

Relational Information in Pharmacology: A Challenge

Sorana BOLBOACĂ

“Iuliu Hațieganu” University of Medicine and Pharmacy, Cluj-Napoca, Romania

sbolboaca@umfcluj.ro

Abstract

A large amount of pharmaceutical information exists and new knowledge's are created every day. Organizing pharmaceutical information is an important task because a correct organization of information allows searching and finding information quickly. The United States National Library of Medicine has already included into Medical Subjects Headings a 'Chemicals and Drugs' chapter and a number of countries translated already the indexes into own medical subjects classifications. The aim of the paper is a proposal of a relational database structure and Visual FoxPro implementation for organization of pharmaceutical standardised information using key terms, a very useful thinks for each country that need to organize pharmaceutical information.

Keywords

Pharmaceutical Information Management; Information Storage; Database Management System

Introduction

Nowadays, a large amount of information is available in all pharmacological areas even if we talk about immunogenic properties [1], validation of a new drug [2, 3, 4], drugs for cancer [5, 6] or any other areas. The pharmacological domain has been included in the

transformation of society's communication, and day-by-day more and more pharmaceutical sites and journals, which contain huge amounts of new knowledge, become available. Thus, the number of databases has exploding in the last decades in number as well as in contents, and organization of information in these databases is based on some standards. Most of these databases are created and maintaining by universities as for example are Drug Resource Center [7], and Drug InfoNet [8], or professional associations as Canadian HIV Trials Network [9], and Clinical Pharmacology [10].

Today, the challenge is to keep up to rapidly expanding of the pharmaceutical knowledge and to learn to access, interpret, and apply this knowledge, and to integrate the pharmacological evidence in day-by-day activities practicing evidence-based medicine. Organizing pharmaceutical information is an important task in managing the huge amount of knowledge. An important step in organizing the pharmaceutical information has made by United States National Library of Medicine, National Institute of Health, when in 1966 stated to use standardization of pharmacological and medical terminology and creating Medical Subject Headings, abbreviate as MeSH [11]. They created the MeSH thesaurus, a controlled vocabulary for subject indexing and searching of journal articles in MEDLINE [12], which is annual update [13].

Looking at the 'Chemicals and Drugs' chapter from the MeSH, tree structures as in figure 1 is founds.

```
graph TD; A[Chemical Actions and Uses [D27]] --> B[Pharmacologic Actions [D27.505]]; B --> C[Therapeutic Uses [D27.505.954]]; C --> D[Anti-Inflammatory Agents, Antirheumatic Agents, and Inflammation Mediators [D27.505.954.194]]; D --> E[Antirheumatic Agents [D27.505.954.194.050]]; E --> F[Anti-Inflammatory Agents, Non-Steroidal [D27.505.954.194.050.030]]; F --> G[Antirheumatic Agents, Gold [D27.505.954.194.050.050]]; G --> H[Gout Suppressants [D27.505.954.194.050.337]]; H --> I[Uricosuric Agents [D27.505.954.194.050.337.900]]
```

Figure 1. The tree-structure of Uricosuric Agents as MeSH term

As it can be seen from the figure 1, each drug term had associated into parentheses a number representing their biochemical, pharmacological or chemical properties as in our example. Most of the time, the drug is classified with the disease. It can say that the information has presented here as a tree structure based on indexed key. Starting from this

idea, the paper presents a proposal of a relational database structure and a Visual FoxPro implementation for pharmacological information management using key terms.

Materials and Method

First step in organizing information electronically is representing by creation of criterions based on which the information can be managed, criterion named generally standard. A standard has defined as *an acknowledged measure of comparison for quantitative or qualitative value*. Today we can talk about International Standardization of pharmaceutical information. The International Organization of Standardization [14] have four standards for pharmaceuticals, represented by ‘*Pharmaceutics in general*’, ‘*Medicaments*’, ‘*Wound dressings and compresses*’, and ‘*Other Standards related to pharmaceuticals*’.

Organising pharmaceutical information has made on based of standardised key terms. From one point of view, these pharmaceutical key terms can be organised as a mathematical graph by considering the key parameters to be nodes connected by each other with arcs corresponding to the relations between the parameters.

Let us take an example. Suppose that the key term is ‘*Growth Substances*’ (figure 2).

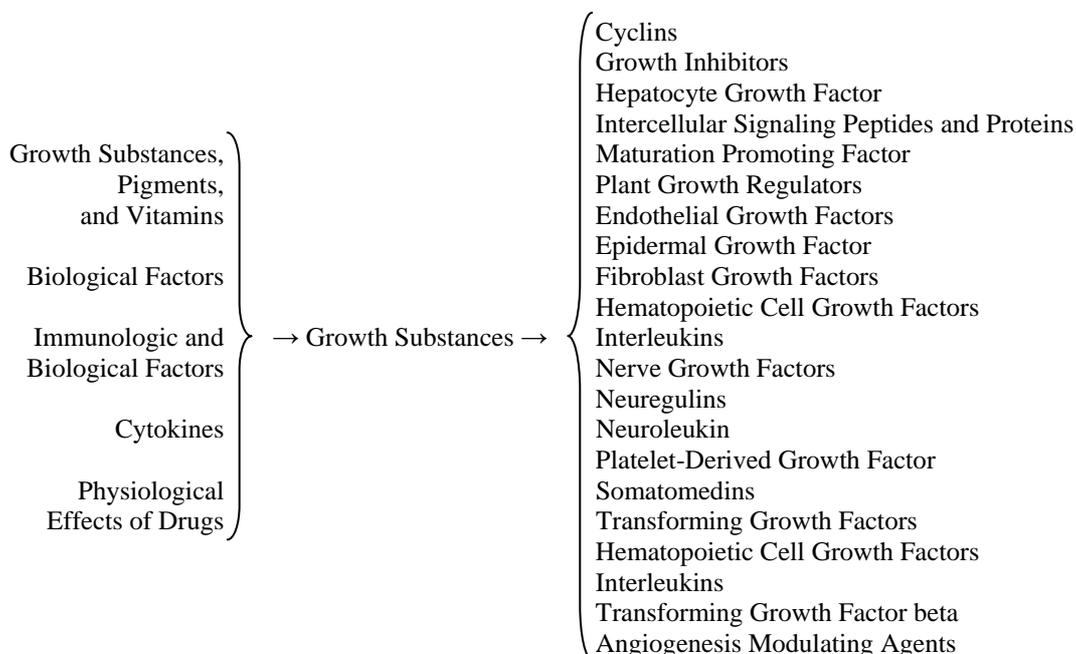


Figure 2. Graph-type relations for ‘*Growth Substances*’ key term node

As it can be seen in figure 2, ‘*Growth Substances*’, is a key term node with five edges

on the left side, from the '*Growth Substances, Pigments, and Vitamins*', '*Biological Factors*', '*Immunologic and Biological Factors*', '*Cytokines*', and '*Physiological Effects of Drugs*' nodes. There are twenty-one edges on the right going to '*Cyclin*', '*Growth Inhibitors*', '*Hepatocyte Growth Factor*', '*Intercellular Signaling Peptides and Proteins*', '*Maturation-Promoting Factor*', '*Plant Growth Regulators*', '*Endothelial Growth Factors*', '*Epidermal Growth Factor*', '*Fibroblast Growth Factors*', '*Hematopoietic Cell Growth Factors*', '*Interleukins*', '*Nerve Growth Factors*', '*Neuregulins*', '*Neuroleukin*', '*Platelet-Derived Growth Factor*', '*Somatomedins*', '*Transforming Growth Factors*', '*Hematopoietic Cell Growth Factors*', '*Interleukins*', '*Transforming Growth Factors beta*', and '*Angiogenesis Modulating Agents*'.

The structure of the key terms, on the other point of view, contains a cycle (figure 3). If we looked at the '*Fertility Agents*' as a key term, it can be found on the arch of '*Physiological Effects of Drugs*' or on the '*Therapeutic Uses*' arch. The '*Physiological Effects of Drugs*' node, as well as the '*Therapeutic Uses*' node is on '*Pharmacological Agents*' arches, attaining with '*Fertility Agents*' an cycle.

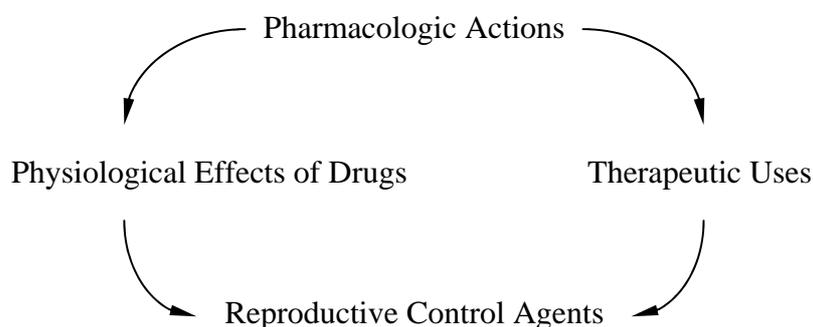


Figure 3. A cycle-structure in the key terms structure

As a method, I choose to work with a rapid application development (RAD) because allows usable systems to be built in as little as 60-90 days and because with conventional methods, there is always a long delay before to obtain any results and in all pharmaceutical fields the information is changing at short periods. I decided to develop the application with Microsoft Visual FoxPro. The structure of the pharmaceutical information described above, has implemented using a relational database. The structure of database is in figure 4. The database contained a number of eight tables called `pnX` (from X = 1 to X = 8) which store the levels of key terms, a table named `rel` that store the relations between different levels of terms and a `ghid` table that store the guideline information.

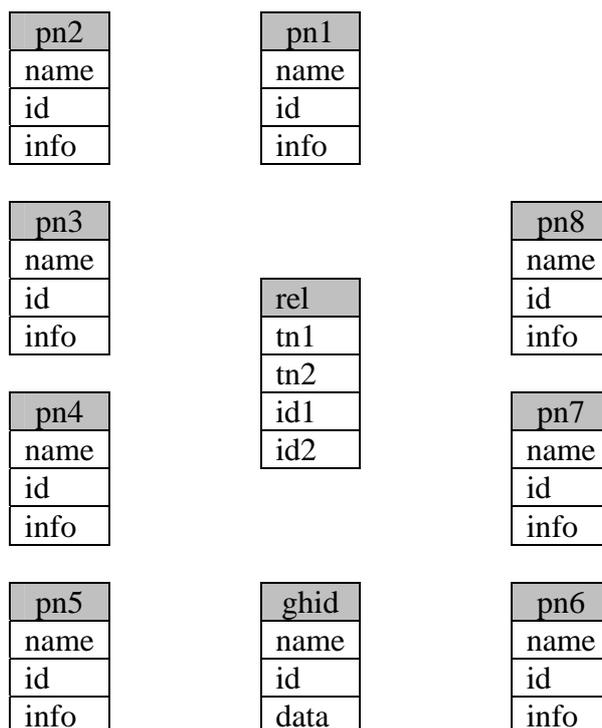


Figure 4. The key terms database structure

The relationships between the `pn...` tables and the `rel` table are in figure 5.

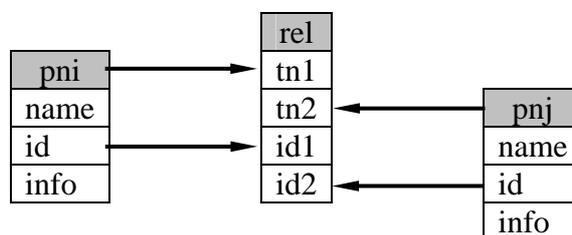


Figure 5. The many-to-many relationships between tables (where $i < j$)

At first looked, the relationship between the `pni` and the `rel` tables looked like a one-to-many relationship but in ensembles, the `rel` table store a many-to-many-to-many-to-many relationship (it had two 1 to n relationships with the `pni` table and two 1 to m relationships with the `pnj` table; where $j > i$). The `rel` table relationship in fact is a four-dimensional one (as example, the term with $id = 52$ from the table `pn2` is related with term with $id = 36$ from the table `pn3` which is related with term with $id = 31$ from the `pn4`).

Results

The program interface consists from eleven forms. The main form's name is 'Browse'. From the main form, we can access every table from the database, by click on the table name, including the table that stored the relations between different key terms (the 'rel' table). The main form allowed also quitting the application ('Quit' button).

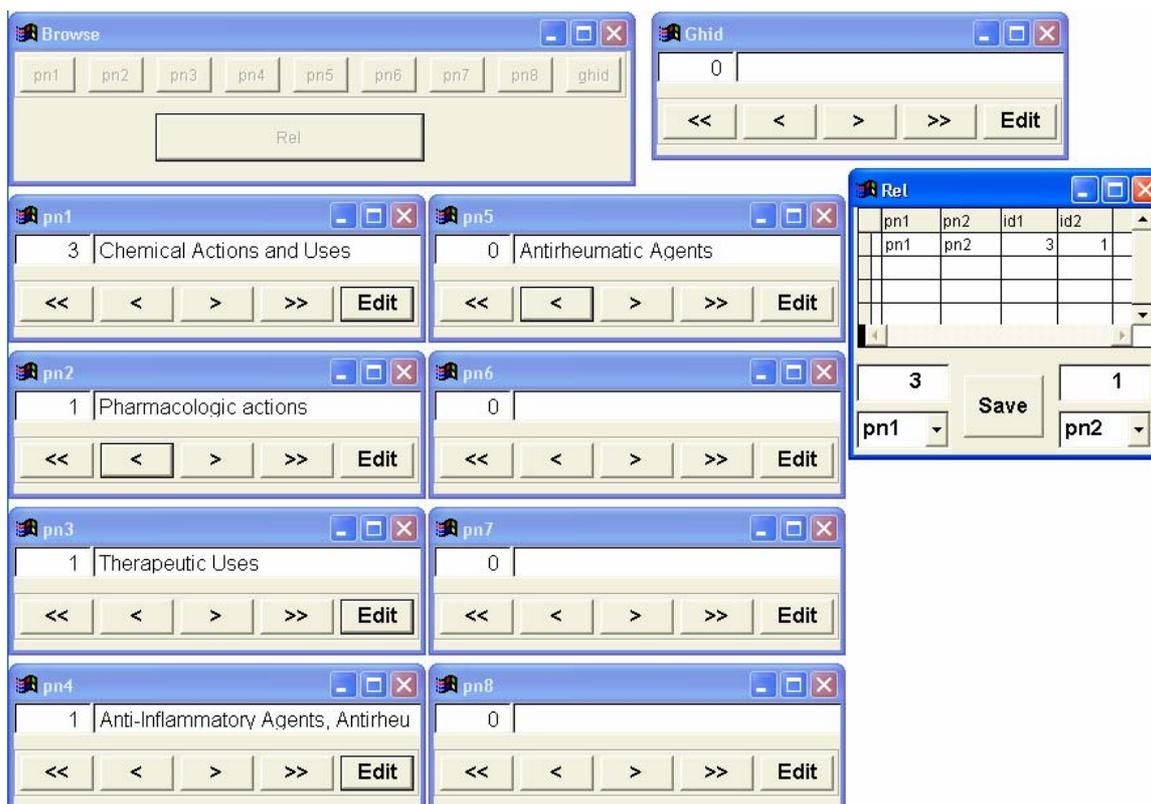


Figure 6. The program interface

Suppose that it necessary to include into the database a relationship for the key term 'Antirheumatic Agents' from the figure 1. First key term that will be included into database is 'Chemical Actions and Uses' in table `pn1`. For that, open the `pn1`, filled the `id` entry and typing the key term, 'Chemical Actions and Uses'.

Each form has two status windows, one that allows editing the information and another one saving the information. After editing the key term by click on 'Edit' button, the information included into database can be save by click on 'Save' button. Any of 'pni' forms can be browsed using the '<<' ('Go to the first record') button, '<' ('Go to the previous record'), '>' ('Go to next record'), and '>>' ('Go to the last record'). The next step is to include the next key level 'Pharmacologic Actions', into the `pn2` form. In order to create the

link between the two terms included into the database the 'rel' form it will be open, select the levels of key term, 'pn1' and 'pn2' forms ($1 < 2$), and then save the information.

Note that even if the interface of the program is nice and easy to use, the work to fill and to create links between key terms is time consuming.

Discussions

MeSH is the best-standardized medical and pharmaceutical terminology database that is used by many medical databases as indexes. Using the MeSH databases in pharmaceutical search strategies is easy and gives the possibilities to use many "mapped" terms, presenting explode capacities (subject categories with more specific terms arranged beneath broader terms) and broaden the search strategies [15]. Even if MeSH has been translated fully or partially into many languages we cannot await to happen in our countries and meantime do nothing. Excluding the languages in which the MeSH has translated, one disadvantage of MeSH is the conceptual and interface language, represented by English language because in the states where the majority of physicians do not have the English language knowledge at a high level, at the level of understanding correctly the medical information the databases and indexes cannot be useful.

The proposed interface, created using Visual FoxPro wants to give a solution for those countries who want to organize their own pharmaceuticals information, which contains the national pharmaceuticals terminology. Why Visual FoxPro was chosen? First reason was because Visual FoxPro provides all environment and tools we need to create and manage high-performance database applications and allows also integrating the Internet into the application. Integrating the Internet can allow the databases to be filled and used at the same time by many users. Microsoft Visual FoxPro [16] offers many properties as speed, power, and flexibility, very useful in creating a database management system allowing to create a database fast and to modify application easily. One of the most important reasons that the application was created using Microsoft Visual FoxPro was its properties to share information with other applications, a property which is very important in increasing the quality of application.

The program is quite easy to use and allows all types of users to work with it even if they have advanced knowledge of working with a computer or not. The work to organize

pharmaceutics information is time-consuming this being a disadvantage of the application. The best host for the application is a server. An Internet interface of our application can be create using a Microsoft Open Database Connectivity - a widely accepted application-programming interface (API) for database access - (ODBC) [17]. This will allows connecting to the database any time and from anywhere.

In order to access rapidly the information it will be very useful to create for every key term a list of entry terms, creating a new table linked with the existent structure; this tasks could be the next step of our research.

Conclusions

Implementation of a relational database for pharmaceutical information managements allows storing of pharmacological data information of any structure type, from tree type, (acyclic graphs) to cyclic graphs.

The application interface allows quickly inserting and searching of information at any tree level and creating directly and visible the relationships between pharmaceuticals key terms.

The physicians, pharmacists, drugs providers and dealers as well as institutions and organizations that develop pharmaceutical databases being a useful tool in organizing pharmaceutical information can use the application.

References

Medical Informatics programs web site: http://vl.academicdirect.ro/medical_informatics/

1. Pendley C., Schantz A., Wagner C., *Immunogenicity of therapeutic monoclonal antibodies. Current Opinion in Molecular Therapeutics*, 2003, 5, p. 172-79.
2. Krause S.O., *Development and validation of analytical methods for biopharmaceuticals, part I: development and optimization*, BioPharm International, 2004, 16, p. 52-61.
3. Krause S.O., *Good analytical method validation practice, part II: deriving acceptance criteria for the AMV protocol*, Journal of Validation Technology, 2003, 9(2), p. 162-178.

4. Krause S.O., *Good analytical method validation practice, part III: data analysis and the AMV report*, Journal of Validation Technology, 2003, 10(1), p. 21-36.
5. Antonini I., Polucci P., Magnano A., Sparapani S., Martelli S., *Rational design, synthesis, and biological evaluation of bis(pyrimido[5,6,1-de]acridines) and bis(pyrazolo[3,4,5-kl]acridine-5-carboxamides) as new anticancer agents*, J. Med. Chem., 2004, 47(21), p. 5244-50.
6. Rustum Y.M., *Thymidylate synthase: a critical target in cancer therapy?*, Front Biosci., 2004, 9, p. 2467-73.
7. Drug Resource Center, Harvard Medical School,
<http://www.intelihealth.com/IH/ihtIH/WSIHW000/8124/8124.html>
8. Drug InfoNet, <http://www.druginfonet.com/>
9. Canadian HIV Trials Network, <http://www.hivnet.ubc.ca/ctn.html>
10. Clinical Pharmacology, <http://www.cponline.gsm.com/>
11. Medical Subject Headings, United States National Library of Medicine,
<http://www.nlm.nih.gov/mesh/meshhome.html>
12. Bachrach C.A., Charen T., *Selection of MEDLINE contents, the development of its thesaurus, and the indexing process*, Medical Informatics, 1978, 3, p. 237-254.
13. Nelson S.J., Schopen M., Schulman J.L., Arluk N., *An Interlingual Database of MeSH Translations*, 8-th International Conference on Medical Librarianship, London, UK, 2000 Jul 4, <http://www.nlm.nih.gov/mesh/intlmesh.html>
14. ISO (International Organization for Standardization), <http://www.iso.org/>
15. MeSH versus Text Words, University of Utah, Spencer S Eccles Health Sciences Library,
http://medstat.med.utah.edu/library/edumaterials/handouts/PubMed_Web/mesh_adv.pdf
16. Microsoft Visual FoxPro development Center, <http://msdn.microsoft.com/vfoxpro/>
17. The Microsoft Open Database Connectivity,
<http://msdn.microsoft.com/library/default.asp?url=/library/en-us/odbc/htm/dasdkodbcoverview.asp>