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COVID-19 Vaccines: A possible solution to ongoing pandemic

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Abstract
The current pandemic situation of COVID-19 incites the researchers to find out vaccines to control SARS-CoV-2. The basis of vaccine designing strategy for COVID-19 has been taken from various published research articles on SARS-CoV and MERS. COVID-19 vaccination efforts have been started in earlier days of infection of COVID-19 in China and a few days later it started worldwide. This pathetic condition evolved race for vaccine development. An accelerated vaccine development program was launched in several countries worldwide in which several steps were done in parallel. In this review we have described the various vaccines *viz*. subunit, mRNA, DNA, inactivated and vector-based vaccine, which have been already signified demonstrated their therapeutic and prophylactic response against SARS-CoV-2, after that released for vaccination. Many vaccines were released to control SARS-CoV-2 with different efficacy and safety.

Keywords: COVID-19, subunit vaccine, mRNA vaccine, DNA vaccine, inactivated vaccine, Vector based vaccine

Introduction
In the current situation, the COVID-19 suffering world resides in the midst of a pandemic era that has desperately urged responses to control SARS-CoV-2 by recently developed vaccination. The pathetic conditions that occurred due to COVID-19 created a huge race for vaccine development worldwide. The vaccine can prevent infectious disease by training and preparing the body's natural defense system (immune system) by specific recognizes and fights off target. The idea for vaccine development was taken from previous reports on SARS-CoV and MERS (Pandey *et al*., 2020) [1]. In some countries, the race for vaccine development was started earlier than the COVID-19 pandemic declared by WHO (Pandey *et al*., 2020) [1]. An accelerated vaccine development program was launched in several countries worldwide in which several steps are done in parallel [Table 1]. Several vaccines mRNA-1273 (Moderna), Ad5-nCoV (Can Sino Biologicals), INO-4800 (Inovio, Inc.), LV-SMENP-DC, Pathogen-specific aAPC (ShinzenGeno-Immune Medical Institute), ChAdOx1 (University of Oxford) have entered the phase I/II clinical trials (https://www.who.int/emergencies/diseases/novel-coronavirus-2019; Kaur and Gupta, 2020) [2]. However, the release of the vaccine against COVID-19 was not successful until late 2020. A landmark achievement was made when Russia's Sputnik V vaccine was released for vaccination in Russia under emergency rules, developed by Gamaleya Research Institute of Epidemiology and Microbiology (https://sputnikvaccine.com/about-vaccine). However, the efficacy of the vaccine at stopping people from developing symptomatic COVID-19 was under debate. Serious concerns were raised against its efficacy and this vaccine was released without the final round of testing (Kaur and Gupta, 2020) [2]. The clouds of uncertainty regarding the development of the COVID-19 vaccine came to an end when the emergency use of Pfizer and BioNTech were granted by UK regulators on 2nd December 2021 after proper clinical trials. This all happens because a good COVID-19 vaccine requires proper confirmation of potency and detrimental effect when it targets a large population of every age person including pregnant women and those who are suffering from respiratory problems. Various strategies of COVID-19 vaccine development have been adopted, namely, virus vectored vaccines, protein subunit vaccines, genetic vaccines, and monoclonal antibodies, with each having own benefits and hindrance (Kaur and Gupta, 2020) [2]. There have been several attempts directed towards the improvement of the development of the COVID-19 vaccine and among the different parts of the virus, the S-protein of SARS-CoV-2 has been chosen as the candidate vaccine part (Dhama

al., 2020) [3]. Pfizer COVID-19 vaccine (BNT162b2) along with two other versions of vaccine AstraZeneca/Oxford COVID-19 manufactured by the Serum Institute of India and SKBio got a green signal for vaccination by WHO (https://www.who.int/health-topics/coronavirus). The most popular vaccines and their mode of action were described below.

Protein subunit vaccines

Synthetic peptides or recombinant antigenic proteins were used for preparing subunit vaccine which is known for their long-lasting immune response and therapeutic response (Fig 1) (Wang *et al*., 2020) [4]. These types of vaccines require adjuvant because of low immunogenicity to express their full potential. An Adjuvant helps to increase the exposure time as well as the half-life of antigenic material (Cao *et al*., 2018) [5]. S protein of COVID-19 is a suitable antigen to induce the neutralizing antibodies. S protein of COVID-19 is made up of S1 and S2 subunit, S1 subunit contains three domains NTD, RBD, and RBM whereas the S2 subunit has two domain FP, HR 1, & 2 (Ou *et al*., 2020) [6]. S-protein helps COVID-19 to enter inside the cell by binding to the hACE2 receptor. So, S-Protein is considered an important target to prepare subunit vaccines (Wang *et al*., 2020) [4]. Triple Antigen Vaccine was developing by Premas Biotech, India using this protein subunit of virus (Kaur and Gupta, 2020) [2].

Viral vectored vaccines

A viral vector-based vaccine is a potential prophylactic approach against the pathogen. These types of vaccines are efficient and specific in terms of delivery of genes and transduction (Fig 1) (Ura *et al*., 2014) [7]. These vaccines induce a long-term immune response and having more protein expression, therefore, triggers cytotoxic T cells (CTL) which finally remove virus-infected cells (Le *et al*., 2020) [8]. Ad5-nCoV is a viral-based vaccine produced by CanSino Biologics Inc and the Beijing Institute of Biotechnology.

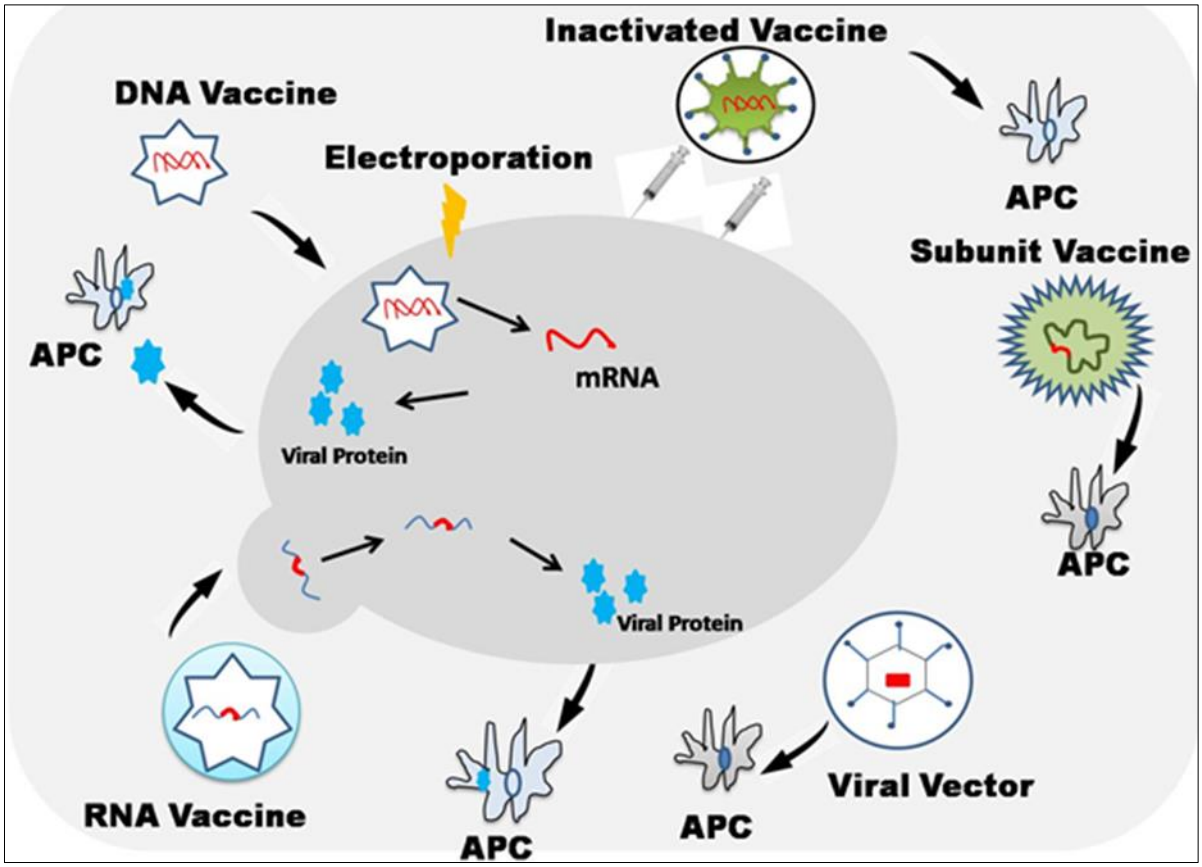

Fig 1: Different type vaccine and their target mode were diagrammatically depicted. (Antigen presenting cell (APC)

Table 1: List of vaccine authorized for emergency use by WHO

Mode of vaccine development	Vaccine, developers/sponsers	Country	Efficacy	Reference
RNA vaccine	Pfizer-BioNTech Covid-19 vaccine (BioNTech, Pfizer)	United states, Germany	95%	(Polack *et al*., 2020) [16]
	Moderna Covid-19 vaccine (Moderna, NIAID, BARDA, CEPI)	United states	94%	(Baden *et al*., 2021) [17]
	Sputnik V Covid-19 vaccine (Gamaleya Research Institute of Epidemiology and Microbiology)	Russia	91.6%	(Logunov *et al*., 2021) [18]
Adenovirus vector vaccine	Oxford-AstraZeneca COVID-19 vaccine (Covishield) (University of Oxford, Astra Zeneca, CEPI)	United Kingdom	62-90%	(Voysey *et al*., 2021) [19]
	Johnson & Johnson Covid-19 vaccine, Janssen Pharmaceutical (Johnson & Johnson), BIDMC	United states, Netherlands		https://www.who.int/health-topics/coronavirus
	Ad5-nCoV (Cnvidicea) CanSino Biologics, Beijing Institute of	China	65.7%	(CanSinoBIO's, 2021) [20]

	Biotechnology of the Academy of Military Medical Sciences			
	BBIBP-CorV, Sinopharm: Beijing Institute of Biological Products, Wuhan Institute of Biological Products	China	79%	(Wee and Qin, 2020) [21]
Inactivated Virus vaccine	CoronaVac, Sinvac	China	50.4%	(CoronaVac's, 2021) [22]
	BBV152 (Covaxin) Bharat Biotech, Indian Council of Medical Research	India	81%	(Bharat Biotech, 2021) [23]
	CoviVacc The Chumakov Centre at the Russian Academy of Sciences	Russia		https://www.precisionvaccinations.com/vaccines/covivac-russia-covid-19-vaccine

mRNA Vaccines

mRNA vaccine contains antigenic genome which further gets translated inside the host cell after vaccination and induce an adaptive immune response (Zhang *et al*., 2019) [9]. mRNA vaccine has high expression and potential along with low cost of production comparatively conventional vaccines (Pardi *et al*., 2018) [10]. mRNA vaccines are completely safe and show good responses with higher efficacy. The mRNA-based vaccine developed by name mRNA-1273 (Moderna TX, Inc) by Moderna, Inc., in collaboration with the National Institute of Allergy and Infectious Diseases (https://www.modernatx.com/mrna-technology/research-engine).

DNA Vaccines

DNA vaccine introduction inside the host cell is the most revolutionary approach in which plasmid DNA encodes for antigen along with adjuvant were injected which able to generate a broad range of adaptive immune response (Fig 1). These types of vaccines are used for both prophylactic and therapeutic purposes (Yang *et al*., 2014) [11]. However, DNA vaccines have to reach the cell nucleus where they are exposed to the possibility of host genome incorporation and mutation (Liu, 2019) [12]. The cells that receive transgene is continuously expressing the transgene protein which somewhat similar to a live virus. INO-4800 (Inovio Pharmaceuticals) is a DNA vaccine that effectively induces T cell activation within 7 days after vaccination (Kaur and Gupta, 2020) [2].

Inactivated and live attenuated vaccines (LAVs)

In inactivated (whole cell-killed) and live attenuated vaccine antigenic components are neutralized by application of heat, radiation, or by chemical means in the laboratory (Fig. 1) (Sharma *et al*., 2011) [13]. After vaccination, specific neutralizing antibodies and T-lymphocytes are generated inside the body which shows a broad range of immunological responses against the pathogen. DelNS1-SARS-CoV2-RBD (University of Hong Kong) is an influenza-based vaccine strain that re-organized to express the RBD domain SARS CoV-2 spike protein on its surface (Anon, 2020) [14].

COVID-19 vaccine in India

India is the second-largest population in the world with one of the biggest pharmaceutical manufacturing capacities, so India has a crucial role in the COVID-19 vaccination effort. India is ranking second-highest number of infections and 156705 confirmed death by 25 February 2021 (https://www.who.int/health-topics/coronavirus), so it is crucial to develop an indigenous vaccine to stop panic driven by the virus. There are two vaccines approved in INDIA namely Covaxin and Covishield whereas ZyCoV-D under release, completed all trial phases.

Covaxin

Covaxin is a kind of inactivated vaccine, which one completely safe. India's first indigenous produced vaccine, by Bharat Biotech International Limited of Bangalore in collaboration with ICMR (Indian Council of Medical Research) and NIV (National Institute of Virology) and 25 800 people have been registered for trials across the country (Thiagarajan, 2021) [15]. DCGI (Drug Controller General of India) provided approval to Covaxin for the human clinical trial in June 2020 and by July completed Phase-I trial. 12 top institutes of India AIIMS) New Delhi, AIIMS Patna, Post Graduate Institute (PGI) of Medical Sciences, Rohtak conducted the Phase-I clinical trials for Covaxin on a total of 365 healthy volunteers. The scientific team of Bharat Biotech has declared that participated volunteers remained healthy after vaccination and no adverse effect of vaccines was observed. Hence, the company has completed 2nd dose in the phase-3 clinical with 13,000 volunteers (NHI, 2020) [24].

Covishield

Covishield is an adenovirus vector-based vaccine that is more popular than covaxin. It is a version of the Oxford University-AstraZeneca vaccine with 70.4% efficacy. This vaccine is manufactured by Serum Institute of India and for phase trial 1600 people registered in Nov 2020 (Thiagarajan, 2021) [15].

ZyCoV-D

ZyCoV-D is a Plasmid DNA vaccine in which specific gene fragments are cloned into a plasmid. This vaccine was developed in India by Ahmadabad-based biopharmaceutical company Zydus Cadila. ZyCoV-D got approval for the Human Clinical Trial phase-I/II after pre-clinical animal trials. A total number of 1,048 volunteers participated in Clinical Trial-I / II and the trial possible when Zydus Cadila collaborated with the Department of Biotechnology (DBT, Govt. of India) (https://www.thehindu.com/sci-tech/health/zydus-cadila-gets-dcgi-nod-to-initiate-phase-3-clinical-trials-for-covid-19-vaccine/article33486423.ece).

Conclusions

Several attempts are being directed towards the development of effective vaccine against COVID-19 employing different mode of action. The currently developed vaccines are completely safe and shows good response with higher efficacy.

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