A Scrutiny on Anti-Covid Activity of Hetrocyclic Compounds

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Abstract- *The coronavirus disease 2019 (COVID-19) pandemic is one of the most serious health problems worldwide. It has caused serious calamities in the world since the blaze of SARS CoV in 2002 and then MERS CoV in 2012.The pandemic caused by SARS CoV-2, a coronavirus that began in China in December 2019, has caused a total of 24,066,076 cases. The World Health Organization reported 3.4 million deaths globally by December 2020.7,010,681 people have died so far from the corona virus COVID-19 outbreak as of April 13, 2024.Yet, there is no medication is feasible against it.For several decades, heterocyclic moeities have been extensively explored for their anticancer, antimalarial, anti-inflammatory, antituberculosis, antimicrobial, antidiabetic, antiviral and many other therapeutic abilities.Therefore, in this review, we emphasize the forecast the role of heterocyclic scaffolds in the design and discovery of the much-awaited anti-SARS CoV-2 therapy, by investigating research articles rendering various heterocyclic moieties.The heterocyclic moties outlined in the review may serve as important asset for the development of SARS coronavirus dealing approaches.*

Keywords- SARS CoV, MERS, SARS CoV-2, Heterocyclic scaffolds, Coronaviruses

I. INTRODUCTION

The IUPAC Gold Book describes heterocyclic compounds as:.Cyclic compounds having as ring members atoms of at least two different elements,e.g. quinoline, 1,2-thiazole, bicyclo[3.3.1]tetrasiloxane[1].Usually they are indicated as counterparts of carbocyclic compounds, whichhave only ring atoms from the same element. Another classical reference book,the Encyclopaedia Britannica, describes a heterocyclic compound, also called aheterocycle, as:Any of a class of organic compounds whose molecules contain one or more rings ofatoms with at least one atom (the heteroatom) being an element other than carbon,most frequently oxygen, nitrogen, or sulfur[2].Heterocyclic chemistry is the branch of chemistry dealing with the synthesis,properties, and applications of heterocycles.Hetrocyclic chemistry has a wide range of applications: they are predominant among the types of compounds used as pharmaceuticals[3] as agrochemicals[4] and veterinary products[5]. They are used as optical brightening agents, as antioxidants,as corrosion inhibitors[6].

Heterocyclic scaffolds play a pivotal role in drug discovery and development as they constitute the key structural component of a majority of biologically active moieties. Their ability to interact with almost every cellular mechanism in living organism has been responsible for their versatile nature. Their interaction with different mechanistic pathways in viruses has continuously been exploited by researches for the designing of heterocycle-based antiviral agents. Several FDA approved drugs currently in the market comprise of differenthetrocyclic scaffolds[7].

Coronaviruses (CoV) are a family of viruses capable of causing mild to severe symptoms of respiratory distress. In the last two decades, the outbreak of two of the coronaviruses, Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS), have emerged as epidemics with severe mortality. Both epidemics were of zoonotic origin, with SARS CoV transmission from civet cats to humans in 2002 in China and MERS CoV transmission from dromedary camels to humans in 2012 in Saudi Arabia. There was emergence of cluster of pneumonia cases of unknown etiology in Wuhan city, Hubei province, China on 31 December 2019 and later declared by China that the outbreak is associated with a seafood market in Wuhan[8]. China shared the genetic sequence of novel coronavirus responsible for the outbreak for diagnostic purposes on 12 January 2020 . On 30 January 2020, World Health Organisation (WHO) declared this 2019-nCoV outbreak as a PHEIC (Public Health Emergency of International Concern) which was declared pandemic on 11 March 2020 . On 11 February 2020, WHO named this novel coronavirus as COVID-19 (corona virus disease 2019) and later International Committee on Taxonomy of viruses renamed it as SARS CoV-2. There were 24,066,076 confirmed cases of COVID-19 and 823,572 deaths, globally as on 26 August 2020. Coronaviruses are single stranded positive sense RNA viruses. COVID-19 is caused by seventh of known coronaviruses which have infected humans, in the sequence: 229E, NL63, OC43, KKU1, MERS-CoV, SARS-CoV, and 2019-nCoV-2[9].

Coronavirus Structure, Vaccine and Therapy Development: All viruses are parasites which can only reproduce within cells. Thus, they are very different from bacteria and fungi, which are self-reproducing, often in soil, water, organic wastes, sewageor within organisms.

Animal and plant viruses fall into two general classes, those in which the genetic material is long DNA molecules, and those in which the genetic material is RNA molecules. Among the DNA viruses are Herpes, Adenoviruses, and wart viruses. Coronaviruses, named for their "sun-like" shape observed in the electron microscope, use RNA molecules to encode their genes, as do influenza viruses, HIV, and rhinoviruses (common cold). SARS-CoV-2, the virus that causes COVID-19, infects mammals and birds. It is closely related to the viruses causing the earlier SARS (Severe Acute Respiratory Syndrome) and MERS (Middle East Respiratory Syndrome) outbreaks[10].

The coronavirus particles are organized with long RNA polymers tightly packed into the center of the particle, and surrounded by a protective capsid, which is a lattice of repeated protein molecules referred to as coat or capsid proteins. In coronavirus, these proteins are called nucleocapsid (N). The coronavirus core particle is further surrounded by an outer membrane envelope made of lipids (fats) with proteins inserted. These membranes derive from the cells in which the virus was last assembled but are modified to contain specific viral proteins, including the spike (S), membrane (M), and envelope (E) proteins.A key set of the proteins in the outer membrane project out from the particle and are known as spike proteins (S). It is these proteins which are recognized by receptor proteins on the host cells which will be infected.A key set of the proteins in the outer membrane project out from the particle and are known as spike proteins (S). It is these proteins which are recognized by receptor proteins on the host cells which will be infected[11].

As the heterocyclic compounds have been rigorously involved in the ailments including viral infections, AIDS, cancer, there exists a profound scope of exploring these multiple nuclei to curb coronaviruses. Therefore, through this review we have tried to summarise some of the treatment options based on the heterocyclic nuclei researched and developed against SARS CoV, MERS-CoV and SARS-CoV-2 epidemics using in vitro, in vivo and in silico approaches, which may be of immense value at this hour of global emergency and in future.

Various Hetrocyclic compounds as anti viral agent:

Indole scaffold has been found in many important synthetic drug molecules and played a faithful way to develop effective targets. Privileged structures bind to multiple receptors with high affinity, thus aiding the development of novel biologically active compounds. Indole is a potent basic pharmacophore presented in a wide variety of antiviral agents which inhibit HSV-1. Abdel-Gawad et al. reported that indole fragment fused with 1,2,4-triazolo[3,4-*b*]-1,3,4-thiadiazine and 1,3-thiazole derivatives displayed potent antiviral activity against HSV-1 grown on Vero cells. A variety of indole derivatives were synthesized and tested with the hope to get better antiviral agents. [12].

Situ Xue et al. were designed, synthesized and screened 22 indole-2-carboxylate derivatives for antiviral activities towards influenza A, influenza B, HSV-1 and Cox B3. The majority of the synthesized compounds exhibited potent activity against the influenza A and Cox B3 viruses[13].

A new series of furan-substituted spirothiazolidinoneshave been designed and synthesized by Apaydın ÇB, Tansuyu M et al. and evaluated for antiviral activity. They characterized new
Zmolecules by IR, ^{1}H NMR, ^{13}C NMR, mass spectrometry and elemental analysis. Six analogues proved to be active against influenza A/H3N2 virus[14].

Some pyrazole-based heterocycles such as pyrrolone, pyridazinone, and imidazole derivatives were synthesized utilizing the pyrazolyl-2(3*H*)-furanone derivative by Youssef M. Youssef, Mohammad E. Azab et al. which was obtained in a good yield via Perkin condensation. Upon antimicrobial screening, they observed that the majority of the compounds were found to be active against Staphylococcus aureus, Haemophilus, and Candida albicans as compared to standard drugs[15].

Osama I el-Sabbagh et al. were synthesized new N-acetyl and N-thiocarbamoyl derivatives of 4,5-dihydropyrazole starting from alpha,beta-unsaturated ketones under the effect of hydrazine hydrate and thiosemicarbazide, respectively.The antiviral activity for such novel compounds against a broad panel of viruses in different cell cultures revealed that N-acetyl 4,5-dihydropyrazole was the only active one at subtoxic concentrations against vaccinia virus (Lederle strain) in HEL cell cultures with a 50% effective concentration (EC(50)) value of 7 microg/ml[16].

Multicomponent synthesis of 4-arylidene-2-phenyl-5(4H)-oxazolones (azlactones) using a mechanochemical approach were reported by Amin F. M. Fahmy, Amira A. El-Sayed and Magdy M. Hemdan. According to them,azlactones

have been reported to exhibit a wide range of pharmaceutical properties including immune suppressive, anticancer. Antimicrobial, antitumor, anti-inflammatory and antiviral[17].

II. CONCLUSION

With the emergence of SARS CoV-2 pandemic there is an urgent need for designing and developing safe, low-cost and potent anti-SARS CoV-2 agents. At present, a number of pharmaceutical industries and research centres throughout the world are working persistently to find a solution to the current pandemic situation. This review gives an insight into the crucial role of heterocyclic moieties as antiviral or anti-SARS CoV and anti- SARS Cov-2 agents.

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