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Adverse Drug Reactions Extraction from Social Media: A Systematic Review

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***Abstract*—The objective of this study is to observe the importance of social media in automatic extraction of Adverse Drug Reactions (ADRs) from different medical forum, social media like Facebook, Twitter etc. studied yet. Drug reaction is major concern in today's health related studies. People share their views on different online medical forum as well as in different social media. A large number of users share their views regarding drugs and its reactions in social media. Natural Language Processing (NLP), several Machine Learning (ML) approaches, Deep Learning (DL) methods have been used for extracting the valuable information from this large pool of raw data taken from the different dataset like PubMed, MEDLINE, Twitters, Facebook and several online medical forums. A systematic review of published work from 2016 to 2020 has been considered in this study. An initial and in-depth screening of 41 research article out of 101 research article have been chosen in the review process. This study shows the performance analysis of different approaches used by many researcher in their study to extract ADRs from social media.**

***Index Terms*— Adverse Drug Reaction (ADRs), Machine Learning (ML), Deep Learning (DL), and Natural Language Processing (NLP).**

I. INTRODUCTION

Adverse drug reactions (ADRs) are unwanted or harmful effect is felt after a specific drug or combination of medication and is one amongst the leading causes of illness and death [1, 2]. Pharmaceutical products are employed in form to stop from various viral or bacterial attacks, basically as a treatment [3]. Regular ADR reporting systems (e.g., clinical trials) are typically under-reported and plenty of ADRs don't seem to be recorded within the systems. It's very difficult to report all the ADRs in clinical trials. Now a days, many of us share their views on several drugs in social media. People choose several social media like online medical forums, Twitter, Facebook, blogs to share their views on drugs and its reactions. During this regards social media plays a vital role to report the ADRs. So, an enormous pool of information come from the various social media. It's greatly needed to develop an automatic system to extract the relevant information from that giant pool of information gathered from social media. The medical reports are wont to detect content that contains ADRs. Thus, it's imperative that ADR knowledge is extracted automatically. Advancement in language processing (NLP) tools and also some advanced machine learning approaches, deep learning approaches have made it possible to develop tools for automatic extraction of ADR information from biomedical literature in social media. The users

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of medication have given their views in several social media platforms like twitter, facebook etc. Now a days, big selection use of social media through the population has made the eye of researchers in various fields. Initially, social media report was considered as a chance to beat the under-reported drug safety in real time in close contact with patients within the area of pharmacovigilance. Several researcher have reported the importance of social media within the area of pharmacovigilance. The twitter data and a few online medical forum data are used as source of knowledge in many studies previously [4, 5]. Now, the information is extracted from alternative sources also [6]. A scientific approaches to automatic extract ADRs from data taken from different social media sources follow some steps. The steps are described within the following figure 1.

Figure 1: ADRs Extraction steps

II. Review of Previous Work on Social Media

A. The Review Process

A systematic approach has been followed to review the literature in this study. This study starts with defining the questions and hence determining the characteristics. The process continues with the retrieval of potential relevant literature. Finally, this study synthesises the relevant information of the literature and reports the result of this review study.

B. The key findings of the review

The key findings of this study are addressed below:
Key findings 1: Datasets Considered
Key findings 2: Methods Applied
Key findings 3: Applications

C. Retrieving information from literature

Some review processes has been reported by researcher which mainly focused on a particular drug or drugs and/or a specific dataset.
This study searches the several published article from different drug related databases that covers mainly the keywords ADRs, social media, Facebook, Twitter. A total of approximately 500 articles has been identified from the year 2010 to 2020. Then 41 research articles has been screened to conduct this review process out of which 20 journal articles and 21 conference proceedings published by IEEE, Springer, Elsevier, etc. in between the year 2016 to 2020. There are many different approaches have been applied over different dataset. The following figure 2 describes the screening process by four steps – i) Identification, ii) 1st round screening based on title of articles, iii) 2nd round screening based on abstract, iv) Articles Included for analysis. The number of journals and conference articles considered for this study for last five years (2016 – 2020) has shown in table II. The following figure 3 depicts the division of number of articles considered in this study for last five years from 2016 – 2020. This review article separates the different approaches and different dataset used by many researcher. Analyzing the findings of this study has been arranged in the following Table I. Table I is also organized as chronological order (recent year at top).

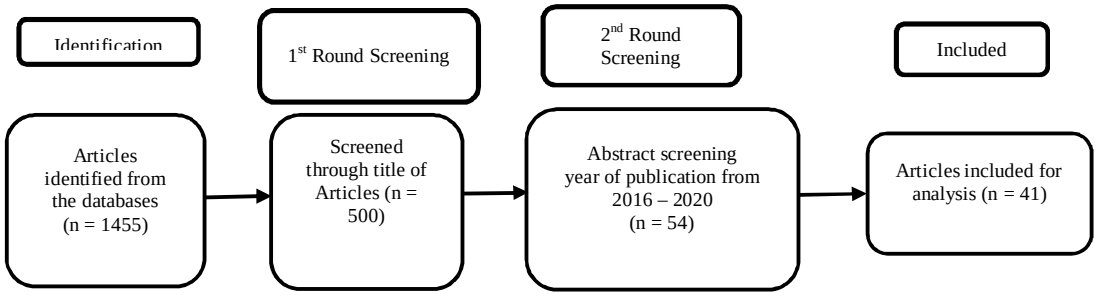

Figure 2: Screening process of Articles

TABLE I: SUMMARY OF REVIEWED LITERATURE

Ref. No.	Title (Year)	Methods	Dataset	Comments
[7]	Adverse drug reaction detection on social media with deep linguistic features (2020)	ADR lexicon	Facebook	Reported better performance than other state-of-art method
[8]	Combining Social Media and FDA Adverse Event Reporting System to Detect Adverse Drug Reactions (2020)	Machine Learning (Bayesian)	Twitter, SRS	Reported Significant improvement in combined system than twitter and SRS alone
[9]	Adverse Drug Reaction Detection in Social Media by Deep Learning Methods (2020)	Deep Learning	Twitter	Reported that More advanced learning result better
[10]	Extended Trigger Terms for Extracting Adverse Drug Reactions in Social Media Texts (2019)	ML(SVM, Naive Bayse, Linear Regression)	Online Forum	Reported the effectiveness in terms of extracting ADRs
[11]	Reporting Social Media-based Adverse Events with Artificial Intelligence: Elaborating the Challenges – Mitigating with Innovation (2019)	Natural Language Processing, Machine Learning	Social Media	Deterministic to remain acquiescent
[12]	Using machine learning and deep learning methods to find mentions of adverse drug reactions in social media (2019)	Natural Language Processing, Machine Learning, Deep Learning	Social Media	Perform better in relaxed system than strict system
[13]	Drug review analytics of neurological disorders (2019)	Machine Learning, Deep Learning	Online dataset	More efficient than other
[14]	The Adverse Drug Reactions From Patient Reports in Social Media Project: Protocol for an Evaluation Against a Gold Standard (2019)	Natural Language Processing, Standardized statistical method	Social Media	Statistical methods to assess the result
[15]	Drugs Reviews Sentiment Analysis using Weakly Supervised Model (2019)	Machine Learning (CNN)	Social Media	Improves capability in ADR detection
[16]	Adverse Drug Event Detection Using a Weakly Supervised Convolutional Neural Network and Recurrent Neural Network Model (2019)	Machine Learning (CNN)	Online health forum	Enhanced ADR identification
[17]	Detecting Adverse Drug Reaction (ADR) Mentions from Social Media (2019)	Machine Learning	Social Media	Five classifier performance analysis
[18]	Parallel ADR detection based on spark and BCPNN (2019)	Machine Learning (CNN)	Online Medical forum	Reported proof of the performance
[19]	A Comparison Study of Search Strategy on Collecting Twitter Data for Drug Adverse Reaction (2018)	Machine Learning (Cluster)	Twitter	Keyword search mechanism
[20]	Causality Patterns for Detecting Adverse Drug Reactions From Social Media: Text Mining Approach (2018)	Machine Learning, Support Vector Machine	Social Media	Reported an average accuracy to detect ADR
[21]	Comparing adverse effects of Hepatitis C drugs using FAERS data (2018)	Data Mining	Online Medical forum	Compares old and new drug for Hepatitis C
[22]	Multi-Task Pharmacovigilance Mining from Social Media Posts (2018)	Machine Learning (SVM, Naïve Bayse)	Twitter	Detect higher phrasal ADRs and single ADRs
[23]	Mining Patients' Narratives in Social Media for Pharmacovigilance: Adverse Effects and Misuse of Methylphenidate (2018)	Data Mining	Social Media	Identify the misuse of drugs
[24]	Detecting Adverse Drug Reaction with Data Mining And Predicting its Severity With Machine Learning (2018)	Machine Learning (SVM)	Online Health Record	Perform safe drug diagnosis
[25]	Automated Detection of Adverse Drug Reactions in the Biomedical Literature Using Convolutional Neural Networks and Biomedical Word Embeddings (2018)	Machine Learning (CNN,SVM)	PubMed	Applying both tools on a choice of word embeddings
[26]	An Attentive Neural Sequence Labeling Model for Adverse Drug Reactions Mentions Extraction (2018)	Machine Learning (Support Vector Machine)	Twitter, PubMed	Effective performance of embedding-level attention mechanism and auxiliary classifier
[27]	Adverse Drug Reactions detection on social media: bias and limitation (2018)	Data Mining	Twitter	Explain the valuable information extraction
[28]	Big Data and Pharmacovigilance: Data Mining for Adverse Drug Events and Interactions (2018)	Natural Language Processing, Data Mining	Online Health Record	Identify new drug-ADE

[29]	MeDIAR: Multi-Drug Adverse Reactions Analytics (2018)	Machine Learning	Online Health Record	Provide signal investigation on ADR reports
[30]	Exploring Joint AB-LSTM with embedded lemmas for Adverse Drug Reaction discovery (2018)	Deep Learning	Online Health Record	Joint AB-LSTM performs better using lemma
[31]	Adverse Drug Reaction Post Classification with Imbalanced Classification Techniques (2018)	Machine Learning (SVM)	Social Media	Boost F-score measure
[32]	Utility of social media and crowd-intelligence data for pharmacovigilance: a scoping review (2018)	Machine Learning	Social Media	Varied methods and approaches yield to better perform
[33]	Spontaneous Adverse Drug Reactions Subgroup report (2018)	Natural Language Processing, Machine Learning	Online Dataset	Availability of more data improves ADR identification
[34]	Identifying Adverse Drug Reactions of hypolipidemic drugs from Chinese adverse event reports (2018)	Data Mining	Online Dataset	Shows the severity of ADRs
[35]	Detecting Potential Serious Adverse Drug Reactions using Sequential Pattern Mining Method (2018)	Natural Language Processing, Data Mining	Social Media	Mining of frequent pattern improves efficiency
[36]	Leveraging Biomedical Resources in Bi-LSTM for Drug-Drug Interaction Extraction (2018)	Machine Learning (SVM)	Online Dataset	Extract DDI
[37]	Recognizing Continuous and Discontinuous Adverse Drug Reaction Mentions from Social Media Using LSTM-CRF (2018)	Deep Learning	Social Media	Recognize continuous and discontinuous ADRs
[38]	Determining Associations with Word Embedding in Heterogeneous Network for Detecting Off-label Drug Uses (2017)	Machine Learning (Random Forest)	PubMed, FEARS	Association rule mining features and word embedding features perform best
[39]	Adverse Drug Extraction in Twitter Data using Convolutional Neural Network (2017)	Machine Learning (CNN)	Twitter	Different word embeddings to sentiment analysis in ADR extraction
[40]	Automated Detection of Adverse Drug Reactions from Social Media Posts with Machine Learning (2017)	Machine Learning (SVM)	Social Media	5-folds cross verification done to compute measurements
[41]	Recognizing Mentions of Adverse Drug Reaction in Social Media Using Knowledge-Infused Recurrent Models (2017)	Deep Learning (LSTM, RNN)	Social Media	Model achieves a good result
[42]	Mining FDA resources to compute population-specific frequencies of adverse drug reactions. (2017)	Natural Language Processing, Data Mining	Online Health Record (FDA)	Generate drug – ADR count
[43]	Adverse Drug Event Detection in Tweets with Semi-Supervised Convolutional Neural Networks (2017)	Machine Learning (CNN)	Twitter	CNN based model evaluated on Twitter dataset used in PSB 2016 Social Media Shared Task
[44]	Prediction of Drug-Drug Interactions Based on Multi-layer Feature Selection and Data Balance (2017)	Machine Learning	Online Dataset	2 times more positive DDI on Canada Vigilance Adverse Reaction online database and 110 DDIs identified in Drugs.com in USA
[45]	An Ensemble Method For Binary Classification Of Adverse Drug Reactions From Social Media (2016)	Machine Learning	Social Media	Ensemble system for binary classification of ADR proposed
[46]	Adverse Drug Reaction Classification With Deep Neural Networks (2016)	Deep Learning	Twitter	Explore different network and analyse their performance
[47]	Using Constrained Information Entropy to Detect Rare Adverse Drug Reactions from Medical Forums (2016)	Machine Learning	Online Medical forum	CIE method to detect ADRs

TABLE II: 5 YEARS REPORTS OF PUBLICATIONS IN THIS STUDY

Year of Publication	No. Journals	No. of Conferences
2016	1	2
2017	1	6
2018	9	10
2019	6	3
2020	3	0
2016 – 2020 (Total)	20	21

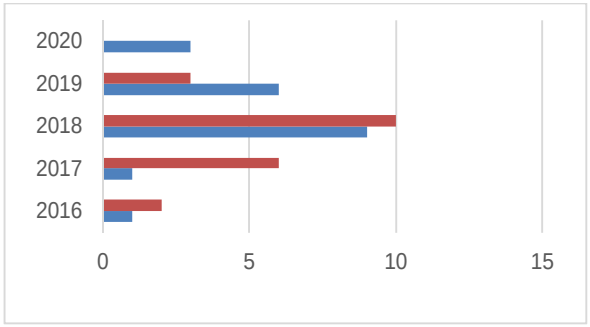

Figure 3: Number of Articles Considered in this study

III. Performance Analysis

The key findings of this study is described as the performance analysis of different datasets and methods used by several researchers.

A. Datasets Considered

The different dataset used by researcher for their studies. In this review study categorized the dataset broadly in two groups – i) Online dataset and ii) Social Media. Online dataset contains the data reported in various online health forum by consultant doctors and also in some public health forum where the patient directly shares their views on a particular drug or drugs. The ADRs care also been detected and extracted from Social Media data mainly based on Twitter and other (like Facebook, blogs etc.). Twitter and other social media platform are being used as collecting information on patients' opinion. There are 23 out of 41 screened research article found in which researcher used twitter and social media as a dataset for detection and extraction of ADRs. The data found from PubMed, MEDLINE, FDA, FEARS, Drugs.com are also being used in search of ADRs by many researchers. The following figure 4 depicts the different datasets are reviewed in this report. The twitter data can easily be accessible through the API. Natural Language Processing (NLP) is being used for the pre-processing of the data.

B. Methods Applied

After screening 41 research articles have selected for this review process. A thorough reading on this research articles, the study shows that the researcher have used Machine Learning, Deep Learning, Mixed of both the techniques and also another approaches to extract ADRs. Basically Natural Language Processing (NLP) is used as a tool to process the English like languages and then any of the above mentioned approaches has been applied on this processed data to extract ADRs. The figure 5 illustrates the different methods applied in detection of ADRs on pre-processed data below.

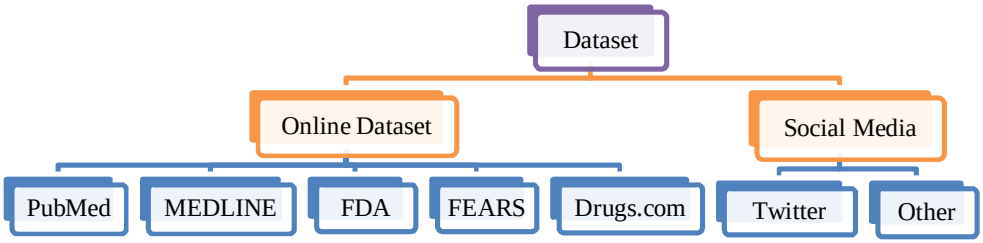

Figure 4: Different dataset used in detection of ADRs

ADR lexicon analysis [7] has been introduced instead of using NLP to extract ADRs. Lexicon analysis is an unsupervised learning mainly depends on dictionary. Several machine learning approaches like SVM [20, 22, 24, 25, 26, 31, 40] and Naïve Bayse [8, 10, 22] which fall under supervised learning have been applied and results better on small size and well formatted database respectively. Other supervised learning technique like Linear Regression has been introduced in [10], which shows the effective results in findings of ADRs. Some unsupervised learning approaches like clustering algorithm [19] reports only the keyword searching, random forest algorithm [38] has been applied based on hypothesis of 2125 potential candidates of off-label drug uses

from the classification result. Convolutional Neural Network (CNN) [15, 16, 18, 25, 39, 43] has also been applied by many researcher in search of better accuracy. It shows the betterment in extraction of ADRs.
Deep learning [9, 30, 36, 37, 41, 46] is able to address more advanced uniqueness in learning information compared to other types of machine learning. Deep learning technique has been applied to gain the advantage of incorporating various semantic features, including topics and concepts results in better accuracy in extraction of ADR.
Both the machine learning and deep learning techniques [12, 13] have applied in some research articles. Ref. [12] reported that relaxed system shows better with respect to strict system and Ref. [13] shows that the combination of these two learning approach gives better than other models.
Data mining [21] approaches used by researcher to compare the old and new drugs for Hepatitis C. The misuse of drugs has been identified and reported in Ref. [23]. Ref. [27] explains the valuable information extraction and standardized statistical method [14] has been used by some researcher to assess the findings of their research. Some mining technique improves the efficiency while frequent data were mined [35]. In a research article identifies the new drug-ADE (Adverse Drug Event) [28], in another the severity has been reported [34]. Article [42] reports the generating a drug-ADR count.

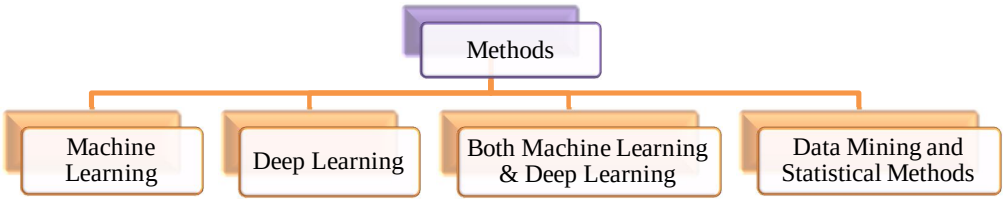

Figure 5: Different methods applied in detection of ADRs on pre-processed data

C. Applications

The application of ADR detection ranges from business, marketing to public health. ADR detection provides a vast application on different drugs to assist pharmaceutical companies in decision making.
ADR extraction can be applied on a various individual drug or a group of drugs that causes harmful reactions to human beings may lead to some uneventful happenings. A study conducted on men and women as well as sex-stratified analyses of all experienced ADRs. This study reported that spontaneous reporting of Global Post Marketing surveillance data suggests that women report higher ADRs than men during adolescence and later and especially during their reproductive years. However, there is a higher proportion of fatal and fatal ADRs in male reports [48]. ADRs also raise awareness of different reactions of drugs. It also acts as a guideline in pharmacovigilance companies. The pharmaceutical organizations also compares old and new Hepatitis C drugs [21].
Supervised learning like SVM [20, 22, 24, 25, 26, 31, 40] and naïve bayse [8, 10, 22] works on comparatively small datasets whereas unsupervised like different cluster algorithms [19, 38] have been applied on a large dataset (twitter and online medical forums) in detection of ADRs.
Convolutional Neural Network approach [15, 16, 18, 25, 39, 43] can also be applied on Twitter data and also on online medical forums data in search of ADRs.
Deep learning [9, 30, 36, 37, 41, 46] can also be used to play an important role in extraction ADRs with high accuracy. All types of machine learning and deep learning techniques reveals the ADRs efficiently. But some of the deep learning techniques needed a huge database for better accuracy. Some of the researcher have applied both machine learning and deep learning techniques to achieve better accuracy.
Lastly, the feedback gathered from the patients play an important role in the application of extracting ADRs which helps the pharmaceutical organizations to take appropriate actions to improve the drug dosage or the services. The analysis on ADRs also allows to detect and improve that are needed to the pharmaceutical organizations. The ADRs can also be detected from several health related data found in hospital and the feedback of the patients but this took a long period of time to create a database of drugs and its ADRs whereas in social media like Twitter, Facebook etc. the patients directly share their views on drug(s). So that the effectiveness and the capability of drug(s) can be assessed by the pharmaceutical organizations.

IV. Conclusion

Research continues to be required to beat technical challenges associated with data extraction, annotation, and filtering, and there's not yet a transparent consensus concerning the systematic exploration and use of social

media in pharmacovigilance. This study may help researchers to figure on extracting ADRs from social media. This paper contributed in three different perspectives: i) Dataset Applied, ii) Methods used, iii) Applications. This study contains year wise improvement of works to extract ADRs with the assistance of several machine learning algorithms including deep learning techniques. Many deep learning approaches like RCNN, CRNN etc. are utilized in different study to boost the performance measurement. Retrieval of real time data from Twitters and several other medical forums have to improve for extracting the ADRs from non ADR and unwanted words by using more advanced NLP methods, deep learning approaches. The applications of this paper demonstrates that the measurement could also be taken by pharmaceutical organizations so as to enhance the dosage of drug(s) and make the attention to the patients for not using some specific drug(s) without consultation of doctors.

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