FDA DDI index calculation

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Abstract: This project presents a Flask-based web tool for evaluating Acute Kidney Injury (AKI) risks associated with specific drugs, both individually and in combinations. Utilizing Reporting Odds Ratio (ROR) calculations and an Association Rule algorithm, the tool processes user-uploaded Excel files to generate a Drug-Drug Interaction (DDI) index. Healthcare professionals can select drugs of interest, receiving insights into AKI risk likelihood.The Flask framework ensures a user-friendly interface, facilitating seamless file uploads and interaction. The tool provides counts of AKI cases related to selected drugs, aiding in medication therapy decisions. The Reporting Odds Ratio (ROR) quantifies the association between drug combinations and AKI risk. This tool enhances understanding and improves patient safety by identifying potential drug interactions.

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1. INTRODUCTION

In the realm of healthcare, ensuring patient safety during medication therapy is paramount. Adverse drug reactions, especially those leading to Acute Kidney Injury (AKI), pose significant challenges for healthcare professionals. This project endeavors to address this challenge by developing a Flask-based web tool designed to assess the risk of AKI associated with specific drugs, both individually and in combination.

The tool utilizes sophisticated algorithms, including Reporting Odds Ratio (ROR) calculations and an Association Rule algorithm, to systematically analyze drug-related data. By allowing healthcare professionals to upload Excel files containing pertinent information, the tool generates a comprehensive Drug-Drug Interaction (DDI) index. This index serves as a quantitative measure of the likelihood of AKI, aiding in identifying potential interactions that may contribute to adverse outcomes.

The user-friendly interface, powered by Flask, ensures seamless navigation and efficient interaction with the tool. Healthcare practitioners can select drugs of interest, receiving detailed insights into AKI risk profiles. The Reporting Odds Ratio provides a quantitative assessment, empowering professionals to make informed decisions about medication therapy.

This project not only introduces a valuable resource for healthcare practitioners but also contributes to the ongoing efforts to improve patient safety by enhancing our understanding of potential drug interactions leading to Acute Kidney Injury.

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2. NOTABLE OBSERVATIONS

During the initial phases of our project, challenges were encountered in extracting data from the designated API, as the extracted information did not align with the FAERS database. Recognizing the significance of accurate data alignment, we engaged in discussions with Professor Feng Cheng for insights into potential solutions.
Following consultations, a strategic decision was made to shift the data acquisition approach. Rather than relying on API-driven data extraction, we have pivoted towards a user-centric model. Users are now empowered to upload Excel sheets containing information specific to the drug of interest. This user-driven methodology ensures that the data used for analysis is consistent and aligns seamlessly with our objectives.
The newly adopted approach enables the calculation of Risk Odds Ratio (ROR), Drug-Drug Interaction (DDI) index, and the identification of cases with and without acute kidney injury (AKI). This user-centric model not only addresses the challenges faced in API data extraction but also provides a more flexible and user-friendly interface. Users can now actively participate in the data input process, ensuring that the analysis is tailored to their specific needs.
This refined methodology not only enhances the accuracy of our data analysis but also promotes user engagement and collaboration. By integrating user-uploaded Excel sheets, our project adapts to the complexities of real-world data, offering a robust solution for the identification of potential drug-drug interactions leading to acute kidney injury.

3. METHODOLOGY

To accomplish the project goal of identifying potential drug-drug interactions (DDIs) leading to acute kidney injury, a systematic approach was undertaken. The following steps outline the key methodologies employed:

2.1 Data Processing and Preprocessing

2.1.1 File Upload:

Users are provided with the ability to upload an Excel file through the web interface. This file should contain relevant information, including columns such as 'Reactions', 'Suspect Product Active Ingredients', 'Suspect Product Names', and 'Concomitant Product Names'.

2.1.2 Data Extraction:

Upon file upload, the Flask application reads the Excel file and extracts the necessary columns ('Reactions', 'Suspect Product Active Ingredients', 'Suspect Product Names', 'Concomitant Product Names') using the Pandas library.

2.1.3 Combining Columns:

A new column, 'Combined Column', is created to consolidate information from 'Suspect Product Active Ingredients', 'Suspect Product Names', and 'Concomitant

Product Names'. This step is necessary to streamline the analysis and facilitate pattern matching.

2.1.4 Lowercasing:

To ensure case-insensitive analysis, the text in the 'Reactions' and 'Combined Column' is converted to lowercase. This normalization step helps in avoiding discrepancies due to case variations.

2.2 Drug Selection

2.2.1 User Input:

Users are prompted to select up to three drugs of interest from a dynamically generated list based on unique values present in the 'Combined Column'. This ensures flexibility in choosing drugs relevant to the analysis.

2.2.2 Drug Combinations:

All possible combinations and permutations of the selected drugs are generated. This step aims to cover scenarios where the impact of individual drugs and their combinations on the specified reaction ('acute kidney injury') is explored.

2.3 Filtering and Analysis

2.3.1. Filtering for Acute Kidney Injury (AKI):

The dataset is filtered to include only those rows where the 'Reactions' column contains the term 'acute kidney injury'. This subset represents cases associated with AKI.

2.3.2. Filtering for Selected Drugs:

- Another subset is created by filtering rows where the 'Combined Column' matches any of the target values derived from the selected drugs. This subset represents cases involving the selected drugs.

2.3.3. Counting Cases:

Counts are calculated for various scenarios:

count_acute_kidney_injury: Total cases of AKI.

count_acute_kidney_injury_drug: Cases of AKI specifically associated with the selected drugs.

count_w_o_acute_kidney_injury_drug: Cases of the selected drugs without AKI.

count_acute_kidney_injury_drug_and_others: Cases of AKI associated with both the selected drugs and other drugs.

count_w_o_acute_kidney_injury_drug_and_others`: Cases of other drugs without AKI.

2.3.4. Reporting Odds Ratio (ROR) Calculation:

The Reporting Odds Ratio (ROR) is computed using the formula:

$$\mathbf{ROR = (n12 \times n21) / (n22 \times n11)}$$

n11= drug A alone with AKI
n12= drug A alone without AKI
n21= drug A + other compounds with AKI
n22= drug A + other compounds without AKI
where n11,n12, n21 and n22 are counts based on the presence or absence of AKI and the selected drugs.

2.3.5. Result Presentation:

The results, including counts and the calculated ROR, are presented to the user through the web interface. Messages are displayed to address special cases where there may be no cases with the selected drugs alone or no cases without AKI with the selected drugs.

2.4 Association Rule Algorithm

2.4.1. Apriori Algorithm:

Employed the Apriori algorithm, a classic association rule mining algorithm, to identify potential associations between drugs and the occurrence of acute kidney injury (AKI).

2.4.2. Rule Generation:

Generated association rules that highlight the relationships between drugs and AKI. Each rule takes the form "If drug A is present, then there is a likelihood of AKI."

2.4.3.Lift Calculation:

Calculated the lift value for each association rule. Lift is a measure of how much more likely it is for AKI to occur when both drug A and drug B are present compared to when only drug A is present.

2.5 DDI Index Calculation

2.5.1. DDI Index:

Calculated the Drug-Drug Interaction (DDI) Index, a customized metric, to assess the strength of the association between drug A and drug B in causing AKI.

2.5.2.Formula:

The DDI Index is computed as the ratio of the lift value of the association rule for drug A and drug B causing AKI to the lift value of another association rule for drug A causing AKI alone.{Drug A =1, Drug B = 1} -> {Acute Kidney Injury = 1 } (drug combination) to the lift value of another association rule {Drug A=1} -> {Acute Kidney Injury = 1 }.

DDI index = lift value of {Drug A =1, Drug B = 1} -> {Acute Kidney Injury = 1 }

2.5.3.Interpretation:

A higher DDI Index suggests a potentially stronger interaction between drug A and drug B in causing AKI. The index provides insights into the synergy or enhancement of AKI risk when both drugs are present compared to the risk associated with each drug individually.

2.6 Result Interpretation

2.6.1. Interpretation of DDI Index:

The ROR serves as an indicator of the association between the selected drugs and the occurrence of AKI. A high ROR suggests a potential association, while a low or zero ROR indicates a less likely association.

2.6.2. Holistic Understanding:

Users are encouraged to consider both the ROR and the DDI Index for a comprehensive understanding of the association between the selected drugs and AKI. The combination of statistical measures and association rules provides a robust basis for interpretation.

4. WEB SERVER DEVELOPMENT

4.1 Flask

Flask is a lightweight and flexible web framework for Python that is widely used for web application development. It is easy to get started with and provides the tools needed to build web applications quickly. Flask is a web application framework written in Python. It was developed by Armin Ronacher, who led a team of international Python enthusiasts called Poocco. Flask is based on the Werkzeg WSGI toolkit and the Jinja2 template engine.Both are Pocco projects.

4.1.1 WSGI

The Web Server Gateway Interface (Web Server Gateway Interface, WSGI) has been used as a standard for Python web application development. WSGI is the specification of a common interface between web servers and web applications.

4.1.2 Werkzeug

Werkzeug is a WSGI toolkit that implements requests, response objects, and utility functions. This enables a web frame to be built on it. The Flask framework uses Werkzeg as one of its bases.

4.1.3 jinja2

jinja2 is a popular template engine for Python. A web template system combines a template with a specific data source to render a dynamic web page.

This allows you to pass Python variables into HTML templates like this:

```
<html>
<head>
    <title>{{ title }}</title>
  </head> <body>
     <h1>Hello {{ username }}</h1> </body>
</html>
```

4.2 HTML

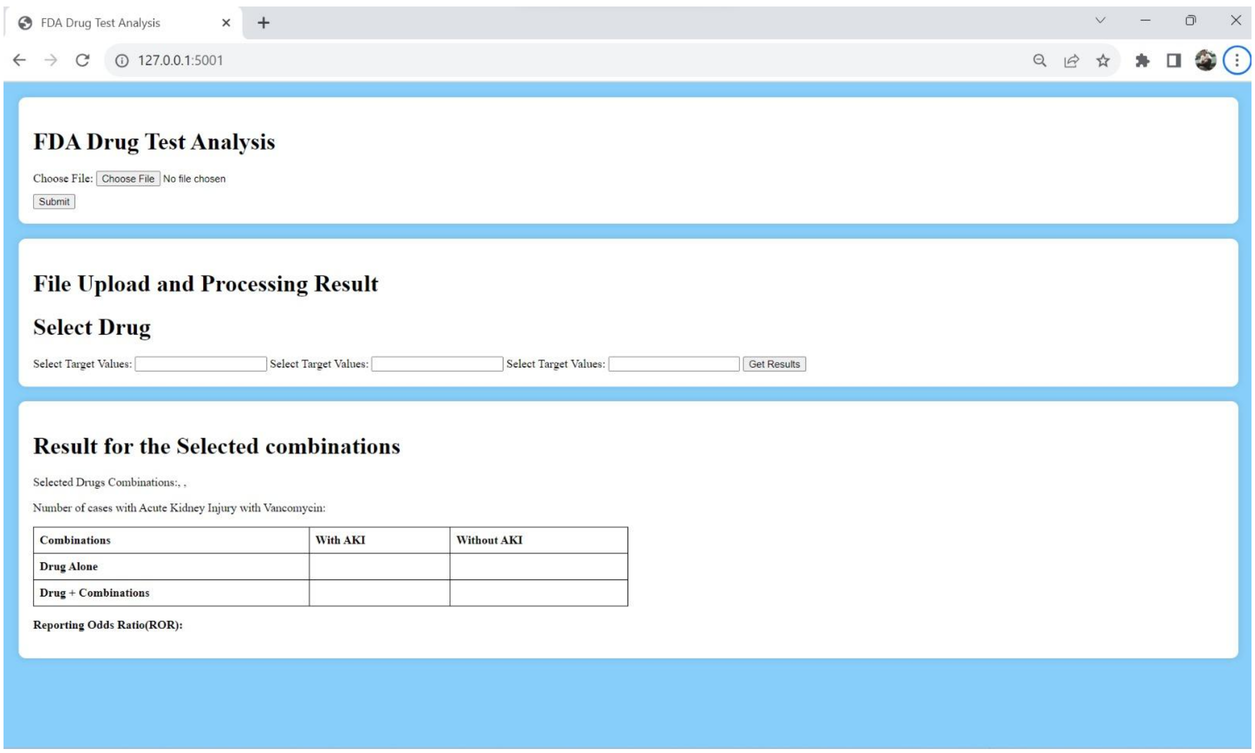
The HyperText Markup Language or HTML is the standard markup language for documents designed to be displayed in a web browser. It is often assisted by technologies such as Cascading Style Sheets (CSS) and scripting languages such as JavaScript.

4.2.1 HTML Elements

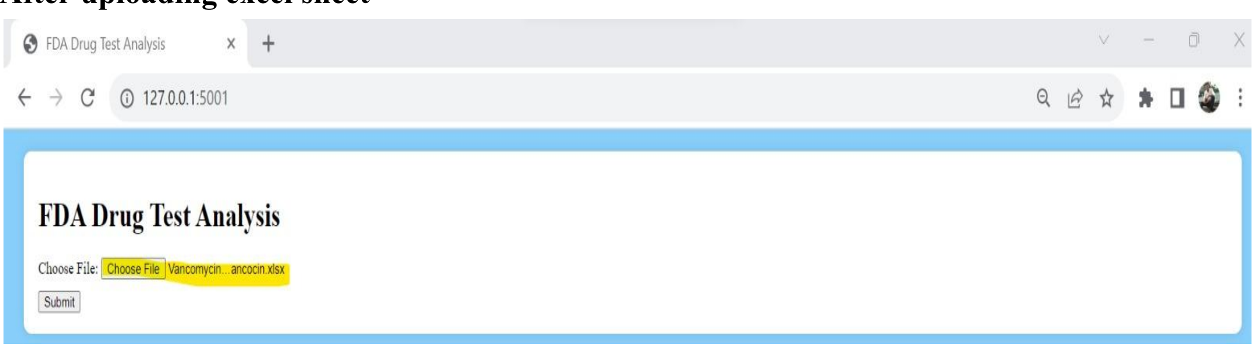
The HTML element is everything from the start tag to the end tag:

<tagname>Content goes here...</tagname>

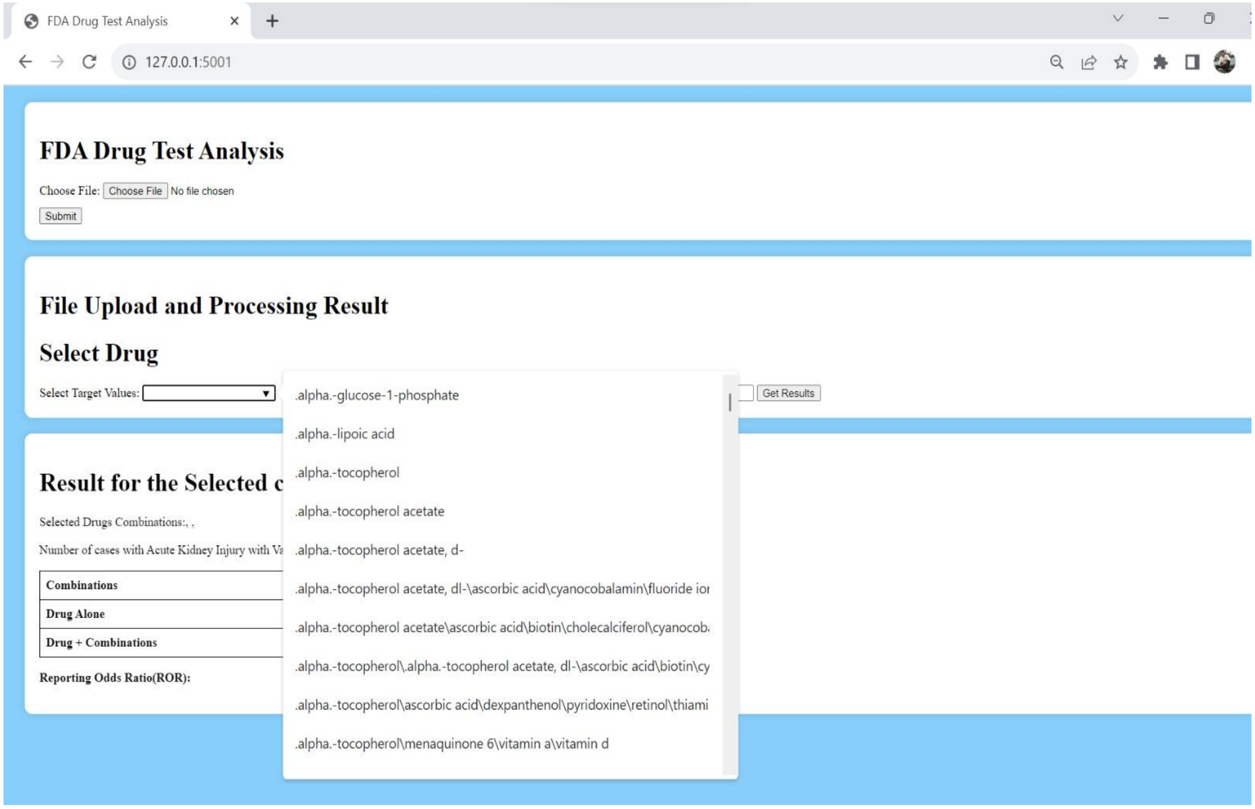
5. SCREENSHOTS OF OUR WEB APPLICATION



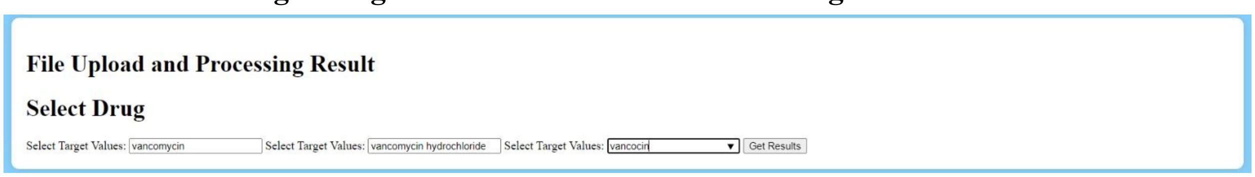
After uploading excel sheet



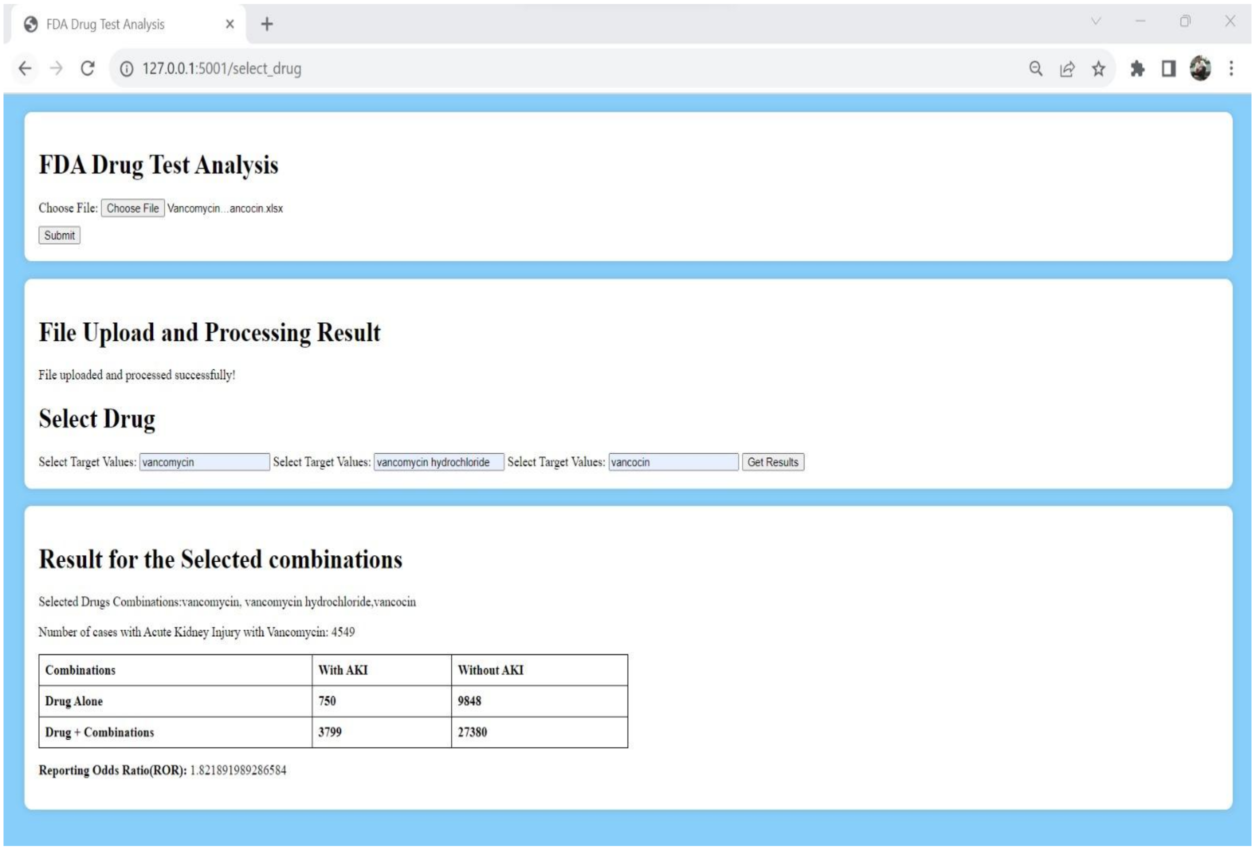
After submitting the excel sheet , user can select required drug to analyze



User can select a single drug or combination of at most 3 drugs

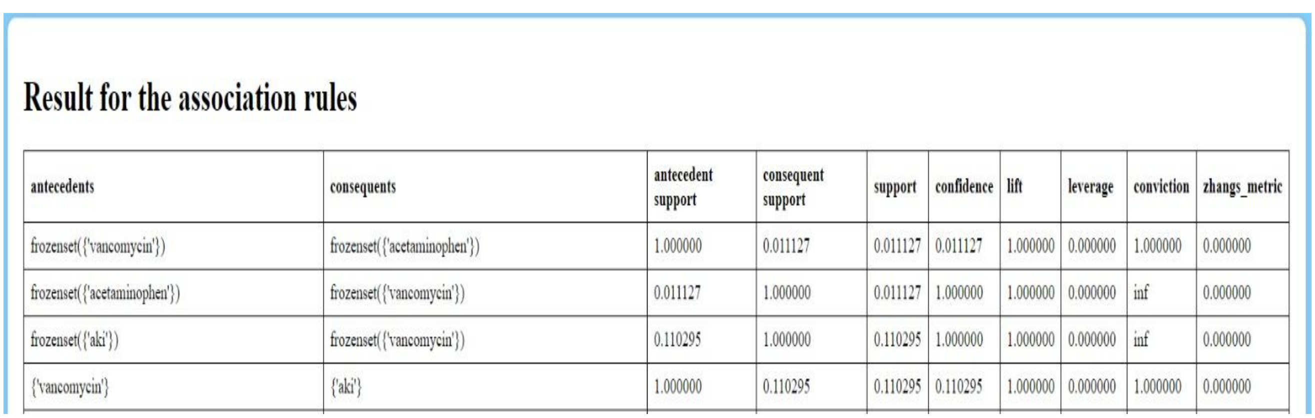


Results providing drug cases With and Without AKI and also the ROR value



Combinations	With AKI	Without AKI
Drug Alone	750	9848
Drug + Combinations	3799	27380

Association Rules results



antecedents	consequents	antecedent support	consequent support	support	confidence	lift	leverage	conviction	zhangs_metric
frozenset({'vancomycin'})	frozenset({'acetaminophen'})	1.000000	0.011127	0.011127	0.011127	1.000000	0.000000	1.000000	0.000000
frozenset({'acetaminophen'})	frozenset({'vancomycin'})	0.011127	1.000000	0.011127	1.000000	1.000000	0.000000	inf	0.000000
frozenset({'aki'})	frozenset({'vancomycin'})	0.110295	1.000000	0.110295	1.000000	1.000000	0.000000	inf	0.000000
{'vancomycin'}	{'aki'}	1.000000	0.110295	0.110295	0.110295	1.000000	0.000000	1.000000	0.000000

6. CONCLUSION

In conclusion, the development of our Flask-based web server represents a pivotal achievement in providing a user-friendly and sophisticated platform for drug interaction analysis. The seamless integration of advanced algorithms, such as the Apriori algorithm for association rule mining and the calculation of the Drug-Drug Interaction (DDI) Index, empowers users with a deeper understanding of potential risks associated with specific drug combinations, particularly in the context of Acute Kidney Injury (AKI). The system's transparent result interpretation and informative messages contribute to the overall user experience, ensuring clarity and informed decision-making.Looking ahead, the web server's scalability, robust architecture, and well-documented codebase position it for future growth and adaptability. Ongoing maintenance, potential updates to algorithms or data sources, and exploration of emerging technologies present exciting avenues for refinement. As the healthcare landscape evolves, our web server stands as a valuable tool in the realm of medical research, providing researchers, healthcare professionals, and stakeholders with a reliable means to explore and comprehend the intricate relationships between drug interactions and adverse health outcomes.

7. FUTURE WORK

One avenue for future work involves the integration of external APIs to enhance the richness of data available for analysis. By tapping into reputable healthcare databases or pharmacological resources, the web server can dynamically fetch and update information about drugs, their interactions, and adverse effects. This not only ensures that the analysis is based on the most current and comprehensive data but also opens avenues for exploring a broader range of drug-related parameters.

Continuous improvement of the user interface is crucial for ensuring a positive and user-friendly experience. Future iterations could involve incorporating interactive data visualizations, such as graphs or charts, to provide users with a more intuitive understanding of the analysis outcomes. Additionally, refining the user input mechanisms, incorporating user feedback, and optimizing the overall design for various devices can contribute to a more seamless and engaging user experience.

8. REFERENCES

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