio. Although PVP is effective at inhibiting both nucleation and crystal growth by restricting molecular mobility, thereby delaying recrystallization, it does not form specific hydrogen bonds or strong interactions with GF(27). This absence of direct intermolecular interaction limits its capacity to thermodynamically stabilize the amorphous form. Consequently, a portion of the drug remains crystalline even at higher polymer concentrations, and the resulting system remains partially amorphous, increasing the risk of recrystallization over time or under stress conditions.

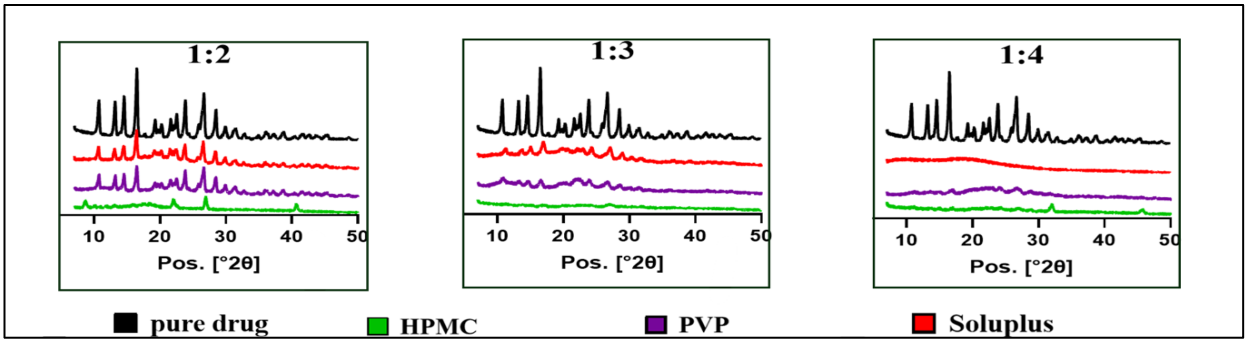


Figure (2): The PXRD analysis of the GF and SD formulations of different polymers (HPMC, PVP, and Soluplus) at different ratios

Selecting the dissolution media

Although 0.54% SLS is recommended by USP, preliminary results showed that it caused rapid and nearly complete dissolution (~80%) of pure GF within the first few minutes. SLS is above its CMC, limiting the ability to detect formulation improvements, “formulation masking” (28). To ensure a discriminative yet biorelevant medium, lower SLS concentrations were screened. Based on the findings, and aligned with the reports that demonstrate that there is linear trend between the increasing SLS concentration and GF solubility in the media (29),0, 0.1%,0.2% 0.3 and 0.5%SLS media were used to dissolve 125mg GF. As shown in Figure 3(A), 0.2% SLS was selected as the optimal medium, offering sufficient solubility while preserving sensitivity to formulation differences. This is consistent with the media used by Kumar et al (30).

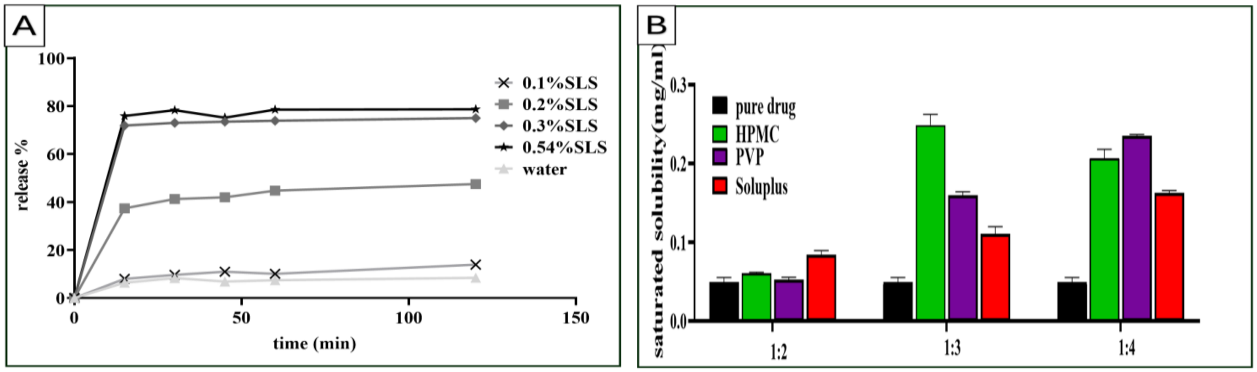


Figure (3): A. Optimizing the SLS concentration in the dissolution media at 37 °C, B. The saturated solubility of GF and SD formulations of different polymers (HPMC, PVP, and Soluplus) at different ratios in water at 25 °C

Saturated solubility study

The solubility of solid dispersion formulations of GF Table 1 was evaluated in distilled water at 25 °C and compared with that of the pure drug. As illustrated in Figure 3(B), both the polymer type and the drug-to-polymer ratio had a significant effect on GF solubility ($p < 0.05$). The pure drug exhibited very low solubility (0.05 mg/mL), which is consistent with previous reports (31). Incorporation of GF into SD formulations markedly enhanced its solubility at different levels due to the hydrophilic nature of the carriers, which facilitated improved drug–

water interaction and dissolution (32). A relatively limited enhancement in solubility was observed at the low polymer ratio (1:2 drug-to-polymer) with only 0.06, 0.05 ,0.08 mg/ml for HPMC, PVP, and Soluplus, respectively. These results~~,~~ accompanied by minimal changes in the physical state as confirmed by PRXD; results in formulations exclusion from further evaluation.

The 1:3 SD formulations of PVP and Soluplus showed significant ($p < 0.05$) improvements in solubility compared with the pure drug, with 0.16 mg/ml for PVP-based formulation and 0.11mg/ml for Soluplus-based one. However, the enhancement was lower than that achieved with HPMC polymer(0.25mg/ml). This was attributed to the relatively high crystalline content detected by XRPD, and thus these formulations were also eliminated from further studies.

SD. P4, SD.H3, SD.H4, and SD. S4 formulas show 0.235mg/ml,0.249mg/ml,0.206mg/ml, and 0.163mg/ml, respectively. The reason for that is HPMC has hydroxyl and hydroxypropyl groups (hydrophilic) and methyl and methoxy groups (hydrophobic) that impart amphiphilic character and surface properties (33). Increasing the HPMC ratio from 1:3 to 1:4 did not show an increase in solubility. This is explained by the high crystalline content of the 1:4 formulation (SD.H4). In addition, previous studies have shown that at higher polymer concentrations, the polymer matrix may conversely reduce the drug dissolution rate. This is attributed to the polymer ability to form a dense diffusion layer around the particles, acting as a barrier to mass transfer and consequently slows drug release from the matrix (34, 35). In contrast, for PVP-based SDs, drug crystallinity decreased remarkably at the 1:4 ratio, as confirmed by XRPD. The reduction in crystallinity is attributed to van der Waals forces and hydrophobic interactions between GF and PVP, which inhibit drug recrystallization and consequently enhance solubility (36).

Soluplus also produced a noticeable enhancement in GF solubility, particularly at higher polymer ratio (SD.S4). This improvement can be attributed to its amphiphilic graft copolymer structure, which enhances wettability and micellar solubilization in aqueous media, and to the complete amorphization of the formula, thereby increasing drug solubility (37).

Overall, all three polymers, when used in sufficient amounts, improved GF solubility by increasing wettability, expanding the solvent–drug interfacial area, and reducing drug crystallinity. These results are consistent with previous findings by Mohammed-Kadhum and Hameed, who reported significant improvements in the saturated solubility of furosemide when PVP and HPMC were used as SD carriers (18).

The best-performing formulations were subjected to dissolution testing, and accordingly, their saturated solubility was assessed in the dissolution medium (1000 ml of 0.2% w/v SLS aqueous solution)at 37 °C to verify sink conditions which means the media volume be three times larger than the volume required to form a saturated solution with the medicinal substance during the dissolution test (38), and the results demonstrated in Table 3.

Table (3): Saturated solubility of the candidate formulas

Formulations	**SD.H3**	**SD.H4**	**SD.P4**	**SD.S4**
Saturated solubility (mg/ml)	0.724	0.633	0.706	0.532

Factors affecting on the dissolution profile of GF formulation

Effect of polymer type:

Based on the saturated solubility screening, formulations SD.H3, SD.H4, SD.P4, and SD.S4 were advanced for dissolution evaluation. As observed in Figure 4(A), all the SDs achieved a higher release percentage at 120 minutes compared to the pure drug, but the initial release rate differed. At 15 min, the Soluplus-based formula (SD. S4) showed the highest burst release (~64%)_, followed by SD.H3 (~60%) and SD.H4 (~58%). For SD. S4, % dissolved rose to ~66% and then gradually declined to ~55% at 120 min. It is attributed to that upon exposure to the dissolution medium, the highly water-soluble stabilizer dissolves rapidly, leaving behind dispersed drug particles in high-energy state (amorphous). This results in transient supersaturation and a peak drug concentration (burst release). However, the system gradually transforms to a thermodynamically more stable crystalline form, which may account for the slight decline observed. This behavior is consistent with a spring-and-parachute profile, indicating that supersaturation was not fully sustained despite the amorphous state that results in drug precipitation (8).

In contrast, the HPMC-based formulations (SD.H3, SD.H4) release percentage continued to increase, reaching ~80% and ~75% by 120 min, respectively. This agrees with previous observations in curcumin amorphous solid dispersions (23).The faster dissolution of HPMC-containing SDs is attributed to HPMC's ability to inhibit nucleation and crystal growth, thereby maintaining drug in a dissolved state and limiting recrystallization

Interestingly, although the PVP-based formulation (SD.P4) displayed high saturated solubility, it failed to achieve a rapid dissolution rate in the early stage, with only 35% drug release in the first 15 minutes, which was even lower than that of the pure drug (37%). *Wang et al.* investigated amorphous solid dispersions of indomethacin and evaluated the effect of PVP K30 addition. They reported that higher PVP levels markedly slowed the dissolution rate and reduced the maximum dissolved concentration, even though no precipitation was detected (39). This paradox may be explained by the fact that PVP, while highly efficient in enhancing equilibrium solubility by inhibiting crystallization, can also increase the viscosity of the medium around drug particles. This may reduce the diffusion rate and hinder the rapid release of the drug. The release enhancement percent can be ordered as HPMC> Soluplus>PVP.

Effect of drug-to-polymer ratio (HPMC):

As shown in Figure 4(B), the optimal ratio was SD.H3 (1:3), which delivered the highest % dissolved across time. XRPD confirmed the lowest residual crystallinity at this ratio, whereas SD.H2 (1:2) and SD.H4 (1:4) showed higher crystallinity, consistent with the solubility screen and their comparatively lower dissolution. Quantitatively, *f*2 analysis showed that SD.H3 and SD.H4 are both not similar to the pure GF a value of 22.7 and 25.2, respectively, while SH2 is 61, which indicates similarity. In addition, SD.H3 and SD.H4 are considered similar as *f*2 was 69.

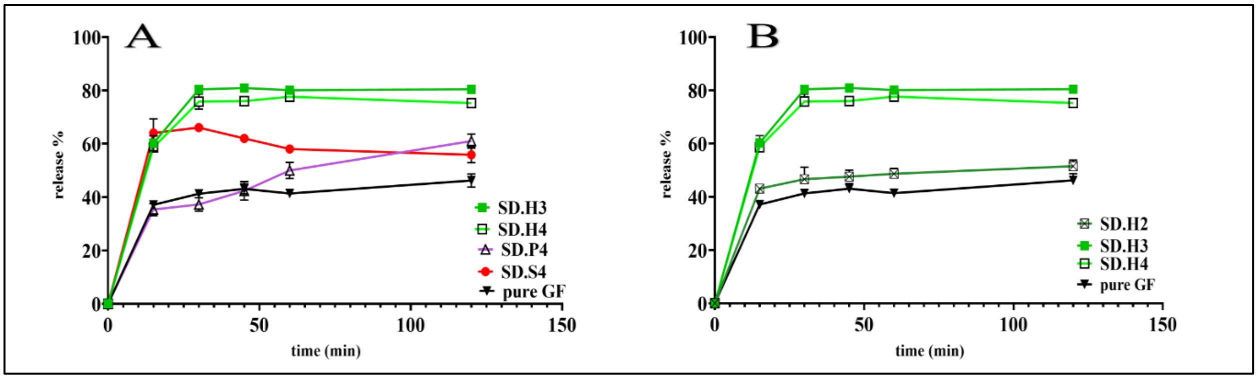


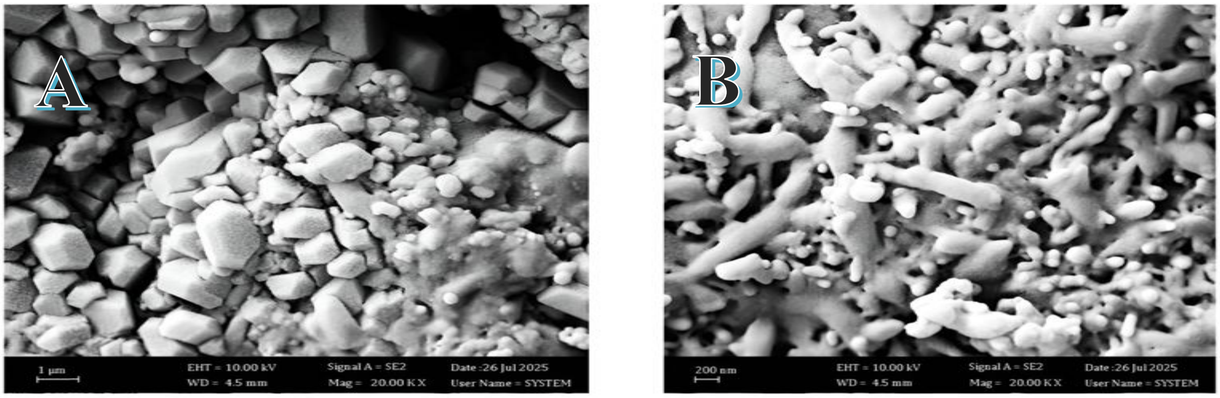
Figure (4): A. The effect of polymer type on the dissolution profile of SD formulations, B. The effect of polymer (HPMC) ratio on the dissolution profile of SD formulations

Selecting the optimum formula:

The optimum formula selection is based on the crystallinity, saturated solubility, and release profile, as shown in Table 4. Formula SD.H3 shows the best result among the others, with the significantly ($p<0.05$) highest saturated solubility (0.249mg/ml) and release percent (80% in the first 30minutes and a total of 81% release percent) with a semi-amorphous state of drug lattice.

Field emission-scanning electron microscopy (FESEM)

The surface morphology of pure GF and the optimum SD formula is described in Figure 5. The pure GF exhibite a octahedral crystal sturucture with smooth surfuces (40). This defined crystalline structure disapeare in the SD formulation, which confirm the efficacy of the solvent evaporation method for the amorphization of the drug particle(40).



Griseofulvin

1:3 HPMC (SD.H3)

Figure (5): FESEM of A. Griseofulvin drug B. Solid dispersion formula of GF: HPMC in a 1:3 ratio.

Stability evaluation

The DSC thermogram (Figure 6A) of the pure GF showed a sharp melting endotherm at 221 °C, consistent with the USP reference value (14), confirming its crystalline nature. The optimized SD formulation (SD.H3) at preparation time exhibited a reduced enthalpy and slightly shifted peak to approximately 218 °C. That is consistent with Furosemide SD prepared by rotary evaporation using HPMC, where the drug melting point shifted and reduced (18). This indicates a decrease in crystallinity and partial amorphization. In addition, broad endothermic events were observed around 50-100°C, which can be attributed to moisture loss (41).

At the 1-month and 3-month time points, the SD formulas maintained their reduced and shifted endothermic peak (219°C and 217°C, respectively) with no signs of recrystallization. This is confirmed as no Bragg peaks reappeared in the PXRD presented in Figure 6B, suggesting the stability of the formulation under harsh conditions (42). Lemtsev et al. developed stable Ibuprofen Solid dispersion with HPMC for more than 6 months when drug content was 20% (43). It is suggested due to the H bonds between GF and the polymer and the crystallization inhibition ability of the polymer (44).

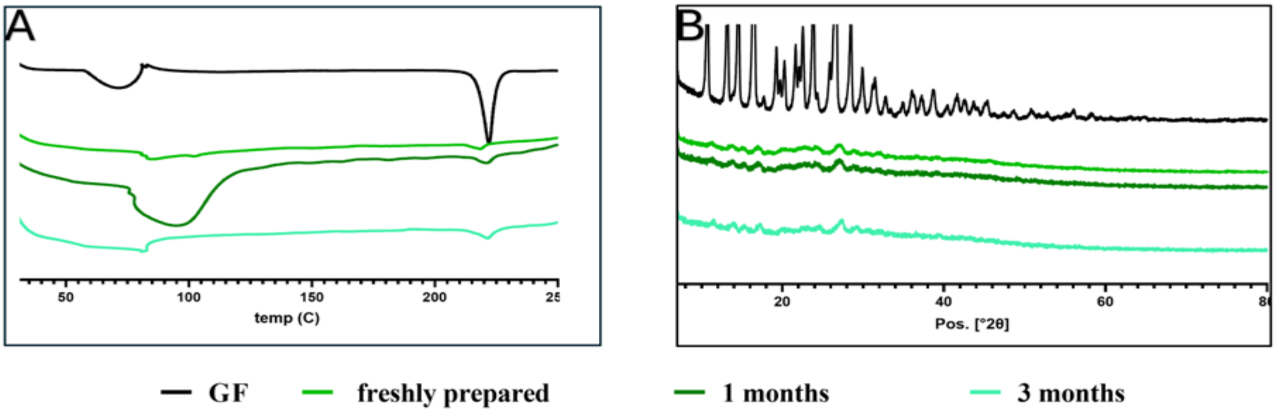


Figure (6): A. DSC B. PXRD of the pure GF and the optimum formula at zero time, after 1 month, and after 3 months.

Conclusion

Solid dispersion via the solvent evaporation method successfully improved the solubility and dissolution rate of GF. Where HPMC at a 1:3 ratio enhances the saturated solubility by ≈ 5 folds compared to the pure drug and achieve 80% drug release from the formulation in the first! % and maintained the supersaturation along the test period. Reduced crystallinity and drug amorphization were confirmed by PXRD, DSC, and FESEM, which may explain the enhanced solubility and dissolution of the drug achieved by this approach.

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