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Research Paper

Drug Repositioning and Covid-19: A Review

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ABSTRACT
Coronaviruses are large family of viruses distributed in birds, humans and other mammals primarily associated with mild to moderate upper respiratory illnesses. The World Health Organization (WHO) named the novel coronavirus disease as Covid-19 after an outbreak of the disease in Wuhan, Hubei province (China). Over 80 clinical trials including drug repositioning have been initiated to get Covid-19 treatment as captured in ClinicalTrials.gov database. The use of drugs in the treatment of various diseases in human and animal medicine has been facing a great deal of setback primarily due to antibiotic resistance, drug tolerance, emerging infectious diseases and drug adverse effects. This necessitates the need for research into getting new drugs or repositioning the existing ones to meet up with the treatment of both infectious and non-infectious diseases affecting humanity. Drug repositioning is the process of finding new indications and therapeutic targets for already known drugs while developing a new molecular entity (drug) is a long, risky, and overly complex processes with extremely high investment and small expectation of success. Drug discovery has only recorded an average success of about 2.01% despite billions of dollars spent on Research and Development (R&D). Drug repositioning takes an average of 3-12 years to be completed while drug discovery takes an average of 10-17 years to be completed and this is because the initial six to nine years required for the development of new drugs is not necessary in repositioning because the research process goes directly to preclinical testing and clinical trials, thus reducing time, risk, and costs. Also, in drug repositioning a range of pharmacological and toxicological information is already available at the beginning process, as drug candidates to be repositioned have undergone developmental processes such as structural optimization, preclinical and clinical trials. Based on statistics, a reasonable number of drugs and vaccines have been successfully repositioned giving them new indications and formulations which consisted of about 30% of all sold drugs in the year 2009 while only one out of one million potential drug candidates have the possibility of entry into clinical studies with a tendency of having a significant number of failures. Hence the urgent need to discover new uses of existing drugs especially with the emergence of human and animal diseases and the high incidence of drug tolerance and resistance. Drug repositioning is therefore considered as an alternative way as it entails the discovery of new therapeutic indications for already existing drugs.

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I. DRUG REPOSITIONING

Discovery of new drug is laborious, costly, time-consuming, highly technical and involves high-risk processes. Report from the Eastern Research Group (ERG) (Sertkaya *et al*., 2014). Drug discovery has only recorded an average success of about 2.01% (Yeu *et al*., 2015) and the success of drug discoveries is said to be infinitesimal as the number of drugs approved by the Food and Drug Administration (FDA) has been declining since 1995 (FDA 2015). Hence, it is important to find a new strategy to discover drugs especially with the emergence of newer diseases affecting the universe. Drug repositioning (DR) which is defined as finding new indications and therapeutic targets for already known drugs can be said to have several advantages. The initial six to nine years required for the development of new drugs is not necessary in repositioning because the research process goes directly to preclinical testing and clinical trials, thus reducing time, risk, and costs. A range of pharmacological, toxicological, and clinical safety information is already available at the beginning of a repositioning process, as drug candidates have already gone through some stages of development such as structural optimization, preclinical and/or clinical trials (Ashburn and Thor, 2004; Padhy and Gupta, 2011; Oprea and Mestres, 2012; Novac, 2013; Zheng *et al*., 2017). In this way, there is a reduction in the risk

associated with failures in the early stages of development which are high in traditional approaches and a possible increase in clinical safety.

II. COVID-19

Coronavirus is an enveloped RNA virus, from the genus *Betacoronavirus*, distributed in birds, humans and other mammals primarily associated with mild to moderate upper respiratory illnesses. The novel corona virus 19-Novel corona virus (2019-nCoV) was named severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) and WHO named this novel corona virus disease as COVID-19 with confirmed cases in more than 117 countries (WHO 2020; Perrella *et al.*, 2020). Six species of coronavirus are known as infectious in humans, four of which are (229E, OC43, NL63, and HKU1) cause common cold symptoms (Zhu *et al.*, 2019). The disease is highly infectious and contagious. During manifestation, a significant viral amplification occurs that led to initial mild to moderate symptoms which later progressed to severe symptoms primarily due to inflammatory cytokine storm and inflammatory cell infiltration causing acute lung injury, thrombosis, ARDS and death at the end stage of the disease (Zhang *et al.*, 2020).

III. COVID-19 AND DRUG REPOSITIONING

The management and prevention of Covid-19 is a global issue as there are no drugs or vaccines approved for the treatment and prevention of the novel coronavirus infection (Li and De Clercq 2020), however there are over 80 clinical trials including drug repositioning that have been initiated to get Covid-19 treatment as captured in clinicaltrials.gov database (Maxmen 2020). No specific therapy has been approved by the US Food and Drug Administration (FDA), but many previously approved drugs have been on the process of being repositioned to discover their therapeutic activities on COVID-19 aside their already approved indications. There are over one thousand registered international research in ClinicalTrials.gov (https://clinicaltrials.gov/). Medications with both antiviral and anti-inflammatory properties have been recommended for repositioning for COVID-19 therapy (Stebbing *et al.*, 2020). Antimalarial agents with anti-inflammatory and immunomodulatory activities such as chloroquine and hydroxychloroquine have shown inhibitory activity for SARS-CoV-2 like previous studies on SARS-CoV-1 and MERS-CoV (Sanders *et al.*, 2020). Based on positive *in vitro* and limited clinical data of chloroquine and hydroxychloroquine use in patient suffering from COVID-19, investigation at clinical stage is ongoing to determine the reliability of the positive result obtained. Azithromycin, a macrolide antibiotic was found to potentiate the action of hydroxychloroquine in the management of COVID-19 hence its recommendation in COVID-19 complementary therapy (Gautret et al., 2020). combination therapy against COVID-19 using lopinavir (human immunodeficiency virus type 1 protease inhibitor) in combination with ritonavir (CYP3A4 inhibitor) has shown positive result at preclinical studies as the combination was suggested to block the main protease of SARS-CoV-1, and inhibits viral replication (Ratia et al., 2008); however, complementary research has failed to confirm this result (Cao et al., 2020).

IV. CONCLUSION

Drug repositioning can be a major determining factor in discovering the drugs for managing COVID-19. Given the considerable time and cost of developing new drugs, a much more effective and efficient option is to reposition the already existing drugs to treat/manage other diseases when possible. The already approved drugs for use in humans and animals are more likely to be safer than drugs that are still undergoing trials. In addition, approved drugs are already optimized to their target proteins, which is an advantage if the target is found to be important in another disease. However, if the drug is being repositioned to an off-target's associated disease, the potent inhibition of the original target may cause adverse effects. It is therefore strongly recommended that awareness on drug repositioning should be intensified and scientific research in pharmacological and toxicological sciences should cover the aspect of drug repositioning to a larger extent since the strategy of repositioning is safer and economically attractive when compared with the cost of new drug development.

CAREER OBJECTIVE

To be actively involved in scientific research; the promotion of public health; the rationale uses of drugs for maintaining and promoting both human and animal health; the diagnosis, treatment, prevention, and control of various zoonotic diseases.

EDUCATION

- University of Maiduguri Borno State. **(MSc. Pharmacology)** **Oct. 2017 – March. 2020**
- University of Maiduguri Borno State. **(DVM)** **Sept. 2006 – Apr. 2014**

PROFESSIONAL CERTIFICATIONS

- Research and Proposal Writing in the Sciences (fSG3Z2wkBy-INASP) **Nov. 2020**
- Fundamentals of Global Health Research (University of Washington) **June 2020**
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PUBLICATIONS

- Acute toxicity and antinociceptive activity of crude ethanol extract of *Securidaca longepedunculata* (Fresen) root bark in albino rats. Int. J. Drug Res. Tech. 2013, Vol. 3 (6), 105-110. ISSN 2277-1506. www.ijdrt.com

RESEARCH/TEACHING EXPERIENCE

- Laboratory Research Assistant I, University of Maiduguri **Oct. 2016 – Aug. 2017**
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