

Sentiment Analysis on Tweets about Adverse Drug Reactions of Hydroxychloroquine: An Aspect-Level Approach

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Abstract: Adverse drug reactions (ADRs) have become the most common cause of deaths in the world despite post marketing drug surveillance. Expensive clinical trials do not uncover all the ADRs and also cumbersome for consumers and healthcare professionals. Majority of existing methods rely on patients' spontaneous self-reports. The recent explosion of micro blogging platforms such as Twitter presents a new information source to discover ADRs. In this study, the authors developed a system to automatically extract ADRs from Twitter messages utilizing Natural Language Processing (NLP) techniques. The outbreak of Coronavirus, namely COVID-19, has created a calamitous situation throughout the world. The cumulative incidence of COVID-19 is rapidly increasing day by day. In the absence of any curative drug, the United States gave Emergency use authorization to the antiviral 'Hydroxychloroquine' for people hospitalized with severe COVID-19. Twitter is an excellent resource for the people since they connect publics who have with similar conditions and experiences. Our system plays a machine learning approach using sentiment analysis using tweet dataset. This research aims to classify these drugs into harmful and safe categories using opinion gained from patients through twitter messages.

Keywords: Hydroxychloroquine, Sentiment Analysis, COVID-19, Twitter, Machine learning

1. INTRODUCTION

An Adverse Drug Reaction (ADR) is an expression that describes the harm associated with the use of given medications at a normal dosage during normal use. It could be an unintended, considerably harmful reaction resulting from an involvement of a medicinal product. The interaction between the human immune system and the pharmaceuticals causes drug hypersensitivity. Currently, it is becoming a dire global problem causing higher numbers of deaths. According to the annual report of the Agency of Healthcare Research and Quality, over 770,000 people are injured or died in each year because of these ADRs. The Journal of the American Medical Association states that prescription drugs have now become the fourth leading medical cause of death in the United State and Canada [1].

Obtaining the knowledge about drug interactions can be done from many resources and using many strategies. Generally the knowledge is compiled from pharmacy experts by conducting a series of experiments whose results are then arranged into text book of drug interactions reference. The rapid expansion of the Internet and computing power in recent years has opened up the possibility of using social media for pharmacovigilance. While this general concept has been proposed by many, central questions remain as to whether social media can provide earlier warnings for rare and serious events than traditional signal detection from spontaneous report data. ADR information obtained from social media can be a valuable despite showing different rates to those measured via traditional sources, according to US and UK researchers [2].

2. Need for Opinion Mining in Medicine

For new medical products, clinical trials are very important for evaluating the safety and efficacy of patients. But, patient selection criteria, small sample sizes, and short durations are given inadequate evidence on unusual harms. This is exemplified by the fact that over one-half of approved drugs have serious adverse events identified that are not detected before approval [3]. In addition, existing post market adverse events reporting

systems are significantly underutilized by clinicians and patients. This has been estimated that 96% of adverse drug events go unreported to regulators.

A high volume of discussions about medical products is occurring online, with patients using social media to publicly share concerns and reactions to medications. There is increasing interest in exploring the use of social media data for pharmacovigilance, but questions remain regarding how to validate and best leverage this data source. Thus, healthcare organization is advanced to coalmine about the health state of Twitter user as well as to give health authorities to simply check about their interior health behavior depend on the Twitter data with the help of opinion mining and machine learning approaches [4].

The purpose of applying opinion mining/sentiment analysis techniques is to process health related opinions of millions of users and conclude them towards useful information. Thus, the result of sentiment analysis has to be modest as well as definite which can be utilized for the purpose of decision making system. The result of sentiment analysis can be in the custom of dual classes demonstrating percentages of positive as well as negative sentiments. If finer level categorization is required the aggregated outcome is distributed among different categories like excellent, good, mediocre, bad, worse etc [5].

3. Twitter

The aim while performing twitter sentiment analysis is classifies the tweets in different sentiment classes accurately. In this field of research, various techniques have evolved, which come up with methods to train a model and then test it to check its effectiveness. Performing sentiment analysis is challenging on twitter tweets. Here we define some reasons for this: [6]

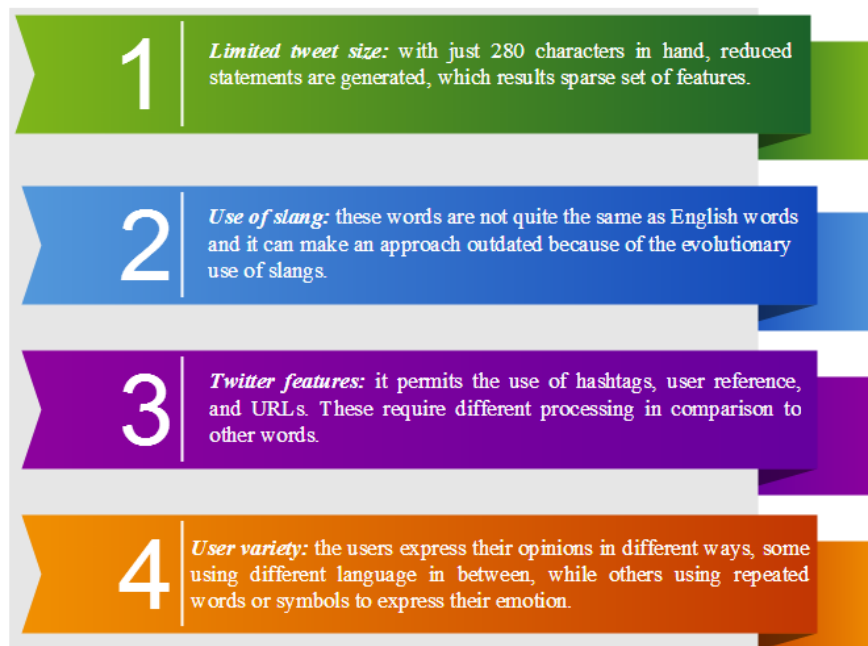


Fig1. Features of Twitter

There are a huge number of messages on Twitter that talk about drugs and their reactions. These messages contain information on medicate use in a lot bigger test sets than any clinical preliminary will ever have. In view of that, this research is beginning to utilize these messages for ADR detection for particular drugs (Hydroxychloroquine). The

objective is to naturally discover applicable messages, to "realize" their substance, and to extricate organized information about the medications and undesirable responses.

This research proposes and evaluates a model which can be used to automatically extract ADR mentioned posts from the Twitter. This model will classify each Twitter message into an Adverse Effect or an Other Effect by analyzing the content of the message by using opinion mining and machine learning approaches. Then the classified Twitter message can be used to identify the known drug effects as well as previously unrecognized drug effects. Ultimately, this research will be beneficial to patients and pharmaceutical companies for monitoring and regulating their drugs usage [7].

4. Significance of Adverse Drug Reactions (ADR) detection

Everyone want also utilize drugs once in a while. However, they can have undesirable symptoms, alluded to as "ADRs (Adverse Drug Reactions)" (ADRs). Although drug manufacturers run extensive clinical trials to identify these ADRs, there are still over two million serious ADRs in every year – and more than 100,000 patients die due to drug reactions, according to the U.S. Food and Drug Administration (FDA). Consequently, we are scanning for creative and powerful approaches to discover ADRs.

Currently, it is becoming a dire global problem causing higher numbers of deaths. According to the annual report of the Agency of Healthcare Research and Quality, over 770,000 people are injured or died in each year because of these ADRs. The Journal of the American Medical Association (JAMA) states that prescription drugs have now become the fourth leading medical cause of death in the United State and Canada [8]. Recognizing ADRs is a significant process for drug producers, government organizations, and general wellbeing. One approach to distinguish them before a medication goes to advertise is through clinical preliminaries. Governments overall additionally have various observation programs so as to recognize ADRs once the medications are being used by purchasers. For example, official websites such as MedWatch allow both patients and drug providers to submit ADRs manually [9]. In any case, just a small partition of all ADRs is submitted to these frameworks specialists gauge that over 90% of all responses go unreported.

The popular social media platform, which is worth to mention is Twitter. As of 1st September 2016, Twitter has over 342,000,000 active users and grows by 135,000 users every day, generating daily 58,000,000 tweets. In this context, Twitter platform is advantageous over others as provides open API for research purposes to download their data, which could be very helpful for the task of ADR revealing and monitoring [7].

5. Proposed Design and Approach

There are five parts in our proposed approach, as shown in following figure. First the tweets are mined and filtered. Then the tweets are preprocessed before features are extracted. Finally, the classifier uses the features to identify the drug side effect related tweets and then the frequency of the side-effects is extracted and updated.

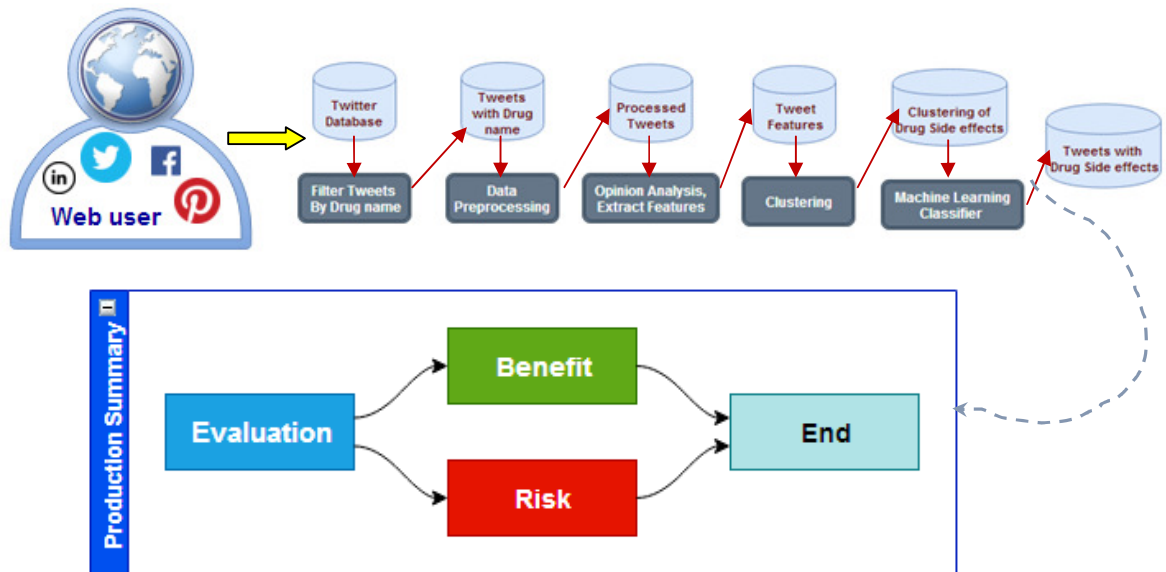


Fig2. Proposed Design and Approach

i. Mining Twitter through R-tool: R-Studio is the environment developed for statistical analysis and a Graphical view of the large data sets. Machine learning methods typically require large amounts of data to provide sufficient predictive power. R-packages are a collection of R functions which is a compiled code on sample data. These functions are stored under the name of R-Library in its environment. During installation period, by default R installs a set of packages. Remaining packages need to be installed and loaded separately as and when they are required by the specific application [10]. For Twitter dataset collection, the proposed system has the following steps:

- i. Creating Twitter Application
- ii. Execute Twitter API code through R-Studio
- iii. Collecting Twitter data archives

ii. Data Preprocessing: Preprocessing is fundamental to all Natural Language Processing (NLP) Task. Steps needed for preprocessing of text in general depends on the targeted requirement or application. Here tweets are preprocessed for analyzing the sentiments. Unlike other text document Twitter may be a domain where people use their freedom to express the messages or comments in a flexible manner. Several attributes have been identified for a Twitter status update or tweets. Maximum length of Twitter message is 140 characters which may include user mention, hash tag, URL etc. In twitter data, the frequency of elongated words, slangs, acronyms and emoticons is much higher than any other domain. Below figure illustrates different steps done in the pre-processing stage [11].

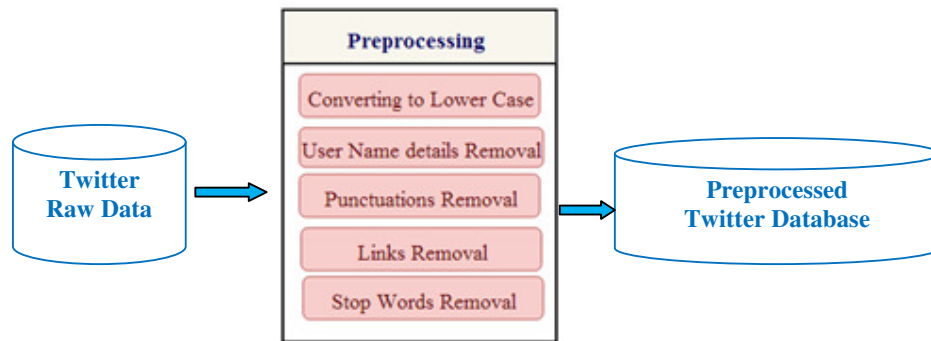


Fig3. Steps in Preprocessing

iii. Feature Extraction: In opinion mining, feature extraction plays a very important role in summarizing reviews. There are some research techniques for extracting features from the online reviews [12]. Some of the features are as follows

- *Terms Presence and Frequency:* These highlights are singular words or n-grams words with their recurrence checks. It either utilizes the term recurrence loads or gives parallel weighting to the words.
- *Parts of speech:* Finding descriptive words/adjectives from the content, as they are important indicators of opinions.
- *Opinion words and phrases:* These are words generally used to express opinions including good or bad, like or hate. Then again, a few watchwords express opinions without utilizing conclusion words.
- *Negations:* The presence of negative words might change the opinion orientation like not good is equivalent to bad.

After the data was preprocessed, the features were then extracted for classification. Selecting the potential features could be very effective in improving the classification. In this research, the main objective of the feature extraction system is to go through the patients' reviews and extract features out of them, and assign them as implicit features to the respective drugs [13]. These features can be regarded as points of interests about '*Hydroxychloroquine*' drugs that can be further used in the patient recommender engine.

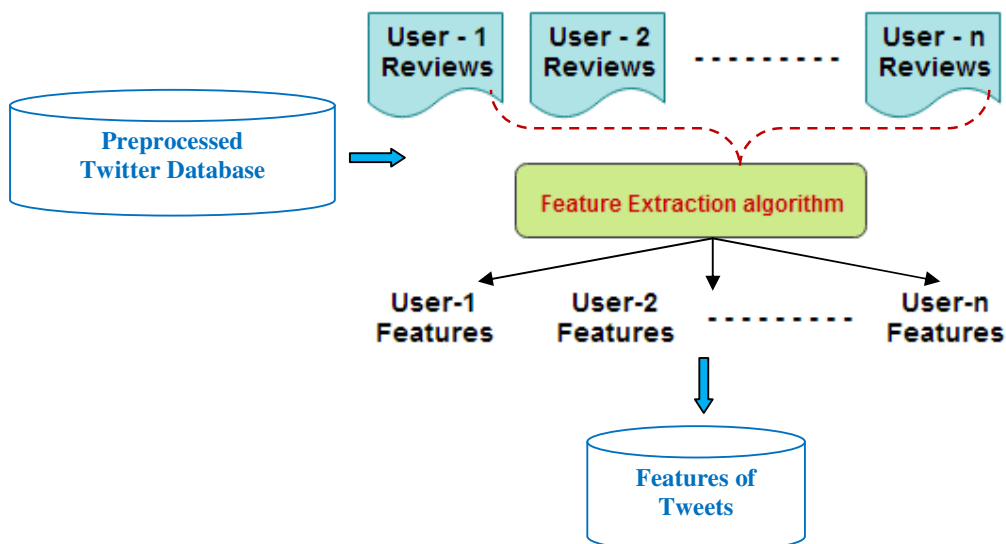
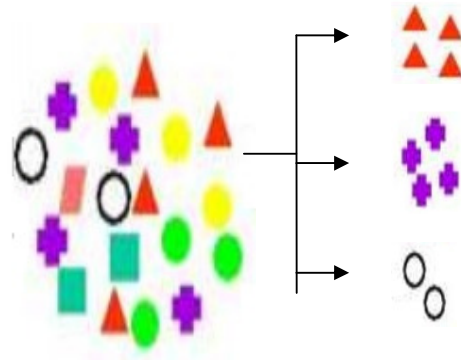


Fig.4 Feature Extraction System

The whole feature extraction procedure is depicted in Figure 4. As seen, patients' reviews are first collected from the twitter database and are preprocessed. Commonly used feature extraction techniques are,

- Principal Component Analysis (PCA)
- Linear Discriminant Analysis (LDA)

iv. Clustering: It is different from classification; it does not have predefined classes. A huge database is divided into number of small subgroups called clusters. It divides the data based on similarities it has. Clustering methods determines collections of the data such that objects in the similar cluster are more identical to every other than other groups.



For the responsibility of assessment mining, many component articulations are phrases comprising of numerous words, e.g., "drugs", "reactions/ side effects "," Hydroxychloroquine". Sharing words are important clues (preexisting knowledge) that can be exploited for our purpose, i.e., feature expressions sharing some words are likely to belong to the same group or cluster. This system will do clustering at word level and those clusters will be groups of words [14]. It can be used for each side effect into clusters, combining clusters into drugs. The different clustering techniques are stated as follows:

Table1. Clustering techniques

S.NO	Clustering techniques	Algorithms
1	Partitioning clustering	K- Means, K-Medoids
2	Hierarchical clustering	Agglomerative, Divisive
3	Density-based clustering	DBSCAN, DENCLUE
4	Grid-based clustering:	STING, CLIQUE

v. Opinion classification: There are basically three types of Opinion classification technique. These three approaches exhibit different techniques as shown in below figure.

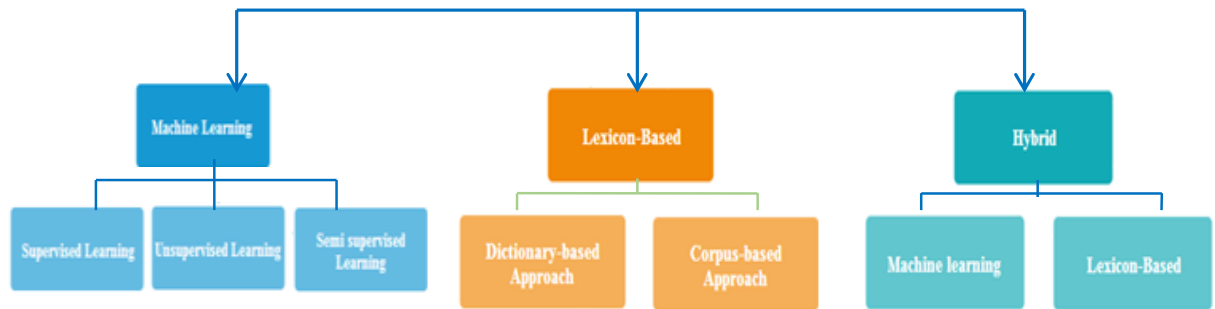


Fig6. Opinion analysis classification techniques

vi. Machine Learning: It is the training the computer such that it becomes capable of taking decision itself. Machine learning involves supervised and unsupervised learning. Supervised learning classifier uses training set to learn and train itself and performance of the classifier is tested using test dataset [15]. There are many kinds of classifier under supervised learning; most common among them are probabilistic classifier and linear classifier.

- *Unsupervised learning:* It doesn't comprise of a class and they don't furnish with the right focuses at all and subsequently depend on grouping.
- *Supervised learning:* It depends on named dataset and along these lines the marks are given to the model during the procedure. These named dataset are prepared to get significant yields when experienced during dynamic. The achievement of both this learning strategies is mostly relies upon the choice and extraction of the particular arrangement of highlights used to distinguish conclusion. The machine learning approach relevant to sentiment analysis that belongs to supervised classification. In an machine learning procedures, two arrangements of information are required:

- i. Training Set
- ii. Test Set

From that point forward, the system train a classifier on the training data. When a supervised classification method is chosen, a significant decision to make is to choose feature data. They can reveal to us how reports are spoken to. The most normally utilized features in opinion characterization are

- Term presence and their frequency
- Part of speech information
- Negations
- Opinion words and phrases

With respect to supervised techniques, support vector machines (SVM), Naive Bayes, Maximum Entropy are some of the most common techniques used. While, semi-supervised as well as unsupervised methods are recommended while it is not potential to have an initial set of labeled opinions to classify the rest of points.

a. Lexicon based approach: It has three common types. They are manual, dictionary based and corpus based approach. Manual based approach is time consuming and limited to some lexicon. It is prone to errors. To generate it more

competent, it is mutual with other two automated methods. Here, two sub classifications methods are there:

- i. **Dictionary-based:** It is based on the usage of terms (seeds) that are usually collected and annotated manually. This set grows by searching the synonyms and antonyms of a dictionary. A model of that dictionary is 'WordNet' that is utilized to improve a lexicon called 'SentiWordNet'. This technique can't treaty with domain also perspective specific directions.
 - ii. **Corpus-Based:** The corpus-based approach have objective of providing dictionaries related to a specific domain. These word references are created from a lot of seed opinion terms that becomes through the hunt of related words by methods for the utilization of either factual or semantic strategies.
 - Techniques dependent on statistics: Latent Semantic Analysis (LSA).
 - Techniques dependent on semantic, for example, the use of synonyms and the utilization of equivalents and antonyms or connections from thesaurus like 'WordNet' may likewise speak to a fascinating arrangement.
- b. Hybrid approach:** In order to improve the performance of sentiment classification, some researchers suggested to combine machine learning with lexicon based approach [16].

6. Literature Survey

Sentiment analysis/ opinion mining is the most significant research territory in business fields. Beforehand investigate was completed for estimation examination in different areas like organization item, film surveys, governmental issues and so forth. A portion of the looks into are portrayed in this area.

Po-Wei Liang et.al, utilized Twitter API to gather twitter information. Their preparation information falls in three distinct classifications (camera, film, portable). The information is named as positive, negative and non-assessments. Tweets containing suppositions were sifted. Unigram Naive Bayes model was executed and the Naive Bayes improving autonomy supposition that was utilized. They likewise disposed of futile highlights by utilizing the Mutual Information and Chi square component extraction strategy. At long last, the direction of a tweet is anticipated. for example positive or negative [17].

Xia et al. utilized a gathering structure for Sentiment Classification which is gotten by joining different capabilities and grouping strategies. In their work, they utilized two kinds of capabilities (Part-of-discourse data and Word relations) and three base classifiers (Naive Bayes, Maximum Entropy and Support Vector Machines). They applied troupe approaches like fixed mix, weighted blend and Meta-classifier mix for conclusion order and acquired better exactness [18].

Luoet. al. [19] featured the difficulties and an effective strategy to mine suppositions from Twitter tweets. Spam and fiercely differing language makes conclusion recovery inside Twitter testing task.

Go and L.Huang [20] proposed an answer for notion investigation for twitter information by utilizing far off oversight, in which their preparation information comprised of tweets with emojis which filled in as loud names. They manufacture models utilizing Naive Bayes, MaxEnt and Support Vector Machines (SVM). Their component space comprised of unigrams, bigrams and POS. They presumed that SVM beat different models and that unigram were progressively successful as highlights.

7. Conclusion

As the coronavirus spread rapidly across the world, Hydroxychloroquine quickly became one of the potential treatment frontrunners. This study aims to classify these drugs into harmful and safe categories using opinion mining and machine learning algorithms. During the last decade we have seen an increasing interest in processing and analyzing unstructured data especially web-based data. In this work, we hypothesized that social media networks, such as Twitter, could be used to extract Adverse Drug Reactions in a matching approach, by identifying tweets related to drugs and their side effects. In this paper, we have briefly examined the opinion mining area and its related techniques involved in this research. The proposed research work will be very helpful and beneficial to the physicians and Covid-19 patients for analyzing the adverse effects of a certain drug based on the patient's reviews.

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