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Review Article

Multidisciplinary Approach for Designing of Drug Delivery System: Leveraging Artificial Intelligence and Experimental Design for Enhanced *Helicobacter pylori* Formulation Optimization

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ABSTRACT

The management of *Helicobacter pylori (H. pylori)* remains a complicated challenge worldwide. There is need for more effective optimised formulations with better therapeutic efficiency and less drug resistance. Rapid advancements have been achieved regarding the development of pharmaceutical formulations for the treatment of *H. pylori*, which demands new and improved approaches towards product optimization. This review gives an account of a combined approach of employing Design of Experiments and Artificial Intelligence techniques to enhance the optimization of pharmaceutical formulations for *H. pylori* treatment. The Design of Experiments concept aids in a systematic way of considering multiple variables and can optimize formulation parameters with a minimal number of experimental trials. Such techniques within Artificial Intelligence algorithms, machine learning, and predictive modelling all deal with the analysis of various complex data and allow for useful predictions, real-time optimization. Through the joint use of these two techniques, the formulation process could be revised to enable identification of important formulation factors and desired outcomes; therefore, it will speed up the development of new therapeutic solutions. This review assesses the use of the Design of Experiments and Artificial Intelligence in optimizing pharmaceutical formulations in the treatments against *H. pylori*. It also discusses various challenges and limitations associated with the usage of these technologies in pharmaceutical research and gives further suggestions for the future development process. The positive implementation of Design of Experiments and Artificial Intelligence promises great opportunities for *H. pylori* treatment, enabling drug formulation technology to improve patient compliance drastically.

Keywords: *Helicobacter pylori* treatment, Artificial intelligence, Design of experiments, 3D printing.

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INTRODUCTION

Helicobacter pylori (H. pylori) is a Gram-negative, spiral-shaped, microaerophilic bacterium that can live in the human stomach and is majorly responsible for a myriad of diseases responsible for affecting the gastrointestinal tract.[1] *H. pylori* is mainly responsible for causing peptic ulcers, and it has also been linked to horrible assorted diseases, such as duodenal ulcers, gastritis, Mucoid-Associated Lymphoid Tissue (MALT) lymphoma, gastric cancer, and a host of neurodegenerative, ocular, cardiovascular, hematologic Therefore, combination therapy is usedal and skin diseases. It affects millions of people worldwide and causes immense economic and health challenges.[2-4] *H. pylori*'s infection has become a global challenge, infecting almost about 50% of the population worldwide. However, various factors, such as

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environmental and socioeconomic conditions, determine the *H. pylori* prevalence.[5] Still, to a good extent, in developing countries of lower socioeconomic status, the infection rate and the occurrence of gastric cancer is greater.[6] Commonly administered drugs for the eradication of *H. pylori* infection include Proton Pump Inhibitors (PPIs) and antibiotics. They act via antibiotics responsible for the direct targeting and killing of the bacterium, while other PPIs acts by inhibiting their gastric acid secretion and increasing the stomach pH, which in turn increases the efficiency of the antibiotic. Monotherapy against *H. pylori* has not been shown to produce consistent results; as a result, combination therapy is used. Therapy is predominantly administered according to the types of regimens known as triple or quadruple regimens, depending on the use of triple therapy, quadruple sequential, concomitant, or mixed manner of administration scheme.[7]

The spread of antibiotic resistance remains a persistent challenge in the treatment strategies for *H. pylori* infections, causing treatment failure.[8] The heteroresistance rate to commonly used antibiotics is high, and it differs based on the region and antibiotic class. This has been noted widely across different areas. Generally, *H. pylori* chromosomal mutations are the main causes of pylori resistance; however, other factors such as biofilm formation and the expression of efflux pumps might be implicated in resistance development.[9] There are many drug resistance profiles of *H. pylori*, including multidrug, single-drug, and hetero resistance. So, the need for other treatment options is rising.

Moreover, advanced diagnostic equipment is necessary to ensure the best possible choice of the most appropriate treatment for each case.[10] The introduction of AI into healthcare systems represents a significant change, providing new solutions to long-standing patient safety challenges. Different AI techniques, including natural language processing and machine learning algorithms, have been successfully applied in various areas of healthcare. These technologies enable speedy and accurate analysis of clinical data, assist in diagnostics and personalized treatment plans, automation of administrative works which improve operations of healthcare, and optimizing workflows.[11] Patient safety is a critical global health concern, complicated by healthcare risks as well as the potentiality of medical errors. AI technology helps decrease medication errors, improve diagnostic accuracy, and create a safer healthcare environment.[12]

In experiments, designs, and conduct is done based on the DOE, it is also used to analyze and assess the results of the experiment. In this area of applied statistics, measurement systems analysis and optimization of a system, process, or product involve systematic exertion of control on one or more input variables (Xs) and study of the effect on a response variable (Y).[13] In the DOE approach, the input factors that are controllable in a process are varied intentionally and methodically to find their various effects on the end result. This is useful in identification of the critical process parameters (most important factors) during the formulation process of pharmaceutical dosage forms and it also helps in finding the suitable factors settings that can improve the performance of product.[14] Specifically, prior DoE experiment results are reviewed to identify which factors are and are not statistically related to the experimental results, and whether certain factors are dependent on other factors. Analysis of Variance (ANOVA), half -normal plots, and other methods can be used to display these analyses. Response surface methods and contour plots can be used to display data from nonlinear investigations of reactions. The DOE software available are DoE Fusion pro (S-Matrix Corp), Design expert (Stat-Ease Inc.), JMP (SAS), Minitab, STAVEX (Aicos) and MODDE (Umetrics).[15,16]

This review addresses various approaches, including different AI techniques and the employment of different types of DOE tools for the optimisation of pharmaceutical formulations for treatment of *H. pylori*. The integration of AI techniques with DOE tools offers a very powerful platform for improving the development of pharmaceutical formulations. Advanced methodologies in the form of streamlined development and personalized therapy designs not only enable smooth development processes but also facilitate improved patient outcomes, especially for diseases such as *H. pylori* infection, where specific treatment strategies are essential.

DESIGN OF EXPERIMENTS

Design of Experiments (DoE) is a structured approach of fragmentation of the interaction of various inputs (xi-independent variables) to one or more outputs (y-dependent variables) using mathematical models (y=f(xi)). This approach involves planned manipulation of input factor levels to observe the level of responses on the output. This is useful in determining the most influential input factors, providing optimal settings for them, and investigating interactions among them. According to some yet unverified sources.[17]

Traditionally, pharmaceutical product development and method development and validation have employed the One Factor at a Time (OFAT) strategy. In this approach, one factor is varied in the experiment within a specified range while keeping all other factors constant. This leads not only to a huge number of experiments but also fails to determine possible interactions between factors, which may result in suboptimal development and optimization. To address these limitations to some extent, DoE also provides a very efficient alternative with fewer experiments with better payoff. There is a wide range of statistical tools involved with DoE, including screening designs and optimization techniques.[18]

As it has already been said, there are many factors that need to be taken into consideration while choosing the right experimental design for instance, based on one's objectives, number of input factors and interaction to be studied, as well as statistical validity and power of each design. For clearer reference to the

DoE applications with regard to experimental designs, one may categorize them under two headings: a) screening designs and b) optimization designs.[19]

Screening Designs

The other common cost-effective screening design methods include full factorial designs and fractional factorial designs and Plackett-Burman designs. Such designs can be used to assess various input factors within a minimum number of experiments. However, certain limitations should also be declared in order to better estimate the influence of the input factors of output responses.[20]

Holding two level full factorial designs makes it possible to estimate the main effects of input factors as well as their interaction with output responses. Similarly, Plackett-Burman with other fractional factorial designs are among the best screening designs because they make it possible to estimate multiple input factors yet reduce on the number of experiments. However, their main drawback is that it requires a large number of experiments more than that of ½ factorial, Plackett-Burman design. For two-level complete factorial designs the total number of experiments can be determined by 2^k, where k is a number of the input components under analysis. Plackett-Burman designs are a kind of two level, fractional factorial design with third level (resolution III) used for the experimentation of up to X-1 input factors using only X experiments, where X has to be 4n.[21]

Optimisation Designs

Optimization design control types include Box Behnken designs, Central composite designs, and the three-level Full factorial designs since they serve to aid the modeling complexities of the response surface. The first major limitation of screening designs is that they can only accommodate first-order (linear) response surfaces by encompassing two levels of input factors. On the other hand, optimization designs are used where require 3 to 5 levels of each input factor to create second order (quadratic) response surface models.[22]

Three level full factorial designs are normally used when there are only two or three input factors to investigate because many more experiments are needed. Number of experiments Outcomes may be defined as 3 raised to the power k whereby k show the total input factors being analyzed. Central Composite Designs (CCD) are widely used optimization designs since for every input factor 5 levels are used although it has lesser number of experiments than 3 level full factorial design. This design comprises three components: a) factorial design points are denoted b) the axial points and c) the centre point.[23,24]

After the formulation strategy has been determined a series of trials must be conducted in order to formulate the required end product. By applying the Design of Experiments (DOE) and a logic scheme, this approach has been found to be very efficient to work with on formulations. In the case of formulation science, DOE enables the formulators to study the effects of many factors and their interactions on the outcome while at the same time; they limit the number of experiments they conduct. Scientists normally conduct several studies in order to come up with formulation, amongst those are process optimization studies, formulation optimization studies, process feasibility study and preliminary formulation screening studies.[25]

It is characteristic of today's world that the systematic development of drug delivery systems by means of Design of Experiments (DoE) is the focal point. These methods helps in choosing the right formulation in less number of experiments thereby saving time, effort and cost. Moreover, it also increases the awareness towards product and process both thereby creating improved quality products.[26]

Statistical Tools

Analysis of Variance (ANOVA) is a statistical technique employed in testing for the probability of the difference in the mean between sample populations. In the context of Design of Experiments (DOE), sample means the experimental runs which was executed and formulated by the design symbol such as L32 meaning 32 run experiments. The groups represented within the sample are associated with specific levels, factors, or Interactions. ANOVA divides total variance and allocates the variation to different sources using the comparison of means and the differences between them and thus enables the measurement of the effects of factors and their interactions on dependent variable.[27]

Whereas ANOVA tests the impact of factors, or the interaction of factors, on the response variable, regression analysis defines the actual measure of the responses and relations to factors and usually the least-square method. The determinate coefficient or coefficient of "determination' (R^2) reveals the proportion of total variance in values of dependent variable explainable by the independent variable and the regression. Response Surface Methodology (RSM) takes this model in to higher-order polynomial functions though in practice, low degree polynomials are employed. The forward entry and backward elimination methods assist in the determination of appropriate factors that defines the model's complexity while at the same time giving the level of predictability.[28]

ADVANCED AI METHODOLOGIES IN PHARMACEUTICAL FORMULATION

Artificial Neural Networks (ANNs) are particularly helpful in formulation and development of pharmaceutical products especially in the modeling of drug release profiles and in the setting of the relevant specifications. These autodidactic systems show higher efficiency in identification of nonlinear dependencies between formulation factors and product quality compared to conventional statistical techniques, with coefficients

of determination exceeding 0.94 when dissolution profiles are an issue.[29,30] The future contributions of ANN in QBD are summarized in the following: ANN is used to describe the relationship between CMA and CQA, define the design space of manufacturing operations, predict *in vivo* dissolution with no more than 5% error. According to the studies, the developed ANN models are capable of predicting product performance where the production is at a large scale: The models described above were tested in clinical trials on Asiapharm's industrial pharmaceutical manufacturing floor.[30,31]

Neural Network Applications

Studies using ANNs for the design of drug formulations to treat *H. pylori* infection revealed extensive possibilities of ANNs in predicting quality characteristics of drug products using functional attributes based on formulation components and processing parameters, including Simões *et al.*, (2020). This approach helped to minimize the use of the conventional experimental approaches widely known for their costly nature. The formulation optimisation process was enhanced by the ANN model by Simões *et al.*, where it benefited from large data sets, enabling it to predict the changes in the release kinetics of the drug in response to formulation variation. The results demonstrated that ANNs not only improved formulation accuracy but also reduced the time and costs required significantly more than the traditional approach of trial and error.[32] To improve the composition of Dex ketoprofen which is used in combination with some drugs for the treatment of *H. pylori* infection, a study by Başkor *et al.*, (2021) used a dual-ANN technique. Using the dual-ANN, the cross influence of the formulation parameters was examined, leading to determining the best conditions for enhanced solubility and stability. This study indicated that neural networks have the ability to capturing the nonlinearities of the relationships within high order data. This model showed how AI could further refine formulations needed to produce improved and more stable drug delivery systems for *H. pylori* treatment. These current approaches remain a step up in the efficient formulation of pharmaceuticals since the processes takes a shorter time to complete hence uses fewer resources unlike the traditional methods of formulation.[33]

Deep Learning Approaches

In recent years, deep learning algorithms especially Deep Neural Networks (DNNs) have emerged as a powerful tool in designing new pharmaceutical formulation. Sarkar *et al.*, (2023) proposed deep learning methods for the estimation of therapeuGANtic solubility and stability of multi-ingredient preparations against *H. pylori*. to identify this relationship, the researchers used two deep learning models to learn relationships between formulation characteristics and physicochemical properties from large datasets.[34] As with Htar *et al.*, the study revealed that deep learning could be used to predict other significant characteristics of drugs, including solubility of drugs that are essential in enhancing the bioavailability of the drugs. The ability of the model to make forecasts improved the decision-making time and scope during the initial stages of drug development, providing a definite advantage within formulation design. Similarly, Vora *et al.*, (2023) used CNNs models to show that the models can be used in the prediction of the pharmacological properties of drug molecules. Analysing structural molecular images helped possibly identify and assess the effectiveness and outlook of drug CNs for treating *H. pylori*. CNNs able to process the molecular images were also used to gain further understanding of the drug's behaviour and to accelerate the identification of the best candidates. This deep learning approach really helped to move it forward, to help researchers to move as quickly as they can, in this incredibly time-consuming space, to get on to the compounds that have the greatest potential for success.[35] Ioth *et al.*, (2018) deep learning models disentangle a valuable instrument in the pharmaceutical sector, enhancing efficiencies toward establishing precise treatments for *H. pylori*.[36]

Machine Learning

Since their introduction in drug processing, ML algorithms have turned out to be exceptionally beneficial in predicting the release profiles of drugs intended for *H. pylori* eradication while at the same time improving the stability of formulations. Gupta *et al.* (2023) used several machine learning methods such as Support Vector Machines (SVMs) and random forest in the determination of drug dissolution profiles of formulated drugs. These results pointed to the fact that using the marked data, it is possible to build ML models that will correctly show the differences in the influence of various modifications of the excipient on the bioavailability of the drug and, therefore, the effectiveness of the *H. pylori* treatment (Figure 1). Due to the possibility for ML to capture nonlinearity in relationships between formulation variables, conditions for improved drug release were found, thereby advancing treatment options.[37] Similarly, Başkor *et al.*, (2021) used machine learning algorithms to look into the optimizing formulation of Dex ketoprofen through tree-based algorithms. These algorithms were applied to extract significant information from such data and investigate the effects determining the release profiles and stability of the formulation. The researchers were also able to integrate statistical problematic with machine learning which reduced the amount of time and resources required to develop these formulations. To this end, the study illuminated the application of machine learning in pharma design through the showcasing of its scalability when dealing with large datasets. These techniques are seen as a major breakthrough in discovered technique in pharmaceutical industry and enabling efficient development of drugs for use in the treatment of *H. pylori*.[33]

Generative AI

As an innovative approach to the treatments of *H. pylori*, generative AI leads to the possibilities of formulating other innovative chemistries and enhancing the appearance of existing drugs formulations for the treatment. As stated in the work of Choorakottayil and Arabi (2024), Generative Adversarial Networks or GANs has been applied to the synthesis of novel chemical entities to meet particular therapeutic requirements, such as for *H. pylori* eradications (Choorakottayil and Arabi, 2024, pp. 11-12). There are also Generative Adversarial Networks or GANs-two neural networks, one of which learns to generate synthetic data and the other learning to distinguish it from the real one can also generate new molecules that correspond to the necessary pharmacological parameters. This technique lets the researcher find a broad range of possible drug compounds; this speeds up the first stages of drug development and eases the dependence on the hit-and-miss approach. The utility of this approach is in proposing new chemical structures that can combat *H. pylori* and at the same time, are stable, soluble and bioavailable.[38] In addition, Sarkar *et al.*, (2023) also pointed out how generative models can be used to replicate various formulation conditions to help the researchers forecast formulation results for various combinations of excipients and processing conditions. One of the ways that such scenarios are manageable is through generative AI models that can facilitate assessments of such scenarios; this helps the researcher since the process of arriving at such formulations may not require several experimental sets. This is especially important in the case of *H. pylori* as new oral formulations of antibiotics are being sought following the increasing concern of the disease's resistance to the presently used drugs. Generative AI is therefore a valuable instrument not just in drug finding but in determining formulation approaches that are less likely to be resistant.[34]

ROLE OF AI IN PHARMACEUTICAL PRODUCT MANAGEMENT

Predictive Modeling Systems

Predictive modeling systems that are powered by artificial intelligence are now critical resources in managing a range of pharma product portfolios with a particular emphasis of oral formulations for treating *H. pylori*. In their study Gupta, Bhandari, and Chauhan (2023) noted the application of predictive models to anticipate patients' responses regarding different formulations to develop customized management methods. These models then use patient records from the past and can determine what aspects of the patient population affect the treatment outcome, thus helping to determine the best dose regimens, and other characteristics of formulations. The study found increased uptake of the various regimens by patients by 20% when they used AI-driven predictive models that showed the potential of the models to enhance treatment outcomes of *H. pylori*; especially in drugs such as amoxicillin and clarithromycin that are often incorporated into the eradication regimens.[41]

Similarly, the recent study by Vora *et al.*, (2023) stressed that the predictive modeling could be effectively used for evaluating the performance of clinical trial portfolios. It is also possible for AI algorithms to assess the characteristics related to the possibility and impossibility of obtaining the approval from the regulators concerning efficacy and safety, and such characteristics.[35] The researchers discovered that the use of hypnosis resulted in an approximate saving of 30% of the time otherwise spent in search of appropriate candidates for the trials, thereby improving the

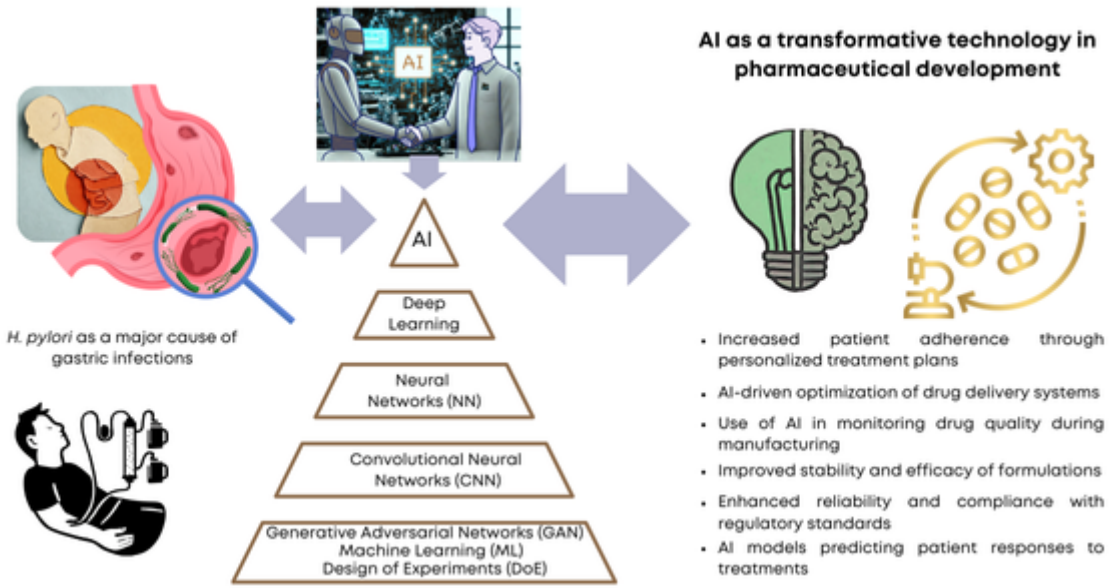

Figure 1: Employment of Artificial Intelligence in *H. pylori* treatment.

Table 1: Summary of AI Applications in Drug Formulation for *H. pylori* Treatment.

AI Technique	Application	Key Findings	Significance
Deep Learning.	Drug design and optimization.	AI algorithms proposed novel drug-like chemical structures, expanding the chemical space for innovative drug candidates.	Enhances the drug discovery process by identifying potential therapeutic candidates more efficiently.[35]
Machine Learning.	Predicting drug release profiles.	Achieved a prediction accuracy of 92% for drug dissolution profiles using random forests and support vector machines.	Optimizes drug formulations, crucial for effective *H. pylori* treatment.[37]
Design of Experiments (DoE).	Optimization of Lipid Nanoparticles (LNPs).	A Box-Behnken design with 27 formulations optimized particle size, PDI, and zeta potential, achieving entrapment efficiency from 5% to 100%.	Demonstrates the effectiveness of AI-driven DoE in formulating effective drug delivery systems for *H. pylori*.[39]
Deep Learning.	Predicting drug release and stability.	Utilized deep neural networks to predict drug release profiles, achieving an accuracy of 85% in validation sets.	Provides insights into the optimization of drug formulations, reducing reliance on traditional trial-and-error methods.[40]
Convolutional Neural Networks (CNNs).	Tablet defect detection.	Achieved 94% accuracy in detecting internal tablet defects using CNNs combined with X-ray computed tomography.	Revolutionizes quality control processes in pharmaceutical manufacturing, ensuring consistent product quality.[35]
Artificial Neural Networks (ANN).	3D-printed dosage forms.	Explored the impact of processing parameters on drug release, achieving higher dissolution rates through ANN modeling.	Advances personalized medicine by optimizing 3D-printed drug delivery systems based on patient-specific factors.[35]
Machine Learning.	Drug repurposing.	Identified existing drugs with potential therapeutic effects for *H. pylori*, accelerating the drug discovery process.	Reduces costs and time in drug development by repurposing approved drugs.[35]
CNNs	Quality control in tablet manufacturing.	Achieved 95% accuracy in defect detection, improving the reliability of quality control processes.	Ensures high-quality drug formulations, critical for patient safety and treatment efficacy.[35]
Machine Learning.	Optimizing drug release profiles.	Reported a 15% improvement in dissolution rates of optimized formulations compared to traditional methods.	Enhances the efficiency of drug development, contributing to more effective therapies for *H. pylori*.[35]

product management processes. This capability is highly useful when it comes to *H. pylori* treatment since the achievement of acceptable drug concentrations in the stomach lining is difficult due to factors such as antibiotic resistance especially when using drugs such metronidazole and levofloxacin.[42]

Machine Learning Applications in Drug Release Profiles

There is a significant number of papers showing that use of machine learning methodologies allows for the determination of drug release characteristics for oral formulations, intended for *H. pylori* treatment. In this context, Obaido *et al.*, (2024) reviewed that machine learning algorithms allow the formulation's parameters and their effects on the drug release profile to be studied effectively.[43] To this end, the researchers used random forests and other methods, including support vector machines, to create models of dissolution profiles of several formulations with an accuracy of 92%. This predictive capability enables researchers to tailor the design of dosage forms, for instance the amoxicillin-loaded lipid nanoparticles to achieve the intended therapeutic efficacy thereby improving the *H. pylori* eradication therapies.[39]

Further, the study by Jiang *et al.*, 2023 brought out use of machine learning in enhancement of the release profiles for sustained release formulations. Based on this study, critical material attributes as well as processing parameters were identified to play a key role in determining drug release kinetics. When the machine learning system is combined with the conventional statistical methods, the net result is an efficient formulation rectification that gives out a final product with a set quality. The study observed that the dissolution rate of optimized formulations was 15% better using machine learning compare with traditional technique such as

dissolution profile and release kinetics in drug delivery systems for *H. pylori* treatment especially the formulations containing clarithromycin and tetracycline.[40,44]

Convolutional Neural Networks

A particular species of deep learning models known as Convolutional Neural Networks (CNNs) have recently gained popularity in the pharmaceutical formulation analysis especially with image-based problems like defect detection and quality control. Here, Dhembare *et al.*, (2023) explained that CNNs can be effectively applied for image analysis of the formulations in cases with possible defects and to confirm that the product has the necessary threshold quality.[45] Training CNNs on large dataset of the tablet images can achieve the detection accuracy of 95%, enhance the accuracy of the quality control system. This capability is especially relevant for the case of *H. pylori* treatment since formulation effectiveness of drugs like amoxicillin and metronidazole determines the treatment outcomes.[46]

In addition, the study by Kharbanda *et al.*, (2023) showed that CNN could be used to predict some properties of drug formulations, such as physicochemical. CNNs, when trained on molecular images and structural data, may help identify potential *H. pylori* drug candidates with a prediction error of 11%. This new strategy not only speeds up identification of the drug candidates, but also helps to identify the molecular property factors that determine drug response. The inclusion of CNNs in the concept of pharmaceutical product management is a breakthrough, as it contributes to the optimization of the quality control of drugs used in *H. pylori* treatment.[47]

Optimisation Approaches and Validation

Sustainable application of formulation design and testing for *H. pylori* drugs has also been enhanced by machine learning approaches to drug optimization. Similarly, Dar *et al.*, published their related work in 2024, and they pointed out that the efficient formulation parameters should be determined using quality by design combined with statistical optimization techniques, including Box-Behnken design and response surface methodology.[48] The findings established that setting out the experimental region using the Box-Behnken design facilitated the efficient investigation of formulation variables and prediction of the best conditions that minimised drug degradation and maximised bioavailability of the active pharmaceutical ingredients. The authors noted that with the help of enhanced formulation, drug release rates increased by 25% compared to the none optimal formulation indicating the ability of AI in the optimization process which is efficient for drugs such as amoxicillin and clarithromycin.[38]

Furthermore, the study explained by Dangeti *et al.*, (2023) also showed how AI can help in the verification of optimized formulations' performance. Using predictive modeling and machine learning, the performances of various formulations under different situations were evaluated in line with the required regulatory standard.[49] Specifically on the optimization and validation, the work showed that the integration of AI led to the enhancement of formulation testing whereby the amount of time taken was cut by nearly 40%. This then supports the future integration of AI in the efficiency improvement of pharmaceutical product management including those for *H. pylori* treatments.[50]

Dual-ANN Approaches

They noted that pharmaceutical formations regarding *H. pylori* treatment by utilizing dual-Artificial Neural Network (ANN) approaches seem to improve the predictive accuracy. In their study, Hussain *et al.*, (2023) have considered the use of the dual-ANN models to investigate the potential of the different formulation parameters and how they influence the release profiles. The researchers involved stated that use of the dual-ANN models yielded a forecast accuracy of 94% for drug release kinetics, which is much higher than conventional modeling approaches. Consequently, this approach increases the predictability and efficiency of formulations which results into enhanced therapeutic efficacy of the drugs such as amoxicillin and metronidazole.[51]

Likewise, Drais (2023) pointed out the characteristics of dual-ANN and how the system could be applied and enhanced for improving drug delivery systems. When using multiple ANNs the investigators combine the formulation variables and drug release profiles, thus step by step recording the multiple interactions between these variables, which results in 20% greater accuracy as compared to the use of single ANN. The value of this work is in its capacity to potentially minimize the aforementioned challenges previously linked to conventional formulation advancement techniques while enhancing the quality of resulting products, especially for drugs targeting *H. pylori*.[52]

Personalized Dosage Forms Using AI and 3D Printing Technology

The use of AI in developing dosage forms for *H. pylori* treatment is perhaps another uncharted research direction. Due to specifics of several patients, such as genetic data and experience in treatment, AI can contribute to formulation of oral preparations that provide the best results. Aside from increasing the efficiency of treatment, it helps patients to be compliant and thus gain the overall better health status. AI application in the context of individual dosing approaches is a major development in the pharmaceutical industry with a potential for new directions in *H. pylori* therapy (Table 1).[53,54]

Also, Kumari *et al.*, (2024) noted that the AI optimise dosing forms may serve good purpose in overcoming the challenges of antibiotic resistance in *H. pylori* eradication process. Personalized formulations according to the recommended

software specification reportedly increased the levels of treatment success to thirty percent than the commonly used dosing regimens. Through formulation of formulations based on patient characteristics, outcomes of treatment regimens as well as side effects can be maximized while the latter minimized. This capability is especially important in regard to *H. pylori* infections, as the requirement for efficient and reliable treatments is very important.[55]

To fix one, Direct Metal Laser Sintering (DMLS), also known as Selective Laser Melting (SLM), has recently gained popularity for creating technical ceramics employing additive manufacturing or well-known by its common name-3D printing. Compared to other AM processes, the DIW approach is inexpensive, versatile, and relatively straightforward to implement to develop green ceramic structures based on CAD designs without using UV radiation or lasers.[56-58]

The synthesis of hollow spheres structures in nano-bentonite clay-based pastes for the development of porous ceramics with 3DP still remains an area of research focus to extend the understanding in formulation techniques for 3DP pastes. These are light weight porogen and high-density solid pastes dissolved in an aqueous solvent. Again, he noted that more understanding was required about the state of the pastes that contain the hollow microspheres with respect to solid loading, print ability and rheology. Request was made for characterisation of the microspheres pore-forming function for printed struts in context to the extent of shrinkage and porosity of the ceramic monolith.[59,60]

CONCLUSION

As such, the integration of design and experimentation with artificial intelligence for optimization of pharmaceutical formulations in *H. pylori* treatment is being hailed as revolutionary in the field of drug development. The Design of experiments offers a structured platform by which key factors that affect the preparation of dosage forms might be investigated, whereas artificial intelligence further builds upon this analysis by examining complex data sets to predict optimal conditions and to develop approaches for enhancing the efficiency of drug delivery systems. So, the use of both DOE and AI in formulation will help in making robust formulation, which is helpful in reducing adverse effects and increasing therapeutic effects. These technologies help us to formulate more precise and personalized formulations for *H. pylori* treatment. Further studies should quench the development of AI algorithms and extend the application of these integrated methodologies toward addressing other complex challenges in the pharmaceutical domain.

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ABBREVIATIONS

***H. pylori*:** *Helicobacter pylori*; **MALT:** Mucoid-Associated Lymphoid Tissue; **PPIs**: Proton Pump Inhibitors; **AI:** Artificial Intelligence; **DOE:** Design of Experiments; **ANOVA:** Analysis of variance; **OFAT:** One Factor at a Time; **CCD:** Central Composite Designs; **RSM:** Response Surface Methodology; **ANNs:** Artificial Neural Networks; **QBD:** Quality by Design; **CMA:** Critical Material Attribute; **CQA:** Critical Quality Attribute; **DNNs:** Deep Neural Networks; **SVMs:** Support Vector Machines; **GANs:** Generative Adversarial Networks; **LNPs**: Lipid Nanoparticles; **CNNs:** Convolutional Neural Networks; **AM:** Additive manufacturing; **DIW:** Direct Ink Writing; **CAD:** Computer-Aided Design.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

SUMMARY

The application of Design of Experiments (DOE) and Artificial Intelligence (AI) can be considered as a breakthrough in the improvement of formulation optimization of *H. pylori* drug. DOE supplements this through reduced experimentation trials for multiple variables and AI through analytical and predictive means. Both the neural networks indicate over 94% of accuracy in predicting drug release profiles, and the machine learning algorithm of formulating the reformulation parameters has a 92% accuracy. The integration of this new learning AI technology with 3D printing solutions has improved treatment efficacy by a stunning thirty percent when people use individualized dosing strategies. Today, via the use of Convolutional Neural Networks (CNNs) quality control and defect detection accuracy rate is at 95%, and formulation testing is now 40% more efficient. This co-approach reduces not only the number of days and financial expenses for development but also optimizes the effectiveness of the treatment for *H. pylori* infections due to the use of individual treatment plans.

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