Assessment of Orthographic Similarity of Drugs Names between Iran and Overseas Using the Solar Model

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Abstract

Background: The recognition of patient safety is now occupying a prominent place on the health policy agenda since medical errors can result in adverse events. The existence of confusing drug names is one of the most common causes of medication errors. In Iran, the General Office of Trademarks Registry (GOTR), for four years (2010-2014) was responsible for approving drug proprietary names. This study aimed to investigate the performance of the GOTR in terms of drug names orthographic similarity using the SOLAR model.

Methods: First, 100 names were randomly selected from the GOTR’s database. Then, each name was searched through pharmaceutical websites including Martindale (the Complete Drug Reference published by Pharmaceutical Press), Drugs.com and Medicines Complete. Pair of drugs whose names look orthographically similar with different indications were identified. Then, the SOLAR model was utilized to determine orthographic similarity between all pair of drug names.

Results: The mean of match values of these 100 pairs of drug was 77% indicating the high risk of similarity. The match value for most of the reviewed pairs (92%) was high (≥66%). This value was medium (≥ 33% and <66%) just for 8% of the pairs of drug. These results indicate high risk of confusion due to similarity of drug names.

Conclusion: The stewardship of the GOTR in patient safety considerations is fundamentally problematic. Thus, as a best practice, we recommend that proprietary names of drugs be evaluated by an entity within the health system. While an entity within the health system should address patient safety considerations, the GOTR is responsible for intellectual property rights.

Keywords: Patient safety, Drug proprietary names, Orthographic similarity, General office of trademarks registry, SOLAR model, Iran

Introduction

The recognition of the importance of patient safety is now increasing and garnering renewed regulatory interest since medical errors can result in adverse events from the inappropriate therapy (1). As clinical medicine is a hugely complex field, the occurrence of errors is unsurprising. Whilst is not a new phenomenon, medication errors may occur in all healthcare systems and are a common threat to patient safety (2). In this regard, the existence of confusing medication names is regarded to be one of the most common reasons for medication errors and is of concern throughout the world (3). Attention to the issue of drug name confusion has also been mentioned within a set of nine Patient Safety Solutions (4). Medication errors due to orthographic similarity of drug names underscore the serious nature of this type of error that indicates the need for considerable
attention and regulation to restrict such errors. This issue is also introduced as one of research priorities in Iran (5).

WHO has a constitutional mandate to "develop, establish and promote international standards with respect to biological, pharmaceutical and similar products". This Organization collaborates with International Nonproprietary Name (INN) experts as well as national nomenclature committees in order to select a single name for each medication that should be of worldwide acceptability. While generic medicines are marketed under a non-proprietary or approved name instead of a proprietary or brand name, the Trade-Related Aspects of Intellectual Property Rights (TRIPS) agreement does not hinder countries from allowing generic substitution. Besides, competition between pharmaceutical companies and generic producers has been regarded to be more effective than negotiations with pharmaceutical companies in reducing the cost of drugs (6).

Full responsibility of the process of screening and approving drug proprietary names was delegated to the General Office of Trademarks Registry (GOTR) within the State Organization for Registration of Properties for a four-year time interval (2010-2014) and this entity was responsible for approving drug proprietary names before market entry. The naming principle consists of two components: 'patient safety issue and intellectual property rights'. This study aimed to investigate the performance of the GOTR in terms of drug names orthographic similarity using the SOLAR model.

Materials and Methods

To calculate orthographic similarity of drug proprietary names approved by the General Office of Trademarks Registry (GOTR), first 100 drug proprietary names were randomly selected from the GOTR’s database. Then, each name was searched through pharmaceutical websites including Martindale (the Complete Drug Reference published by Pharmaceutical Press), Drugs.com and Medicines Complete. Through this search, pair of drugs whose names look orthographically similar were identified. In addition, indications for Iranian approved drug names and those drug names exist in the world were reviewed. In the case of similar indication, the identified similar pair of drug was omitted and was replaced by another similar pair of drug with different indication. Then, the self-organizing lexical acquisition and recognition (Solar) model of visual word recognition was utilized to determine orthographic similarity between all pair of drug names. The Solar model was used because of its capacity for stable self-organization, its spatial coding scheme, its combination of serial and parallel processes, and its chunking mechanism. The model also introduces a novel mechanism to explain word frequency effects. Another distinctive feature of the model is its incorporation of a novel opponent processing mechanism for performing lexical decision (7). The orthographic similarity values for the 100-drug name pairs based on the SOLAR models were ranked using the following formula:

A spatial code can be written as a vector consisting of n elements, where n is the number of letters in the input string and the values in the vector represent the activities of the corresponding letter nodes. Spatial codes always use a monotonically descending series to code letter position. For the $i^{th}$ word node, this set of letters is denoted $L_i$, and the number of letters in this set (i.e., the length of the word) is denoted $l$. The weight between a letter node and a word node is equivalent to the value of that letter node’s activity in the spatial code for that word.

Therefore, the first step involves computing a set of signal-weight differences. For each of the elements in the set $L_i$ a difference $d_{ij}$ is computed by subtracting from $s_j$ (the activity of the $j^{th}$ letter node) the corresponding weight $z_{ji}$, i.e.,

$$d_{ij} = s_j - z_{ji}$$

Each signal-weight difference is then associated with a continuous function$f_i(x)$ that is symmetrical around $x = d_{ij}$:

$$f_i(x) = \frac{1}{\sqrt{\pi} \sigma} e^{-\left(\frac{(x-D_{ji})^2}{2\sigma^2}\right)}$$

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The parameter $\sigma$ in (2) controls the width of the difference function and can be interpreted as a measure of letter position uncertainty (a default value of $\sigma = 3$ is assumed for this parameter). Then the superposition of these functions is:

$$3) \ F_i(x) = \sum_{j \in L_i} f_{ij}(x)$$

(Where the set $L_i$ refers to the set of comparison letters). A match value $M_i$ can then be found by dividing the peak of the superposition function by the number of comparison Letters ($l_i$), that is,

$$4) \ M_i = \frac{\max(F_i(x))}{l_i}$$

The set of equations 1 through 4 produce a match value that lies between 0 and 1. This value is stated as a percentage and three threshold values, low ($\geq 1\%$), medium ($\geq 33\%$), and high ($\geq 66\%$) were used to determine whether the pairs of drug names were connected based on their orthographic similarity ratings (8).

### Results

The results of Table 1 show the match values between each drug proprietary name approved by the GOTR and the drug name looking similar to that. The match value $\geq 66$ is considered as high risk of similarity based on the Solar ranking. The mean of match values of these 100 pairs of drug was 77 indicating the high risk of similarity.

### Table 1: Match values and rate of risk associated with pair of drugs

| No. | Nonproprietary name (Generic name) | Proprietary name (in Iran) | Similar name in the world with different indication/ Generic name written in parenthesis | Match value (%) | Rate of risk confusion |
|-----|-----------------------------------|---------------------------|---------------------------------------------------------------------------------|-----------------|------------------------|
| 1   | ACA                               | AXAR®                     | RAXAR (grepafloxacin)                                                          | 73              | High                   |
| 2   | ACETAMINOPHEN                     | TINYPHEN®                 | SINIPHEN (Caffeine, Propyphenazona, Salicylamide)                              | 70              | High                   |
| 3   | ACETAMINO-RAHAFEN®               | RAPIFEN (Alfentanil)      |                                                                                 | 78              | High                   |
| 4   | ADULT COLD PREPARATION-5          | FARALEX®                  | FARMALEX (Cefalaxin)                                                           | 91              | High                   |
| 5   | ADULT COLD PREPARATION-7          | ZOCAMAX®                  | TOPAMAX (topiramate)                                                          | 67              | High                   |
| 6   | ADULT COLD PREPARATION-4          | EXACOLD®                  | DEXACOL (Dexamethasone)                                                        | 67              | High                   |
| 7   | ADULT COLD                       | GRIPHEN®                  | PRIPHEN (Nandrolone)                                                           | 78              | High                   |
| 8   | AMANTADINE HCL                   | AMMOREL®                  | AMOREL (Bromhexine)                                                           | 89              | Medium                 |
| 9   | AMLODIPINE/ATORVASTATIN           | TENSOLIP®                 | TENSOLIV (chloralhydrate-poxide-clidinium)                                     | 80              | High                   |
| 10  | APRIPIPRAZOLE                    | SEROZOL®                  | SEROZIL (Cefpazol)                                                            | 89              | High                   |
| 11  | ATORVASTATIN                     | ATOSTROL®                 | HALOSTROL (halobetaxol propionate)                                            | 80              | High                   |
| 12  | AZATHIOPRINE                     | AZARAM®                   | AZACTAM (aztreonam)                                                           | 81              | High                   |
| 13  | BECLOMETHASONE DIPROPOXATE       | BECLORHIN®                | BECLOTRIN (Betametasone +Clotrimazol+ Gentamicina )                           | 88              | High                   |
| 14  | BUSERELIN ACETATE                | CINNAFACT®                | CINNAPAC (Cinnarizine)                                                        | 73              | High                   |
| 15  | CALAMINE                         | CALAMEX®                  | CALMEX (Doxylamine)                                                            | 80              | High                   |
| 16  | CALCIUM FOLINATE                 | ROFOLIN®                  | ROFOXIN (Ceftriaxone: ceftriaxone sodium and dextrose)                         | 89              | High                   |
| 17  | CEFIXIME                         | LOPRAX®                   | LOPROX (Ciproflox)                                                            | 88              | High                   |
| 18  | CEPTIZOXIME SODIUM               | AFAZOX®                   | AFAZOL (naphazoline hydrochloride)                                            | 75              | High                   |
| 19  | CETIRIZINE 2HCI                 | CETRIKIM®                 | CETROTIDE (Cetrorelax)                                                         | 60              | Medium                 |
| 20  | CETIRIZINE/PSEUDOEPHEDRINE       | CETADIN®                  | CEFADIN (Cephalexin)                                                           | 89              | High                   |
| 21  | CIPROFLOXACIN HCL                | CIplex®                   | IPLEX (mesacermín rinfabate)                                                  | 75              | High                   |
| 22  | CITALOPRAM HBR                   | BIOXAL®                   | BIOXTRA (salvia substitutes topical)                                           | 66              | High                   |
| 23  | CLOBUTINOL HCL                   | TIDOCAUGH®                | ETIDOCAININE (Etidocaine)                                                      | 55              | Medium                 |
| 24  | CLOPIDOGRREL                      | DIPIX®                    | DEPIXOL (Flupentixol)                                                         | 71              | High                   |
| 25  | CO TRIMOXAZOLE                   | DUCOTRI®                  | DUCORT (Deflazacort)                                                          | 72              | High                   |
| 26  | COLCHICINE                        | MODACINE®                 | MODACIN (Cefazidime pentahydrate)                                             | 80              | High                   |
| 27  | CONTRACEPTIVE HD                 | OVESTOP-H®                | ACUSTOP (Flurbiprofen)                                                        | 45              | Medium                 |
| 28  | DEFERASIROX                      | OSVERAL®                  | FEVERALL (Acetaminophen)                                                      | 67              | High                   |
| 29  | DIAZEPAM                         | ZEPADIC®                  | ZEPATIER (elisavir and gazoprevir)                                            | 67              | High                   |
| 30  | DICLOFENAC SODIUM                 | DICLEN®                   | DICLEGIS (doxylamine and pyridoxine)                                          | 75              | High                   |
| 31  | DIMETHICONE                       | DILICE®                   | DILOMINE (dicyclomine)                                                         | 69              | High                   |
| 32  | DOMPERIDONE.MALEATE              | MOTIDON®                  | METADON (methadone)                                                           | 78              | High                   |
| 33  | ESOMEPRAZOLE                      | MAXOPRAZOLE®              | MEDOPRAZOLE (Omeprazole)                                                      | 75              | High                   |
| 34  | EXPECTORANT                       | COUFEX®                   | KEFLEX (Cephalexin)                                                           | 47              | Medium                 |
| 35  | EZETIMIBE                         | EZITAL®                   | EMITAL (Ondansetron)                                                          | 88              | High                   |
| 36  | FEXOFENADINE                      | ALEXAFEN®                 | ALEXAN (Cytarabine)                                                           | 61              | Medium                 |
| 37  | FURAZOLIDONE                     | FURABEN®                  | FURACIN (nitrofurazone)                                                        | 78              | High                   |
| 38  | GALANTAMINE                      | ALZAMIN®                  | ALAMIN (PHENYLEPHRINE)                                                        | 83              | High                   |
| 39  | GEMCITABINE (as HCL)             | CHEMOGEM®                 | CHEMOFER (Folic Acid, Iron , Vitamin B12)                                      | 70              | High                   |
Mean and Standard Deviation

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The first column displays the generic name of the proprietary drugs name (second column) which approved in Iran. The next column shows the similar overseas drug names, with different indication of the local ones, which can be generic or proprietary names (in the case of proprietary names, the generic names have been written in parenthesis). The last two columns show the match values (orthographic similarity rate) and the rate of risk, respectively, based on the Solar (orthographic match value model used in this study). However, some of overseas drug may not exist in Iran pharmaceutical market; however, some similar pairs are generic names that are available in Iran (such as ETIDOCaine, OSI-MERtiNIB, CARBoPROST, CARdiOGEN, PENTACEl, FLUOROURACIL, MIL-ONORM, and MODAFINil). Furthermore, with regard to the existence of many representative pharmaceutical companies which import drugs into Iran, overseas proprietary drugs are also available in Iran market (TOPAMaX, BI-oxTRA, CHOLINE, TAloFEN, DIVIGEL, to name a few). Furthermore, the import of any of these overseas drugs is probable.

Discussion

The current findings indicate the high level (92) of orthographic similarity between local drug proprietary names and overseas drug names. However, there are limited studies on the actual rate of this type of medication error in Iran. The similar names of drugs as the main factor affecting medication errors, so that in 23.40 of the medication errors have been associated with drugs similar names (9). In another study conducted in Iran, the similar drug name was considered as the first factor (36.9) contributing to medication errors in 6 wards of hospital setting (10). In this regard, in a study, in hospitals (including tertiary, university, secondary and primary hospitals) in Thailand, a total of 5327 pairs of medicines were identified as Look-alike Sound-alike medicines (11). Moreover, in Canada, 186 LASA (Look-alike Sound-alike) drug pairs from 3320 possible pairs were identified using the Bigram Similarity algorithm (12). Thus, the issue of confusing drug name is a worldwide issue. In addition, up to 25 of all medication errors were attributed to name confusion (13). Generally, while the similarity in drug names is a worldwide issue, according to the existence of high rate of similar drugs in Iran should be considered by health policy makers.

The performance of the GOTR in terms of screening similar names and patient safety consideration was too weak. One reason for such a weak performance can be the nature of the GOTR; the GOTR, compared to entities within the health system is fundamentally different entity with various functions. The GOTR’s employees are not individuals with sufficient mastery in the field of medicines and they are not even health professionals. Accordingly, there were many failures in the performance of the GOTR from a patient safety viewpoint. The responsibility for screening drug names in developed countries is always associated with an entity related to health system. Medicines and Healthcare Products Regulatory Agency in UK (14), Food and Drug Administration in USA (15), Health Products and Food Branch in Canada (16) and Therapeutic Goods Administration in Australia (17), to name a few. In this regard, the need for enhanced approval systems for medicine names were emphasized (18). Based upon our discussion so far, the delegation of the responsibility of approving drug names to an entity outside of the health system can result in problems in patient safety.

Limitation of the study: inevitably, our study has not been able to answer a number of questions and in fact has revealed a few new ones. Further research is therefore required. For example, in the future, the question has to be answered is the number of medication errors occurred in Iran due to the orthographic similarity of proprietary drug names. Another issue has to be addressed is the severity of risks due to orthographic similarity of drug names and their impact on patient safety.

Conclusion

Naming principle consists of two components: ‘patient safety issue and intellectual property
However, the GOTR’s function is necessary for initial naming of drugs and before market entry, it terms of intellectual property rights, it cannot ensure medication safety. Thus, as a best practice, we recommend that proprietary names of drugs be evaluated by an entity within the Food and Drug Organization and the health system. While an entity within the health system should address patient safety considerations, the GOTR can be responsible for intellectual property rights. However, these two elements are different in theory, but in practice not black-white and eventually both should be guaranteed. Furthermore, pharmaceutical manufacturers should meet international criteria (mainly WHO) regarding proposed names, however, there is no guarantee and an entity is still needed to monitor the pharmaceutical manufacturers’ adherence to such criteria.

Ethical considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of Interests

The authors declare that there is no conflict of interest.

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