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Original Article

Integration of Artificial Intelligence-Assisted Open-Source Programming in Pharmaceutical Research and Development: A Multi-Domain Evaluation of Dose Calculation, Granulation Process, Formulation Optimization, and *In vitro-In vivo* Modeling

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ABSTRACT

Background: The integration of artificial intelligence with open-source programming languages such as Python and R has the potential to enhance computational efficiency and analytical precision in pharmaceutical research and development. **Objectives:** This study aimed to evaluate the feasibility and reliability of artificial intelligence-assisted open-source programming across multiple pharmaceutical application domains, including dose calculation, process computation, formulation optimization, and pharmacokinetic modeling. **Materials and Methods:** Artificial intelligence- assisted Python scripts were developed for paediatric dose calculations using standard empirical equations and for wet granulation process computations. Statistical optimization of formulations was performed using RStudio (version 4.3.3) through Response Surface Methodology with a 2^3 factorial design. *In vitro-in vivo correlation modeling* was conducted using deconvolution techniques and regression analysis in R. **Results:** The computational outputs generated using Python were consistent with manual calculations and standard references, confirming accuracy in dose and process computations. In formulation optimization, the predicted optimal conditions (8% w/v cryoprotectant, 100 mg drug loading, 15 min trituration) achieved 98.25% drug content, 16.28 mg/mL solubility, and 44.60% drug release at 10 min. In *in vitro-in vivo correlation* modeling, nonlinear polynomial regression demonstrated superior predictive performance (R^2=0.8698, RMSE=0.1420, MAE=0.1271) compared to linear models, with an absorption rate constant (k_a=0.0845) consistent with known pharmacokinetics. **Conclusion:** Artificial intelligence-assisted open-source programming using Python and R demonstrated reliable performance across diverse pharmaceutical applications. These tools provide cost-effective, flexible, and scalable alternatives to proprietary software, supporting their broader adoption in pharmaceutical research and development.

Keywords: Artificial Intelligence, *IVIVC*, Open-Source Programming, Pharmaceutical Research and Development, Python, R Programming.

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INTRODUCTION

Pharmaceutical Research and Development (R&D) relies heavily on precise experimental design, accurate quantitative analysis, and robust data interpretation. Conventional laboratory-based approaches often involve complex calculations, iterative formulation optimization, and pharmacokinetic modeling, which are time-consuming and susceptible to human error. These limitations can compromise the efficiency, reproducibility, and decision-making in pharmaceutical workflows. In recent years, the integration of Artificial Intelligence (AI) with computational tools has significantly transformed pharmaceutical R&D by enabling automation, improving analytical accuracy, and supporting data-driven decision-making. Several proprietary software platforms, including Schrödinger Suite, Discovery Studio, Design-Expert, Minitab, and GastroPlus, are widely used across different domains of pharmaceutical sciences. These tools

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facilitate molecular modeling, formulation optimization, statistical design of experiments, and pharmacokinetic simulations, thereby reducing experimental burden and accelerating development timelines.

Despite their advantages, these proprietary platforms are often associated with significant limitations, including high licensing costs, dependence on specialized expertise, restricted accessibility, and limited interoperability. Such constraints can hinder their adoption, particularly in academic and resource-limited research environments. Open-source programming languages such as Python and R have emerged as powerful alternatives due to their flexibility, transparency, and cost-effectiveness. Python enables efficient automation, scripting, and reproducible workflows, whereas R, particularly RStudio, provides extensive capabilities for statistical modeling, data visualization, and optimization. The incorporation of AI-assisted code generation further enhances the usability of these platforms by reducing the technical barrier for non-expert users. Although AI-assisted open-source programming has gained increasing attention, its practical applicability and reliability across diverse pharmaceutical domains remain unexplored. A systematic evaluation is necessary to establish whether these tools can effectively replicate or complement the functions of established proprietary software. Therefore, the present study aims to evaluate the feasibility and reliability of AI-assisted Python and R programming across multiple pharmaceutical applications, including (i) dose calculation and wet granulation computation, (ii) statistical optimization using Response Surface Methodology (RSM), and (iii) development of *in vitro-in vivo Correlation* (*IVIVC*) models using deconvolution and regression approaches. By integrating these case applications within a unified framework, this study investigates the potential of AI-assisted open-source tools as scalable and cost-effective solutions in pharmaceutical R&D.

MATERIALS AND METHODS

In vivo animal studies were performed with the approval of the Institutional Animal Ethics Committee (IAEC Approval No. CPS GMC/IAEC-1/24/16) and according to the guidelines of the CCSEA, Government of India.

Study design and computational framework

This study was designed as a multi-domain evaluation of AI-assisted open-source programming tools across representative pharmaceutical applications. Four computational modules were developed and assessed, encompassing (i) dose calculation, (ii) wet granulation process computation, (iii) statistical formulation optimization, and (iv) *IVIVC* modeling.

AI-assisted code generation was employed to develop scripts in Python and R, enabling automation of calculations, statistical modeling, and pharmacokinetic analysis. The outputs obtained from these computational tools were compared with conventional manual calculations and established theoretical models to assess accuracy, reliability, and reproducibility.

Module 1. Dose calculation based on age

Paediatric dose calculations were performed using standard empirical equations from posology:

Dilling's formula (12-20 years)

$$\text{Child dose (C.D)} = \frac{(Age(years) \times Adult\ Dose)}{20}$$

Fried's formula (up to 24 months)

$$\text{Child dose (C.D)} = \frac{(Age(months) \times Adult\ Dose)}{150}$$

Young's formula (1-12 years)

$$\text{Child dose (C.D)} = \frac{(Age(years) \times Adult\ Dose)}{Age + 12}$$

AI-assisted Python scripts were developed to automate the calculations (Figure 1). User-defined inputs (age and adult dose) were processed to generate paediatric doses. The outputs were validated by comparison with manually calculated values.

Module 2. Wet granulation process computation

A model formulation of Paracetamol 500 mg tablets prepared by wet granulation was selected for computational analysis. The formulation comprised Paracetamol, starch paste (10% w/v), starch powder (10% w/w), talc (1% w/w), and magnesium stearate (1% w/w).

The granulation process involved blending of Paracetamol with a portion of starch powder, followed by wet massing using starch paste. The wet mass was granulated, dried, and passed through sieve no. 66. The dried granules were then placed over sieve no. 44, and the granules retained on sieve no. 44 were collected. The fines passing through sieve no. 44 were separated, and an amount equivalent to 15% of the retained granules was reintroduced into the formulation. The remaining starch powder (equivalent to 5% of the drug weight), along with talc and magnesium stearate, was incorporated into the granules using geometric dilution. The final blend was then compressed.

AI-assisted Python scripts were developed to compute ingredient quantities, fines adjustment, and yield parameters based on formulation composition and process constraints (Supplementary Figure 1). The computational outputs were validated against manual calculations to assess accuracy and consistency.

Module 3. Statistical optimization of solid dispersions

Statistical optimization of omeprazole-milk based solid dispersion was performed using RStudio (version 4.3.3) under Response Surface Methodology (RSM).[1] A three-factor, two-level

(2^3) full factorial design with center point replication was employed. The central point (0, 0, 0) was studied in quintuplicate to estimate experimental error and assess model adequacy.[2] Three independent variables selected were; the concentration of cryoprotectant (X_1), drug loading (X_2), and trituration time (X_3), with solubility (Y_1), % drug content (Y_2), and cumulative % drug release at 10th min (Y_3). Each factor was evaluated at three levels: low (-1), medium (0), and high (+1), corresponding to the actual values presented in Table 1. The experimental runs generated based on the factorial design are shown in Supplementary Table 1.[3]

AI-assisted R-based programming was used to develop polynomial regression models incorporating main effects and interaction terms. The general form of the model is expressed as:

$$Y=\beta_0+\beta_1X_1+\beta_2X_2+\beta_3X_3+\beta_{12}X_1X_2+\beta_{13}X_1X_3+\beta_{23}X_2X_3$$

The statistical significance of the model and factor interactions was evaluated using Analysis of Variance (ANOVA) developed through AI- assistance in RStudio. Model adequacy was assessed through lack-of-fit testing and residual analysis. Contour plots and three-dimensional response surface plots were generated to visualize the interaction effects and to identify optimal formulation conditions.[4,5]

Module 4. *In vitro-in vivo* correlation

IVIVC modeling was performed for the rosuvastatin-hydroxypropyl-β-cyclodextrin (RS-HP-β-CD) inclusion complex using RStudio (version 4.3.3) (Supplementary Figure 2).[6,7] A model-based analytical deconvolution approach was employed to estimate the fraction of drug absorbed from plasma concentration-time data. Both Wagner-Nelson (one-compartment model) and Loo-Riegelman (multi-compartment model) methods were applied to derive the fraction absorbed.[6,7] The obtained absorption profiles were correlated with *in vitro* dissolution data using linear and nonlinear regression models to establish *IVIVC* relationships.[8-16] AI-assistance was utilized in R-based programming code generation and execution of deconvolution analysis, regression modeling, and parameter estimation. Model performance and predictive accuracy were evaluated using statistical parameters including Coefficient of Determination (R^2), Root Mean Square Error (RMSE), Mean Absolute Error (MAE), Akaike Information Criterion (AIC), and Bayesian Information Criterion (BIC). Model validation and robustness were further assessed through sensitivity analysis and bootstrap resampling techniques to evaluate the stability, reliability, and predictive capability of the developed *IVIVC* models.[6,7]

RESULTS

AI-assisted open-source computational tools demonstrated consistent and reliable performance across all evaluated pharmaceutical applications.

Modules 1 and 2. Dose calculation and Wet granulation computation

The AI-assisted Python models developed for paediatric dose calculation generated outputs identical to those obtained through manual calculations using standard empirical equations. Similarly, the Python-based computational model for wet granulation process calculations accurately estimated ingredient quantities, fines adjustment, and yield parameters. The results obtained were consistent with manual calculations, demonstrating the reliability of the developed scripts in handling formulation process computations.

Module 3. Statistical optimization of solid dispersions

The statistical optimization of omeprazole-based solid dispersions using RSM successfully identified the optimal formulation conditions. The optimized parameters were 8% w/v cryoprotectant concentration, 100 mg drug loading, and 15 min trituration time, which resulted in 98.25% drug content, 16.28 mg/mL solubility, and 44.60% cumulative drug release at 10 min.

The developed polynomial regression models revealed that cryoprotectant concentration (X_1) and trituration time (X_3) exerted a positive influence on all response variables, whereas drug loading (X_2) showed a negative effect. The polynomial equations describing the relationship between the independent variables and responses are as follows:

Table 1: Factors with their levels and response selected.

Factors	Levels used		
Coded values	Low (-1)	Medium (0)	High (+1)
X1= Concentration of cryoprotectant (%w/v)	2	5	8
X2= Drug loading (mg)	100	150	200
X3 =Trituration time (min)	5	10	15
Response	Constraints		
Y1= Drug content (%)	≥ 75		
Y2=Solubility (mg/mL)	≥ 10		
Y3=Cumulative % drug released at 10th min (%)	≥ 35		

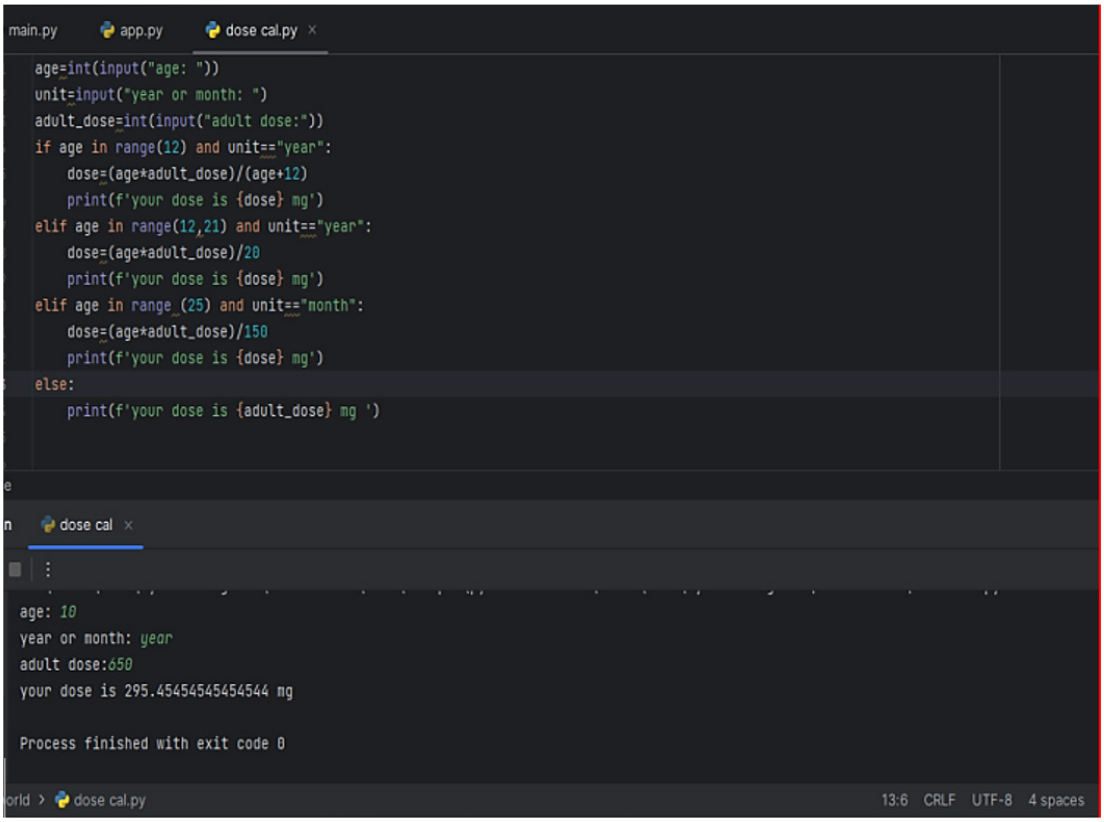


Figure 1: AI-assisted Python codes for dose calculations.

$$Y_1=93.9717+ 2.17\ X_1 -1.225\ X_2 + 0.6175\ X_3 -0.58\ X_2X_3 \ldots\ldots\ldots\ldots (1)$$

$$Y_2= 13.803 + 1.2571\ X_1 -0.7963\ X_2 + 0.8182\ X_3 + 0.2726\ X_1X_2 -0.1873\ X_1X_3 \ldots. (2)$$

$$Y_3=40.1301 + 1.7105\ X_1 -1.0925\ X_2 + 1.335\ X_3 -0.5425\ X_1X_2 + 0.7132\ X_1X_3 + 0.5467\ X_2X_3 \ldots\ldots\ldots\ldots (3)$$

ANOVA confirmed the statistical significance of the developed models, with significant contributions from both main effects and interaction terms (Table 2).[17] The contour and three-dimensional response surface plots (Figure 2) further illustrated the interaction effects and supported the identification of optimal formulation conditions.[4,5]

Module 4. *In vitro-in vivo* correlation modeling

The *IVIVC* analysis demonstrated a clear relationship between *in vitro* dissolution and *in vivo* absorption profiles of the RS-HP-β-CD inclusion complex.[6,7] The fraction of drug absorbed, obtained through deconvolution, showed good agreement with the dissolution data (Table 3).

Comparative evaluation of regression models indicated that the nonlinear polynomial model exhibited superior predictive performance compared to the linear model. The polynomial model achieved an R^2 value of 0.8698, RMSE of 0.1420, and MAE of 0.1271, whereas the linear model showed lower predictive accuracy (Table 4).[6,7]

The estimated absorption rate constant (k_a=0.0845) was consistent with reported pharmacokinetic characteristics of rosuvastatin. Additionally, lower AIC and BIC values for the polynomial model further confirmed its suitability for describing the IVIVC relationship.[6,7]

Sensitivity analysis and bootstrap resampling indicated stable model performance of the model parameters (Figures 3 and 4).

DISCUSSION

The present study systematically evaluated the feasibility and reliability of AI-assisted open-source programming tools, such as Python and R, across multiple pharmaceutical application domains, including dose calculation, formulation process computation, statistical optimization, and pharmacokinetic modeling. The findings collectively demonstrate that such tools can effectively perform diverse pharmaceutical computations with a high degree of consistency when compared to conventional approaches.

In the context of paediatric dose calculation, the Python-based models generated outputs identical to those obtained using standard empirical equations, indicating accurate implementation of established posological principles. Given that manual dose calculations are prone to human error, particularly in repetitive

clinical or academic settings, the use of automated computational tools can significantly improve calculation reliability and operational efficiency. Similarly, the wet granulation computation module accurately reproduced formulation calculations, including ingredient quantification and process-related adjustments such as fines correction. Considering the multi-step and calculation-intensive nature of granulation processes, the adoption of such computational tools may reduce variability and enhance standardization in formulation development workflows.

The statistical optimization study further highlights the capability of open-source tools in handling complex experimental designs. The application of RSM using RStudio successfully identified optimal formulation conditions and generated statistically significant polynomial models describing the relationship between formulation variables and response outcomes. The observed positive influence of cryoprotectant concentration and trituration time, along with the negative effect of drug loading, is consistent with expected formulation behaviour in solid dispersion systems. The use of contour plots and response surface analyses enabled effective visualization of factor interactions and design space, demonstrating that open-source platforms can provide analytical outputs comparable to those obtained from proprietary statistical software packages.

The *IVIVC* modeling results provide further evidence of the applicability of AI-assisted open-source tools in advanced pharmacokinetic analysis. The successful implementation of both Wagner-Nelson and Loo-Riegelman deconvolution methods enabled estimation of drug absorption profiles and their correlation with *in vitro* dissolution data. The superior performance of the nonlinear polynomial model over the linear model suggests that the relationship between dissolution and absorption for the studied system is inherently nonlinear.[6,7] The estimated absorption rate constant was consistent with reported pharmacokinetic characteristics of rosuvastatin, supporting the reliability of the developed model. Additionally, the application of sensitivity analysis and bootstrap resampling indicates that the model parameters exhibit stable behaviour under varying conditions, reflecting the robustness of the computational approach.[6,7]

A key implication of this study is the demonstration that AI-assisted open-source programming can serve as a viable alternative to proprietary software in pharmaceutical R&D. Unlike commercial platforms, which are often associated with high costs and limited accessibility, open-source tools such as Python and R provide flexible, transparent, and customizable environments for computational analysis. The integration of AI-assisted code generation further reduces the technical barrier for researchers, enabling broader adoption without the need for specialized programming skills.

Despite these advantages, certain limitations should be acknowledged. This study evaluated selected application domains under controlled conditions, and the generalizability of these

Table 2: ANOVA table of polynomial equation for the response % drug content (Y_1), solubility (Y_2), response cumulative % drug release (Y_3).

	Degree of freedom	Sum of Squares	Mean Square	F value	Pr (>F)
FO (X_1, X_2, X_3)	3	52.727	17.5755	191.84	0.001398
TWI (X_1, X_2, X_3)	3	2.810	0.9368	10.226	0.01421
Residuals	5	0.458	0.0916		
Lack of fit	2	0.458	0.2290	4.0629e+25	<2.2e-16
Pure error	3	0.000	0.0000		
	Degree of freedom	**Sum of squares**	**Mean Squares**	**F value**	**Pr (>F)**
FO (X_1, X_2, X_3)	3	23.0711	7.6904	2.1554e+02	1.05e-05
TWI (X_1, X_2, X_3)	3	1.1084	0.3695	1.035e+01	0.01385
Residuals	5	0.1785	0.0357		
Lack of fit	2	0.1785	0.0892	7.43e+26	<2.2e-16
Pure error	3	0	0		
	Degree of freedom	**Sum of squares**	**Mean Squares**	**F value**	**Pr (>F)**
FO (X_1, X_2, X_3)	3	47.212	15.7373	9.47e+01	7.97e-05
TWI (X_1, X_2, X_3)	3	8.815	2.9382	1.77e+01	0.004299
Residuals	5	0.831	0.1662		
Lack of fit	2	0.831	0.4155	1.18e+27	<2.2e-16
Pure error	3	0	0		

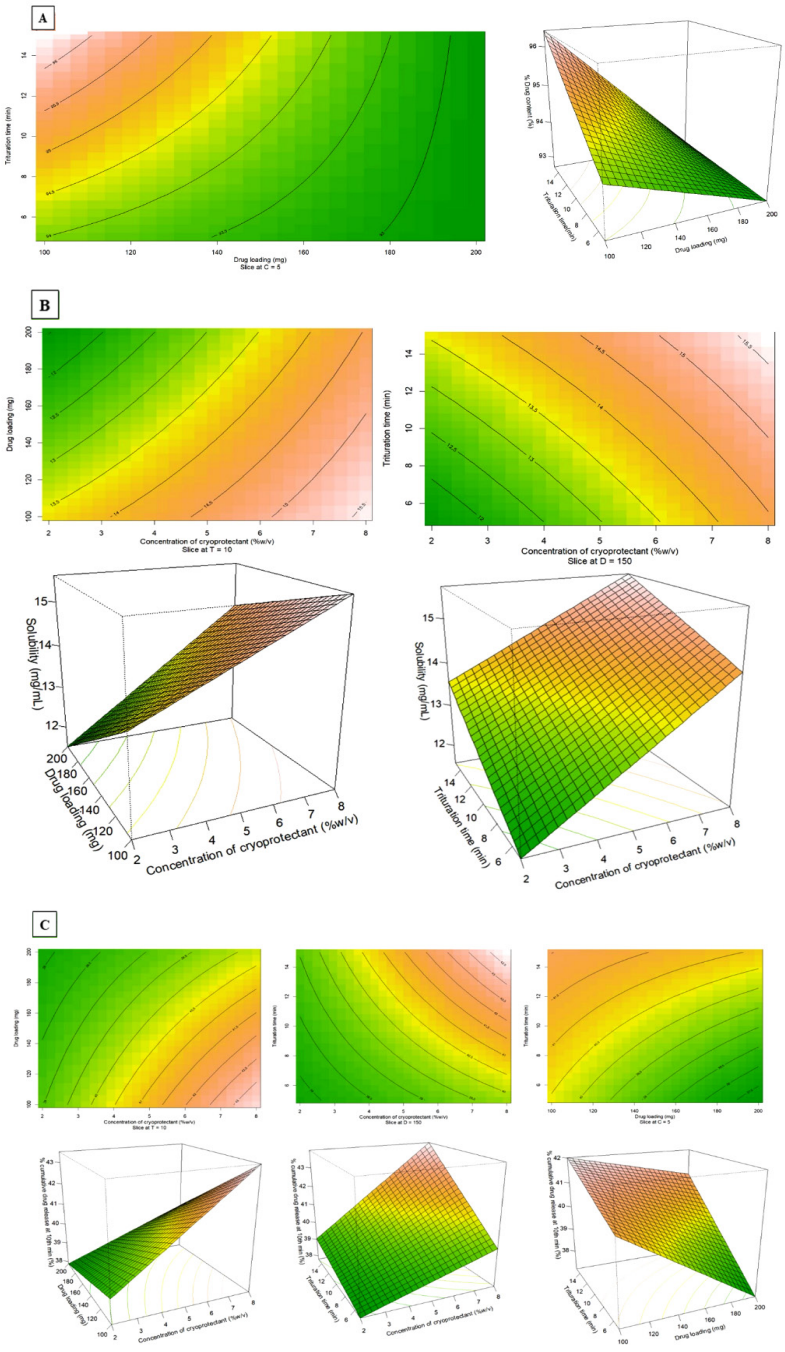


Figure 2: Contour and perspective plots for the effect of independent variables on (A) Y_1, (B) Y_2 and (C) Y_3.

Table 3: Predicted fraction absorbed.

Time (h)	Plasma concentration (ng/mL)	Fraction absorbed	Percent dissolved (%)
0.0	0.0000	0.0000000	0.000
0.5	135.3690	0.5466891	15.367
0.1	254.7350	1.0593061	26.247
0.2	249.3540	1.1519676	40.818
0.3	202.2684	1.0690685	59.683
0.4	176.5741	1.0537158	73.005
0.6	142.3510	1.0633466	99.996

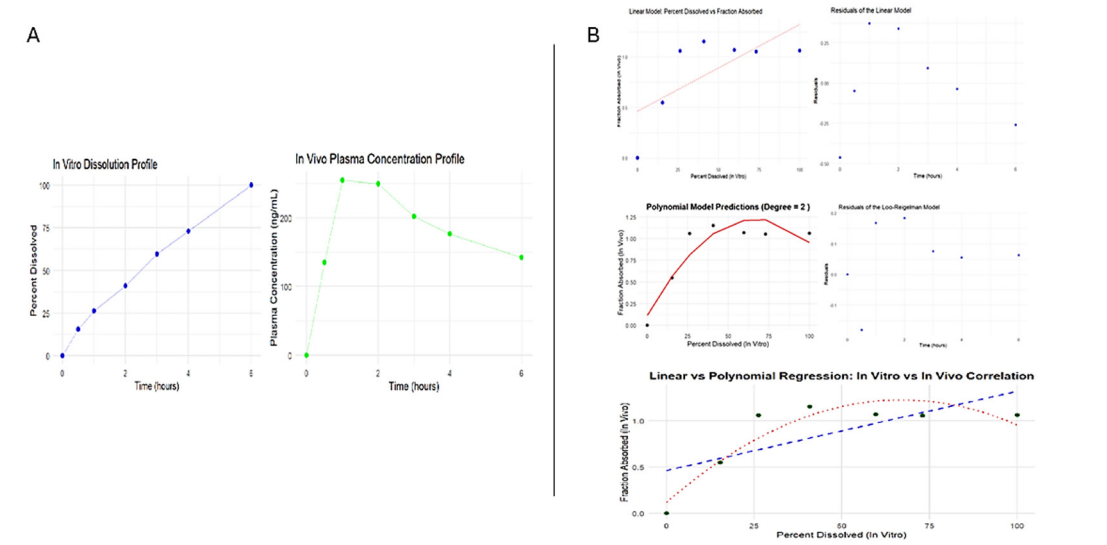


Figure 3: (A) *In vitro* dissolution profile and *in vivo* plasma concentration profile. (B) Evaluation of linear and Loo-Reigelman model.

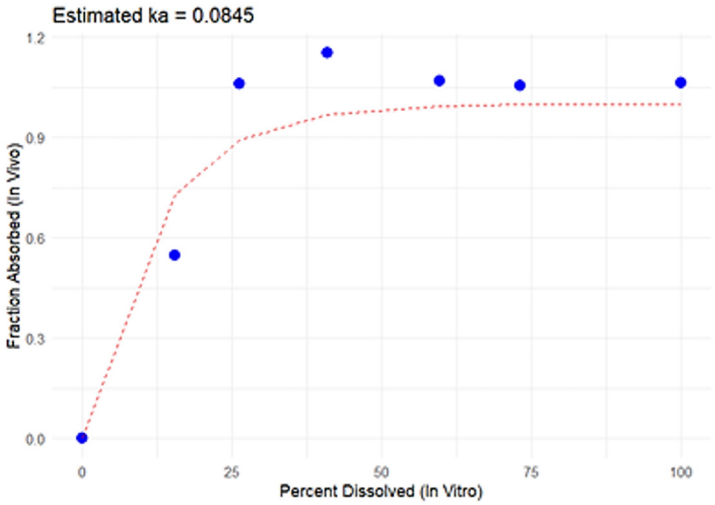


Figure 4: Estimation of absorption rate constant.

Table 4: Comparison between linear and polynomial models.

Parameter	Linear model	Polynomial model
R^2	0.4969	0.8698
RMSE	0.2792	0.1420
MAE	0.2298	0.1271

findings to more complex industrial-scale processes require further investigation. Additionally, while the computational models demonstrated consistency with manual calculations and theoretical expectations, their performance is inherently dependent on the accuracy of input data and model assumptions. In the *IVIVC* analysis, minor deviations in predicted absorption profiles may arise due to model simplifications or experimental variability, which should be considered during interpretation.

CONCLUSION

The present study demonstrates that AI-assisted open-source programming using Python and R can effectively support diverse pharmaceutical applications, including dose calculation, formulation process computation, statistical optimization, and pharmacokinetic modeling. The computational outputs generated across all evaluated domains showed consistency with conventional methods, indicating reliable performance of the developed models.

The integration of AI-assisted code generation further enhances the accessibility and usability of these tools, enabling researchers to implement complex computational workflows without extensive programming skills. Compared to proprietary software, open-source platforms offer significant advantages in terms of cost, flexibility, transparency, and scalability.

These findings highlight the potential of AI-assisted open-source tools as practical and efficient alternatives for pharmaceutical research and development. Their adoption may facilitate improved computational accuracy, workflow efficiency, and broader accessibility, particularly in academic and resource-limited settings.

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ABBREVIATIONS

AI: Artificial Intelligence; **AIC:** Akaike Information Criterion; **ANOVA:** Analysis of Variance; **BIC:** Bayesian Information Criterion; **C.D:** Child Dose; **IVIVC:** *In vitro-in vivo* Correlation; **MAE:** Mean Absolute Error; **R&D:** Research and Development; **RMSE:** Root Mean Square Error; **RS-HP-β-CD:** Rosuvastatin–Hydroxypropyl-β-Cyclodextrin; **RSM:** Response Surface Methodology.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ETHICAL APPROVAL

In vivo animal studies were performed with the approval of the Institutional Animal Ethics Committee (IAEC Approval No. CPS GMC/IAEC-1/24/16) and according to the guidelines of the CCSEA, Government of India.

SUMMARY

The study assessed the use of open-source programming languages like Python and R in conjunction with AI for a range of pharmaceutical Research and Development (R&D) tasks. As part of this study, pharmaceutical applications such as dose calculation, wet granulation process calculations, statistical formulation optimization and IVIVC modeling were selected. AI integrated Python and R were applied to develop programmes to automate calculations, to carry out statistical optimization, and to build predictive models. The results generated were compared with those of conventional or existing methods. RSM was used to determine the effect of the critical formulation parameters on the product performance for the optimization. A statistical model was established to assess the extent of the relationship between the response variables and formulation factors, and significant effects were validated by analysis of variance. Deconvolution methods were used in IVIVC studies to determine the correlation between *in vitro* drug release and *in vivo* absorption profiles. A series of mathematical models were evaluated in order to determine their predictive ability and their usefulness for modeling the observed data in this study.

The results indicated that AI-powered open-source tools can be successfully employed for pharmaceutical calculations, formulation development, statistical optimization and pharmacokinetic modeling. These tools were effective in providing accurate, reproducible and efficient results, and in minimizing reliance on proprietary software. In conclusion, the research underscores the promise of AI assisted open-source tools for the pharmaceutical sector, which are versatile, accessible, and cost-effective.

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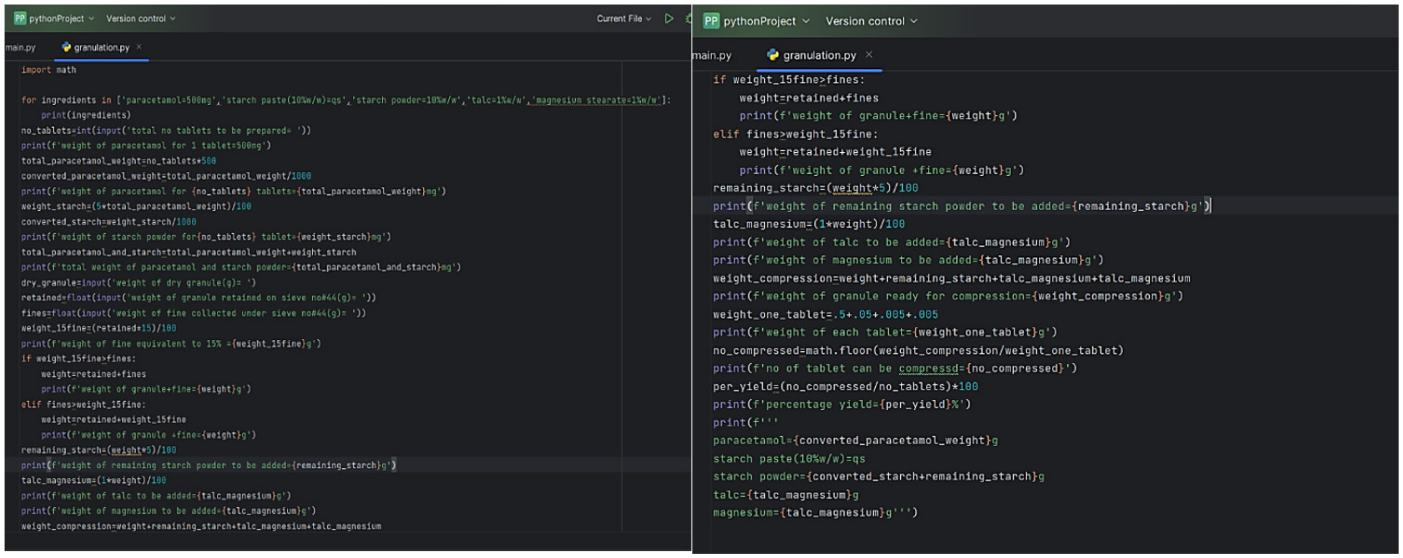
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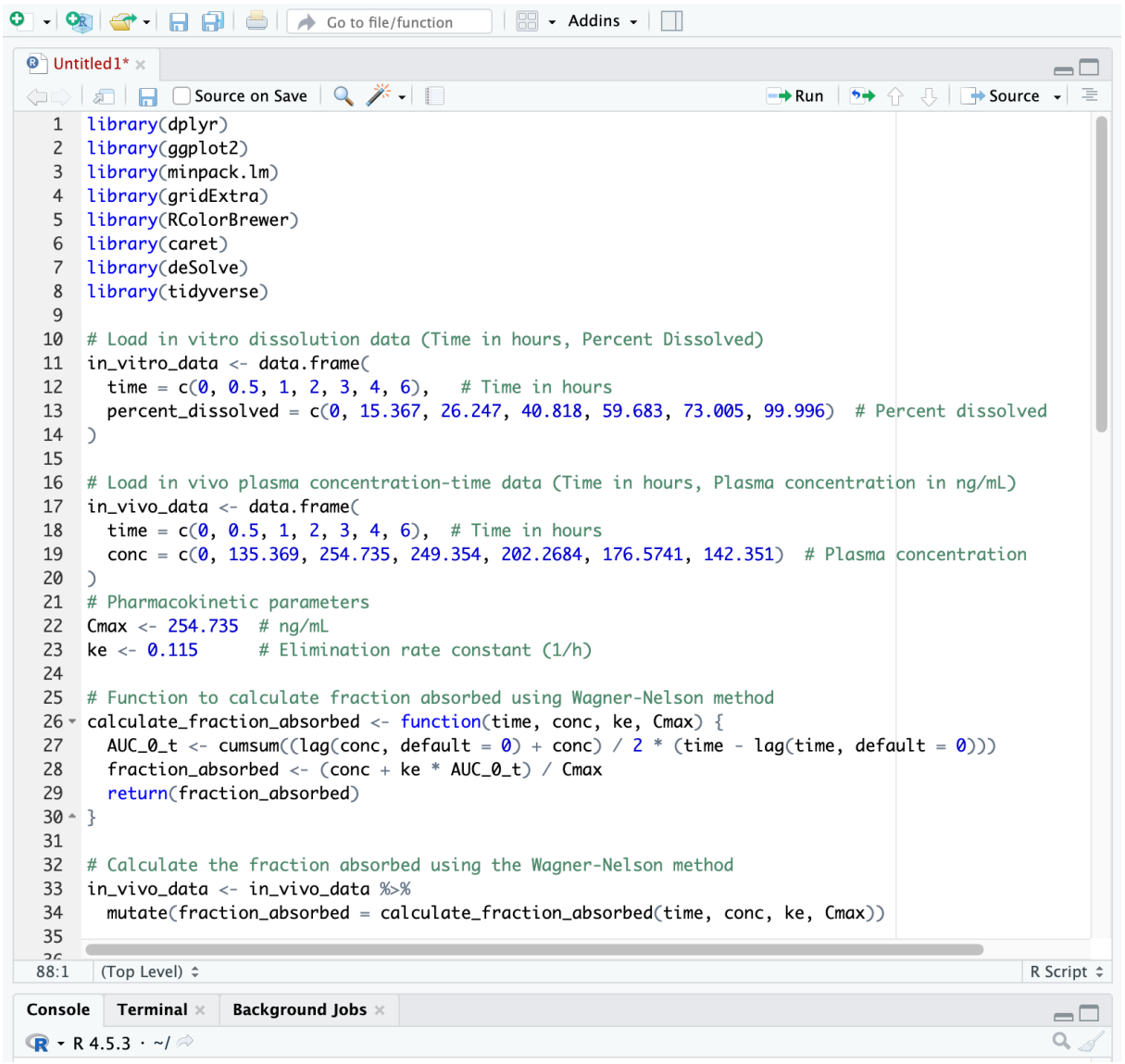
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Supplementary Table 1: Predicted trial runs for optimization.

Sl. No.	Run order	Std order	X_1	X_2	X_3	C	D	T
1.	1	11	0	0	0	5	150	10
2.	2	8	1	1	1	8	200	15
3.	3	2	1	-1	-1	8	100	5
4.	4	10	0	0	0	5	150	10
5.	5	12	0	0	0	5	150	10
6.	6	3	-1	1	-1	2	200	5
7.	7	1	-1	-1	-1	2	100	5
8.	8	6	1	-1	1	8	100	15
9.	9	7	-1	1	1	2	200	15
10.	10	5	-1	-1	1	2	100	15
11.	11	4	1	1	-1	8	200	5
12.	12	9	0	0	0	5	150	10



Supplementary Figure 1: AI- assisted Python codes for the calculations involved in the wet granulation process.



Supplementary Figure 2: R script used for IVIVC modelling and deconvolution analysis.