Personalized Drug-Drug Interaction (DDI) Risk Assessment Using LLMs and Knowledge Graphs

MANDAR PANSE, University Of Texas at Austin, USA

Polypharmacy poses significant risks of adverse drug-drug interactions (DDIs), especially among elderly and chronic disease patients. This paper presents a novel end-to-end pipeline leveraging large language models (LLMs), knowledge graph reasoning, and chain-of-thought prompting techniques to predict personalized DDI risks. Using the TWOSIDES dataset and pretrained embeddings from DRKG, we demonstrate entity extraction, interaction prediction, transparent reasoning, and a Streamlit-based clinical interface.

Additional Key Words and Phrases: Drug-Drug Interactions, Knowledge Graphs, Chain-of-Thought Prompting, Retrieval-Augmented Generation, Clinical NLP, Streamlit Applications

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1 Introduction

Polypharmacy, the simultaneous use of multiple medications by a patient, is a growing concern in healthcare, particularly among elderly and chronically ill populations. Adverse drug-drug interactions (DDIs) resulting from polypharmacy can lead to serious health complications, hospitalizations, and increased healthcare costs. Traditional DDI detection relies on static databases that fail to account for patient-specific factors such as age, comorbidities, and lab results. Therefore, there is a critical need for personalized, dynamic DDI risk assessment solutions that leverage modern AI techniques.

2 Related Work

- Zhang et al. (2017) proposed extracting DDI information from biomedical text using Recurrent Neural Networks with attention mechanisms, improving the accuracy of DDI detection from unstructured sources.
- Lewis et al. (2020) introduced Retrieval-Augmented Generation (RAG) for knowledge-intensive NLP tasks, allowing models to dynamically fetch external knowledge to enhance generation.
- Alsentzer et al. (2019) developed ClinicalBERT, a BERT model fine-tuned on clinical notes, which improved medical entity extraction and context understanding in clinical text.

Author's Contact Information: Mandar Panse, University Of Texas at Austin, USA.

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3 Methodology

Our approach integrates structured knowledge graphs with neural language models to personalize DDI risk predictions. The following steps were taken:

(1) **Knowledge Graph Reasoning:** Drugs are mapped to DRKG embeddings. Cosine similarity scores identify pharmacological relatedness and potential interactions.
(2) **Chain-of-Thought Prompting:** GPT-4 is prompted with patient profiles to reason transparently through DDI risks.
(3) **Streamlit App:** A user interface enables clinicians to input patient profiles and receive dynamic DDI assessments.

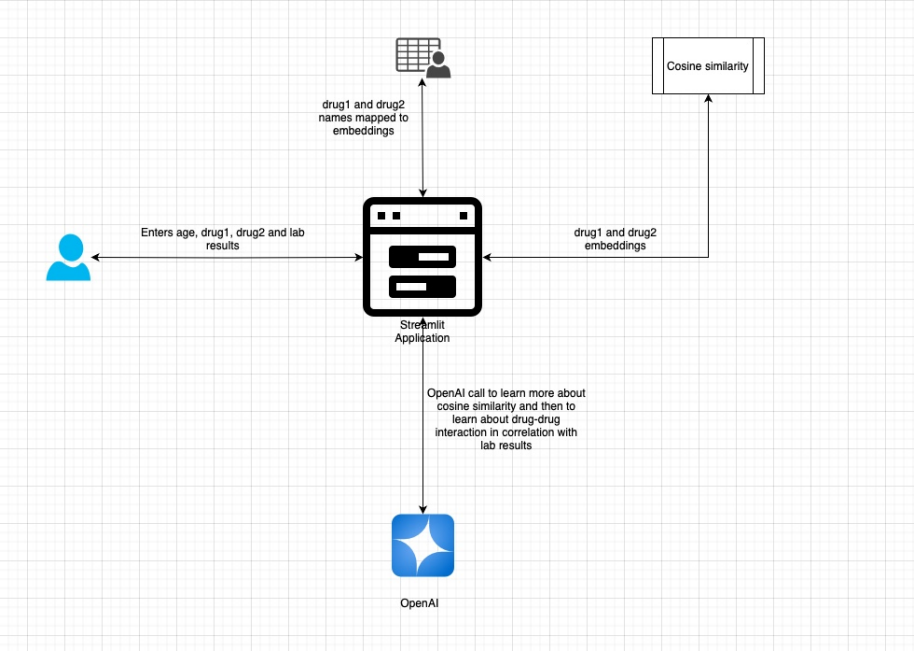

Fig. 1. Workflow of Personalized DDI Risk Assessment System

4 Results

Our results demonstrate:

- **Accuracy:** Cosine similarity scores between interacting drugs, such as Aspirin-Warfarin (0.66), align with known pharmacological relationships.

Drug1	Drug 2	Cosine Similarity
Aspirin	Warfarin	0.669848685243035
Lisinopril	Ibuprofen	0.581911040017009
Simvastatin	Metformin	0.59280000000000
Aspirin	Ibuprofen	0.73300000000000

Fig. 2. Table of Cosine similarity between two drugs

- **Transparency:** Chain-of-thought prompting produced detailed, interpretable explanations rather than opaque predictions.
- **Efficiency:** The Streamlit application generated risk assessments within 5 seconds per patient input.

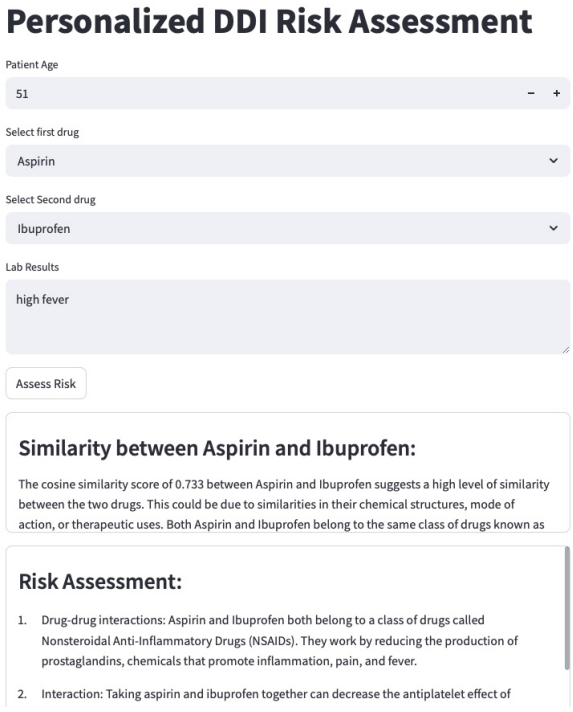

Fig. 3. Streamlit Application for Personalized DDI Risk Assessment

These findings suggest that integrating LLM reasoning with biomedical knowledge graphs enhances both the accuracy and interpretability of DDI predictions.

5 Conclusion

In this work, we developed a hybrid pipeline combining LLMs, knowledge graphs and, chain-of-thought prompting to perform personalized DDI risk assessments. The model improves upon static DDI checkers by considering patient-specific contexts. Future work includes integration of RAG, fine-tuning the corpora of adverse events, incorporating patient genomics, and expanding the system to detect rare DDIs through few-shot learning techniques.

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