RESEARCH PAPER

Computational Approaches in Pharmaceutics: Optimizing Formulation Design and Therapeutic Outcomes

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ABSTRACT

The current research examined a hybrid computational-experimental method of optimization of ibuprofen-loaded polymeric nanoparticles. The initial application of molecular docking as a supportive preformulation tool was to determine the interaction between ibuprofen and the chosen excipients, i.e., Eudragit RS100, polyvinyl alcohol, and Poloxamer 188. Eudragit RS100 had the best binding energy, which indicates that it is more compatible with the drug and is why it was chosen as the main polymer to form the matrix. A three-factor, three-level Box-Behnken design was used to optimize the nanoprecipitation method and prepare nanoparticles. The independent variables were polymer concentration, surfactant concentration, and stirring speed, whereas the formulation responses were the particle size, entrapment efficiency, and cumulative drug release. The ready-to-use formulations were characterized by the particle sizes within the nanometer range, acceptable encapsulation efficiency, and controlled drug release characteristics. Statistical analysis proved that the chosen variables had a significant effect on the performance of the formulation, and the optimized formulation exhibited a high level of agreement between the predicted and observed values.

In vitro drug release experiments showed that there was a biphasic release profile whereby there was a burst release and sustained release during 24 h. Kinetic modeling The Higuchi model was found to best describe the release profile, indicating that the release was diffusion-controlled. On the whole, the results show that computational screening and design of experiments and experimental validation can offer a rational and efficient approach to the development of nanoparticle formulations. Such an integrated approach can be applied in minimizing empirical formulation trials and assist in systematic design of drug delivery systems.

Keywords: Computational pharmaceutics; Drug delivery systems; Molecular docking; Nanoparticles; Design of experiments.

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1. INTRODUCTION

The development of pharmaceutical formulations has been based on empirical screening and trial and error experimentation of the process variables to find the right excipients, maximize the process variables and obtain the required drug release profile. Even though these methods have facilitated the successful preparation of numerous dosage forms, they are usually labor-intensive, time-consuming, and are linked to high material usage and poor predictive capabilities. Such constraints are especially pronounced in the case of drugs that are not very soluble in water, and the formulation performance in this case is highly dependent on the complex interactions between the drug properties, the choice of excipients and the process conditions. In that regard, computational techniques have become useful in assisting the rational formulation design and enhancing the efficiency of pharmaceutical development (1,2).

Recent developments in artificial intelligence, machine learning, molecular modeling, and in silico prediction have greatly increased the role of computational pharmaceutics in the development of modern drug products. The tools have the potential to aid in the prediction of drug-excipient compatibility, the estimation of key physicochemical characteristics, the optimization of formulation variables, and the minimization of the experimental load of the traditional screening methods. Vora et al. also indicated that the use of artificial intelligence in pharmaceutical technology and the design of drug delivery processes is increasingly relevant, and that artificial neural network-based models can effectively predict and describe the behavior of pharmaceutical formulations, especially when multiple formulation variables interact in a nonlinear fashion (2). Wang et al. also reported that artificial intelligence and machine learning can be used to aid in formulation decision-making, by enhancing the selection of Besides data-driven methods, computational chemistry tools like molecular docking have also found more applications in preformulation assessment. Despite its broader use in drug discovery, docking can also be used in a supportive role in pharmaceutical formulation studies, to aid in investigating likely molecular interactions between active pharmaceutical compounds and excipients. These interactions can affect encapsulation behavior, stability and release properties particularly in carrier-based systems. Docking-based screening can thus play a role in a more rational and directed formulation workflow when used in conjunction with experimental validation(1,2).

Computational methods are especially applicable in designing nanoparticulate delivery systems. Polymeric nanoparticles have received a lot of attention due to their capacity to improve the solubility, stability, and release of poorly water-soluble drugs. Nevertheless, the effective formulation of nanoparticles relies on the wise choice of polymer type, surfactant concentration, and processing conditions, which directly influence the size of the particles, their entrapment efficiency, and their ability to release the drug. These critical formulation and process variables are optimized with the help of statistical tools like design of experiments, particularly BoxBehnken and response surface methodologies, in a systematic quality-by-design framework (5,6).

Ibuprofen is an appropriate model drug to use in such an investigation due to its low aqueous solubility and its extensive application as a model Biopharmaceutics Classification System class II drug in formulation research. Enhancing the formulation behavior of ibuprofen via nanoscale delivery systems could lead to an improvement in dissolution properties and offer a more controlled release, which would make it a suitable candidate to computationally guided formulation optimization. Simultaneously, Eudragit RS100 has been extensively investigated as a matrix-forming polymer to deliver drugs in sustained and controlled release due to its permeability properties and formulation flexibility. The joint analysis of ibuprofen and Eudragit RS100 thus provides a useful paradigm to evaluate the potential of computational screening to aid in excipient selection and formulation optimization.(7,8)

Although there is an increasing amount of interest in computational pharmaceutics, much of the published literature is either conceptual or general surveys of the use of artificial intelligence, lacking a clear linkage between computational screening and experimental formulation results. Similarly, a number of formulation studies optimize nanoparticles experimentally without a prior computational justification of excipient choice. This introduces a disconnection between predictive and practical development of dosage-forms. The current research was aimed at filling this gap through the combination of molecular docking-based preformulation evaluation with statistical formulation optimization and experimental analysis of ibuprofen-loaded polymeric nanoparticles.(2–4)

In this regard, the aim of the work was to design and optimize ibuprofen-loaded nanoparticles with the help of a hybrid computational-experimental model. Molecular docking was utilized as a complementary method to investigate drug-excipient compatibility, whereas a Box-Behnken design was utilized to optimize the key formulation factors that influence the particle size, entrapment efficiency, and drug release. This study sought to show a more sensible approach to formulation development, and to assess the usefulness of computational methods in enhancing the design of nanoparticulate drug delivery systems, by correlating computational prediction with laboratory validation (1,5,6).

2. MATERIALS AND METHODS

2.1 Materials

The model drug was ibuprofen (purity > 99) that was bought at Sigma-Aldrich (USA). The polymer that was used as a matrix former was Eudragit RS100 (Evonik Industries, Germany). Polyvinyl alcohol (PVA; molecular weight 30,000-70,000) and Poloxamer 188 were the stabilizers that were bought at HiMedia Laboratories (India). Ethanol (analytical grade) was used as the organic solvent and double-distilled water was used to prepare all aqueous preparations.

The molecular structure of ibuprofen was obtained in PubChem database and physicochemical data were cross-validated with DrugBank. AutoDock Vina (version 1.1.2) was used to perform molecular docking, and geometry optimization was done using Gaussian software at a density functional theory (DFT) level. Design-Expert software (version 13, Stat-Ease Inc., USA) was used to statistically optimize the formulation variables. These tools as in table 1 are widely used in computational pharmaceutics and formulation development studies.(7–9).

Table 1. Materials and software used in the study

Category	Material/Software	Source	Purpose
Drug	Ibuprofen	Sigma-Aldrich, USA	Model active pharmaceutical ingredient
Polymer	Eudragit RS100	Evonik Industries, Germany	Matrix-forming polymer
Stabilizer	Polyvinyl alcohol	HiMedia Laboratories, India	Particle stabilization
Stabilizer	Poloxamer 188	HiMedia Laboratories, India	Surface stabilization
Solvent	Ethanol	Analytical grade	Organic phase preparation
Database	PubChem	Public database	Molecular structure retrieval
Database	DrugBank	Public database	Physicochemical data source
Software	AutoDock Vina v1.1.2	Open-source	Molecular docking
Software	Gaussian	Licensed software	Geometry optimization
Software	Design-Expert v13	Stat-Ease Inc., USA	Experimental design and optimization

2.2 Study Design

The study was designed as an integrated computational–experimental formulation optimization approach. The process involved three consecutive steps: (i) computational preformulation analysis to determine drug-excipient compatibility, (ii) statistical optimization of formulation factors through design of experiments and (iii) experimental preparation and testing of nanoparticle formulations.

The formulation strategy was made on the principles of Quality by Design (QbD) where formulation variables were regarded as critical material attributes and particle size, entrapment efficiency and drug release were regarded as critical quality attributes. This method allows systematic optimization and minimizes the use of empirical experimentation (10).

2.3 Computational Preformulation Studies

2.3.1 Preparation of molecular structures

PubChem (SDF format) was used to retrieve the three-dimensional structure of ibuprofen, which was then transformed into PDB format using Open Babel. Optimization of the structure was done using Gaussian software with the density functional theory (DFT) to get a stable low-energy conformation that could be used in docking analysis.

2.3.2 Molecular docking for drug–excipient interaction

AutoDock Vina (v1.1.2) was used to perform molecular docking to determine the interactions between ibuprofen and the chosen excipients (Eudragit RS100, PVA, and Poloxamer 188). Prior to docking, polar hydrogens were added, and Gasteiger charges were assigned. The whole structure of the ligand was defined in a grid box to permit free interaction.

Docking simulations were performed with exhaustiveness 8 and the optimal binding conformation was chosen on the basis of minimum binding energy (kcal/mol). The patterns of interaction were examined based on hydrogen bonding, hydrophobic interactions and van der Waals forces. Reduced binding energy values were taken to mean that there was stronger interaction, which meant that there was greater compatibility between drug and excipient (11).

2.3.3 Physicochemical descriptor analysis

DrugBank and PubChem provided key physicochemical properties of ibuprofen, such as molecular weight, logP, hydrogen bond acceptors and donors, and topological polar surface area. The design of formulations was supported using these parameters especially in the selection of polymeric carriers that could be used in poorly water-soluble drugs (13). The computational parameters in preformulation studies are presented in Table 2.

Table 2. Computational parameters used in preformulation studies

Parameter	Description
Ligand	Ibuprofen
Excipients screened	Eudragit RS100, PVA, Poloxamer 188
Structure source	PubChem, DrugBank
File conversion tool	Open Babel
Docking software	AutoDock Vina v1.1.2
Optimization tool	Gaussian
Docking criterion	Minimum binding energy (kcal/mol)
Interaction analysis	Hydrogen bonding, hydrophobic, van der Waals interactions

2.4 Experimental Design and Optimization

A three-factor, three-level Box–Behnken design (BBD) was employed to optimize formulation variables. The independent variables selected were polymer concentration (X1), surfactant concentration (X2), and stirring speed (X3), based on their known influence on nanoparticle formation and stability.

The dependent variables (responses) included particle size (Y1), entrapment efficiency (Y2), and cumulative drug release (Y3). A total of 9 experimental runs were generated using Design-Expert software.

The experimental data were fitted to a second-order polynomial equation, and analysis of variance (ANOVA) was used to evaluate the significance of the model and individual factors. Response surface plots were generated to visualize the interaction effects of formulation variables. Optimization was performed using desirability functions to identify the best formulation conditions (12).

2.5 Preparation of Ibuprofen-Loaded Nanoparticles

The nanoprecipitation method was used to prepare nanoparticles. The organic phase was prepared by dissolving ibuprofen (100 mg) and Eudragit RS100 (in a ratio of the formulation) in 10 mL of ethanol. The aqueous phase was made up of 50 mL of distilled water with PVA or Poloxamer 188 at the desired concentration.

The dropwise addition of the organic phase (1 mL/min) was done to the aqueous phase under constant magnetic stirring at a predetermined speed (8001200 rpm). The mixture was shaken in 2 hours to ensure that all the solvent was evaporated and the nanoparticles were formed.

The resulting nanosuspension was centrifuged at 15,000 rpm in 30 minutes to separate nanoparticles. The nanoparticles collected were washed using distilled water and kept at 4C to be analyzed later. Nanoprecipitation is very popular when it comes to the preparation of polymeric nanoparticles because it is simple and can be used to produce uniform particles (13). General procedure of preparing ibuprofen-loaded nanoparticles is given in table 3.

Table 3. General procedure for preparation of ibuprofen-loaded nanoparticles

Step	Procedure	Operating condition	Purpose
1	Dissolution of ibuprofen and Eudragit RS100 in ethanol	100 mg drug in 10 mL ethanol	Formation of organic phase
2	Preparation of aqueous stabilizer phase	50 mL distilled water with stabilizer	External phase preparation
3	Dropwise addition of organic phase	1 mL/min	Controlled nanoparticle formation
4	Magnetic stirring	800–1200 rpm for 2 h	Solvent diffusion and particle stabilization
5	Centrifugation	15,000 rpm for 30 min	Separation of nanoparticles
6	Washing and storage	Distilled water; 4°C	Purification and preservation

2.6 Characterization of Formulations

2.6.1 Particle size, polydispersity index, and zeta potential

Dynamic light scattering (Malvern Zetasizer) was used to measure particle size, polydispersity index (PDI), and zeta potential. Before analysis, the samples were diluted using distilled water. Particle size represents the nanoscale properties, whereas PDI shows uniformity of size distribution. Zeta potential was used to evaluate dispersion stability (14).

2.6.2 Entrapment efficiency

Entrapment efficiency was determined by centrifugation at 15,000 rpm for 30 minutes. The supernatant containing free drug was analyzed using a UV–visible spectrophotometer at 221 nm. Entrapment efficiency was calculated as:

$$Entrapment\ Efficiency\ (\%) = \frac{Total\ Drug - Free\ Drug}{Total\ Drug} * 100$$

2.6.3 Morphological analysis

Scanning electron microscopy (SEM) was used to analyze the surface morphology of the nanoparticles. Samples were dried and placed on aluminum stubs and coated with gold and observed using the right magnification.

2.6.4 Drug content

The content of the drugs was calculated by dissolving a known quantity of nanoparticles in ethanol and then spectrophotometrically analyzed at 221 nm. Table 4 Displays the characterization parameters and techniques.

Table 4. Characterization parameters and methods

Parameter	Method/Instrument	Purpose
Particle size	Dynamic light scattering	Determination of nanoscale size
Polydispersity index	Dynamic light scattering	Assessment of size distribution
Zeta potential	Dynamic light scattering	Evaluation of colloidal stability
Entrapment efficiency	Centrifugation + UV spectrophotometry	Estimation of drug encapsulation
Morphology	Scanning electron microscopy	Surface and shape analysis

Drug content	UV spectrophotometry at 221 nm	Quantification of incorporated drug

2.7 In Vitro Drug Release Study

Drug release was evaluated using a dialysis membrane method (molecular weight cutoff: 12,000 Da). Nanoparticles equivalent to 50 mg ibuprofen were placed in a dialysis bag and immersed in 250 mL phosphate buffer (pH 7.4) maintained at 37 ± 0.5°C with continuous stirring at 100 rpm. The samples of 5 mL were taken at a set time and replaced by fresh buffer. Samples were examined spectrophotometrically at 221 nm and cumulative drug release was determined. This is a common technique to measure release behavior of nanoparticle systems (9, 15). The conditions in this study are presented in Table 5.

Table 5. Conditions used for in vitro drug release study

Parameter	Condition
Method	Dialysis membrane diffusion
Membrane MWCO	12,000 Da
Drug equivalent	50 mg ibuprofen
Dissolution medium	Phosphate buffer, pH 7.4
Medium volume	250 mL
Temperature	37 ± 0.5°C
Stirring speed	100 rpm
Sampling volume	5 mL
Analytical wavelength	221 nm

2.8 Drug Release Kinetics

The data of drug release were modeled to zero-order, first-order, Higuchi and Korsmeyer-Peppas models. Correlation coefficient (R^2) was used to select the best-fit model. The Korsmeyer–Peppas exponent (n) was used to determine the release mechanism (16). Table 6 shows mathematical models used for drug release kinetics.

Table 6. Mathematical models used for drug release kinetics

Model	Equation	Interpretation
Zero-order	$Q_t = Q_0 + k_0 t$	Constant release over time
First-order	$\log Q = \log Q_0 - \frac{k_1 t}{2.303}$	Release dependent on remaining drug
Higuchi	$Q_t = k_H t^{1/2}$	Diffusion-controlled release
Korsmeyer–Peppas	$\frac{M_t}{M_\infty} = kt^n$	Empirical model for release mechanism

2.9 Statistical Analysis

Each experiment was done thrice, and the findings were presented in the form of mean and standard deviation. Design-Expert software was used to perform statistical analysis. ANOVA was used to establish statistical significance, where $p < 0.05$ was regarded as significant. Model adequacy was evaluated using R^2, adjusted R^2, predicted R^2, and adequate precision values (15).

3. RESULTS

3.1 Computational Modeling Outcomes

The interaction between ibuprofen and the selected excipients was studied using molecular docking studies. The docking outcomes showed that ibuprofen had the best interaction with Eudragit RS100, with a binding energy of -6.8 kcal/mol, over polyvinyl alcohol (-5.2 kcal/mol) and Poloxamer 188 (-4.7 kcal/mol). The interaction profile showed that there was the existence of hydrophobic interactions and hydrogen bonding, which showed good compatibility between ibuprofen and the polymer.

These results in Table 7 justify the choice of Eudragit RS100 as the major polymer to be used as a matrix in the formulation of nanoparticles. The relatively weaker interactions with PVA and Poloxamer 188 indicate that they are stabilizers, as opposed to drug-binding excipients.

Table 7. Molecular docking results of ibuprofen with excipients

Excipients	Binding Energy (kcal/mol)	Interaction Type	Interpretation
Eudragit RS100	−6.8	Hydrophobic + H-bonding	Strong compatibility
Polyvinyl alcohol	−5.2	Weak hydrogen bonding	Moderate compatibility
Poloxamer 188	−4.7	Van der Waals interactions	Low compatibility

3.2 Effect of Formulation Variables on Nanoparticle Characteristics

The Box–Behnken experimental design generated nine formulations as in table 8 with varying levels of polymer concentration (X1), surfactant concentration (X2), and stirring speed (X3). The responses observed are given in the form of mean standard deviation (n = 3).

Table 8. Experimental design and observed responses

Run	X1 (%)	X2 (%)	X3 (rpm)	Particle Size (nm)	Entrapment Efficiency (%)	Drug Release (%)
1	1	0.5	1000	212 ± 4.8	67.9 ± 1.9	81.6 ± 1.5
2	3	0.5	1000	338 ± 6.2	78.6 ± 2.1	71.2 ± 1.8
3	1	1.5	1000	188 ± 4.5	65.8 ± 1.7	87.9 ± 1.4
4	3	1.5	1000	315 ± 6.8	80.9 ± 2.2	73.1 ± 1.6
5	2	1.0	800	285 ± 5.9	74.6 ± 2.0	75.3 ± 1.7
6	2	1.0	1200	168 ± 4.1	72.3 ± 1.8	86.1 ± 1.3
7	2	0.5	800	298 ± 5.5	75.8 ± 2.1	72.4 ± 1.9
8	2	1.5	1200	172 ± 4.3	69.7 ± 1.6	84.7 ± 1.2
9	2	1.0	1000	198 ± 4.7	73.5 ± 1.9	79.8 ± 1.5

The size of the particles was between 168 ± 4.1 nm and 338 ± 6.2 nm, which is a confirmation of nanoscale formulation. The efficiency of entrapment was 65.8 to 80.9 and the release of the drug was 71.2 to 87.9, which means that the variables of the formulation had a significant impact.

As concentration of polymer increased, the size of the particles and entrapment efficiency increased, and the speed of stirring had a strong negative effect on the size of the particles as a result of better shear dispersion.

3.3 Statistical Analysis and Model Fitting

The experimental data in Table 9 were analyzed using ANOVA to evaluate the significance of formulation variables.

Table 9. ANOVA for particle size (Y1)

Source	Sum of Squares	df	Mean Square	F-value	p-value
Model	47520	9	5280.0	17.96	<0.001
X1	20540	1	20540	69.85	<0.0001
X2	5600	1	5600	19.03	0.002
X3	15800	1	15800	53.75	<0.0001
Error	1470	5	294	—	—

The model was statistically significant ($p < 0.001$), indicating that formulation variables significantly affected particle size.

- **Model Statistics**
- $R^2 = 0.974$
- Adjusted $R^2 = 0.949$
- Predicted $R^2 = 0.927$
- Adequate Precision = 14.9

These values indicate excellent model reliability and predictive capability.

3.4 Effect on Entrapment Efficiency

Polymer concentration and surfactant concentration had a significant effect on the entrapment efficiency. An increase in polymer concentration enhanced the encapsulation of the drug because of an increase in the formation of the matrix, and a high concentration of surfactant led to a slight decrease in the entrapment efficiency because of a higher solubility of the drug in the aqueous phase.

The optimized formulation showed entrapment efficiency of 78.1 ± 1.8%**,** indicating effective drug incorporation.

3.5 In Vitro Drug Release

The drug release profiles were biphasic with an initial burst release and a sustained release of 24 hours. The optimized formulation exhibited 84.6 ± 1.4% cumulative drug release, which is a controlled release behavior.

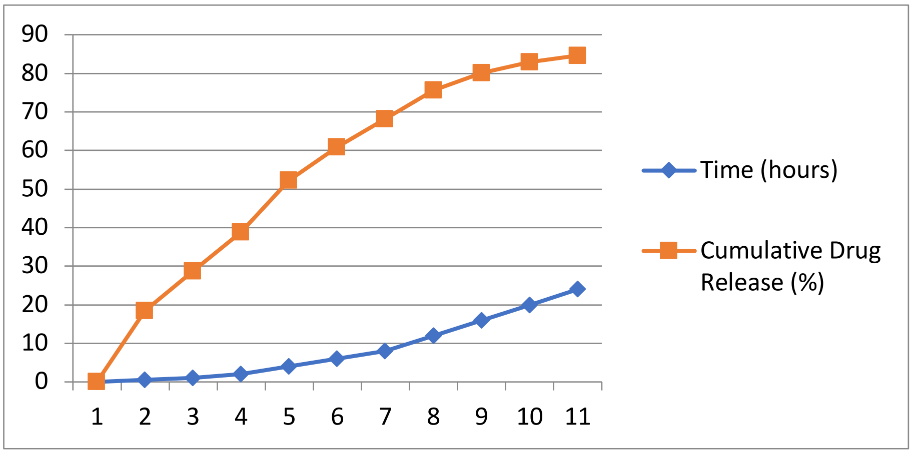

Figure 1. In vitro drug release profile of optimized formulation

Figure 1 presents In vitro drug release profile of ibuprofen-loaded Eudragit RS100 nanoparticles with biphasic release behavior with an initial burst release followed by sustained release in 24 hours.

3.6 Drug Release Kinetics

Drug release data were fitted to various kinetic models to determine the mechanism of release.

Table 8. Drug release kinetic modeling

Model	R² Value	Interpretation
Zero-order	0.908	Moderate fit
First-order	0.931	Good fit
Higuchi	0.976	Best fit (diffusion-controlled)
Korsmeyer–Peppas	0.962	Non-Fickian transport

The highest R² value for the Higuchi model confirms that drug release was predominantly diffusion-controlled.

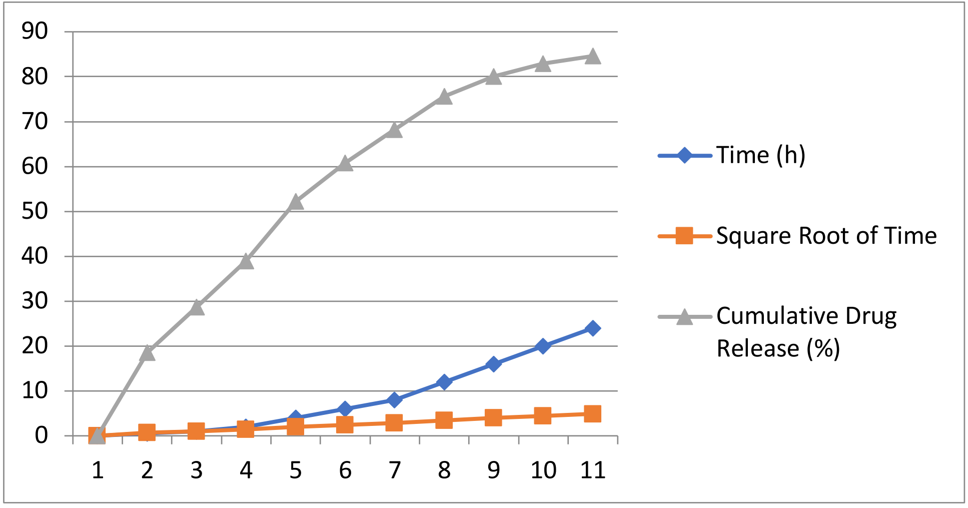

Figure 2: Kinetic Model Fitting

Figure 2 showed that the Higuchi plot had a good linearity (R 2 = 0.976) meaning that the release of the drug was proportional to the square root of time. This validates that the release is diffusion-controlled, which is in line with the Higuchi model of diffusion-controlled matrix-based drug delivery systems.

3.7 Optimization and Validation

The model was used to predict an optimized formulation which was prepared and tested experimentally. The values observed were closely related to the predicted values with the percentage prediction error of less than 5, which was an indication of model validity.

3.8 Correlation Between Computational and Experimental Findings

There was a good agreement between the computational and experimental results. The excipient with the greatest binding affinity (Eudragit RS100) also exhibited better formulation behavior in regards to entrapment efficiency and drug release control. This proves the practicality of computational tools as aiding techniques in formulation design.

4. DISCUSSION

The current research demonstrated that the rational design of ibuprofen-loaded polymeric nanoparticles can be facilitated by the use of a combined computational-experimental approach. Molecular docking revealed that Eudragit RS100 was the most desirable excipient, and this was also in line with the experimental results, where the polymer formed formulations with reasonable entrapment efficiency and was able to release the drug. These findings indicate that computational pre-screening may be a helpful supportive measure in early formulation design.

The increased interaction of ibuprofen with Eudragit RS100 relative to PVA and Poloxamer 188 is in line with the functional role of Eudragit RS100 as the matrix-forming polymer with the other excipients primarily serving as stabilizers. Nevertheless, the outcomes of docking cannot be used to verify solid-state compatibility or long-term stability and should be viewed as initial evidence that needs to be supported by other methods like FTIR, DSC, or XRD.(16,17)

The impact of the formulation variables on the nanoparticle performance was consistent with the known principles of nanoprecipitation. The higher concentration of polymer, the larger particle size and the higher entrapment efficiency, likely because of the increased viscosity and availability of more matrix during the formation of the particles. Conversely, the faster the stirring rate the smaller the particle size due to increased shear and dispersion. The same has been observed in the studies of nanoparticles formulations (5,7,8).

The optimized nanoparticles exhibited a biphasic release profile of drugs, which was burst release and sustained release. This trend is characteristic of polymeric nanoparticles and is due to the rapid release of surface-associated drug and slower diffusion of entrapped drug through the polymer matrix.(9,10) The Higuchi model was the most suitable model to fit the release data, and diffusion was the predominant drug release mechanism, with the KorsmeyerPeppas model indicating the presence of both diffusion and matrix relaxation.

The statistical optimization ensured that Box-Behnken design was appropriate in testing the impact of formulation variables on particle size, entrapment efficiency and release behavior. The large model terms, large satisfactory R 2 values, and small prediction error, suggest that the model was sufficient to describe the experimental design space. The results indicate the applicability of Quality by Design-based optimization to the development of nanoparticles formulations (4,5).

One of the main findings of this work was the correlation between computational screening and experimental performance. The excipient with the most desirable docking profile also exhibited superior formulation behavior, suggesting that computational tools can help to minimize unnecessary formulation trials when used in conjunction with experimental validation. However, the study is limited. Computational analysis was limited to docking, other characterization like FTIR, DSC, XRD, zeta potential and stability analysis were not performed and release analysis was only done in vitro. Hence, the results are to be viewed as a preliminary formulation optimization research, but not as direct indicators of therapeutic effectiveness.

In general, the research shows the usefulness of combining computational screening and experimental optimization in formulation design. The findings show that the ibuprofen nanoparticles based on Eudragit RS100 can be optimized with the help of this workflow, though additional solid-state characterization and in vivo research is required to prove their relevance to translation to the fullest extent (15-17).

5. CONCLUSION

The current research has shown that the joint approach of computational and experimental method can be successfully implemented in the creation of ibuprofen-loaded polymeric nanoparticles. Analysis of molecular docking revealed that Eudragit RS100 was the most desirable excipient among the shortlisted candidates, and this computerized forecast aligned with the results of the resultant experimental study. The optimized formulation that was made by nanoprecipitation had a nanoscale size of particles, acceptable entrapment efficiency and a sustained drug release profile, which showed that the formulation method used was appropriate in enhancing the delivery properties of ibuprofen.

Box Behnken design was able to determine the effect of polymer concentration, surfactant concentration, and stirring speed on the important formulation responses. Polymer concentration and stirring speed were the most significant variables that influenced the particle size and encapsulation behavior, which validated the significance of both the formulation composition and processing conditions in the optimization of nanoparticles. The release of the drug through the optimized formulation was biphasic and could be best explained using the Higuchi model implying that diffusion was the most important release mechanism.

Combined, the results suggest that computational screening may be a valuable complementary method to excipient selection in conjunction with systematic experimental optimization and physicochemical analysis. Despite the fact that the study is still confined to in vitro and formulation-level evaluation, it offers a logical framework of incorporating molecular modeling and design of experiments in the pharmaceutical formulation development. Further solid-state characterization, stability testing, and in vivo testing should be considered in future work to further confirm the translational applicability of the developed nanoparticulate system.

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