

AI-Assisted Solubility Enhancement of Lornoxicam : A Comprehensive Review of Conventional and Emerging Formulation Strategies

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ABSTRACT

Lornoxicam is a nonsteroidal anti-inflammatory drug with poor water solubility, which limits its oral bioavailability and therapeutic effectiveness. This study was conducted to review and evaluate various strategies used to enhance the solubility of lornoxicam, as well as to examine the emerging role of computational tools in formulation development. Traditional approaches such as the use of solubility-enhancing excipients, liquid-based systems, particle size reduction techniques and complex formation have been widely explored. However the selection of optimal formulations has largely relied on trial-and-error methods, making the process time-consuming and resource-intensive. Recent advancements in computer-aided techniques, including machine learning and predictive modeling, have provided new opportunities to improve formulation design. These tools can predict drug-excipient interactions, solubility behavior and stability profiles, enabling faster and more efficient screening of potential formulations. The findings of this review indicate that integrating computational methods with conventional formulation strategies can significantly reduce development time and improve the success rate of identifying effective solubility-enhancing systems. In conclusion, the application of modern computational approaches in pharmaceutical research holds great promise for improving oral drug delivery. Such integration can enhance the performance of lornoxicam and similar poorly soluble drugs, leading to more efficient and reliable drug development processes.

Key words : Lornoxicam, Solubility enhancement, Artificial intelligence, Solid dispersion, Machine learning, Nanotechnology.

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Highlights :

- Reviews physicochemical challenges limiting solubility and bioavailability of lornoxicam
- Summarizes nanotechnology-based approaches for enhancing dissolution and drug performance
- Explores the role of artificial intelligence in predicting and optimizing pharmaceutical formulations.

1. Introduction

Lornoxicam is used to treat conditions like arthritis that cause inflammation. It does not work well for many people because it does not dissolve well in water¹⁻⁴. This makes how fast it dissolves a factor in how well it works when taken orally^{5,6}. Traditional methods to make it work better have been tried. However these methods take a lot of trial and error. Are not very good, at predicting what will work. Lornoxicams effectiveness is often limited because of its water solubility⁷⁻⁸.

This solubility issue directly affects how well Lornoxicam works when taken by mouth⁹⁻¹³. Lornoxicams rate of dissolution plays a role in its oral bioavailability. The conventional formulation approaches have attempted to address this challenge. They often require experimentation and lack predictive accuracy¹⁴⁻¹⁵

2. Physicochemical Challenges of Lornoxicam

Lornoxicam has some properties that make it hard to work with in medicines. It is a substance with strong bonds between its molecules, which makes it hardly dissolve in water at all^{16,17}. The Biopharmaceutics Classification System says lornoxicam is a Class II drug. This means its solubility is the issue when it comes to absorption, in the body¹⁸. Lornoxicam dissolves better in pH levels. This happens because its parts start to ionize. In the stomachs acidic environment it does not dissolve well which leads to slow and delayed absorption. The medicine also does not mix well with stomach fluids. This is because it has wettability and is very crystalline. As

a result it does not dissolve quickly. These issues mean we need to use techniques. These techniques can help make lornoxicam dissolve better mix with stomach fluids and release quickly in oral medicines. Lornoxicam solubility and wettability need to be improved. Lornoxicam dissolution rate is also a concern. Lornoxicams properties affect its absorption^{19,12}

3. Conventional Solubility Enhancement Techniques

The major conventional solubility enhancement techniques are illustrated in figure.1

3.1 Solid Dispersion

Solid dispersion is one of the most extensively studied approaches for improving the solubility of poorly water-soluble drugs^{22,23}. In this technique, the drug is dispersed within a hydrophilic polymer matrix, which enhances wettability and reduces particle aggregation²⁴. Additionally, the transformation of the drug from a crystalline to an amorphous state leads to higher free energy and improved solubility.

However, despite its advantages, solid dispersion systems are often associated with physical instability. The amorphous form of the drug tends to recrystallize²⁵. over time, particularly under conditions of high humidity and temperature, which can reduce the solubility advantage.

3.2 Liquisolid Systems

Liquisolid technology involves dissolving the drug in a non-volatile solvent followed by its adsorption onto carrier and coating materials to produce a dry, free-flowing powder. This method enhances dissolution by maintaining the drug in a solubilized form within the formulation^{26,27}

Although liquisolid systems significantly improve dissolution rates, challenges such as poor flow properties and the need for large quantities of carrier material may limit their large-scale application.

3.3 Inclusion Complexation

Inclusion complexation, particularly with cyclodextrins, improves drug solubility by encapsulating hydrophobic molecules within a hydrophilic cavity^{28,29}. This approach enhances the apparent solubility and stability of lornoxicam. However, limitations such as high cost and restricted drug loading capacity must be considered during formulation design.

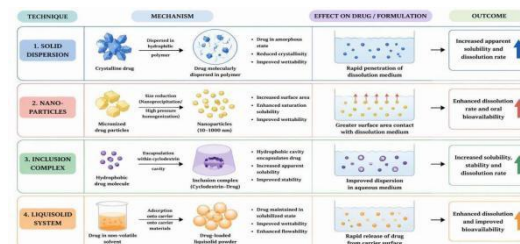


Figure.1. Conventional Solubility

Enhancement Techniques

3.4 Nanotechnology-Based Approaches

Nanotechnology offers a highly effective approach to solubility enhancement by reducing particle size to the nanometer range^{30,31}. This results in increased surface area and improved dissolution rate, Nanosuspensions and polymeric.

nanoparticles have shown promising results in enhancing the bioavailability of poorly soluble drugs. Despite these advantages, issues related to physical stability, aggregation and manufacturing complexity remain challenges.

4. Limitation of Conventional Methods

- Extensive Trial-and-error experimentation
- High development cost and time
- Limited predictive capability
- Scale-up challenges^{32,33}.

These limitations necessitate advanced computational approaches.

5. Role of AI In Formulation Development

Artificial intelligence has revolutionized pharmaceutical formulation by enabling predictive modeling and data-driven decision-making^{34,38}

5.1 Types of AI Models

Different types of AI models are discussed in figure.2

1. Artificial Neural Networks (ANN): Capture nonlinear relationships
2. Support Vector Machines (SVM): Effective for small datasets
3. Random Forest (RF): Robust ensemble learning
4. Deep Learning (DL): High predictive accuracy for complex data

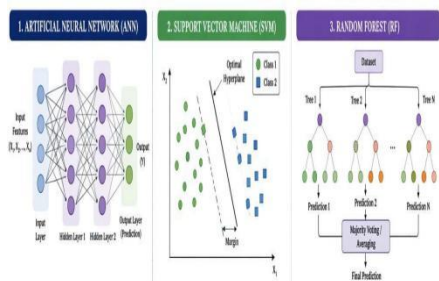


Figure.2. Types of artificial intelligence models in pharmaceutical formulation

In Table.1

Model	Application	Accuracy	Advantages	Limitations
Artificial neural network (ANN)	Dissolution prediction, solubility modeling	85–95%	Handles nonlinear data, high predictive power	Requires large datasets, low interpretability
Support Vector Machine (SVM)	Classification of drug properties, solubility prediction	80–92%	Effective in small datasets, robust	Difficult to tune parameters, less scalable
Random Forest (RF)	Excipient selection, formulation optimization	85–93%	Reduces overfitting, handles complex data	Less interpretable, computationally intensive
Deep Learning (DL)	Drug release prediction, molecular modeling	88–97%	High accuracy, automatic feature extraction	Requires big data, high computational cost

Table1. Comparison of Artificial Intelligence Models in Pharmaceutical Formulation

In the pharmaceutical formulation comparison of ce These models can predict key properties such as solubility, permeability and dissolution behavior³⁹⁻⁴¹. Reducing reliance on traditional trial-and-error approaches.

AI also enables optimization of formulation parameters, leading to improved efficiency and reduced development time.

5.2 AI Workflow In Formulation

1. Data collection
2. Feature engineering
3. Model training and validation
4. Prediction of formulation outcomes
5. Optimization using algorithms (e.g., Bayesian optimization)

The work flow of AI in formulation development is presented in figure.3

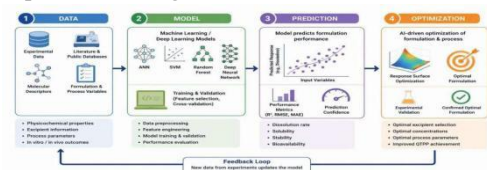


Figure.3. Workflow of artificial intelligence in formulation development

5.3 AI vs Design of Experiments (DoE)

AI models outperform DoE in capturing nonlinear interactions and handling high-dimensional datasets, though they require larger datasets and validation are disussed with DOE in figure.4

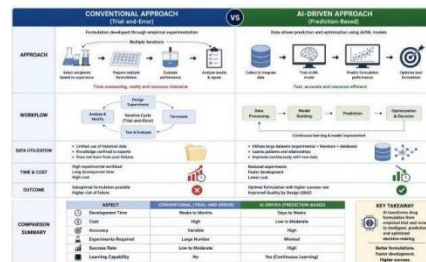


Figure.4. Comparison between artificial intelligence and design of experiment

6. AI-Assisted Solubility Enhancement

6.1 AI in Solid Dispersion Design

AI-based tools can predict drug–polymer compatibility and identify suitable carriers for solid dispersion systems^{42,43}. Machine learning algorithms analyze molecular descriptors and physicochemical properties to forecast formulation stability and performance.

6.2 AI in Dissolution Prediction

Machine learning models are increasingly used to simulate drug release profiles and predict dissolution kinetics⁴⁴. These models help in selecting optimal formulation parameters without extensive laboratory experiments.

6.3 AI in Nanoparticle Optimization

AI assists in optimizing nanoparticle characteristics such as size, surface charge and stability⁴⁵. This improves formulation efficiency and ensures consistent drug delivery performance.

6.4 AI in Excipient Selection

AI-driven platforms can evaluate large datasets to identify optimal excipients for enhancing solubility and stability^{46,47}. This reduces development time and improves formulation success rates.

Representative case studies demonstrating the application of AI in solubility enhancement and pharmaceutical formulation are summarized in Table.2

Table 2. Case studies of AI-Assisted solubility enhancement

Drug	Technique	AI Model	Outcome
Lornoxicam	Solid dispersion optimization	Artificial Neural Network (ANN)	Improved dissolution rate by ~2–3 fold; prediction accuracy > 90%
Ibuprofen	Nanoparticle	Random	Reduced particle

	formulation	Forest (RF)	size; enhanced solubility and stability
Carbamazepine	Nanoparticle formulation	Support Vector Machine (SVM)	Accurate prediction of dissolution profiles ($R^2 > 0.88$)
Curcumin	Nanoformulation optimization	Deep Learning (DL)	Increased bioavailability and solubility; >85% prediction accuracy
Fenofibrate	Lipid-based formulation	ANN	Enhanced solubility and improved oral bioavailability
Ritonavir	Amorphous solid dispersion	Gradient Boosting (XGBoost)	Improved stability and dissolution; reduced experimental trials
Indomethacin	Cyclodextrin inclusion complex	ANN	Significant increase in aqueous solubility
Nifedipine	Nanosuspension	Random Forest (RF)	Optimized particle size distribution and dissolution rate

7. Challenges of AI in pharmaceutical formulation

- > Limited availability of High-quality datasets
- > Interpretability issues (black-box models)
- > Regulatory challenges

8. Comparative Analysis

A comparison of different solubility enhancement techniques is present in Table.3

Traditional methods for enhancing solubility have shown considerable advancements in drug dissolution, however they frequently necessitate comprehensive experimentation and optimization. In comparison, AI-driven techniques offer predictive insights that make the formulation development process more efficient⁴⁸⁻⁵².

Table 3. Comparison of Solubility Enhancement Techniques

Techniques	Mechanism	Advantages	Limitations
Solid dispersion	Amorphization	High release	Stability issue
Liquid solids	Solubilization	Fast dissolution	Flow issue
Nano particles	Surface area ↑	High bioavailability	Cost
Inclusion complex	Encapsulation	Stable	Limited loading

9. Integration of AI With Nanotechnology

The integration of artificial intelligence with nanotechnology represents a significant advancement in drug delivery systems. AI-based models can be employed to optimize nanoparticle formulations by predicting key parameters such as particle size, stability and drug loading efficiency. This combined approach improves formulation precision, reduces development time and enhances reproducibility. As a result, it is expected to play an important role in the future of pharmaceutical innovation.

10. Critical Evaluation of Startiges

Each solubility enhancement technique has its own advantages and limitations. Conventional approaches are generally simple and cost-effective, but they may face issues related to stability and scalability. In contrast, nanotechnology-based systems offer improved performance, although they are often associated with greater complexity and higher cost.

Artificial intelligence helps address some of these challenges by enabling predictive formulation design. However, factors such as data dependency

and limited interpretability should also be taken into account. Overall, a combined approach may provide a more balanced and effective solution.

11. Recent Advances

Recent advancements in pharmaceutical research have concentrated on merging AI with sophisticated drug delivery systems. Combining nanotechnology with AI in hybrid methods has demonstrated encouraging outcomes in enhancing drug formulations⁵³⁻⁵⁶.

12. Future Perspectives

The future of enhancing solubility is connected to the merging of AI with personalized medicine and cutting-edge manufacturing technologies⁵⁷⁻⁵⁹. AI could create formulations tailored to individual patients and improve drug delivery systems according to specific requirement.

13. Conclusion

The solubility enhancement of lornoxicam continues to be a significant challenge in pharmaceutical formulation due to its poor aqueous solubility and resulting limitations in oral bioavailability. Although conventional approaches such as solid dispersion, liquisolid systems and inclusion complexation have provided useful initial solutions, they are often associated with issues related to stability, scalability and limited predictability.

In recent years, advanced strategies based on nanotechnology and artificial intelligence have gained considerable attention for their ability to address these limitations more effectively. Nanotechnology-based systems improve drug dissolution by reducing particle size, increasing surface area and enhancing interaction with biological membranes. At the same time, artificial intelligence enables predictive modeling and optimization of formulation parameters, thereby reducing the need for extensive experimental trials. The integration of these technologies offers a more systematic and efficient approach to formulation development. By combining data-driven insights with advanced drug delivery systems, it becomes possible to design formulations with improved performance and consistency. Such an approach is expected to significantly enhance drug delivery efficiency and support the development of optimized formulations for poorly soluble drugs, including lornoxicam.

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