Review Article

International Journal of Research in Pharmaceutical Sciences

Published by JK Welfare & Pharmascope Foundation Journal Home Page: www.ijrps.com

Current update on COVID-19 vaccines

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Article History:

Received on: 09 Feb 2021
Revised on: 20 Mar 2021
Accepted on: 25 Mar 2021

Keywords:

COVID-19 Vaccines,
Virology,
Platform technologies,
SARS-CoV-2,
Spike protein,
Vaccine safety

Abstract

Novel Coronavirus, also known as SARS-CoV-2, is an infectious disease that primarily affects the respiratory tract and gastrointestinal tract. The viral spread occurs through respiratory droplets produced while coughing and sneezing. Major vaccine targets for COVID-19 are spike protein, M protein, envelope protein, receptor binding domain, nucleic acids etc. Different mechanisms through which a vaccine can be developed to evoke an immune response include virus inactivated vaccine, live attenuated vaccine, subunit vaccines, virus-like particles, replicating and non-replicating viral vectors and nucleic acid-based vaccines. The mainstay of COVID-19 treatment is supportive and symptomatic therapy with dexamethasone, hydroxychlorquine and anti-viral agents like Darunavir, Ribavirin, Remdesivir, Interferons. Maintaining social distance, personal hygiene, use of N-95 masks aids in limiting the spread of the infection. There is a vital requirement for an ideal and potent vaccine with a favorable benefit-risk profile to evoke an immune response against SARS-CoV-2 infection. There are currently 11 approved vaccines in the market of which the Pfizer/ BioNTech vaccine have produced the most efficacy (95%), followed by Moderna (94%), Sputnik (91.6%), Covaxin (90%), Janssen (90%) and Astra Zeneca (70%). Vaccine hesitancy, vaccine-related adverse reactions and the high cost of the vaccine can be a major barrier to public acceptance and global access to the vaccine.

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ISSN: 0975-7538

DOI: https://doi.org/10.26452/ijrps.v12i3.4721

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INTRODUCTION

Severe acute respiratory syndrome-CoV-2 (SARS CoV-2) is a highly pathogenic virus with a zoonotic origin identified initially in Wuhan, China which subsequently spread all over the world, turning out to be a pandemic termed as COVID-19. Coronavirus belongs to a diverse family of RNA viruses called Coronaviridae, causing a wide array of clinical manifestations on the upper respiratory, gastrointestinal, hepatic and central nervous system (Hageman, 2020).

The novel SARS Coronavirus-2 has 90% similar amino acids (except Spike protein) as that of SARS, with 79% of its genomic sequence indistinguishable from SARS-CoV. The arrangement of SARS-CoV-2 comprises a densely enveloped trimeric glycoprotein called the Spike protein (S-protein), expressed superficially on the virus and is the lead hope for vaccine development as it binds to ACE 2 receptors on host cells resulting in attachment and penetration to host cells. The S-protein has two core subunits S1 and S2; S1 controls receptor binding whereas S2 governs membrane fusion, these spike proteins also undergo a conformational change from pre-fusion to post-fusion state attained by drag-

ging and fusing the host cell with viral membranes together (Sharma *et al.*, 2020).

Current treatment modalities for the management of COVID-19 focus on symptomatic treatment such as oxygen therapy, fluid management, anticoagulation and ventilator support. Virus-specific therapies include antiviral medications such as protease inhibitors, monoclonal antibodies and anti-cytokines (Ramezankhani *et al.*, 2020).

However, COVID-19 can be restrained from being transmitted by developing herd immunity either with an effective vaccine or with at least 80% of the population getting infected, the latter of which can come with quite a serious societal impact (Chung *et al.*, 2020). Thus, there is an urgent need for an efficacious and economic vaccine at present to develop the necessary herd immunity to prevent further spread of the virus and the development of more potent infections strains.

Methodology

A thorough literature search was conducted in Pubmed to detect relevant articles pertaining to the research question. Studies published in Pubmed till February 2021 corresponding to the search criteria were included for consideration. Article search was conducted to identify original research articles related to the current vaccines in the pipeline, vaccine target platforms, the public perception towards vaccines, vaccine hesitancy and safety regarding the currently marketed COVID-19 vaccines. The search terms used were: SARS-CoV-2 AND COVID-19 vaccines OR virology OR immunology OR vaccine platforms OR vaccine targets. Letters to editors, narrative reviews and data presented at conferences were excluded from consideration. Once all the relevant articles were extracted, relevant studies addressing the current status of COVID-19 vaccines were selected.

Virology of SARS-COV-2

Structurally, the SARS-CoV-2 genome has a polarity of +28kb to +32kb with non-structural and structural poly-proteins. The non-structural poly-proteins undergo cleavage to generate 16 non-structural proteins and the four structural proteins, along with five accessory proteins (ORF3a, 6, 7, 8, 83 9) which make up the final protein ensemble in the virus. The four structural proteins are the spike surface glycoprotein (S), membrane protein (M), envelope (E), nucleocapsid protein (N). The spike protein is essential for host cell attachment and penetration into the cell and therefore is an appropriate target against the virus for vaccine development. The exact mechanism behind the activation of the silent COVID-19 infection in an asymptomatic person into an active infection characterized by respiratory symptoms is not clearly understood.

It is assumed that the spike protein, which binds to the host cell receptor (ACE-2 in lungs) and undergoes division with the help of a host protease enzyme into 2 subunits, N-terminal S1 subunit and C-terminal S2 subunit (membrane-bound), plays a vital role in the pathophysiology and virulence mechanism of the virus.

Binding of S1 subunit to ACE-2 receptor results in the shedding of a part of the S1 subunit ('down' conformation of S1 subunit) and the shift of the S2 subunit into a highly steady post-fusion conformation state and the receptor binding domain (RBD) of S1 subunit undergo a hinge-like conformation which is the primary determinant of the receptor binding ('up' conformation of S1 subunit) (Li *et al.*, 2020).

Although SARS-CoV and SARS-CoV-2 are structurally similar, variations in the spike protein in SARS-CoV-2 increases its affinity towards the ACE-2 receptor 10-20 times that of SARS-CoV making them highly infectious.

Thus, S-protein and receptor-binding domain (RBD) are prominent central targets for the development of vaccines.

Once entered into the pulmonary alveolar epithelial cells through ACE-2 receptors, SARS-CoV-2 undergoes rapid replication. The viral RNA strands then undergo translation and invade adjacent cells (Parasher, 2020).

This elicits a vigorous immune response leading to cytokine storm syndrome and subsequent pulmonary tissue damage, acute respiratory distress syndrome (ARDS) and multiple organ impairment. Hyperactivity of cytokines leads to functionally exhausted T-cells producing a decline in immune function and worsening prognosis (Wang *et al.*, 2020).

Introduction to Vaccine Development

Developing a COVID-19 vaccine in 1-2 years is a significant challenge as it normally takes 10-15 years to develop a vaccine. Vaccine development has principally 5 stages: Exploratory, Preclinical, Development, Regulatory Review and Approval and the final step is the Manufacturing and Quality control (World Health Organization, 2014).

The exploratory stage of vaccine development includes fundamental laboratory research and computational modeling to identify natural and synthetic antigens that can be transformed into potential vaccine candidates.

Table 1: Vaccine Candidates based on Platforms in Clinical Phase

Platform		Candidates (No.)	Candidates (%)
PS	Protein subunit	20	32%
VVnr	Viral Vector (non-replicating)	10	16%
DNA	DNA vaccines	8	13%
IV	Inactivated Vaccines	9	14%
RNA	RNA vaccines	7	11%
VVr	Viral Vector (replicating)	3	5%
VLP	Virus Like Particles	2	3%
VVr+ APC	VVr + Antigen Presenting Cell	2	3%
LAV	Li ve Attenuated Virus	1	2%
VVnr+ APC	VVnr + Antigen Presenting Cell	1	2%

(Corey *et al.*, 2020)

Table 2: FDA approved marketed COVID-19 vaccines

S. No.	Name	Vaccine platform	Primary developer and country of origin	Doses	Storage
1.	COVID-19 Vaccine Astra Zeneca; also known as Covishield	Adenovirus vaccine	BARDA, OWS (UK)	2	2-8°C
2.	Covaxin	Inactivated vaccine	Bharath Biotech, ICMR (India)	2	-20°C
3.	BBIBP-CorV	Inactivated vaccine	Beijing institute of Biological Products; Sinopharm (China)	2	2-8°C
4.	Convidicea	Recombinant vaccine (Adenovirus type 5 vector)	CanSino Biologics (China)	1	2-8°C
5.	EpiVacCorona	Peptide Vaccine	Federal Budgetary Research Institute State Research Centre of Virology and Biotechnology (Russia)	2	2-8°C
6.	Sputnik V	Non-replicating viral vector	Gamaleya Research Institute, Acellena Contract Drug Research and Development (Russia)	2	-18°C - 0°C
7.	Moderna COVID-19 Vaccine	mRNA-based vaccine	Moderna, BARDA, NIAID (US)	2	-20°C
8.	Comirnaty	mRNA-based vaccine	Pfizer, BioNTech, Fosun Pharma (Multinational)	2	-70°C
9.	CoronaVac	Inactivated vaccine (formalin with alum adjuvant)	Sinovac (China)	2	2-8°C
10.	No name	Inactivated Vaccine	Wuhan Institute of Biological Products, Sinopharm (China)	3	2-8°C
11.	JNJ-78436725; also known as (Ad26.CoV2.S)	Non- replicating viral vector	Janssen vaccines – Johnson and Johnson (Netherlands,US)	1	2-8°C

(Frederiksen *et al.*, 2020)

Table 3: Current status of COVID-Vaccine candidates in pipeline

S. No.	Candidate Name	Vaccine Platform	Status	Sponsor
1.	CVnCoV	mRNA- based vaccine	Phase 2b/3	CureVac; GSK
2.	NVX-CoV2373	Nanoparticle vaccine	Phase 3	Novavax
3.	ZF2001	Recombinant vaccine	Phase 3	Anhui Zhifei long-com Biopharmaceutical Institute of the Chinese Academy of science
4.	Bacillus Calmette-Guerin (BCG) vaccine	Live attenuated vaccine	Phase 2b/3	University of Melbourne and Murdoch Children's Research Institute: Radbund University Medical Center Z;Faustman Lab at Massachusetts General Hospital
5.	ZyCoV-D	DNA Vaccine (plasmid)	Phase 3	Zydus Cadila
6.	INO-4800	DNA Vaccine (plasmid)	Phase 2/3	Inovio Pharmaceuticals
7.	VIR-7831	Plant -based adjuvant vaccine	Phase 2/3	Medico
8.	No Name	Adenovirus-based vaccine	Phase 2/3	ImmunityBio; NantKwest
9.	UB-612	Multitope peptide- based DNA Vaccine (plasmid)vaccine	Phase 2/3	COVAXX
10.	Abdala CIGB66)	Protein subunit vaccine	Phase 2	Finlay institute of Vaccine
11.	BNT162	mRNA- based vaccine	Phase 1/2/3	Pfizer,BioNTech
12.	AdCLD - CoV19	Adenivirus -based vaccine	Phase 1/2a	Korea University Guro Hospital
13.	Nanocovax	Recombinant vaccine (spike protein)	Phase 1/2	Nanogen Biopharmaceutical
14.	EuCorVac-19	Nanoparticle vaccine	Phase 1/2	EuBiologics
15.	Mambisa (CIGB 669)	Protein subunit vaccine	Phase 1/2	Finlay institute of Vaccine
16.	IIBR -100	V Vesicular stomatitis virus (rVSV) vaccine	Phase 1/2	Israel Institute for Biological Research
17.	No Name	SF9 cell vaccine candidate	Phase 1/ 2	Westchina Hospital, Sichuan University
18.	Soberana 1 and 2	Monovalent/Conjugate vaccine	Phase 1/ 2	Finlay institute of Vaccine
19.	VLA2001	Inactivated Vaccine	Phase1/2	Valneva; National institute For Health Research (NIHR
20.	No Name	Adjuvanted Protein subunit Vaccine	Phase 1/2	CEPI
21.	AGO301-COVID-19	DNA Vaccine	Phase 1/2	AnGes, Inc.
22.	GX-19N	DNA Vaccine	Phase 1/2	Genexine

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Table 3 continued

23.	ARCT-021 (LUNAR -COV-19)	Self -replicating RNA Vaccine	Phase 1/2	Arcturus Therapeutics Duke -NUS Medical School
24.	No Name	Protein subunit vaccine	Phase 1/2	Sanofi GlaxoSmithKline
25.	No Name	Inactivated Vaccine	Phase 1/2	Chinese Academy of Medical sciences,Institute of Medical Biology
26.	HDT-301(HGC019)	RNA Vaccine	Phase 1/2	University of National Institutes of Health Rocky Mountain Laboratories: HDT Bio Corp; Genova Biopharmaceuticals
27.	AV-COVID-19	Dendritic cell vaccine	Phase 1b/2	Aivita Biomedical,Inc.
28.	PTX COVID-19-B	mRNA- based vaccine	Phase 1	Providence Therapeutics;Canadian government
29.	COV-VAC	Intranasal vaccine	Phase 1	Codagenix; Serum Institute of India
30.	CORVax12	DNA Vaccine (plasmid)	Phase 1	Onco Sec; Providence Cancer Institute
31.	MVA-SARS-2-S	Modified vaccinia virus ankara (MVA) Vector vaccine candidate	Phase 1	UniversitatsklinikumHamburg-Eppendorf; German Center for University Marburg Medical center, Ludwig-Maximilians-University of Munich
32.	COH04S1	Modified vaccinia virus ankara (MVA) Vector vaccine candidate	Phase 1	City of Hope Meical Center; National cancer Institute
33.	pVAC	Multiple-peptide vaccine candidate	Phase 1	University Hospital Tubingen
34.	AdimrSC-2f	Protein subunit vaccine	Phase 1	Adimmune
35.	bacTRL-Spike	Monovalent oral vaccine (bifdobacteria)	Phase 1	Symvivo
36.	COVAX-19	Monovalent recombinant protein vaccine	Phase 1	Vaxine Pty.Ltd
37.	DelNS1-2019-nCoV	Replicating Viral Vector	Phase 1	Xiamen University, Beijing Wantai Biological Pharmacy
38.	GRAd-COV2	Adenovirus-based vaccine	Phase 1	ReiThera; Leukocare; Univercells
39.	UQ-CSLV451	Protein subunit vaccine	Phase 1	CSL; The University of Queensland

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Table 3 continued

40.	SCB-2019	Protein subunit vaccine	Phase 1	Glaxosmithkline, Sanofi, Clover Biopharmaceuticals, Dynavax and Xiamen Innovax CEPI
41.	VXA-CoV2-1	Recombinant vaccine (Adenovirus type 5 vector)	Phase 1	Vaxart
42.	AdCOVID	Intranasal vaccine	Phase 1	Altimmune
43.	AAVCOVID	Gene -based vaccine	Pre-Clinical	Massachusetts Eye and Ear; Massachusetts General Hospital University of Pennsylvania
44.	ChAd-SARS-CoV-2-S	Adenovirus-based vaccine	Pre-Clinical	Washington University School of Medicine in St. Louis
45.	HaloVax	Self- assembling vaccine	Pre-Clinical	Voltron Therapeutics Inc; Hoth Therapeutics Inc.
46.	Linea DNA	DNA Vaccine	Pre-Clinical	Takis Biotech
47.	MRT5500	mRNA- based vaccine	Pre-Clinical	Sanofi, Translate Bio
48.	No Name	li-Key peptide COVID-19 Vaccine	Pre-Clinical	Generex Biotechnology
49.	No Name	Protein subunit vaccine	Pre-Clinical	University of Sasktechewan Vaccine and Infectious Disease Oranization – International Vaccine Centre
50.	No Name	mRNA- based vaccine	Pre-Clinical	Chulalongkorn University's Center of Excellence in Vaccine Research and Development
51.	No Name	Gp96-based vaccine	Pre-Clinical	Heat Biologics
52.	No Name	Inactivated Vaccine	Pre-Clinical	Shenzhen Kangtai Biological Product
53.	PittCoVacc	Recombinant Protein subunit vaccine (delivered through microneedle array)	Pre-Clinical	UPMC/University of Pittsburgh School of Medicine
54.	T-COVIDTM	Intranasal vaccine	Pre-Clinical	Altimmune
55.	LNP-nCoVsaRNA	Self- amplifying RNA vaccine	No longer being studied	Imperial College London
56.	V590	Recombinant vaccine (Vesicular stomatitis virus)	No longer being studied	Merck; IAVI
57.	V591	Measles vector vaccine	No longer being studied	University of Pittsburgh; Themis Bioscience; Institute Pasteur

(Frederiksen *et al.*, 2020)

Preclinical-stage encompasses cell or tissue culturing and conducting vaccine trials on animals to determine the ability of the vaccine candidate to evoke an immune response along with a preliminary assessment of safety and efficacy (Sharma *et al.*, 2020). In the clinical stages of development, vaccines are tested on humans, giving a more enhanced understanding of vaccine safety and efficacy from the animal data (World Health Organization, 2014).

Vaccine Platform Technologies

These technologies vary from inactivated and target attenuated live pathogens to delivering synthetic peptide agents and recombinant protein antigens, nucleic-acid based vaccines, replicating and non-replicating viral vectors, polysaccharide-protein conjugation and Virus-like Particles(VLPs) (Frederiksen *et al.*, 2020). Some of the techniques used in vaccine development include inactivated virus vaccines, adenovirus vector, mRNA based vaccines, DNA vaccines, protein vaccines (Raja *et al.*, 2020). The list of vaccine candidate based on platform technologies is listed in Table 1.

Inactivated Vaccine

These are developed by inactivating the live organism using formalin or phytochemical method using UV light and riboflavin, which selectively targets nucleic acids preserving the viral antigens and protein integrity of the virus, which will evoke an immune response in the individual without causing the disease. This methodology has been followed for the preparation of SolaVAX by the University of Colorado. These vaccines primarily induce immunity through the production of protective antibodies against epitopes on the hemagglutinin S-glycoprotein binding site (Rawat *et al.*, 2020).

The conventional development of inactivated vaccines possess major safety concerns as it requires bio-safety level 3 facilities to culture high titers of the SARS-CoV-2, also incomplete virus inactivation would lead to a disease outbreak among the vaccinated individuals, which can potentially lead to a health care crisis (Frederiksen *et al.*, 2020).

Live Attenuated Vaccines

Live attenuated vaccine utilizes a weakened live pathogen to generate an immune response without causing an infection, thereby mimicking the properties of a natural infection. This type of vaccine can induce a strong lifelong humoral and cellular immune response compared to the inactivated vaccine with two doses. The vaccine formulated against COVID-19 by the Serum Institute of India has utilized the viral gene deoptimization method, which involves computer-aided gene design with chemical synthesis.

Live attenuated vaccines on intranasal administration can produce IgA and provide a local mucosal immunity (Rawat *et al.*, 2020). They have several advantages over other vaccine platforms as they can induce an immune reaction against several variations of the antigens formed by the virus (Frederiksen *et al.*, 2020).

Despite its effectiveness and advantages, these vaccines are not devoid of disadvantages. As the SARS-CoV-2 virus is excreted through faeces, the live attenuated strains may also get excreted post-administration through the same route. Thus it can potentially generate an infection in unvaccinated individuals or via recombination of live attenuated strains with any wild type CoV post elimination in the faeces produce virulent strains (Frederiksen *et al.*, 2020).

Protein Subunit Vaccines

These vaccines are generated based on recombinant proteins or synthetic peptides of the target pathogen. They use only specific viral antigenic fragments and are devoid of any other components of the pathogenic virus thus surpassing any potential pathogenic effect incurred when administering whole viral particle. This type of vaccine candidates possesses additional advantages such as a better safety profile, cost-effectiveness and long-lasting therapeutic immune response with adjuvants (Rawat *et al.*, 2020). These vaccines can only produce a humoral response.

Clover Biopharmaceuticals has developed a SARS-CoV-2 S-trimer subunit vaccine candidate and the University of Queensland had used molecular clamp stabilized spike protein technology for the development of the COVID-19 vaccine (Rawat *et al.*, 2020). The University of Pittsburgh has used a micro-needle array based recombinant technology, which comprises administering recombinant immunogens.

Viral-vectored Vaccines

This technique involves a modified virus used as a vector to deliver a gene that instructs cells to produce SARS-CoV-2 spike protein, expressing it on the surface of human cells, thereby triggering an antibody production evoking an immune response.

Several viruses such as influenza, stomatitis virus, measles virus have been used to develop viral vector vaccines (Le *et al.*, 2020; Lundstrom, 2020). Adenovirus and poxviruses can be used in both replicating and non-replicating viral vector forms. The replicating viral vectors include measles virus, poliovirus, yellow fever virus and vesicular stom-

atitis virus and non-replicating vectors include adenovirus, alphavirus and herpes virus (Rawat *et al.*, 2020).

Lately, Adenovirus is also used as one of the viral vectors as it can be produced on a large scale, are easy to design and can generate high levels of recombinant protein expression. One of the major drawbacks of these vectored vaccines is if the vaccine fails to provide an immune response, then using the same vector vaccine for any other infection in those patients can trigger an immune response against viral vector making the subsequent vaccine ineffective to evoke an immune response (Frederiksen *et al.*, 2020).

The vaccines developed by Oxford University-AstraZeneca is an example of viral vector vaccines and has been approved by WHO and marketed as "Covishield" for use among frontline healthcare workers and public and comes in two doses and should be refrigerated at 2-8°C.

DNA Vaccine

A DNA vaccine delivers genes that encode immunogenic antigens to the host cell through vectors such as DNA plasmids, which can induce both humoral and cell-mediated immune response. This kind of formulation provides genetic instructions which reach the host cell nucleus and instructs it to build harmless spike proteins. Antigen presenting cells receive the genetic material, after which the mammalian promoter gets stimulated and initiates the transcription of the gene. Some of the advantages of DNA vaccines are low-cost production, high stability, can be stored for a long time with less need for refrigeration at very low temperatures and can be produced efficiently on a large-scale (Silveira *et al.*, 2020).

mRNA Vaccine

Messenger RNAs are a significant and viable therapeutic tool for vaccine development. It is a non-integrating and emerging vaccine platform with less or reduced risk of insertional mutagenesis. The mode of action and efficacy of mRNA vaccines are superior as it does not need to reach inside the cell nucleus (Silveira *et al.*, 2020). Messenger RNA is an unstable molecule but can be designed and developed into a nucleoside-modified mRNA enclosed in lipid nanoparticles to improve its stability, induce a defensive and protective antibody response and improve the efficiency of protein translation. These vaccines consist of an mRNA that codes for a protein antigen. When entered into the body, the host cells can take in the mRNA and initiate translation into proteins (Jackson *et al.*, 2020; Lederer *et al.*, 2020).

There are currently two mRNA vaccines from Pfizer/BioNTech and Moderna approved for marketing. Moderna vaccine is permitted for use in 18 years and older and Pfizer vaccine allowed for use in people of 16 years or older by WHO.

Virus-Like Particles (VLPs)

These are multimeric structures that are assembled similar to viral structural proteins to trigger immune cells instantly by mimicking the 3D conformation of the SARS COV-2 virus. Though they do not hold any genetic material, they morphologically resemble the SARS-CoV-2 virus, thereby triggering an immune response (Swann *et al.*, 2020). These vaccines can penetrate the host cell using a functional viral protein (Spike protein) therefore ensuring cell entry. They induce a humoral immune response by stimulating antibody production via a high density B – cell epitope and intracellular T-cell epitope, respectively. VLPs are safer than attenuated and inactivated form of vaccines (Ghorbani *et al.*, 2020). Studies have revealed that using a mammalian expression system would help in sustaining the exact configuration of glycosylated proteins (Xu *et al.*, 2020; Chan *et al.*, 2020).

Premas Biotech in India used a triple antigen vaccine, which involves co-expressing recombinant S, M and E protein in genetically engineered *Saccharomyces cerevisiae* (Kaur and Gupta, 2020).

Current Status of Vaccine Candidates In Pipeline

Currently, there are more than 50 vaccine candidates on the run with 3 frontrunner vaccines developed by Pfixer/BioNTech, Moderna and Oxford/AstraZeneca. As of 4^{th} March 2021, there are 177 vaccines in Pre-clinical trials, 19 vaccines in Phase 1, 25 vaccines has reached Phase 2 and 21 vaccines have entered Phase 3 (Polack *et al.*, 2020). FDA approved marketed vaccines and the current status of vaccine candidates in the pipeline is listed in Table 2, Table 3 respectively.

Vaccine Safety

Vaccine related adverse effects are one of the major public concerns. An extensive and thorough analysis should be done to avoid any immuno-potentiation reaction (Raja *et al.*, 2020).

A clinical trial conducted on the safety and efficacy of Pfizer (Germany/US) vaccine has shown that the vaccine has 95% efficacy against COVID-19 infection in people older than 16 years. Mild adverse vaccine reactions such as fatigue, mild-moderate pain at the site of injection and headaches were noted, which improved within 2-3 days (Polack *et al.*, 2020).

Moderna vaccine (US) has shown 94.1% efficacy against COVID-19, whereas the safety profile

included mild local and systemic reactions during the second dose and serious adverse events were rare (Baden *et al.*, 2021).

Clinical Trials of Oxford/AstraZeneca (UK/US) have shown that the vaccine induces a peak T-cell response by the 14^{th} day and IgG response was identified on the 28^{th} day after the 1^{st} dose, which was further improved with the second dose of immunization. 91% of antibody neutralization response was seen after the first dose and 100% antibody neutralization after the second shot. The efficacy of this vaccine was found to be 70.1% and the safety profile reveals adverse effects such as fever, headache, generalized weakness and body ache. It was found that these effects subsided with a dose of Acetaminophen (Prub, 2021). It can be administered in pregnant women as well.

Janssen Vaccine (Netherlands/US) in Phase2a trials had exhibited 90% neutralizing antibodies with first dose immunization. Fever and injection-site pain is common vaccine-related systemic adverse effect along with muscle pain, fatigue and headache (Kaur and Gupta, 2020).

Sputnik V Vaccine (Russia) and Novavax (US/UK) has shown a strong immune response with a good safety and efficacy profile. Phase 3 trial data revealed 91.6% vaccine efficacy against SARS-CoV-2 infection. 94% of the participants have shown Grade1 reaction towards vaccine (Logunov *et al.*, 2021).

A clinical trial of Covaxin (India) has shown an interim clinical efficacy of 81% in preventing SARS-CoV-2 infection with a 2 dose regimen, 28 days apart. The preclinical trial has demonstrated strong immunogenicity and protective efficacy in animals. Covaxin is developed by inactivating whole-virion in Vero cell (Polack *et al.*, 2020). Contraindication of this vaccine includes a history of drug/food allergies, fever, bleeding disorder, those who are on anticoagulants or antiplatelet medication, immune-compromised individuals, pregnant women and lactating mothers (Ella *et al.*, 2021).

CONCLUSIONS

COVID-19 has become a dreadful pandemic affecting millions of lives all over the world and has contributed to a wide array of psychiatric illness. Vaccine mediated immunity is essential to prevent the spread of the SARS-CoV-2 virus. Developing a vaccine with high efficacy, mild or no adverse effects, single-dose suitable for all ages, lactating and pregnant women is important. Discovering an appropriate and acceptable target for vaccine development is vital to produce a safe and efficacious vaccine. Protein subunit technology is used in majority of the vaccines (32%). Currently, there are 11 vaccines approved for use and approximately 60 vaccines are under clinical development and over 170 candidates are in the pre-clinical phase. As of 23^{rd} February 2021, approximately 12 million doses of vaccines have been given in India.

Funding Support

The authors declare that they have no funding support for this study.

Conflict of interest

The authors declare that there is no conflict of interest for this study.

REFERENCES

Baden, L. R., Sahly, H. M. E., Essink, B. 2021. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. *New England Journal of Medicine*, 384(5):403–416.

Chan, S. K., Du, P., Ignacio, C., Mehta, S., Newton, I. G., Steinmetz, N. F. 2020. Biomimetic Virus-Like Particles as Severe Acute Respiratory Syndrome Coronavirus 2 Diagnostic Tools. *ACS Nano*, 15(1):1259–1272.

Chung, Y. H., Beiss, V., Fiering, S. N., Steinmetz, N. F. 2020. COVID-19 Vaccine Frontrunners and Their Nanotechnology Design. *ACS Nano*, 14(10):12522–12537.

Corey, L., Mascola, J. R., Fauci, A. S., Collins, F. S. 2020. A strategic approach to COVID-19 vaccine R and D. *Science*, 368(6494):948–950.

Ella, R., Vadrevu, K. M., Jogdand, H., Prasad, S., Reddy, S., Sarangi, V., Ganneru, B., Sapkal, G., Yadav, P., Abraham, P., Panda, S. 2021. Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBV152: a double-blind, randomised, phase 1 trial. *The Lancet Infectious Diseases*, pages 1–10.

Frederiksen, L. S. F., Zhang, Y., Foged, C., Thakur, A. 2020. The Long Road Toward COVID-19 Herd Immunity: Vaccine Platform Technologies and Mass Immunization Strategies. *Frontiers in Immunology*, 11.

Ghorbani, A., Zare, F., Sazegari, S., Afsharifar, A., Eskandari, M. H., Pormohammad, A. 2020. Development of a novel platform of virus-like particle (VLP)-based vaccine against COVID-19 by exposing epitopes: an immunoinformatics approach. *New Microbes and New Infections*, 38:100786.

Hageman, J. R. 2020. The Coronavirus Disease 2019 (COVID-19). *Pediatric Annals*, 49(3):e99–e100.

Jackson, L. A., Anderson, E. J., Rouphael, N. G., Roberts, P. C., Makhene, M., Coler, R. N. 2020. An mRNA vaccine against SARS-CoV-2-preliminary report. *New England Journal of Medicine*, 383:1920–1931.

Kaur, S. P., Gupta, V. 2020. COVID-19 Vaccine: A comprehensive status report. *Virus research*, page 198114.

Le, T. T., Andreadakis, Z., Kumar, A., Román, R. G., Tollefsen, S., Saville, M., Mayhew, S. 2020. The COVID-19 vaccine development landscape. *Nature Reviews Drug Discovery*, 19(5):305–306.

Lederer, K., Castaño, D., Atria, D. G. 2020. SARS-CoV-2 mRNA Vaccines Foster Potent Antigen-Specific Germinal Center Responses Associated with Neutralizing Antibody Generation. *Immunity*, 53(6):1281–1295.

Li, H., Liu, S. M., Yu, X. H., Tang, S. L., Tang, C. K. 2020. Coronavirus disease 2019 (COVID-19): current status and future perspectives. *International journal of antimicrobial agents*, 55(5):105951.

Logunov, D. Y., Dolzhikova, I. V., Shcheblyakov, D. V., Tukhvatulin, A. I., Zubkova, O. V., Dzharullaeva, A. S. 2021. Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia. *The Lancet*, 397(10275):671–681.

Lundstrom, K. 2020. Application of Viral Vectors for Vaccine Development with a Special Emphasis on COVID-19. *Viruses*, 12(11):1324.

Parasher, A. 2020. COVID-19: Current understanding of its Pathophysiology, Clinical presentation and Treatment. *Postgraduate medical journal*, pages 1–9.

Polack, F. P., Thomas, S. J., Kitchin, N. 2020. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. *New England Journal of Medicine*, 383(27):2603–2615.

Prub, B. M. 2021. Current State of the First COVID-19 Vaccines. *Vaccines*, 9(1):1–30.

Raja, A. T., Alshamsan, A., Al-jedai, A. 2020. Current COVID-19 vaccine candidates: Implications in the Saudi population. *Saudi Pharmaceutical Journal*, 28(12):1743–1748.

Ramezankhani, R., Solhi, R., Memarnejadian, A. 2020. Therapeutic modalities and novel approaches in regenerative medicine for COVID-19. *International Journal of Antimicrobial Agents*, 56(6):106208.

Rawat, K., Kumari, P., Saha, L. 2020. COVID-19 vaccine: A recent update in pipeline vaccines, their design and development strategies. *European Journal of Pharmacology*, 892:173751.

Sharma, O., Sultan, A. A., Ding, H., Triggle, C. R. 2020. A Review of the Progress and Challenges of Developing a Vaccine for COVID-19. *Frontiers in Immunology*, 11:2413.

Silveira, M. M., Moreira, G. M. S. G., Mendonça, M. 2020. DNA vaccines against COVID-19: Perspectives and challenges. *Life Sciences*, 267:118919.

Swann, H., Sharma, A., Preece, B., Peterson, A., Eldridge, C., Belnap, D. M., Vershinin, M., Saffarian, S. 2020. Minimal system for assembly of SARS-CoV-2 virus like particles. *Scientific Reports*, 10(1):1–5.

Wang, H., Li, X., Li, X. 2020. Treatment and prognosis of COVID 19: Current scenario and prospects. *Experimental and Therapeutic Medicine*, 20(6):1.

World Health Organization 2014. Principles and considerations for adding a vaccine to a national immunization programme: from decision to implementation and monitoring. pages 1–136.

Xu, R., Shi, M., Li, J., Song, P., Li, N. 2020. Construction of SARS-CoV-2 virus-like particles by mammalian expression system. *Frontiers in bioengineering and biotechnology*, 8.