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Visualization of a graph model of medical drugs and their classes with subject to incompatibility

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Abstract

Currently, the world is actively undergoing digital transformation, which is associated with the introduction of digital technologies in various fields. Methods for predicting and combating various types of diseases are being developed more and more actively. A separate place in this issue is given to pharmacology and reducing the risks of poly-pharmacotherapy. Works in this area have become more and more active in the last three years, and relate primarily to the problems of experimental medicine - the search for new drugs or classification of patients by images. In this connection, the development of algorithms for processing big data in the field of clinical pharmacology, including regulatory documents, instructions for the use of drugs, reliable medical resources for machine learning and building a knowledge base focused on practical application in real medical practice, is becoming increasingly important.

One of the considered approaches for solving the problems described above is the search for an effective vector representation of the found concepts (word embedding) to build models of recommendations for the practical use of drugs based on the diagnosis and models for identifying their compatibility. The article presents a software tool for visualizing a graph model of medicines and their classes, considering their incompatibility. The problem of incompatibility of medicines is being investigated. The considered database of medicines, obtained from various sources, and the advantages of its use are described. The article presents the results of the developed prototype of a software tool that allows you to visualize a complete graph of relationships between drugs, a graph of incompatible drugs for a selected drug, and a graph of compatibility of two drugs. Graph model visualization provides a visual representation of complex relationships and allows researchers and pharmacologists to better understand interactions between drugs. The software offer the necessary tools to make informed decisions when prescribing medications and improve safety when using medicines.

Keywords: pharmacology, poly-pharmacotherapy, big data, vector representation, mathematical modeling, neural networks, graph models.

1. Introduction

The importance of drug incompatibility cannot be overstated in the context of modern medicine. In a world where numerous drugs are available for the treatment of various diseases, it is important to pay special attention to the results of their interaction. The results of the incompetent use of medicines can have long-term and very serious health consequences. Often, such situations arise due to the incompatibility of certain drugs.

Drug incompatibilities can have serious consequences for patients, including poor health, unwanted side effects, and even life-threatening situations. It is important to note that incompatibility between drugs can occur due to various factors, which include: chemical interactions, pharmacological effects and adverse reactions [1]. Drug interactions are complex and

varied, sophysicians, pharmacists, and other healthcare professionals need to be aware of possible incompatibilities in order to make informed drug therapy decisions.

In this context, the development and visualization of a graph model of medicines taking into account incompatibility is of great importance. The presentation of such information in graphs provides a visual representation of the relationships and interactions between drugs and classes, which can help professionals in the field to better understand the potential risks associated with the combined use of drugs.

At the moment, a large number of studies have been carried out and there is a wide range of accumulated knowledge related to the medications used and their side effects when various drugs are used together [2,3]. This avoids repeat medical studies, which allows the use of already existing datasets.

Thus, the aim of the research is to develop a software prototype that allows taking into account the incompatibility of several drugs and possible adverse reactions, which will ultimately help to present the results in a visual format convenient for human perception. It is also worth considering the possibility of using the results obtained in the future as part of a more complex system, which implies the presence of an API (Application Programming Interface) and receiving a response in machine form.

2. Overview of existing approaches

To date, there are various tools and approaches that help in solving the problem of visualizing a graph model of medicines and their classes, taking into account incompatibility. They include:

• Graph databases: Specialized databases such as Neo4j [4] that store and manage information about medicines, their classes and relationships. Such structures allow you to operate with great query capabilities and algorithms for analyzing and visualizing graphs.

• Visualization tools: Various graph visualization tools that can be applied to the model of medicines and their classes. These include software products Gephi [5], Cytoscape [6] and NetworkX [7], which provide flexible tools for visualization and analysis of graph structures.

• Bioinformatics and data integration: There are various resources and databases in this area containing information on chemical compounds, pharmacological properties and drug interactions, such as ClinVar [8]. Integrating this data with graph models and visualizing allows you to gain a deep understanding of interactions between medicines.

• Machine learning and data analysis: The use of machine learning and data analysis methods allows you to identify hidden patterns and patterns in the data of medicines, as well as solve the problem of division into classes, which helps in building more accurate and informative graph visualization models [9].

In general, thanks to the development of information technology and research efforts in the field of medicine and pharmacology, at the moment there is a set of tools and approaches that contribute to the effective visualization of a graph model of medicines and their classes, taking into account incompatibility. However, all of them are a text model with the ability to check for compatibility only a few specific drugs, without a visual component and without the ability to see a list of all negative reactions for one drug.

3. Data selecting and preprocessing

To test the algorithms of the software prototype and solve the problem of visualizing the graph model of medical drugs and their classes a database in the PostgreSQL format [10] obtained from the DrugCentral website [11] was chosen. This choice was driven by several factors that make this database attractive for this task. DrugCentral is a comprehensive drug database including information on chemical structures, pharmacological properties, pharmacokinetics, side effects, drug interactions and more. It brings together data from various sources, including scientific articles, clinical trials and official drug registries. Such a variety of data provides a rich context for the analysis and visualization of a graph model of medi-

cines. One of the advantages of DrugCentral is its relevance and constant updating of data. The database is regularly updated with new scientific research and developments in the field of pharmacology. This allows taking into account the latest achievements and changes in the field of medicine, which is especially important when analyzing the incompatibility of medicines. In addition, it is possible to use an open copy of the database, which allows you to directly configure a remote connection in order to have access to up-to-date data in real time. This ensures that the analysis and visualization of the graph model is based on up-to-date and reliable data, which is an important factor in achieving accurate and relevant results. Using a remote database also provides convenience and flexibility when working with data, allowing you to quickly receive updates and make changes to the analyzed graph model.

In the context of the research, the most interesting is a bunch of five tables, which serves as the basis for visualizing the graph model. These tables contain data about drugs, their classes, and side effects between them. The choice of these tables is determined by the goals and objectives of the study. These tables provide the necessary and sufficient information to build a graph model (Fig. 1).

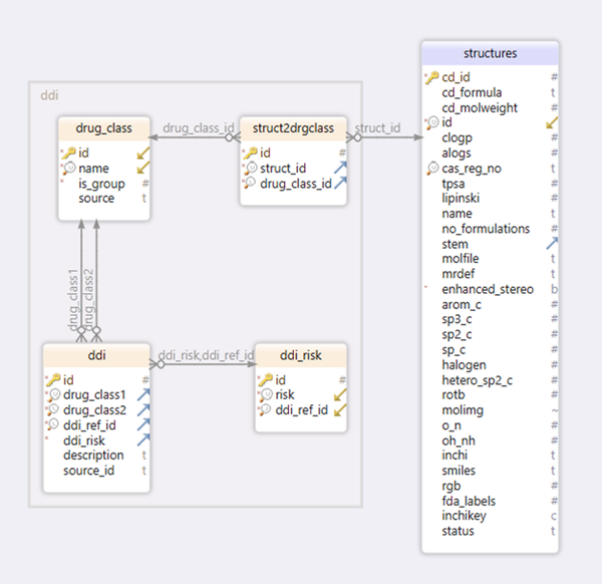

Figure 1. Tables and their relationships that serve as the basis for the visualization of the graph model

It is important to note that the drug-drug interactions described in the selected pairing of tables represent an aggregation of data from two main sources: drugdb [12] and lexicomp [13]. Drugdb is a database that contains information about various aspects of medicines, including their composition, pharmacological properties, and interactions. Lexicomp, on the other hand, is an authoritative source of information about medicines, providing data on drug interactions, possible side effects and recommendations for their use.

For the convenience of data visualization and analysis, it was decided to use the CSV format. To obtain the necessary data and their subsequent visualization into a format, SQL queries were developed. Using these queries, the necessary tables and relationships between them were selected in order to obtain information on interactions between medicines, taking into account incompatibilities. An example of the developed SQL queries is shown in fig. 2.

```
SELECT s.name, sc.drug_class_id AS class_id
FROM structures s
LEFT JOIN struct2drgclass sc ON s.cd_id = sc.struct_id
ORDER BY s.name;

SELECT dc1.name AS class_name1,
       dc1.id AS class_id1,
       dc2.name AS class_name2,
       dc2.id AS class_id2,
       ddi.ddi_risk,
       ddi.description
FROM ddi
JOIN drug_class dc1 ON ddi.drug_class1 = dc1.name
JOIN drug_class dc2 ON ddi.drug_class2 = dc2.name
```

Figure. 2. An example of the developed SQL queries for obtaining data

The results of SQL queries are saved to two files in CSV format. The first file contains a list of drug names and consists of 5692 lines. This file provides information about specific medicines that were included in the analysis and visualization of the graph model.

The second file contains the results of interactions between drugs and consists of 7621 lines. This file is a set of pairs of interactions, where each line corresponds to a set of two classes of drugs and the effect of their interaction.

4. Implementation

It should be taken into account that the software product being developed is primarily planned to be used for operation by medical staff. In this connection, for ease of perception, it is necessary to present data in an intuitive form.

To solve the described problem in the software, it was decided to develop algorithms that allow implementing and visualizing a graph model based on the available data, with the ability to change the target medicines for which this model is being built.

Rendering a complete graph does not require any parameters. In html format, an interactive graph is displayed, built on the basis of all the data received from the database (Fig. 3.).

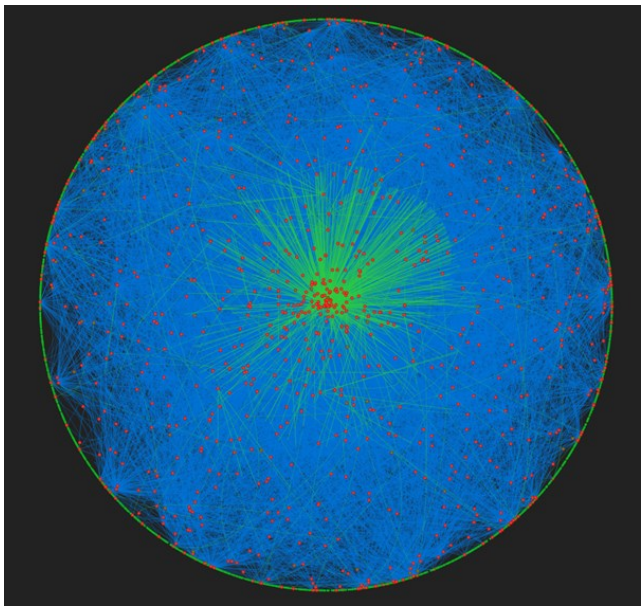

Figure 3. Interactive graph built on the basis of all data

Red nodes represent drug classes. These classes are interconnected by blue edges, indicating the incompatibility of the two classes with each other, and each node has its own signature with a comment about a possible side effect. Green nodes represent medicines that are associated with classes by green edges.

This visualization allows you to understand the scope of the study area and gain an overview of the relationships and interactions between all drugs in the system, which helps to understand the structure and complexity of the drug network. Also, thanks to this visualization, it is possible to highlight the central elements, which include key drugs or classes of drugs that play an important role in the health care system. This can help in decision making and identify potential areas for improvement and optimization.

In addition, for ease of presentation, the graph is interactive and allows you to change the location of the graph nodes in real time, moving them around the workspace. For this, the Barnes-Hut physical model is used, which implements a hierarchical tree to determine the forces of interaction between different nodes [14].

The advantage of this approach is its time efficiency, even with a large number of vertices. This is achieved by reducing the number of pairwise interacting vertices, taking into account the distance between them. The force $\vec{F}$ of the action of the vertex $A = (A_x, A_y, A_z)$ on the vertex $B = (B_x, B_y, B_z)$ can be calculated through their coordinates (formula 1)

$$\vec{F} = \vec{B} - \vec{A} = (B_x - A_x, B_y - A_y, B_z - A_z) \quad (1)$$

To calculate the direction of such a force, the parallelogram rule is used, and the size of such a force is calculated using the distance formula (formula 2)

$$|\vec{F}| = \sqrt{(B_x - A_x)^2 + (B_y - A_y)^2 + (B_z - A_z)^2} \quad (2)$$

In addition, the vertices are rigid bodies, and a torque can act on them. Thus, it is necessary to calculate the resultant force. Taking into account the direction (formula 3). Force calculations are simplified by the fact that the vertices are perfect circles.

$$\vec{r} \times \overrightarrow{F_R} = \sum_{i=1}^{N} (\vec{r_i} \times \vec{F_i}) \quad (3)$$

However, this graph is too large and inconvenient for a more detailed study of specific relationships and the search for specific drugs. For this, it was decided to implement the presentation in the form of an html page with the ability to select one single drug for study (Fig. 4).

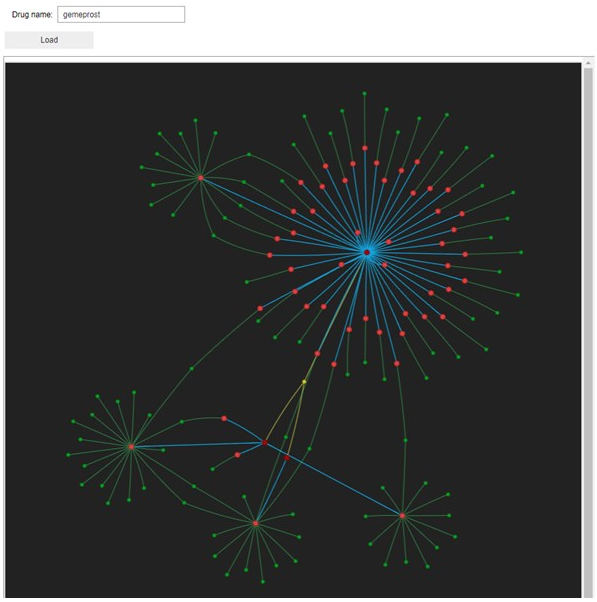

Figure 4. An example of an html page with a single drug to study

After entering the name of the drug to be considered, a new graph is built. The yellow node denotes the drug in question. It is connected by yellow edges to the dark red classes it belongs to. These classes are connected by blue edges with classes with which negative effects are ob-

served when interacting. Thus, this graph allows you to visually consider the medicinal products and classes of drugs with which the investigational medicinal product should not be mixed.

So, in the below image, the drug “gemeprost” is being examined. It can be seen that it belongs, among other things, to the classes “CYP3A4 Substrates” and “CYP2D6 Substrates”. For the “CYP3A4 Substrates” class, there is a negative interaction with the “fusidic acid” class, described as “may increase the serum concentration of CYP3A4 Substrates” (Fig. 5).

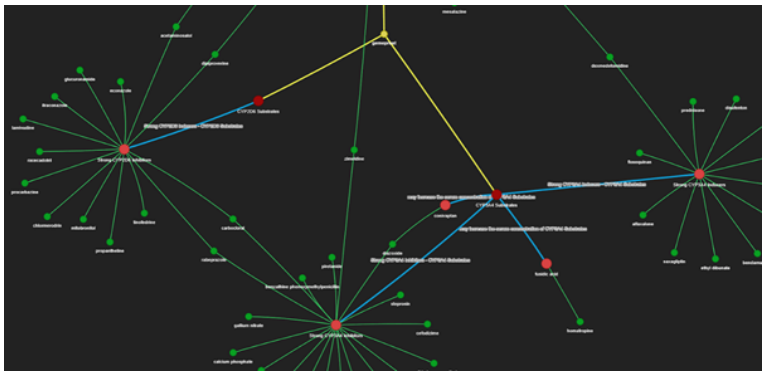

Figure 5. An example of an html page demonstrating the negative interaction between classes

Therefore, “gemeprost” cannot be combined with drugs of the “fusidic acid” class and directly with homatropine. In addition, some drugs may have incompatibilities across multiple classes, such as “gemeprost” incompatibility with “carbocloral” and “rabeprazole”.

In addition, it is possible to visualize two drugs and the presence or absence of incompatibility links between them, this can be done using another html file consisting of two input fields (Fig. 6).

Rice. 6. An example of an html page demonstrating the visualization of two preparations

Based on this example, it can be seen that the drugs “maltose” and “phenosulfazole” are incompatible, since the drug class “Monoamine Oxidase Inhibitors” is incompatible with the classes “Alpha/Beta Agonists” and “Indirectly Acting Sympathomimetic Amines”. In addition, this visualization shows possible side effects, such as hypertensive crisis, on the combined use of study drugs.

In addition to human-friendly visualization, consideration must be given to the possibility of using the software tool as a component of a larger program. To do this, a number of API functions were implemented in Python 3.10, which simplify interaction with the software product.

One of these functions worth noting is the function for translating data from html to json format. As an input parameter, the name of the drug is passed to its input, after which a tree

of all classes corresponding to the drug is built, while each contains incompatible classes with a description of the side effect and a list of the corresponding drugs (Fig. 7).


```
"iodoform": {
    "sevelamer": {
        "levothyroxine sodium": {
            "description": "LEVOTHYROXINE SODIUM/SEVELAMER HCL [VA Drug Interaction]",
            "drugs": [
                "quazepam"
            ]
        },
        "liothyronine": {
            "description": "LIOTHYRONINE SODIUM/SEVELAMER HCL [VA Drug Interaction]",
            "drugs": []
        },
        "ciprofloxacin": {
            "description": "CIPROFLOXACIN/SEVELAMER HCL [VA Drug Interaction]",
            "drugs": [
                "bufexamac"
            ]
        }
    }
}
```


Figure 7. An example of the API function for converting data from html to json format

For example, the drug “iodoform” belongs to the “sevelamer” class, which is incompatible with three classes, including “ciprofloxacin”, to which the drug “bufexamac” belongs. So "iodoform" and "bufexamac" are incompatible.

In addition, it is worth noting the function that allows you to check for the presence of adverse reactions between two drugs and form a final list based on them. For example, you can check the compatibility of "maltose" and "phenosulfazole". Thus, during the operation of the implemented algorithm, a list of two side effects of joint use will be displayed, which will describe both the classes of drugs that cause these effects and the degree of risk (Fig. 8).


```
[
    {
        "name1": "Monoamine Oxidase Inhibitors",
        "name2": "Alpha/Beta Agonists",
        "risk": "Potentially significant",
        "description": "MAO Inhibitors may enhance the hypertensive effect of Alpha/Beta-Agonists"
    },
    {
        "name1": "Monoamine Oxidase Inhibitors",
        "name2": "Indirectly Acting Sympathomimetic Amines",
        "risk": "Contraindicated",
        "description": "potentially fatal hypertensive crisis"
    }
]
```


Figure 8. An example of the API function for checking for adverse reactions between two drugs

5. Conclusion

This article describes the software implementation of visualization tools for the graph model of medical drugs and their classes, taking into account incompatibility. A review of the subject area and existing solutions was carried out. The main problems associated with the incompatibility of drugs, as well as the importance and relevance of this topic in the medical field are presented.

To solve the problem, a software prototype that allows visualizing the subject area and relationships between drugs and their classes was developed. The database of medicines was taken as a basis, obtained from DrugCentral, formed on the basis of drugdb and lexicomp data. This provided a variety of data, including information on drug interactions. Using SQL queries, the results were saved in CSV format, which made it possible to use them for visualization in a convenient format.

Within the framework of the developed software tool, three main types of visualization were implemented: a complete graph of relationships between drugs, a graph of incompatible

drugs for a selected drug, and a graph of compatibility of two drugs. Each of these types of visualization provides valuable information and helps in understanding the relationships and dependencies between medicines.

The developed software tool is very useful for medical personnel, researchers and other interested parties who want to explore and analyze the relationship between medicines. Visualization of the graph model contributes to more accurate decision-making and improves safety in the application of drug therapy.

However, it should be taken into account that this model is a complex knowledge base, the main task of which is to support the medical decision-making of specialists in the field. Further development of the software tool may include expanding functionality, improving the interface, and further using a wider range of data to more fully and accurately reflect the complex relationships in the medical field. However, the main goal is to apply the implemented algorithms within a more complex decision support system using artificial intelligence methods.

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