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A Study On Potential Drug Target For SARS-CoV-2-And Combinatorial Therapeutic Approach To Combat COVID-19

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Abstract

The COVID-19 pandemic caused by (SARS-CoV-2) a threat, leading to numerous deaths and socioeconomic disruptions. Spurred intense research efforts effective treatment. Our study provides a brief overview COVID-19. Urgent need for effective treatments has prompted extensive research to identify potential drug targets against disease. Review shows most promising drug and their associated therapeutic approaches for combating COVID-19. Key targets include the spike protein, which facilitates viral entry into host cells, and proteases essential for viral replication. Additionally, RNA-dependent RNA polymerase (RdRp) inhibitors have been explored to inhibit viral RNA replication, highlighting their mechanisms of action, potential therapeutic benefits, and challenges in drug development. Host factors, such as the ACE2 receptor and immune response modulators, are also targeted. Combination therapies and overcoming challenges in the drug development are crucial for successful COVID-19 treatment. In this review the molecular docking study is discussed here. The future perspective of drug targets for COVID-19 encompasses a range of innovative approaches aimed at combating the virus and preparing for future outbreaks. The review also discusses the challenges faced and future directions in the field of drug target research for COVID-19. This review will provide an overview of the anticipated advancements in drug target discovery and development for COVID-19, highlighting key areas of focus and potential strategies.

Keywords: COVID-19, SARS-CoV-2, Drug targets, Molecular docking, Phytochemicals, Synthetic drugs, Therapeutic approaches

Introduction

A pandemic has been genarated by SARS-CoV-2 or, COVID-19, a critical worldwide, driving to mortality, and financial disturbances. The SARS-CoV-2 shows a specific structure is appeared (Figure 1).

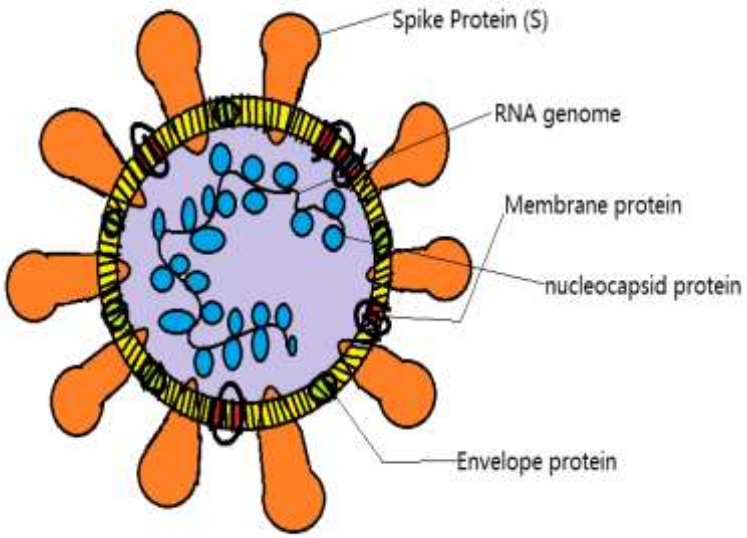

Fig. 1: Cross section of SARS-CoV-2 Coronavirus

Recognizable proof and characterization of particular targets for drugs empower drugs advancement that can meddled with the viral lifecycle, viral replication can be repressed. (or, more straightforwardly) tweaked the safe framework reacts moderate the seriousness of the malady. The understanding of these sedate targets and their intuitive with the infection and have components contributed the improvement of successful treatment alternatives for COVID-19. The most medicate targets talked about in this survey incorporate the spike protein intervenes viral section significant for viral replication, e.g., proteins and enzymes. Moreover, the survey will look at the utilize of monoclonal antibodies and repurposed antiviral drugs in focusing on these particular components. It'll emphasize the significance of worldwide collaborations and continuous investigate endeavors in tending to these challenges and progressing the advancement of successful treatments against COVID-19.

1. Drug-able Targets of COVID-19: Spike Protein, RNA-Dependent RNA Polymerase (RdRp), Angiotensin-Converting Enzyme 2 (ACE2) Receptor, Proteases (Proteases are 3 types, for example: chymotrypsin-like protease, Papain-like protease, Main protease or, primary protease), Transmembrane protease, serine 2 (TMPRSS2) **(Sánchez et al.; 2022)**.

2. Usable Drugs

A. Phytochemicals: Artemisinin **(Uckun et al.; 2021)**, Kuwanon C **(Kim et al.; 2022)**, Ellagic Acid **(AbouAitah et al.; 2021)**, Quercetin **(Imran et al.; 2022)**, Quercetin-3-O-Glucuronide **(Kim et al.; 2021)**, Kaempferol-3-O-Glucuronide **(Deng et al.; 2021)**, Kaempferol-3-O-Rutinoside **(Wang et al.; 2015)**, Myricetin **(Li et al.; 2021)**, Naringenin **(Salehi et al.; 2019)**, Epigallocatechin Gallate **(Wang er al.; 2022)**, Procyanidin B1 **(Okamoto et al.; 2014)**, Δ-viniferin **(Di Matteo et al.; 2020)**, Cnicin **(Avula et al.; 2022)**, Silibinin **(Speciale et al.; 2021)**, Amentoflavone **(Hossain et al.; 2023)**, Limonin **(Meeran et al.; 2021)**, Glycyrrhizic Acid **(Li et al.; 2021)**, Mulberrofuran G **(Kim et al.; 2022)**, Gallic Acid **(Umar et al.; 2021)**, Caffeic Acid **(Adem et al.; 2021)**, Ferulic Acid **(Pasquereau et al.; 2022)**, Chlorogenic Acid **(Abomughaid et al.; 2022)**, Catechin **(Diniz et al.; 2021)**, Cyanidin-3-O-Glucoside **(Semmarath et al.; 2022)**, Kaempferol **(Hossain et al.; 2023)**, Rutin **(Rizzuti et al.; 2021)**, Withanoside IV **(Kuboyama et al.; 2006)**, Withanoside V **(Dhanjal et al.; 2021)**.

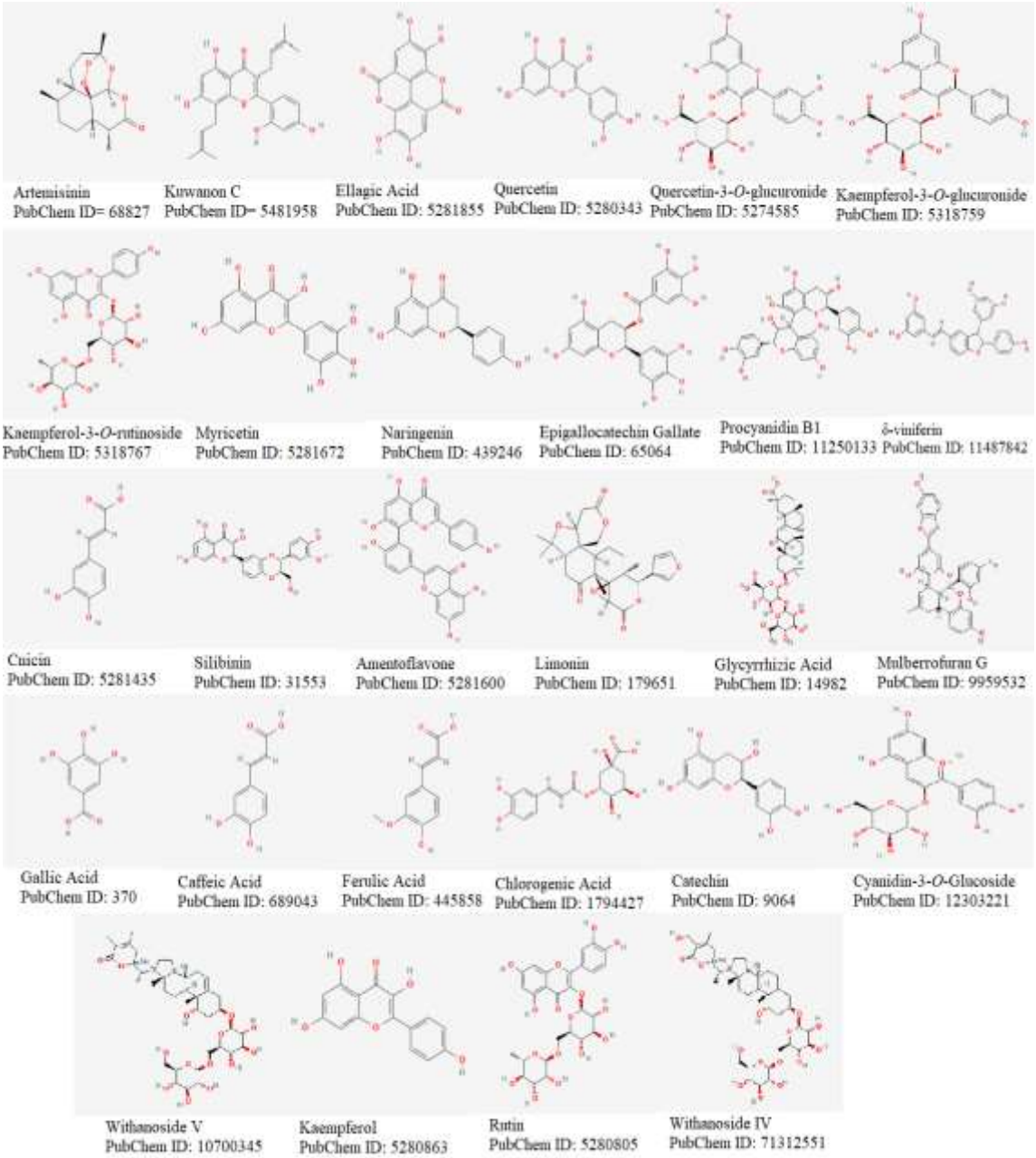

Fig. 2: Structures and PubChem IDs of phytochemicals (Figure was drawn by using MS Paint).

B. Synthetic Drugs: Remdesivir **(Malin et al.; 2020)**, Chloroquine **(Chang, Sun; 2020)**, Ciclesonide **(Kimura et al.; 2020)**, Niclosamide **(Singh et al.; 2022)**, Lopinavir **(Maciorowski et al.; 2020)**.

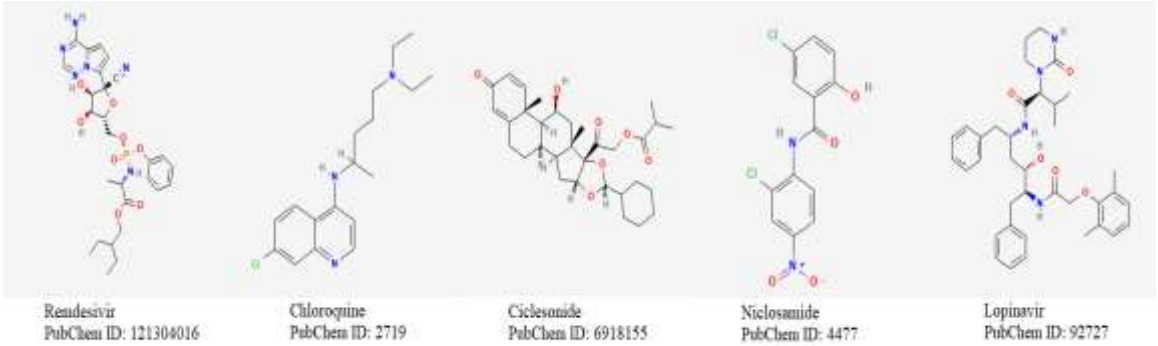

Fig. 3: Structures and PubChem IDs of synthetic drugs (Figure was drawn by using MS Paint)

Table 1: Comparison of binding affinity of different phytochemicals and Synthetic Drugs and their target proteins.

Target Protein	Drug Molecules types	Names	Docking Score	Reference
Spike Proteins	Phytochemicals	Artemisinin	-5.06	(Rafiq et al.; 2023)
		Kuwanon C	-7.1	
RdRp	Phytochemicals	Ellagic acid	-7.6	(Souid et al.; 2022)
		Quercetin	-7.2	
		Quercetin-3-O-Glucuronide	-8.0	
		Kaempferol-3-O-Glucuronide	-7.9	
		Kaempferol-3-O-Rutinoside	-9.2	
		Myricetin	-7.2	
		Naringenin	-5.7	
		Epigallocatechin Gallate	-5.7	
		Procyanidin B1	-9.8	
		Δ-viniferin	-8.3	
		Cnicin	-9.7	(Rafiq er al.; 2023)
		Silibinin	-7.15	
		Amentoflavone	-9.4	
ACE2	Phytochemicals	Limonin	- 8.2	(Vardhan and Sahoo, 2022)
			- 8.3	
			- 8.3	
		Glycyrrhizic Acid	- 8.5	
			- 8.7	
			-8.4	
		Mulberrofuran G	-7.4	
	Synthetic Drugs	Remdesivir	-5.62	(Zhang et al.; 2020)
		Chloroquine	-4.2	
		Ciclesonide	-5.53	
		Niclosamide	-4.31	
		Lopinavir	-5.5	
Mpro	Phytochemicals	Gallic Acid	-4.5	(Souid et al.; 2022)
		Caffeic Acid	-5.7	
		Ferulic Acid	-5.4	
		Chlorogenic Acid	-6.0	
		Catechin	-7.9	
		Cyanidin-3-O-Glucoside	-8.4	
Mpro/3CLpro	Phytochemicals	Kaempferol	-6.4	(Rafiq et al.; 2023)
		Rutin	-9.19	
TMPRSS2	Phytochemicals	Withanoside V	-7.96	
		Withanoside IV	-6.92	

Conclusion

Several drug targets have been investigated for COVID-19, and host immune response modulators. Targeting these components aims to inhibit viral entry, disrupt replication, modulate inflammation, and enhance the host immune response. Promising drug candidates have emerged, along with synthetic drugs. These drugs have shown efficacy in reducing viral load, suppressing inflammation, and improving clinical outcomes in certain patient populations. Combination therapies involving multiple drug targets are being explored to enhance treatment efficacy and overcome potential drug resistance. By Molecular Docking the result we found that, in antiviral medicines maximum phytochemicals are used because it is more non-toxic and herbal than synthetic drugs. In this case synthetic drugs are less used because of it's side effects.

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