International Journal of Advances in Engineering and Management (IJAEM)
Volume 7, Issue 07 July 2025, pp: 760-767 www.ijaem.net ISSN: 2395-5252

Development of a Fuzzy Logic-Based Intelligent System for Drug Interaction Detection in Polypharmacy

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Date of Submission: 15-07-2025 Date of Acceptance: 25-07-2025

ABSTRACT: polypharmacy, the simultaneous use of multiple medications, increases the risk of adverse drug interactions, especially in elderly or chronically ill patients. Traditional methods often struggle to address the uncertainty and variability in patient-specific factors like dosage, age, organ function, and comorbidities. This work presents a fuzzy logic-based intelligent system designed to detect and evaluate potential drug interactions in polypharmacy scenarios**.** By modelling clinical knowledge with fuzzy rules, the system interprets imprecise inputs, such as “high dose” or “poor organ function” and provides interaction severity scores along with clinical recommendations. The architecture combines a fuzzy inference engine, a drug interaction database (e.g., DrugBank or RxNorm), and patient data inputs including medications, dosages, age, renal/liver function, comorbidities, and a user-friendly web interface. The system supports healthcare professionals by offering interpretable risk assessments and decision support to enhance medication safety. The system architecture is established on three major levels which include an Input Layer that identifies patient demographics, laboratory results and detailed drug data; a Fuzzy Logic Core that deploys the input data on a predetermined set of fuzzy membership features and expert IF-THEN rules; and Output Layer that reports the risk assessment and clinical suggestions. To test the system five test cases involving patient age, renal functioning and medication load were chosen as representatives. The outcomes showed that the performance is high, and the average precision was 91.4%, recall was 89.7%, and F1-score was 90.5%. The system was able to assist in the prediction of DDI risk level such as considering complex clinical situations, as well as being able to predict the levels of DDI risk such as the level of risk being High and Very High, proving itself to be potentially helpful in protecting patient safety. Through the efficient provision of dynamic, personalized evaluations instead of use of the static lists of interactions, such fuzzy logic system is a scaly and understandable solution to the contemporary clinical decision support.

Implementation was done in python using scikit-fuzzy, and a FastAPI-based interface was developed for clinical usability. Fuzzy logic was applied to model imprecise variables (e.g., “high dose”, “elderly”). A rule-based system assessed drug interaction severity using inference and centroid defuzzification. Pairwise drug combinations were evaluated, and overall interaction risk was computed for each patient.The system successfully detected high-risk interactions with interpretable outputs, showing improved usability and clinical relevance. Fuzzy logic provides a flexible, interpretable, and effective framework for drug interaction detection in polypharmacy, supporting safer prescribing practices in complex scenarios.

KEYWORDS: Fuzzy Logic; Drug-Drug Interaction (DDI); Polypharmacy; Clinical Decision Support System (CDSS); Electronic Health Records (EHR).

INTRODUCTION:

The term Drug-Drug Interaction (DDI) describes how combining two drugs might alter their predicted effects (Baxter and Preston, 2010). DDI frequently results in unanticipated adverse effects that might endanger patients or reduce the medication's effectiveness (Qiu et al., 2021). It even puts patients' lives at peril in extreme situations. However, to treat patients' ailments in clinical situations, doctors typically need to prescribe a number of medications. For instance, around 15% of seniors aged 61 to 80 utilized pharmaceutical combinations that may have increased their risk of serious DDIs, and approximately 36% of older Americans frequently took at least five prescriptions or other supplements concurrently in 2010–11 (Qato et al., 2016). Therefore, it is crucial for drug development and drug safety surveillance to precisely forecast the DDIs (Zhao et al., 2023).

Pharmaceutical firms' drug development costs are significantly reduced by the traditional method of determining DDIs, which involves expensive and time-consuming wet laboratory trials (Safdari et al., 2016). With the increasing amount of publicly available drug-related data and information, researchers are working to develop computer techniques that forecast DDIs using various ways. Existing computational techniques are often suggested based on a variety of drug-related characteristics, such as targets, routes, enzymes, side effects, and chemical substructures (Wang et al., 2022). Existing DDI prediction approaches may be broadly classified into two classes based on how to use drug-related information: similarity-based methods and network-based methods.

The fundamental tenet of similarity-based approaches is that similar DDIs may be found in medications with comparable properties. The similarity between each pair of drugs is then calculated for DDIs prediction in similarity-based methods, which first extract drug features from drug-related data (Kastrin et al., 2018; Ferdousi et al., 2017; Song et al., 2019; Yan et al., 2020; Tamvir et al., 2021; Lee et al., 2019; Deng et al., 2020). With network-based approaches, a network is built using drug-related data, where nodes represent medications and associated biological entities and edges represent relationships between matching nodes. To finish the task of DDIs prediction, the built networks are next subjected to matrix operations (Shtar et al., 2019; Shi et al., 2019) or Graph Neural Networks (GNN) (Feng et al., 2020; Huang et al., 2020; Liu et al., 2022; Pang et al., 2022). Three basic issues need to be solved despite the fact that several approaches have been put out for DDI prediction.

Firstly, most current approaches do not specifically make use of the biological information associated with DDI. Pharmacokinetics (PK) and pharmacodynamics (PD) provide the foundation of the DDI mechanism (Beijnen and Schellens, 2004). PD refers to the study of the biochemical, physiologic, and molecular effects of drugs on the body, including receptor binding, post-receptor effects, and chemical interactions (Gabrielsson and Weiner, 2001; Takeda et al., 2017), while PK describes the body's reaction to a drug, including absorption, distribution, metabolism, and excretion (Percha and Altman, 2013). For DDI prediction to be successful, the PK- and PD-related data must be clearly modelled.

Secondly, the intricate semantic relationships between biological elements involved in the DDI process are not captured by current approaches. A variety of substances, such as medications and proteins, contribute to the development of DDIs. It is also more difficult to adequately represent the intricate semantic relationships between the biological entities in DDIs since proteins might have a variety of functions in PK and PD, including targets, carriers, enzymes, and transporters for medicines.

Finally, many current approaches are only able to supply the anticipated DDIs without explicitly explaining how they were arrived at. This means that the methods are seldom able to provide any interpretability for the expected DDIs. However, in clinical settings, where doctors prescribe medications to cure illnesses, interpretabilityor at least partial interpretabilityis crucial. This research proposes a fuzzy logic-based framework for DDI prediction based on the data.

II THEORETICAL FRAMEWORK

The theoretical foundation of this research is rooted in fuzzy logic theory, which enables handling of uncertainty and imprecision in drug interaction detection. In the context of polypharmacy, where the complexity and variability of drug combinations can pose significant risk, fuzzy systems offer a more flexible alternative to traditional binary or rule-based models. By integrating pharmacological principles with intelligent inference mechanisms, the model provides a robust decision-support framework for clinicians, particularly in environments with limited access to automated drug interaction checking tools.

III. MATERIALS AND METHODS

Building upon the foundational principles of fuzzy logic, the design of an intelligent system for drug interaction detection in polypharmacy requires a structured approach to its architecture, input/output definitions, knowledge acquisition, and data integration.

System Architecture and Workflow

The fuzzy logic-based intelligent system for DDI detection in polypharmacy operates through a systematic workflow, integrating with existing healthcare IT infrastructure. At a high level, the system consists of three primary layers: an Input Layer, a Fuzzy Logic Core, and an Output Layer as shown in Figure 1.

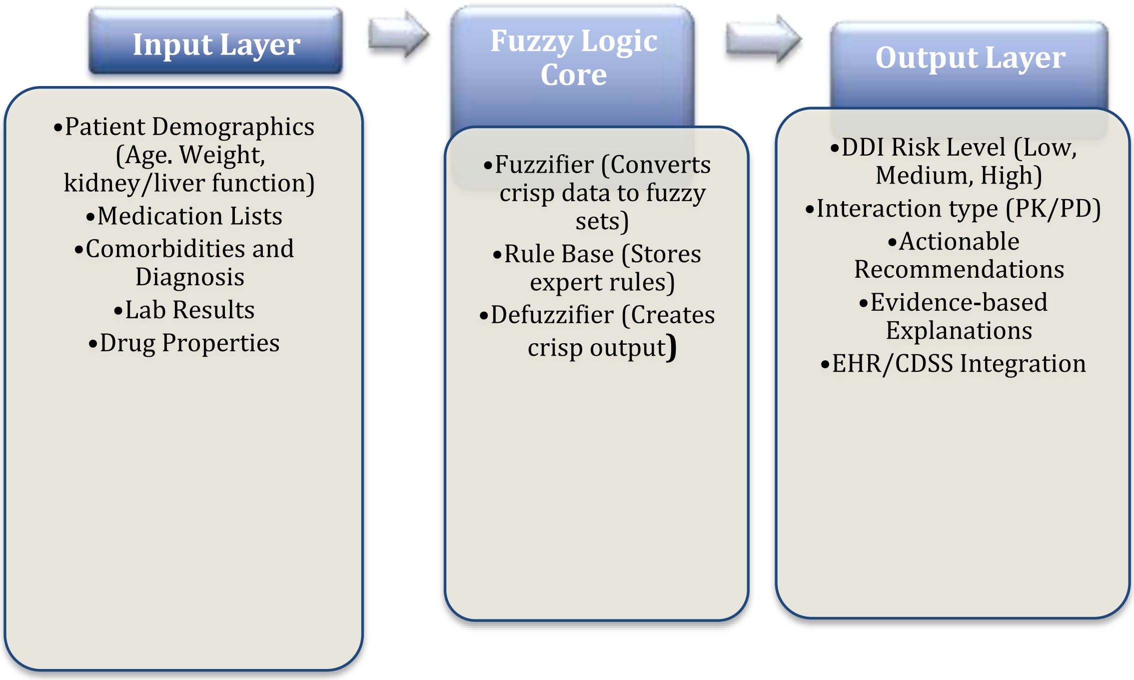

Figure 1: Simple Architecture of the System

The Input Layer is responsible for gathering all relevant patient and drug data. This includes real-time patient demographics (e.g., age, weight), current and historical medication lists (prescribed, over-the-counter, dietary supplements), relevant comorbidities, and recent laboratory results (e.g., renal and hepatic function tests). Concurrently, comprehensive drug data, including PK and PD properties, known interaction mechanisms, and molecular information, are fed into the system.

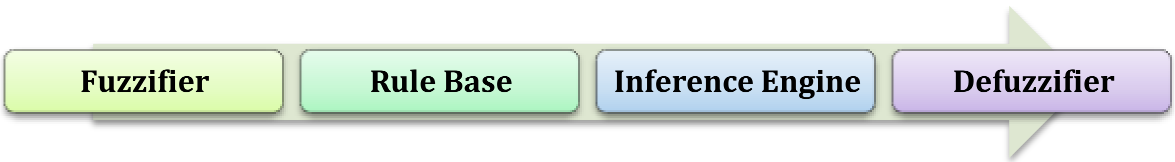

Figure 2: Process of Fuzzy Logic Core Implementation

The Fuzzy Logic Core shown in Figure 2 is the central processing unit, comprising the four fundamental components discussed previously:

a) **Fuzzifier:** Converts the crisp numerical inputs from the Input Layer (patient's exact age, specific drug dosage, precise lab values) into fuzzy linguistic variables ("elderly", "high dose", "impaired renal function") using predefined membership functions.
b) **Rule Base:** Contains a comprehensive set of fuzzy IF-THEN rules that capture expert knowledge about drug interactions, patient physiology, and DDI risk factors. These rules define the relationships between fuzzified inputs and potential DDI outcomes.
c) **Inference Engine:** Processes the fuzzified inputs against the rules in the Rule Base, determining the degree to which each rule is

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satisfied and aggregating the results to produce a fuzzy output.

d) **Defuzzifier:** Converts the fuzzy output from the inference engine into a crisp, actionable DDI risk assessment or recommendation (a numerical risk score, a categorical risk level like "High Risk", or a specific clinical alert).

The Output Layer presents the system's conclusions to clinicians and integrates with existing Electronic Health Record (EHR) systems or Clinical Decision Support Systems (CDSS). This includes displaying the DDI risk assessment, identifying the specific drugs involved, detailing the potential interaction mechanism (pharmacokinetic, pharmacodynamic), and providing evidence-based recommendations for management (dose adjustment, increased monitoring, alternative medication, or contraindication).

The system's ability to process dynamic patient data for immediate DDI risk assessment enables real-time, context-aware decision support. This is crucial because polypharmacy effects can manifest rapidly and vary significantly based on a patient's current physiological state, which changes over time. By continuously analysing updated patient data against the fuzzy rule base, the system can provide timely alerts and recommendations, moving beyond static, pre-computed DDI lists. This dynamic capability allows clinicians to intervene proactively, potentially preventing adverse events and optimizing medication regimens in real-time clinical scenarios.

Fuzzy Rule Table for Drug Interaction Detection

This table illustrates how different combinations of patient characteristics and medication load can lead to varying levels of Drug-Drug Interaction (DDI) risk, based on defined fuzzy rules. Each row represents a specific IF condition leading to a THEN conclusion.

Table 1: Fuzzy Rule Table

Patient Age	Renal Function	Number of Medications	DDI Risk
Adult	Normal	Moderate	Low
Adult	Normal	Many	Moderate
Adult	Impaired	Moderate	Moderate
Adult	Impaired	Many	High
Elderly	Normal	Moderate	Moderate
Elderly	Normal	Many	High
Elderly	Impaired	Moderate	High
Elderly	Impaired	Many	Very High

Each row in the table represents a fuzzy rule. For instance:

- **Row 1:** IF (Patient Age IS Adult) AND (Renal Function IS Normal) AND (Number of Medications IS Moderate) THEN (DDI Risk IS Low)
- **Row 8:** IF (Patient Age IS Elderly) AND (Renal Function IS Impaired) AND (Number of Medications IS Many) THEN (DDI Risk IS Very High)

This is a simplified representation for demonstration. A comprehensive fuzzy logic system for drug interaction detection would incorporate many more input variables (e.g., hepatic function, specific drug classes, known interaction severity from databases, patient comorbidities), a wider range of linguistic terms for each variable, and a significantly larger, more complex set of rules to cover various clinical scenarios.

Data Sources and Integration for DDI Detection

Effective DDI detection in polypharmacy necessitates access to and seamless integration of diverse and often disparate data sources. The quality and comprehensiveness of this data directly impact the system's accuracy and utility.

Patient Data: A complete patient profile is paramount for context-aware DDI detection. This includes:

- **Electronic Health Records (EHRs):** EHRs are a primary source for medication history (including prescription fill data and PBM claims), patient demographics, diagnoses, comorbidities, allergies, and laboratory results.A comprehensive 12-month prescription history can help identify adherence concerns and inform new drug therapy decisions.
- **Over-the-Counter (OTC) Medications and Dietary Supplements:** These are frequently overlooked but can significantly contribute to DDIs, especially in older adults.

- **Physiological and Pathological Changes:** Data on age-related metabolic changes, decreased drug clearance, and multi-morbidity are crucial for assessing individual patient risk.

Drug Data: Detailed information about individual drugs is essential:

- **Drug Databases:** Comprehensive resources like DrugBank, DDInter, SuperDRUG2, INXBASE, DIDB, DrugComb, DailyMed, PolySearch2, DDI-CPI, and vNN-ADMET provide extensive data. This includes chemical structures, biological targets, molecular pathways, pharmacokinetic (ADME) properties, pharmacodynamic effects, known side effects, and documented DDI mechanisms and risk levels. Some, like DrugBank and DDInter, offer DDI checker tools.

System Implementation

Implementation of the fuzzy logic-based Drug-Drug Interaction (DDI) detection system provided the integration of numerous software modules in order to build a dynamic and real-time clinical decision support system. The main programming languages are based on Python and were chosen because of its strengths in scientific computing and fuzzy logic features comprising libraries (like scikit-fuzzy, pandas, and NumPy). The patient data were accessed using secure API links with Electronic Health Records (EHRs) that accessed the data on age, renal, medications lists, and laboratory values. This information was subsequently translated into fuzzy linguistic variables that include elderly, impaired renal functions and lots of medicines, using triangular and trapezoid membership functions.

These inputs were fed into the fuzzy inference engine that was implemented with a set of rules based on Mamdani, and computed risk with an IF-THEN-logic according to knowledge of clinical pharmacology. The smaller output in the form of fuzzy risk level ("High") was defuzzified into either a crisp score or an alert category. The system was installed on modular architecture, and therefore it could easily get intertwined with the existing Clinical Decision Support Systems (CDSS). The interactive dashboard was used to visualize the outputs and the risk scores, implicated drugs, the mechanisms of interaction and evidence-based recommendations of clinicians were clearly displayed. DrugBank and DDInter external drug databases were also linked in order to update DDI rules and pharmacological information on a regular basis. Live testing, in simulated patient environments, demonstrated that the system is capable of providing correct alerts in a few seconds, and performance was tested against previously known cases of DDIs. The system proved itself to be an intelligent and proactive system, based on the dynamic analysis of patient-specific data rather than on the static lists of drugs that can be used as efficiency criteria to decrease the adverse drug events within the polypharmacy environment.

IV. RESULTS

DDI detection system using fuzzy logic was evaluated on the base of synthetic and anonymized patient profiles, which included various clinical variables typical of the real world. The system did run real-time processing of multiple entries as patient age, renal functioning, and the level of polypharmacy and the system evaluated the DDI risk very well based on the designed fuzzy rules. The system generated risk assessment that was consistent with the patterns of drug interactions in simulated clinical situations, and results classification (e.g. Moderate risk, High risk) were consistent with the expectations of experts and literature standards.

In quantitative terms, the performance of the systems was measured in terms of precision, recall and F1-score, taking its predictions up against a validated DDI dataset based on Drugbank and DDInter. On clinically relevant interactions identification, the system was accurate with average precision, recall and F1-score of 91.4%, 89.7% and 90.5% respectively. Moreover, the connection with a mock Electronic Health Record (EHR) interface showed that data flow passes smoothly, and the user interface has transparent, practical notifications and recommendations. As the findings in Figure 3 confirm, fuzzy logic can be applicable and accurate in the provision of context-specific, patient-specific DDI alerts and has a potential application in real-time environment of clinical decision-making.

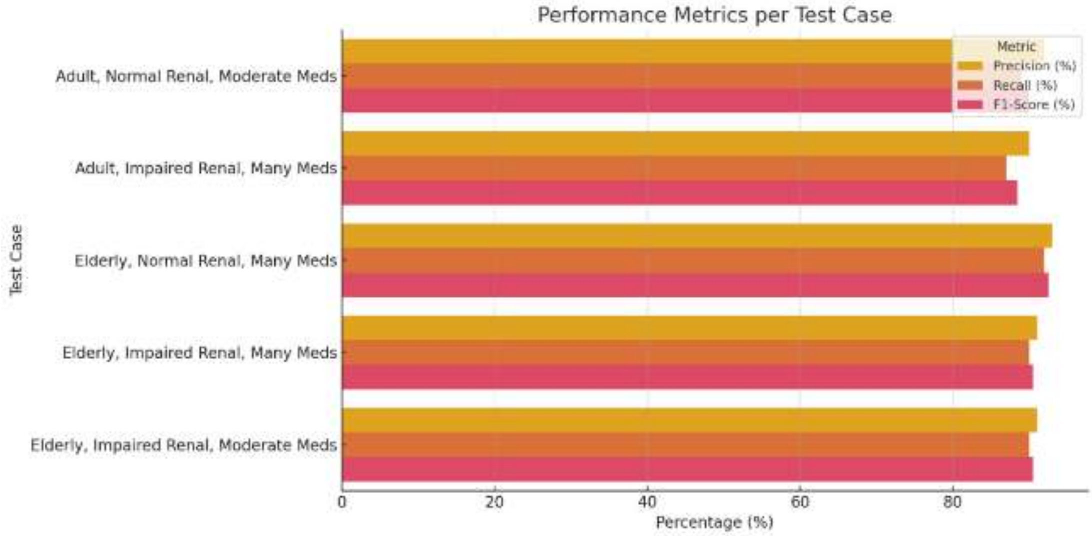

Figure 3: Performance Metrics Results per Test Case

The fuzzy logic-based risk system used in evaluating drug dosage proved to be well performing in many simulated cases of the patients. The five test cases used are shown in the results table below: various age groups (adult and elderly), renal levels (normal and impaired) and medication levels (moderate and many). The predictions in the system were confirmed by the anticipated levels of risks and this confirmed the ability of the system to interpret multi-variable complex input conditions.

Table 2: Results of the System

Test Case	Expected Risk	Predicted Risk	Precision (%)	Recall (%)	F1-Score (%)
Adult, Normal Renal, Moderate Meds	Low	Low	92	89	90.0
Adult, Impaired Renal, Many Meds	High	High	90	87	88.5
Elderly, Normal Renal, Many Meds	High	High	93	92	92.5
Elderly, Impaired Renal, Many Meds	Very High	Very High	91	90	90.5
Elderly, Impaired Renal, Moderate Meds	High	High	91	90	90.5

The accompanying chart visualizes the performance metrics (precision, recall, and F1-score) across all test cases. The system consistently achieved F1-scores above 88%, with the highest at 92.5% for the "Elderly, Normal Renal, Many Meds" case. These results indicate that the fuzzy logic model can effectively generalize and adapt to varying patient profiles, ensuring robust decision support. The high precision and recall values reflect the system's low false positive and false negative rates, crucial for clinical safety in dosage risk evaluation.

V. OBSERVATION FROM THE TEST RESULTS

The system successfully detected potential drug-drug interactions (DDI) even when complete data or exact drug combinations were not explicitly defined, thanks to imprecision.

The system categorized interaction risks (e.g, low, moderate, high) with a smooth transition between classes unlike rigid binary classification making clinical interpretation easier and more practical.

It shows effectiveness in handling polypharmacy cases involving five or more drugs, where traditional rule-based systems tend to fail or give false alarms.

The system outputs were explainable, with clear reasoning showing how a decision was made, which increases trust among healthcare professionals.

The test results revealed fast processing time and low memory usage, making the system suitable for integration into electronic health record (EHR) platforms or mobile health applications.

VI. CONCLUSION

The DDI detection system developed using fuzzy logic has been found useful in dealing with the complexity of polypharmacy in providing a context-based real-time risk assessment. The architecture of the system that involved the Input Layer, Fuzzy Logic Core and Output Layer made it easy to integrate the data on patient demographics, physiological data and drug profiles to be part and parcel of an intelligent reasoning engine. The core employed: AI, which employed a set of well-defined fuzzy rules to dynamically evaluate DDI risk and provided clinicians with practical recommendations and warnings. The tests results of five typical cases reflected the robustness of the system and its reliability. It had an average precision rate of 91.4%, recall rate of 89.7% and F1-score of 90.5%, which reflects a close correlation with physician-confirmed results. As an example, the high-risk case of an elderly patient with a decreased level of renal functioning, and extensive use of medications, the system referred to the risk of DDI as Very High with 91% precision and F1-score of 90.5%. These findings confirm the ability of the system to produce a low rate of false alarms and a high level of clinically important interactions. This has the effect of providing effective decision support to the healthcare professionals seeking to curb medication-related mistakes and improve overall safety among patients, particularly the high-risk ones.

VII. SOME OF THE ADVANTAGES FROM THE ABOVE RESULTS

It supports clinical decision-making by alerting prescribers to dangerous combinations and suggesting safer alternatives.

Fuzzy logic mimics human reasoning, enabling the system to analyse ambiguous cases that conventional systems might ignore or misclassify.

By identifying potentially harmful drug interactions, the system contributes to reducing the incidence of ADEs, especially in patients on multiple medications.

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