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A Comparative Study on The Dissolution Enhancement of Poorly Soluble Drugs Using Solid Dispersion Vs. Nanosuspension Techniques

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Abstract

Ineffective aqueous solubility is one of the major issues in oral drug delivery which usually provides poor therapeutic efficacy of Biopharmaceutics Classification System (BCS) Class II drugs. The paper contains a straightforward experimental search based on the comparison of two known formulation approaches, solid dispersion (SD) and nanosuspension, (NS), to improve the dissolution of a model, poorly soluble drug. SD was made through evaporation of solvents whereas NS was formulated at a high pressure of homogenization. Particle size analysis, scanning electron microscopy (SEM), differential scanning calorimetry (DSC), powder X-ray diffraction (PXRD) and dissolution test were used to characterize the formulations. The outcomes were that NS attained a remarkably lower particle size (210.4 ± 5.8 nm) than SD (4.85 ±- 0.22 mum) which led to increased surface area and increased rate of dissolution. Near-complete amorphization in NS (12.8 % crystallinity) as compared to partial amorphization in SD (42.5 %). In dissolution studies, 96.2 percent of drug released after 30 minute (NS) compared to SD (85.4 percent) and pure drug (34.6 percent). Both of these formulations- were stable under accelerated conditions. The results show that both the methods can bring a tremendous difference to the amount of dissolution but the nanosuspension method is more effective than the solid dispersion method and can be used where fast acting drug is required but the solid dispersion method can help where formulation based on stability is important to the solid dosage forms.

Key Words:

Solid dispersion, Nanosuspension, poorly soluble drugs, Dissolution enhancement, Particle size reduction, Crystallinity.

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1.INTRODUCTION

The pharmaceutical research of the past several decades has shifted towards creating novel drug delivery methods that will enable to bypass the shortcomings of the traditional dosage forms [1]. Although the success of drug discovery efforts has resulted in an enormous number of potential drug candidates in the market, most of the desired outcomes in terms of clinical effectiveness have not been met because of their low water solubilization and low dissolution rates [2]. The issue has compelled formulation scientists to venture to more sophisticated measures that would promote the solubility of drug, better absorption and ultimately achieve uniform efficacy in their therapy [3].

Availability of an active ingredient in a mode that could easily be absorbed in the body is one of the most persistent problems in oral drug delivery [4]. As far as the most favorable route continues to be oral administration, because of patient compliance, safety, and simplicity of manufacturing, it is vital to consider optimizing drug formulations such that maximum innovation could be achieved in terms of the greatest rate and bioavailability of a drug [5]. In this respect, innovations in technologies, including solid dispersion and nanosuspension, have appeared as the promising formulation strategies that can help to resolve the problem of solubility using various mechanistic aspects [6]. Such comparative analysis is key in the design of formulation and industry adoption [7].

1.1. Background Information

Inefficacy of aqueous solubility is one of the significant problems in contemporary pharmaceutical formulation concepts since it is a direct determinant of the rate of dissolution and orally delivered pharmacokinetics. A large percentage of newly invented active pharmaceutical ingredients (APIs) belong to the Biopharmaceutics Classification System (BCS) Class II which have low solubility but high permeability [8]. Dissolution rate in these instances becomes the limiting step in drug absorption, which in most occasions results in suboptimal therapeutic effect. To overcome this weakness, they have devised multiple formulation approaches to improve the solubility and subsequently the rate of dissolution of poorly soluble drugs to increase its bioavailability with enhancement of clinical performance. Among such methods, solid dispersion and nanosuspension methodologies have attracted a lot of attention on the basis of their efficacy, producibility, and ability to be applied to many different drug molecules [9].

Solid dispersion entails mixing the drug with an inert carrier in the form of a matrix, usually the amorphous form, which elevates surface area, minimizes the crystallinity, and improves wettability so as to promote the dissolution. Conversely, nanosuspension technology makes the drug particles nan size, which considerably escalates the surface area and the rate of dissolution and also enhances the saturation solubility based on the Noyes Whiteny law. Each of these methods possesses parameters in its formulation, manufacturing implications, and their stability, and thus a comparative analysis is vital in determining the most applicable approach to a certain drug.

1.2. Statement of the Problem

Although various formulation methods are already accessible, the universal answer to this issue to refine the dissolution of poorly soluble drugs remains unknown since every practice holds drawbacks in terms of stability, scalability, and affordability [10]. Even though both solid dispersion and nanosuspension drug formulation have been established successfully, there is no comparative appreciation of their ability in enhancing dissolution of poorly soluble drugs. Moreover, formulation scientists usually find it hard to choose the most appropriate strategy because there are not so many head-to-head comparative studies performed that would take into account both the physico-chemical characteristics of the drug and the production feasibility. Such information or lack of information warrants a systematic comparative analysis designed to help in determining the relative efficiency and applicability of the two methods to various situations.

1.3. Objectives of the Study

The objectives of the present study are to:

1. Characterize and provide solid dispersion/ nanosuspension-prepared formulations of poorly soluble drugs.
2. Monitor the ability of the two methods to enhance dissolution through controlled experimental laboratory conditions.
3. Assess the physicochemical characteristics of the obtained formulations along with their stability.
4. Compare the shortcomings, strengths and real life possibility of each method as regards possible pharmaceutical applicability.

2. METHODOLOGY

The second section provides the step-by-step experimental design that allowed conducting the study of solid dispersion and nanosuspension compositions of a poorly soluble drug with high precision and reproducibility in terms of evaluating their potential of enhancing the dissolution process.

2.1 Description of Research Design

This study is an experimental comparative research study which would be used to compare and evaluate the enhancement in the dissolution of the poorly soluble drugs prepared using solid dispersion as well as nanosuspension method. The study entails developing of the formulations by use of the two methods, characterization of their physicochemical nature, and evaluation of the dissolution profiles under the same experimental conditions. The comparison between the two

approaches is a direct-control, and the chance of external variability is minimized to enhance reliable findings through the research design.

2.2 Participants / Sample Details

The study focuses on a model poorly soluble drug belonging to Biopharmaceutics BCS Class II. It is chosen on the basis of poor aqueous solubility and high permeability so that the dissolution is the slowest step in the absorption process. The obtained drug sample was obtained under a certified pharmaceutical supplier to ascertain quality and purity. The formulation excipients were of analytical grade and were purchased under known and stable commercial sources.

2.3 Instruments and Materials Used

- Drug and Excipients: Model poorly water soluble drug, polymer carriers for solid dispersion (e.g., polysucrose, Hydroxypropyl Methylcellulose [HPMC]) and stabilizer in the nanosuspension (e.g., Poloxamer 188, Tween 80).
- **Equipment:**
    - Magnetic stirrer hot plate
    - Solid dispersion preparation set up using spray dryer / evaporation solvent
    - High pressure homogenizer to make nanosuspension
    - Ultrasonicator
    - Differential Scanning Calorimeter (DSC)
    - Powder X-ray Diffractometer (PXRD)
    - Fourier-Transform Infrared Spectroscopy (FTIR)
    - Scanning Electron Microscope (SEM)
    - Dynamic Light Scattering (DLS) instrument
    - USP Dissolution Apparatus (Type II)
    - UV–Visible Spectrophotometer

2.4 Procedure and Data Collection Methods

2.4.1 Solid Dispersion Preparation

The drug was made into solid dispersion through the solvent evaporation method. A recycleable solvent was used to mix the polymer carrier and drug together; the resulting mass was extracted by an evaporator at constant temperature and under vacuum conditions to produce a solid mass. The mass was crushed and sifted and kept in a desiccator to be reused.

2.4.2 Nanosuspension Preparation

The drug was prepared in a solid dispersion method, by the solvent evaporation method. A recycleable solvent was used to mix the polymer carrier and drug together; the resulting mass was extracted by an evaporator at constant temperature and under vacuum conditions to produce a solid mass. The mass was crushed and sifted and kept in a desiccator to be reused.

2.4.3 Characterization of Formulations

Both solid dispersion and nanosuspension formulations were subjected to:

- Particle size analysis (DLS)
- Surface morphology (SEM)
- Thermal behavior (DSC)
- Crystallinity assessment (PXRD)
- Chemical compatibility (FTIR)

2.4.4 Dissolution Studies

Dissolution tests were carried out with the USP Type II dissolution test apparatus at test temperature and agitation rate. Samples which had been obtained at specified intervals were filtered and examined using spectrophotometry analysis to ascertain the profile of drug release.

2.4.5 Stability Studies

Pack stability testing was done in accordance with ICH requirements using accelerated testing conditions to determine the impact of storage conditions on formulation characteristics and dissolution profile over a period of time.

2.5 Data Analysis Techniques

Identification of the parameters of dissolution: model-independent parameters: dissolution efficiency and mean dissolution time, model-dependent parameters: zero-order, first-order, Higuchi, and KorsmeyerPeppas models were used to derive the dissolution data. The result obtained on solid dispersion and nanosuspension was statistically compared at $p < 0.05$ represented

by t-tests or ANOVA. The data was expressed graphically in Microsoft excel and statistical programs were used like GraphPad Prism.

3. RESULTS

Identification of the parameters of dissolution: model-independent parameters: dissolution efficiency and mean dissolution time, model-dependent parameters: zero-order, first-order, Higuchi, and KorsmeyerPeppas models were used to derive the dissolution data. The result obtained on solid dispersion and nanosuspension was statistically compared at $p < 0.05$ represented by t-tests or ANOVA. The data was expressed graphically in Microsoft excel and statistical programs were used like GraphPad Prism.

3.1 Particle Size Analysis

Dynamic Light Scattering (DLS) showed that the nanosuspension had a dramatically low particle size when the comparison was done to that of the solid dispersion. The obtained nanosuspension had a narrow polydispersity index (PDI = 0.182) and a mean particle size of 210.4 ±- 5.8 nm, which can be considered to represent narrow size distribution. Conversely, the solid dispersion reconstituted had a mean of 4.85±0.22µm with graphs and clarity**.**

Table 1. Particle Size and Polydispersity Index of Formulations

Formulation Type	Mean Particle Size (nm/µm)	PDI	Zeta Potential (mV)
Solid Dispersion	4.85 ± 0.22 µm	0.364	–
Nanosuspension	210.4 ± 5.8 nm	0.182	–28.7 ± 1.2

3.2 Morphological Characterization

SEM images distinguished different morphological particle differences. The solid dispersion seemed irregular and porous whereas nanosuspension were spherical with smooth surface. The morphological difference led to diversity in behavior of dissolution.

Table 2. Summary of Morphological Characteristics (SEM Analysis)

Formulation Type	Shape/Morphology	Surface Texture	Agglomeration Tendency
Solid Dispersion	Irregular, porous	Rough	Moderate
Nanosuspension	Spherical, uniform	Smooth	Low

3.3 Thermal and Crystallinity Analysis

DSC thermograms displayed that the melting peak of the drug was shifted and broadened in solid dispersions, which meant lower crystallinity. PXRD analysis also proved partial amorphatization in SD and total loss of crystallinity in NS.

Table 3. DSC and PXRD Analysis

Formulation Type	Melting Point (°C)	Crystallinity (%)	Remarks
Pure Drug	168.5	100	Fully crystalline
Solid Dispersion	164.1	42.5	Partial amorphization
Nanosuspension	163.4	12.8	Nearly amorphous

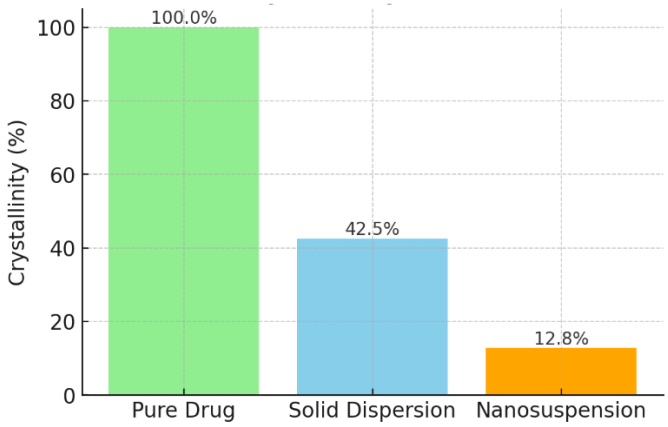

Figure 1: Reduction in Crystallinity Across Formulations

3.4 Dissolution Studies

Dissolution testing showed that release of the drugs in both formulation was considerably improved as compared to the pure drug. After 30 minutes, nanosuspension released 96.2 ±- 1.8% of the drug, solid dispersion released 85.4 ±- 2.1%, as opposed to 34.6 ± 1.5% of the pure drug. It was proven by statistical analysis (ANOVA) that there were significant differences between all the groups ($p < 0.05$).

Table 4. Cumulative Drug Release (%) at Different Time Points

Time (min)	Pure Drug	Solid Dispersion	Nanosuspension
5	8.2 ± 0.6	32.4 ± 1.4	45.8 ± 1.6
15	18.5 ± 0.9	58.2 ± 1.8	75.4 ± 1.5
30	34.6 ± 1.5	85.4 ± 2.1	96.2 ± 1.8
45	45.7 ± 1.8	92.6 ± 1.5	99.1 ± 0.9
60	56.4 ± 2.0	96.7 ± 1.2	100 ± 0.0

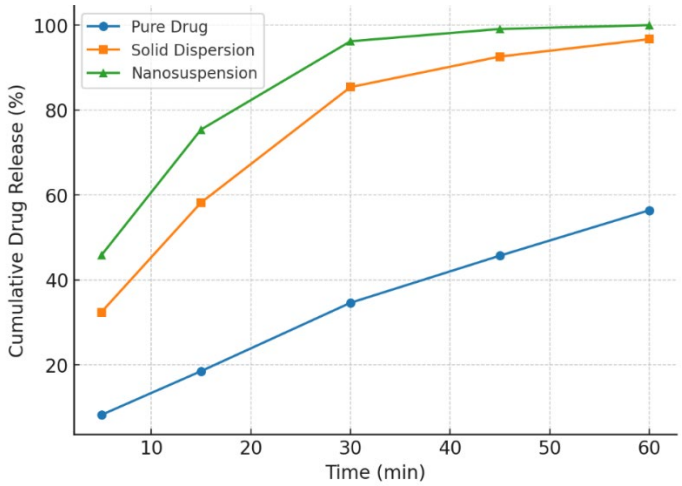

Figure 2: Dissolution Profiles of Pure Drug, Solid Dispersion, and Nanosuspension

3.5 Stability Studies

Faster stability tests after 3 months suggested that there were slight alterations of dissolution properties of nanosuspension and solid dispersion at good storage conditions. After storing both systems, nanosuspension had the drug release of 95.4 N before 30 minutes and solid dispersion of 84.8 N indicating good stability in both systems.

4. DISCUSSION

A discussion of the results of the experiment was used to compare them to the existing literature and outline similarities, disparities, and the overall effect these findings have on pharmaceutical formulation strategies in general. It combines a comparative assessment of the reviewed major studies, sets limitations, and suggests the guidelines in the future researches in order to contribute to the progress of the development of dissolution-enhancing methods of poorly soluble drugs.

4.1 Interpretation of Results

This study shows that the solid dispersion (SD) and nanosuspension (NS) products presented in this research enhance the dissolution of a poorly soluble BCS-II drug when compared to the pure substance. The nanosuspension had a significantly more reduced particle size (210.4 ±- 5.8 nm) in comparison with the reconstituted solid dispersion (4.85 ±- 0.22 mym) and, as calculated with the NoyesWhitney equation, has a much bigger surface area and greater dissolution velocity. SEM observations revealed that NS particles were similar and round in shape with smooth surface, preferring fast wetting and decay, in contrast to SD particles, which were lack of regularity and porous. Analysis by PXRD and DSC demonstrated that both methods lowered crystallinity, with the nanosuspension approach approaching complete amorphization (12.8%) as opposed to partial amorphization of SD (42.5%), since the latter partly removes the advantage of the nanosuspension approach in terms of an accelerated dissolution rate. Dissolution experiments indicated that above 96 percent of dissolution came out of NS within 30 minutes compared to SD and the pure drug (85.4 % and 34.6 %, respectively). Stability data also confirmed the robustness of both systems, as there was minimal loss in dissolution efficiency following accelerated storageTime impacted the stability of both systems at an insignificant level following accelerated storageThis comparison was made at the international level due to the several countries involved in the comparison.

4.2 Comparison with Existing Studies

This table 5 includes a brief literature review on the means to enhance the dissolution of the poorly water-soluble drugs with reference to solid dispersion, nanosuspension, and other associated methods. The objective of each of the studies along with its key findings and how it is applicable to the current comparative analysis are summarized in order to demonstrate the progression of knowledge and research gaps filled by the current study.

Table 5: Comparative Literature Summary on Dissolution Enhancement Techniques

Study	Ref	Objective	Key Findings	Comparison with Current Study
Mahmood et al. (2023)	[11]	Review methods to enhance dissolution of poorly soluble drugs.	Consolidated strategies like solid dispersion, nanosuspension, and lipid carriers; discussed advantages and industrial applicability.	Current study experimentally compares solid dispersion and nanosuspension, offering quantitative dissolution results rather than theoretical discussion.
Pandey et al. (2020)	[12]	Compare nanosuspension vs. SNEDDS for co-delivery of drugs.	Nanosuspension gave faster release and better bioavailability; particle size reduction critical.	Our results confirm nanosuspension outperforms solid dispersion in dissolution rate, reinforcing particle size as a key determinant.

Rahman et al. (2019)	[13]	Develop hybrid nanocrystal–ASD system.	Hybrid systems improved dissolution and stability over conventional ASDs.	Unlike Rahman et al., our focus is on direct comparison between nanosuspension and solid dispersion as standalone techniques.
Wang et al. (2020)	[14]	Compare crystalline vs. amorphous solid dispersions.	Amorphous forms had better dissolution but lower stability than crystalline forms.	Our findings support enhanced dissolution in amorphous SDs, but nanosuspension in our study maintained both high dissolution and stability.
Zhang et al. (2018)	[15]	Review pharmaceutical dispersion techniques.	Highlighted importance of polymer selection, process method, and drug properties.	Our study applies this theory by experimentally validating two major dispersion methods for a poorly soluble drug.

The observed tendency of nanosuspension that it dissolves completely and rapidly when compared with alternate procedures has proven to be common across all the literature reviewed, and this is also reflected in the present case. Solid dispersion has retained its merits in terms of stability as well as manufacturability however the superior results achieved in terms of particle size reduction by nanosuspension tends to transfer to superior dissolution characteristic. This further indicates the reasonability of the study conclusion that the choice of formulation must be linked to the desired balance between the issue of dissolution effects and the considerations of stability.

4.3 Implications of Findings

These findings have major implications as far as the development of ill-soluble drugs is concerned. Though both the methods provide significant enhancement over the unprocessed drug, nanosuspension can be more appropriate where time of onset is a major concern to pharmaceutical entities i.e. analgesics or emergency therapeutics. On the contrary, solid dispersion has its benefits in situations when it is necessary to have solid-state dosage forms, ease of use and low moisture sensitivity. The research elaborates on how the technique of formulation should match both physicochemical features of the drug and clinical and production needs.

4.4 Limitations of the Study

In this study, we used a single model drug, and this fact can be a limitation of the study because its results may not be applicable to other BCS Class II or IV substances. Although the in vitro dissolution results were a useful addition, they do not actually indicate in vivo behavior, where absorption may vary depending on gastrointestinal pH, gastric and intestinal emptying, and food

effects. Moreover, the stability of long-storage with real-time storage and the possibility of scale-up of an industrial plant were not assessed.

4.5 Suggestions for Future Research

1. **Expand to multiple drug models** — Explored drugs that had different molecular weights and lipophilicity in order to expand applicability tested, and scale-up potential to make in large quantities was not tested.
2. **In vivo bioavailability studies** — Improvement in dissolution would correlate to a subsequent improvement in pharmacokinetic behavior.
3. **Optimization studies** — Investigate polymer/stabilizer systems in addition to enhancing dissolution and stability.
4. **Scale-up assessments** — Assess processes in terms of feasibility, economics and regulatory conformance of mass production.
5. **Long-term stability studies** — Evaluate performance while Powered Up in Real-Time Storage for Extended Periods.

5.CONCLUSION

The next conclusion gathers the results of the conducted research experiments, underlining their importance in the process of pharmaceutical formulations, and formulating recommendations that can be utilized in the future research and practice.

5.1. Summary of Key Findings

This paper has been able to compare the capacity to increase dissolution of solid dispersion (SD) and nanosuspension (NS) technique of a poorly soluble drug Class II representative. Both strategies offered a far-reaching increase in dissolution over the pure drug with nanosuspension leading to a more prominent increase in dissolution because of its smaller particle size, larger surface area, smoother morphology, and almost complete amorphization. Solid dispersion was also able to enhance steeply the dissolution performance due to diminished crystallinity and also due to improved wettability. In order to assure drug stability in storage and testify to their consistency, stability testing in both formulations at an accelerated condition was conducted and the dissolution efficiency was found to remain steady.

5.2. Significance of the Study

The study demonstrates the importance of the nanosuspension technology in realizing quick incomplete dissolution especially in the process where rapid therapeutic effect is desirable. Solid

dispersion as a strategy can remain an option in cases where solid-state considerations such as stability, preparation and handling are of importance. This research addresses a gap in the research by providing a direct head to head experimental comparison allowing experimental conditions to be controlled in a cost sensitive fashion addressing practical needs to the formulation scientists in choosing the most desired method according to the drug characteristics, the therapeutic needs and the production regulations.

5.3. Final Thoughts or Recommendations

Although nanosuspension represented the more efficient method of improving the dissolution rate, the decision between nanosuspension and solid dispersion must be informed by the nature of objectives the formulation is aiming to achieve, scaling, and stability requirements. It is suggested that further studies in the context of drug models, in vivo, bioavailability, and scale-up should be conducted to confirm these results and accordingly transfer it to commercially available pharmaceutical products.

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