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April-June 2021

INTERNATIONAL JOURNAL OF MEDICAL, PHARMACEUTICAL AND BIOLOGICAL SCIENCES

eISSN : 2832-787X, pISSN : 2832-7888

Review Article | Volume-1 | Issue-1 | Article ID: 0006

COVID-19 VACCINES APPROVED FOR EMERGENCY USE AND UNDER DEVELOPMENT AROUND THE GLOBE – AN OVERVIEW

Harshal Ashok Pawar[1,*], Anjali Harshal Pawar[2], Sandip Ashok Pawar[3], Prashant Ashok Pawar[4]

[1]Assistant Professor, Department of Pharmacognosy, Dr. L. H. Hiranandani College of Pharmacy, Ulhasnagar-421003, Maharashtra, India.
[2]Naturopathiest, Aai Nature Cure, Ram Baug Lane-1, Kalyan (W)-421301, Maharashtra, India.
[3]Manager, Manufacturing Science and Technology, Sandoz - A Division of Novartis, Kalwe, Navi Mumbai - 400708, Maharashtra, India.
[4]Assistant Manager-External Manufacturing, Glenmark Pharmaceuticals Pvt. Ltd., Andheri (E), Mumbai-400099, Maharashtra, India.

***Corresponding Author: Email:** anjhp83@gmail.com*

Received: 17 April 2021/ Revised: 24 May 2021 / Accepted: 27 June 2021 / Available online: 30 June 2021

ABSTRACT

COVID-19 has caused extensive human casualties with significant economic impacts around the globe, and has imposed new challenges on health systems worldwide. When the genetic sequence of SARS-CoV-2 was revealed, global vaccine companies and scientists have stepped forward to develop a vaccine, triggering a race toward vaccine development that the whole world is relying on. Several vaccines against SARS-CoV-2, the virus that causes COVID-19, have been developed. The first vaccines available in the US (by Pfizer-BioNTech and Moderna) are messenger RNA (mRNA) vaccines. Another mRNA vaccine is available in Europe (CureVac). Other vaccines (by Janssen-Johnson & Johnson, Astra-Zeneca, Sputnik-V, and CanSino) are made using human and primate adenovirus vectors. A third type of vaccine available outside of the US is an inactivated whole-virus SARS-CoV-2 vaccine (by Bharat Biotech, Sinopharm and Sinovac). An effective and safe vaccine could play a pivotal role in eradicating COVID-19. However, few important questions regarding SARS-CoV-2 vaccine development are explored in this review. The present review gives an insight into the current status of vaccine development and associated outcomes reported at different phases of trial.

Keywords *– COVID-19, Vaccine, Coronavirus, Covaxin, Moderna, Covishield.*

1. INTRODUCTION

Rapid spread of severe acute respiratory syndrome coronavirus (SARS-CoV-2), the infection that causes coronavirus disease 2019 (COVID-19), has affected millions of lives since its emergence in December 2019 in Wuhan, China [1]. Public health and mitigation measures, such as social distancing, masks, and hand washing to prevent the spread of SARS-CoV-2, has been met with some resistance and resulted in mixed success based on implementation efforts [2]. As a result, there has been a global urgency for vaccine development. Within a month of the outbreak, scientists sequenced the SARS-CoV-2 genome and used similarities between SARS-CoV-1 and SARS-CoV-2 to accelerate the vaccine discovery process.3 Currently, there are over 180 vaccines in various stages of development worldwide [3]. Recently, two vaccines have received Emergency Use Authorization (EUA) by the Food and Drug Administration (FDA) and 20 others are undergoing phase 3 clinical trials in the United States (US).

Equitable access to safe and effective vaccines is critical to ending the COVID-19 pandemic, so it is hugely encouraging to see so many vaccines proving and going into development. WHO is working tirelessly with partners to develop, manufacture and deploy safe and effective vaccines. But it's not vaccines that will stop the pandemic, it's vaccination. We must ensure fair and equitable access to vaccines, and ensure every country receives them and can roll them out to protect their people, starting with the most vulnerable [4].

2. TYPES OF VACCINES UNDER DEVELOPMENT FOR COVID-19

As per WHO, currently 287 vaccine candidates are under development, out of which 102 are in clinical phase and 185 are in preclinical phase. Several different types of potential vaccines for COVID-19 are in development, including:

- *Inactivated or weakened virus vaccines*, which use a form of the virus that has been inactivated or weakened so it doesn't cause disease, but still generates an immune response.

Example: Covaxin

- *Protein-based vaccines*, which use harmless fragments of proteins or protein shells that mimic the COVID-19 virus to safely generate an immune response.

Example: Novavax

- *Viral vector vaccines*, which use a safe virus that cannot cause disease but serves as a platform to produce coronavirus proteins to generate an immune response.

Example: Sputnik-V

- *RNA and DNA vaccines*, a cutting-edge approach that uses genetically engineered RNA or DNA to generate a protein that itself safely prompts an immune response.

Example: Moderna, Covigen [4,5]**.**

3. VACCINES UNDER DEVELOPMENT AND APPROVED FOR EMERGENCY USE IN DIFFERENT CONTRIES

Vaccines from Pfizer-BioNTech, Moderna, and Johnson & Johnson are being administered in the U.S. right now, and others are on track to do the same. Even though you will likely not be able to choose which vaccine you will get, it's still helpful to know how each one is different. With that in mind, we mapped out a comparison of the most prominent vaccines so far.

3.1 Pfizer & BioNtech Vaccine

This was the first COVID-19 vaccine to receive an approval for emergency use in the US and in the European Union (under the name Comirnaty). It was approved by majority of countries but not yet approved in India. It is mRNA-based vaccine. It has showed 95% efficacy in preventing symptomatic disease. This vaccine was found to be more than 95% effective against the variants first detected in the United Kingdom (B.1.1.7) and South Africa (B.1.351). It is recommended for use in individuals with age more than 12. It is given in two shots with a gap of 21 days. The commonly found side effect includes chills, headache, pain, tiredness, and/or redness and swelling at the injection site, all of which generally resolve within a day or two of rest, hydration, and medications like acetaminophen. (If symptoms don't resolve within 72 hours or if you have respiratory symptoms, such as cough or shortness of breath, call your doctor.) On rare occasions, mRNA vaccines have appeared to trigger anaphylaxis, a severe reaction that is treatable with epinephrine (the drug in Epipens®). For that reason, the Centers for Disease Control and Prevention (CDC) requires vaccination sites to monitor everyone for 15 minutes after their COVID-19 shot, and for 30 minutes if they have a history of severe allergies or are taking a blood thinner. It has required shipping in ultra-cold temperature-controlled units (-94 degrees Fahrenheit).

In mid-February, the company submitted new data to the FDA demonstrating the stability of the vaccine at temperatures more commonly found in pharmaceutical refrigerators and freezers. Approval would make the vaccine easier to distribute. [6-9]

3.2 Moderna Vaccine

It was the second COVID-19 vaccine approved for emergency use in the US and in the European Union. Similar to Fizer vaccine, it was also approved by majority of countries but not yet approved in India. It is also mRNA-based vaccine. It is 94.1% effective in preventing symptomatic infection in people with no evidence of previous COVID-19 infection. It is recommended for an adult with an age 18 and older. It is administered in two shots, 28 days apart. The common side effects can include chills, headache, pain, tiredness, and/or redness and swelling at the injection site, all of which generally resolve within a day or two. On rare occasions, mRNA vaccines have appeared to trigger anaphylaxis, a severe reaction that is treatable with epinephrine (the drug in Epipens®). For that reason, the CDC requires vaccination sites to monitor everyone for 15 minutes after their COVID-19 shot, and for 30 minutes if they have a history of severe allergies. The Moderna vaccine can be shipped and kept in long-term storage in standard freezer temperatures, and stored for up to 30 days using normal refrigeration, making it easier to distribute and store [10-14].

3.3 Johnson and Johnson

This is one more COVID-19 vaccine approved for emergency use in the US and in the European Union. It is not yet approved in India for use. It is a carrier, or virus vector-based vaccine. It has 72% overall efficacy and 86% efficacy against severe disease in the U.S. There was 64% overall efficacy and 82% efficacy against severe disease in South Africa, where the B.1.351 variant was first detected. This vaccine is recommended for an adult with an age 18 and older. It is given as a single shot. The common side effects include Fatigue, fever headache, injection site pain, or myalgia (pain in a muscle or group of muscles), all of which generally resolve within a day or two. It has had noticeably milder side effects than the Pfizer and Moderna vaccines, according to the FDA report released in late February. No one suffered an allergic reaction in clinical trials for the vaccine, according to the company. In comparison to the Pfizer and Moderna vaccines, this one is easier to store (in refrigerator temperature) [15-18].

3.4 Oxford-Astrazeneca Vaccine

It is s**old under the brand names Covishield and Vaxzevria.** It is not yet approved in the U.S., but authorized for use in the European Union (under the name Vaxzevria) and in India (Covishield). It is a viral vector-based vaccine. AstraZeneca updated its data analysis of its phase 3 trials in March, showing its vaccine to be 76% effective at reducing the risk of symptomatic disease 15 days or more after receiving the two doses, and 100% against severe disease. The company also said the vaccine was 85% effective in preventing COVID-19 in people over 65. A paper in early February (not yet peer-reviewed) cited 74.6% efficacy against the B.1.1.7 variant. However, the vaccine did not protect as well against mild and moderate cases in people infected with the B.1.351 variant. On 22 May 2021, Public Health England published an analysis showing that, for symptomatic COVID-19 infection after the second dose, the vaccine is 66% effective against B.1.1.7 (alpha) variant, and 60% against B.1.617.2 (delta) variant. It is recommended for adults with an age 18 and older. It is given in two doses, four to 12 weeks apart. The common side effect includes tenderness, pain, warmth, redness, itching, swelling or bruising at the injection site, all of which generally resolve within a day or two. It can be stored, transported, and handled in normal refrigeration for at least six months [19-23].

3.5 Novavax Vaccine

It is a Subunit / virus-like particle (SARS-CoV-2 recombinant spike protein nanoparticle with Protein adjuvant). It is under development and is not yet approved for use. It is 96.4% efficacy in reducing mild and moderate disease, 100% against severe disease from the original strain of COVID-19. It is found to have 86.3% efficacy in the United Kingdom, where the B.1.1.7 variant is circulating. The vaccine is being studied in adults ages 18-84. It is recommended in two doses, three weeks apart. While the

Novavax vaccine is still being studied, early trials have shown no adverse events. It is also simpler to make and can be stored in a refrigerator [24-30].

3.6 Sputnik-V Vaccine

This vaccine was initially approved for distribution in Russia and then in 59 other countries (as of April 2021) on the preliminary results of Phase I–II studies eventually published on 4 September 2020. On 12 April 2021, India approved the use of Sputnik V vaccine for emergency use against COVID-19 based on strong immunogenicity data. It is a non-replicating Viral vector (Modified Adeno). On 2 February 2021, an interim analysis from the trial was published in The Lancet, indicating 91.6% efficacy without unusual side effects. It can be administered in an adult with age 18 and older. It is given in two shots, second dose after 28 days. No serious side effects have been recorded after taking the Sputnik V shot. There have been instances of hypertension, hemorrhagic stroke, and thrombosis, but there's no confirmation of the vaccine shot being the reason behind it. The vaccine can be formulated in two ways: as a ready-to-use solution in water that is frozen at the common home-freezer storage temperature of −18 °C or 0 °F or lower; and as a freeze-dried powder, "Gam-COVID-Vac-Lyo", whose storage temperature is above freezing, 2–8 °C or 36–46 °F, at the common home-refrigerator temperature. The freeze-dried powder must be reconstituted with water before use. *Sputnik*-Light, a single-dose version, is also being developed to speed up vaccination outside Russia. It will offer less protection than the two-dose versions, but it is still expected to reach an efficacy of 85%. In India, Dr. Reddys Laboratories Limited and Sputnik LLC are jointly conducting multi-centre, phase II/III adaptive clinical trial to assess safety and immunogenicity of Gam-COVID-Vac combined vector vaccine [31-37].

3.7 Covaxin Vaccine

This is the first domestically-produced vaccine to receive approval from the Drug Controller General of India for its emergency or conditional usage. It is inactivated virus-based COVID-19 vaccine. On 3 March 2021, Bharat Biotech reported that Covaxin showed 81% efficacy in a phase 3 trial with 25,800 participants. In December 2020, a new SARS-CoV-2 variant, B.1.1.7, was identified in the UK. An in vitro study on this variant was carried out and preliminary results show Covaxin to be effective in neutralizing this strain. In April 2021, the Indian Council of Medical Research reported that the vaccine has shown promising results in neutralizing the strain B.1.617. In May 2021, a joint investigation by the scientists of National Institute of Virology (NIV) India, found the vaccine effective in neutralizing the P.2 (previously known B.1.1.28) strain. COVAXIN has been approved for restricted use in emergency situation in individuals 18 years of age and older. In May 2021, Drugs Controller General of India (DCGI) approved clinical trials in the age group of 2 to 18 years. The trails are conducted at AIIMS Delhi and Patna. As many as 54 children had registered at the AIIMS Patna. It is given in two shots, second dose after 28 days. The side effects that have been reported in the fact sheet of Bharat Biotech COVID-19 vaccine (COVAXIN) include Injection site pain, swelling, redness, itching, headache, fever, malaise/body ache, nausea, vomiting, and Rashes. A severe allergic reaction may very rarely occur after getting a dose of COVAXIN. These may not be all the possible side effects of COVAXIN. Serious and unexpected side effects may occur. COVAXIN is still being studied in clinical trials. Covaxin can be easily and conveniently stored at 2–8 degrees celsius, which is a regular refrigerator temperature [38-41].

4. CONCLUSION

The quantity of morbidities and mortalities identified with COVID-19 is expanding step by step. Worldwide and neighborhood economies are very nearly gloom, which is fueling philanthropic emergencies across the globe. A large portion of the nations have forced lockdown and stay-at-home-procedure to break the chain of the local area transmission; notwithstanding, these preventive

techniques are not supportable for quite a while. In that capacity, there is a desperate requirement for an immunization against COVID-19. A proficient immunization is the most ideal alternative for controlling and counteraction COVID-19 pandemic.

The COVID-19 antibodies produce security against the infection, because of fostering a resistant reaction to the SARS-Cov-2 infection. Creating resistance through inoculation implies there is a diminished danger of fostering the ailment and its outcomes. This invulnerability assists you with battling the infection whenever uncovered. Getting immunized may likewise secure individuals around you, since, supposing that you are shielded from getting tainted and from illness, you are less inclined to contaminate another person. This is especially critical to ensure individuals at expanded danger for extreme disease from COVID-19, like medical services suppliers, more established or older grown-ups, and individuals with other ailments.

5. ACKNOWLEDGEMENT

Authors are very much thankful to Dr. Paraag Gide, Principal, Hyderabad (Sindh) National Collegiate Board's Dr. L. H. Hiranandani College of Pharmacy, Ulhasnagar for his continuous support, guidance, and encouragement.

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