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Detection of Drug Interactions via Android Smartphone: Design and Implementation

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ABSTRACT

Despite the morbidity and cases of widespread drug poisoning, clinical guidelines are largely written by taking into account only one treatment at a time. The cumulative impact of multiple treatments is rarely considered. Drug treatment for people with several diseases produces a complex regimen called "polypharmacy" with a potential combination of harmful and even lethal drugs that can be prevented. This polypharmacy causes in many cases the death of some people due to drug interactions. The vast majority of these deaths can be prevented by detecting interactions before taking these medications. But the problem is that such information exists in a state that is difficult to access for the general public, much less for people with little knowledge in the field. Although the pharmacist is unmistakable and most viable source to avoid such a problem, he cannot know what the patient does not mention because he is not aware of what may affect his treatment. To remedy this, we aim in this paper to develop an ergonomic Android application that will inform the patient about the potential risks of such drug interactions. The application is optimized to handle various databases and operate automation of QR code.

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1. INTRODUCTION

Adverse effects caused by drugs are a major cause of additional cost and mortality [1]. Drug interactions are one of the main preventable causes [2]. In 2015, a committee of US experts [3] defined a drug interaction as "a clinically relevant alteration of a drug's effect caused by the co-administration of another drug". This alteration can cause the occurrence of an adverse event or change the therapeutic effect of the drug. A clinically relevant drug interaction is "an interaction that results in toxicity or a loss of therapeutic efficacy that warrants the attention of a health professional". A potential drug interaction is defined as "the co-prescription of two drugs known to interact and exposing the patient to the risk of a drug interaction occurring" [3]. A drug interaction is therefore an event that causes an adverse effect and a potential drug interaction is the risk of developing this event.

In practice, drug interactions can come from many different mechanisms. In some situations, drug interac- tions are voluntarily sought. This is for example the case of naloxone, a morphine receptor antagonist administered during an overdose of morphine. Many contextual elements can alter the risk of developing a drug interaction. They may be related to the drug such as the dosage, duration of administration and route of administration or related to the physiopathological characteristics of the patient such as age (elderly), sex, pathologies (severe renal or hepatic impairment) and pharmacogenomics (slow or fast metabolizer) [3]. Figure 1 shows presentation of the INN.

Figure 1. Presentation of the INN

Polypathologists and the elderly are particularly at risk because the multiplicity of conditions increases the number of drugs and the fragile field makes more dramatic the occurrence of an undesirable effect [4]. The risk of drug interactions is a concern for health professionals when prescribing and dispensing. The risk of drug interaction between two molecules can be estimated from randomized studies, clinical observations, and signal detection in a database or extrapolations from in vitro studies [5].

In an active world where evolution can be seen with the naked eye, the motivation to develop better and more efficient ways of communication and exchange of information is becoming increasingly important. This motivation leads us to a revolution carrying out the use of all embedded devices for personal and daily needs.

Recent years have seen an exponential growth of mobile devices that have spread like wildfire in the develop-ing world and revolutionizing the communications field. In this environment, old mobile phones do not do everything, but smartphones appear to break with the opinions of its predecessors and give another dimension to this technol- ogy while incorporating new contributions and services to mobile telephony and attracting customers through to its revolutionary and attractive ease of use.

Starting from the idea of optimizing the utility of a smartphone, the application development has emerged. After doing some research on the pharmacological field while establishing our own statistics, it was concluded that there is a growing number of people with many diseases, thus subject to polypharmacy (heart medications, diabetes, hypertension) [6]. The bitter fact faced by doctors is: how to coexist several drugs simultaneously in the same patient by avoiding interactions that could harm the physical integrity of the patient? Based on a scientific database having corollary avoidance of adverse drug interactions, it seemed that it was possible to develop an application that would make a great service to the medical prescription and the extension support information to the patient. The usefulness of smartphones will change significantly managements of patients' life [7]. These mobile devices will act as link between the drug and the doctor and the drug and the patient [8]. They provide individual users and communities with valuable access to a range of information services for personal purposes.

The remainder of this paper is organized as follows: in Section II, basic concepts are presented. We begin by defining a drug followed by a drugs classification then present the various drug interactions. The Section III discusses the Android system: their features, their applications especially those used in medical field. QR code and their caracteristics constitute the content of Section IV. The Section V is reserved to the application developpment, and the conclusion and directions for future works are presented in the last section.

2. FUNDAMENTALS CONCEPTS

The drug comes from the Latin word ″medicamentum″ meaning remedy. Today, the drug is subjected to a rigorous definition. Medicaments are products designed to prevent, treat, or even detect disease. They can fight the cause, so antibiotics against bacterial infections or mitigate events such as analgesics used to relieve pain. The drugs generally contain substances or active ingredients, where the effect extends to the whole body. It is possible to modulate their absorption and duration of action by altering the chemical structure or by choosing the appropriate form. There are many forms of drugs: (i) Oral forms: tablet, capsule, syrup, etc., (ii) Forms for external application: ointment, cream, gel, powder, etc., (iii) Forms for the nose, ears or eyes: auricular solution, eye drops, etc., (iv) Injectable forms: injection, infusion.

2.1. Drug Classification

There are more than ten thousand drugs. Each drug is used for a specific purpose and for different medical specialties. There are many ways to classify drugs. The two most important are:

2.1.1. Classification by INN (International Nonproprietary Name)

A drug is classified according to its active ingredients. This type of classification allows finding a drug in any country of the world and regardless of the brand name it bears. As an example we quote: Dafalgan®, Efferalgan®, Doliprane®, Claradol®, Dolko®, Dolotec®, Geluprane®. The international name for all these drugs is paracetamol.

2.1.2. Classification by Therapeutic Action

It is called the "Pacotherapeutic Families". While a family may include several active ingredients, Table 1 lists some examples:

Table 1. Some Examples of Therapeutics Classes

Therapeutic families	Action	Active ingredients
Analgesics	Soothe and removes the pain of a pathology	Paracetamol, Morphine, Codeine
Anti-Infective	helps fight infection	Antibiotics, antiviral and vaccines
Nonsteroidal Anti-Inflammatory	Decreasing the effects of inflammation	acetylsalicylic acid (Aspgic), Diclofenac Potassium, Sodium

2.2. Drug Interaction

A drug interaction [9] is a qualitative or quantitative modification of a drug with another drug, food or drink. The interaction may also occur with chemical agents to the environment. However, for this work, we will retain only the interactions taking place between drugs. Some drug interactions have serious clinical consequences; others have only effects without seriousness criteria and / or are sometimes asymptomatic [10]. When talking about the addition of several drugs, we should specify the parent molecule (or active ingredient) of each of them because it determines its position against the interaction. It's not all drugs that are affected by these interactions because it knows that these drugs are beneficial, but they sometimes act in contradiction with each other.

These contradictions are listed in four levels: (1) the most serious level is the "against-indication". This is absolute and must not be transgressed. It can have a toxic effect, which enters in what is called iatrogenic (negative result due to treatment or medical procedure), (2) the "recommended combination" should be mostly avoided. If both drugs are needed and after careful consideration of the benefit/risk ratio, close monitoring of the patient is necessary [11], (3) the most common case is the "safety precaution". The association is possible therefore when are met, especially in early treatment: dose adjustment, strengthening the clinical, biological, electrocardiogram, (4) at the fourth level, there is no practical recommendation. However, the risk of drug interaction exists, and usually corresponds to an addition of adverse effects. It is the doctor to assess the appropriateness of the drug combination.

2.2.1. Pharmacological Consequences of Drug Interactions

The pharmacological effects of drug interactions are quantitative changes of one or more effects (therapeutic or undesirable) of one or more drugs in the combination. If we consider a given effect, drug interactions affect either intensity or duration, or both parameters simultaneously. We can count three consequences:

a. Synergy: The action of a drug can be increased in speed, intensity, duration, and simultaneous administration of another drug with a pharmacological activity qualitatively similar. Figure 2 depicts the synergy mechanism. There are three types of synergy: (i) Full additive synergy: the observed action is equal to the sum of two partial actions, (ii) Partial synergy: the observed action is less than the sum of the two partial actions, (iii) The potentiating synergy: the observed action is greater than the sum of the two partial actions.

   The synergistic drug interactions are frequently observed. For example, they are observed: (i) When we prescribe two antihypertensive drugs, the risk of orthostatic hypotension is naturally more frequent, (ii) Blood pressure lowering with an antidepressant; the risk of orthostatic hypotension is increased.

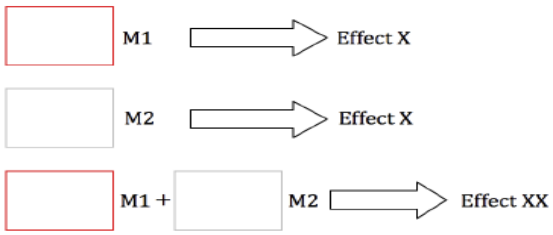

Figure 2. Synergy mechanism

b. Potentiation: The sum of the effects of the two drugs is greater than their simple addition.
c. Antagonism: An interaction between two substances of the same or different pharmacological activity in which one substance partially or completely inhibits or counteracts the effects of the other. Antagonism can be total or partial. Figure 3 illustrates the antagonism mechanism.

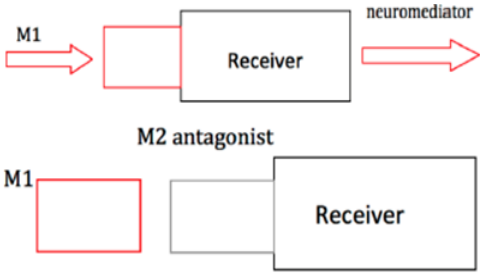

Figure 3. Antagonism mechanism

d. Total antagonism: Total antagonism occurs when the effects of the two substances vanish completely.
e. Partial antagonism: Partial antagonism occurs when the global effect of the combination is less than each of the two components taken separately [12].
Fixing the M1 on the receiver causes the release of neuromediator. M1 cannot bind to the receptor occupied by M2; there is no release of neurotransmitter.

2.2.2. Types of Drug Interactions

The mechanisms of drug interactions are numerous, but they can be classified into two groups: pharmacokinetic interactions and pharmacodynamic interactions. Pharmacokinetic interactions: It is the modification of the relationship between dose and concentration of the active drug. Pharmacokinetic aims to study the future of a drug in the body. Pharmacokinetic interactions occur when one drug alters the handling of another by altering its absorption, distribution, metabolism or excretion. Pharmacodynamic interactions: Pharmacodynamic interactions occur when two drugs act on the same drug target (e.g. cell surface receptor, enzyme) or physiological system (e.g. blood clotting, blood pressure, central nervous system, plasma electrolyte concentration) [9].

3. ANDROID SYSTEM

Smartphones and other smart mobile devices (tablets, watches, television) use different operating systems. The main popular operating systems used in the world are Android, Windows Phone, iOS and Apple (iPhone OS) etc. The mobile operating system clearly has a significant impact on the phone market where the presence of the giants of the computer industry likes Google and Apple. Each of them develops its own operating system, Android for Google and iOS for Apple.

Android is an open source operating system and is based on Linux. Android is designed for mobile devices. Not restricted to the phones it opens up other possibilities of using tablets, laptops, and smartwatches. To promote this new open operating system, Google has federated around it a consortium of thirty companies: the Open Handset Alliance (OHA) formally established on November 5, 2007. All of these

companies are involved, more or less directly, in the market of mobile telephony accounting for telephone operators, semiconductor manufacturers, mobile devices, and software.

Their main objective was to develop open standards for mobile devices in order to find a reliable solution to compete with Apple iOS, Microsoft and Nokia withWindows Mobile and Research In Motion with Blackberry OS. In October 2008, appears the first version of Android that did not receive name. This version has proven to be the beta version of the system.

Implemented in a mobile terminal, Android exploits the features of the latter using downloaded applications in a platform called Google Store. The OS offers a unified approach to application development for mobile devices, which means that developers must only develop under Android, and their applications should be able to run on different devices operating by Android. The source code for Android is available under license of free and open software. One of the other advantages of Android is that it is customizable by manufacturers and mobile operators. While undergoing several changes, the heart of the system remains common enabling application interoperability.

3.1. Android Apps and Diversity of Deployment

Android applications are generally developed in java using a specific development kit with it. This is a program that is loaded on the mobile user, having previously been downloaded or without payment at the option of the publisher who created it. Once downloaded, the application is represented as a small icon that appears on the smartphone screen. It then uses thereafter by simply pressing the icon in question, via the touch screen.

An application, as its name suggests, performs a function, a specific utility can be very varied. It offers a multitude of different uses from the game through information, purchasing, reservations, listening to music and so on. Theirs applications are available at a platform called Google Play Store and can be uploaded by any Android user just having a Gmail account. This operation is performed in a downlink, otherwise where will a developer who wants to charge its application on this platform, once developed, this application can be sold or offered according to the wishes of his publisher on platforms. With hardware capabilities incorporated into terminals (camera, GPS, etc.), smartphones and tablet applications can integrate specific features and dedicated to users, and to enrich the functional spectrum and uses imagine not covered so far. These applications are present in many areas, evoking a daily or professional functionality.

We will mention a few that have revolutionized the world of Android and especially the health field: in [13], authors design and implement a health monitoring system capable of detecting, monitoring and transmitting subject's physiological parameters such as ECG, blood pressure, blood oxygenation, respiration and temperature. The monitoring system is small, portable, low-cost, and easy-to-use without the limit of time and places. The use of Bluetooth standard communication protocol for data transmission and Android operating system for software development make the monitoring system more interchangeable.

Z. Pirani [14] build an application that could ease the everyday life of a person affected by Alzheimers disease. This application provides various functionalities such as tracking movements of the patient through GPS, providing medicine and food timing notifications, daily routine tracker and quiz to increase cognitive functioning of the patient. In [15], authors present a comprehensive discussion of the various applications utilizing smartphone-based technologies in cardiology. The project presented in [16] shows the patient's vital parameters such as ECG, heart rate, Sp02, pulse rate and temperature are measured using a patient monitoring system. These values are stored into a database and are uploaded into a web-based server manually. The entire details of the patient suffering from various chronic diseases like cancer, Alzheimer's etc. can be sent to a doctor sitting abroad in order to analyze and recommend the type of treatment and medicines for the diagnosis of the disease.

4. QR CODE REVOLUTION

The barcode is a representation of a digital or alphanumeric data in the form of a symbol consisting of bars and spaces that vary in thickness depending on the symbology used (transposition system between a text and a bar code by coding) and the encoded data to facilitate access to information. We distinguish one-dimensional barcode, which are represented by vertical bars as it is illustrated in Figure 4 (left). The increased demand for more information guided their evolution in two-dimensional barcodes Figure 4 right part.

Figure 4. Barecode (left) and QR code (right)

4.1. Presentation of the QR Code

The QR code [17, 18] is a barcode in two dimensions means that it is scanned in both vertical and horizontal directions. It was created and protected by DensoWave Japanese company in 1994 and later in 2000 it was recognized and defined by the industry standard ISO/IEC 18004. QR stands for Quick Response, which emphasizes its ability to read and decode at high speed. It is called as Flash Code [19].

4.2. Characteristics of QR Code

a. Capacity: The QR code can contain a lot of information: 7089 numeric characters 4296 alphanumeric characters, while the normal barcodes can only store 10 to 13 characters or 2953 bytes.
b. Code structure: As previously reported the QR code is two-dimensional, it consists of a black and white assembly squares.

4.3. Sub section 2

The QR code is used to encode a URL such as that of a blog, a product, SMS, email to send, contact (name, address, telephone number of a person to record it quickly in the contact list after have scanned the QR code through the mobile's camera), etc. In view of the proliferation of smartphones, the QR code has been loosely spread in different areas of expertise included: i) In advertising field by directing the reader to the site of their product, ii) As a method of payment, exclusively in Japan, iii) Operations of records: Visas, train tickets or open doors.

5. APPLICATION DEVELOPMENT

There are various techniques and approaches to develop an application in general. It is preferred to consider the conditions believed to be the most difficult. Thus, it has a clear view of whether it is possible to complete the stakeholder of our application; its success will give an advance momentum for development. The difficult challenges of our application focus around the exploitation of QR code reader introduced previously and interactions with different databases within the application [20]. The complexity of integration and the pile of obstacles bypassed do not allow us to mention all the steps and maneuvers of the development process. However, we will present them briefly into three parts: 1) Integrating QR code reader, 2) Create, import and use of databases, 3) GUI Development with explanation by different scenarios.

5.1. Integrating QR Code Reader

There are various applications using this feature. Our application is chosen to be "standalone" i.e it can read and interpret a QR code without the need for another application or service already available on the device. Its realization was not easy, due to the countless compatibility constraints of different systems and APIs (Android Package Index).

The QR code reader module we chose is the "Zebra Crossing" or "ZXing Code Reader" due to the flexibility of its source code, its continuous updating and viability of the service while supporting the former-dimensional bar code. The integration of the QR code reader begins by importing source code named "core.jar" by Maven Repository. Then we create an application folder that can be considered as a sub-application called "CaptureActivity" which will contain the elements of the ZXing and will deal exclusively ensure the reading and interpretation service QR code. Figures 5 show the scan of two drugs containing respectively a QR code and a one-dimensional barcode. Note that the interpretation of QR code often requires Internet connection in order to extract additional information and display the results in full.

5.2. Create, Import and Use of Databases

The type of database used is SQLite. This choice is obvious given the ease of handling in the Android system and speed of treatment. In our work, we create two separate databases: one dedicated for processing profiles and another for interactions between drugs.

Figure 5. QR code and barecode scan mediation

5.2.1. Database Processing Profiles

This database will contain records of various treatments entered by the user to facilitate the exploitation of these data (which are other than the medication list in a single treatment). The database is created in the "SQLite Database Browser" and contains three tables: (i) The first table contains basic information such as: id, name, and medication list, (ii) The second table contains the version of the database required for the update, (iii) The third table is automatically generated for drawing lines. Although there has been content to record information in the field and avoid the database, our method has several advantages: (i) Greatly optimize resources because the information is stored in a file and not in RAM, (ii) The ability to have different treatments recorded at a time and display them in an ergonomic list, iii) The speed of access to information.

5.2.2. Interactions Database

This is the most sensitive part in our work. So far, there is not a universal database of all drug interactions of each trade name. Given the complexity and the large number of these interactions, it is difficult to automate the whole process. That's why we started first by interactions Drug-to-Drug (a drug with another) based on "Thesaurus drug interactions" made by ANSM (National Agency of Drug Safety and products health) with the version of "January 2016" to establish our own database. In the foreground, it will compare two drugs by their INN (International Nonproprietary Name or name of the parent molecule). These databases will be in files that must import into our application that will be compiled into the "APK" file (Android Package Kit), which will then be copied to the Android mobile. The files are first deposited in the "Assets" folder to have access to Java classes. The import of these databases will be done through a class, which contains the different import and verification procedures and methods of access to data.

5.3. GUI Development and Explanation of Different Scenarios

The GUI is the graphical interface through which the user will interact. Several standards and rules are needed to ergonomics and ease of use. For this, we tried to make an interface as intuitive as possible while maintaining a pleasant aesthetic and not crowded. The design of the GUI can be very complex if you want to make an attractive interface, which makes it a specialty in itself since we used external programs. In our application, the development of the GUI was done in two parts:

1. The design of the buttons, images and funds by Adobe Illustrator then deposit images into the folder" Drawable"
2. The creation and setting XML layouts.

The launch of the application display the main interface corresponding to "MainActivity". Figure 6 shows the application home page. This interface contains three buttons and each button opens the appropriate interface. The interface allows us to see the profile of treatment, check if there is interaction between two drugs or a drug scanner through its QR code.

First, we present an example of treatment that will test with a drug: treatment against tonsillitis and fever. The recommended drugs are: aspirin (aspegic), antibiotics (Clamoxyl) Rhinathiol syrup (Promethazine). After a hypertension [21] the doctor prescribes to the same patient an antihypertensive (Atabek). Pressing the key "treatment profile" displays in a listview the list of profiles recorded with a button to add others that will guide us to an interface to complete and recorded a new treatment spotted by its profile name as shown in Figure 7.

Profile names are extracted from the database processing profiles and displayed in a "ListView" that can drag and click on content. This is ensured by several additional classes and layouts called the "Adapter" with the sole role of adapting the content to the display. Subsequently, after a recording is made, the profile name will be added to the list of profiles.

Figure 6. Application displays

Figure 7. List of profiles

The buttons behind each "TextField" are used to automatically enter the INN of medicament by opening the "Scanner" but given the non-standardization of the QR code format; it is very difficult at the moment to extract the INN with a single scan. Figure 8 shows add treatment and Figure 9 shows check between profile and drugs.

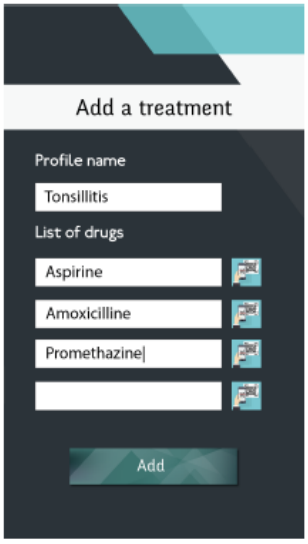

Figure 8. Add treatment

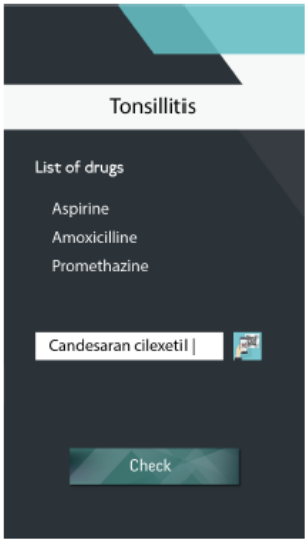

Figure 9. Check between profile and drugs

By clicking on a profile name in the ListView, the associated interface will be displayed with the drug field to be checked in which the INN Atabek is entered (the INN is obtained from the example of the scan performed previously). Then, clicking the "Check" button displays the interface given by Figure 10. Informations of the result are obtained after processing the interactions database. Details of the interaction are not available for all, but in the foreground, we display its severity with interacting INN. In another scenario where we want to check the two drugs, the operation is fairly linear and does not require the involvement of the database processing profiles. By clicking the second button in the main window, then entering the relevant drugs and validating the corresponding result is obtained as shown in Figure 11.

Figure 10. No interaction

Figure 11. Check between two drugs

6. CONCLUSION

The work presented in this paper is based on the development of a program for mobile devices such as smartphone, tablet, etc. allowing a person already following a specific medical treatment to evaluate the level of the drug interaction if this patient added one drug and another medication to his treatment. So, this application can manage various therapies followed by the patient based on the medication he takes. This application is also beneficial for patients and for the medical profession (doctor, pharmacist).

The application aims to provide a simple and ergonomic interface, untied of any complexity and unnecessary detail, which will allow a patient with little knowledge to know the risks of interactions between a drug and another. It will therefore translate the raw information and extract it as necessary to gauge the severity of interaction. Given the deployment of the new QR code in the newest drugs, the use of the application will be fully automated with a simple scan of the drug by the camera and give simple and interpretable results to everybody. As an extension to this work, possible perspectives are needed: (i) Enriching the database with more interactions, (ii) Add interactions with substances, (iii) Finalize the automatic entry of drugs QR code scans, (iv) Add a reminder of the time taken to drugs registered in treatment.

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Sidi Mohammed Hadj Irid received Engineer and Magister degrees in electronic and communication engineering from Tlemcen university, Algeria, in 1996 and 2000 respectively. Then he studied digital communication in Valenciennes University, France in 2001. He has been a network supervisor at IBM Montreal, Canada, then a project manager at Orascom Telecom Algeria. Since 2008, he is lecturer at university of Tlemcen. His research interests are in the area of digital and array signal processing.