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REVIEW PAPER

A Review on India's First Domestic Covid-19 Vaccine: Covaxin

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ABSTRACT

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a highly contagious and pathogenic coronavirus that causes respiratory tract infections in humans. SARS-CoV-2 is the causative agent of coronavirus disease 2019 (COVID-19) that emerged in late 2019. This disease has provided various scopes for researchers to develop vaccines and antiviral drugs. After the COVID-19 was declared a pandemic by the World Health Organization (WHO), India joined the global race of developing safe and effective vaccines to protect its citizens as well as the global community from life-threatening disease. The vaccine is the main weapon to fight against COVID-19..COVID-19 vaccination in India was initiated with two types of vaccine: Covaxin and Covishield. This review is aimed at providing an overview of the Covaxin vaccine; ingredients, development, mechanism of action, clinical research data, efficacy, dose, administration, storage, side effects, contraindication and post-vaccination infection rate of the vaccine.

Keywords: - *SARS-CoV-2, COVID-19, vaccine, Covaxin.*

INTRODUCTION

SARS-CoV-2, a newly identified beta-coronavirus, is an enveloped, positive-sense, single-stranded RNA virus that belongs to the family of Coronaviridae.[1] The SARS-CoV-2 genome sequence shares ~80% sequence identity with severe acute respiratory syndrome coronavirus (SARS-CoV) and ~50% with middle east respiratory syndrome coronavirus (MERS-CoV). SARS-CoV-2 contains four structural proteins: spike (S), envelope (E), membrane (M), and nucleocapsid (N), of which Spike mediates virus entry into host cells.[2]. The spike protein of SARS-CoV-2 is a potential target for the development of specific drugs, antibodies, and vaccines.[3]

On 10 May 2020, the Indian Council of Medical Research(ICMR), New Delhi, India - National Institute of Virology(NIV), Pune, India transfers the novel coronavirus strain to Bharat Biotech International Limited (BBIL) for the development of COVID-19 vaccine.[4] On 2 January, the Drugs

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Controller General of India (DCGI) granted emergency use authorization to BBV152 or Covaxin. The world's largest COVID-19 vaccination campaign started in India on 16 January 2020. COVID-19 vaccination in India was initiated with two types of vaccines: Covishield and Covaxin.[5]

COVAXIN

The Indian Company Bharat Biotech partnered with the NIV and the ICMR to develop an inactivated virus-based COVID-19 vaccine called Covaxin.[6]

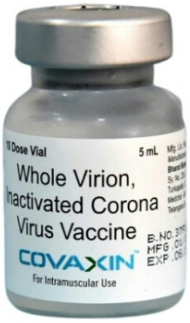


Figure 1: A vial of Covaxin

Ingredients

Active ingredient: 6 micrograms of Whole-virion inactivated SARS-CoV-2 antigen (Strain: NIV-2020-770).

Inactive ingredients: Aluminium hydroxide (alum), Toll-like receptor (TLR) 7/8 agonist – Imidazoquinoline (IMDG), 2-Phenoxyethanol and Phosphate buffer saline.[7]

Development of the vaccine

The SARS-CoV-2 strain(NIV-2020-770) containing the Asp614Gly mutation isolated from a COVID-19 patient and sequenced at the ICMR - NIV, was provided to BBIL. Biosafety level 3 manufacturing facilities and a well established Vero cell manufacturing platform were used for the rapid development of Covaxin.[8]

First, the researchers produced large numbers of the SARS-CoV-2 then poured them into a chemical called Beta-propiolactone. This organic compound deactivates the coronaviruses by binding to their genes. The inactivated SARS-CoV-2 could no longer replicate but their proteins, including the spike, remained undamaged.

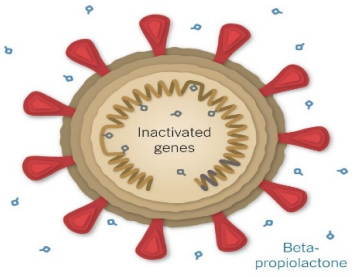
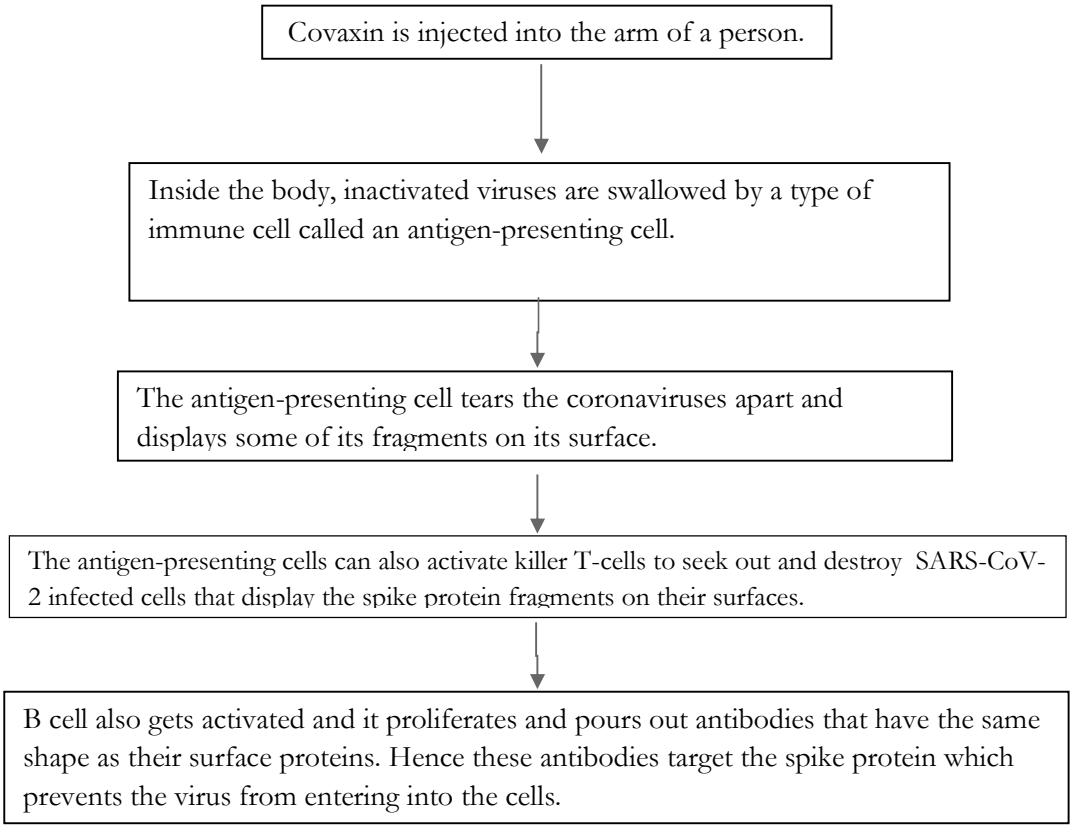


Figure 2: Inactivated SARS-CoV-2

The researchers then extracted the inactivated SARS-CoV-2 and mixed them with a small amount of an aluminium-based compound called an adjuvant.[6] The vaccine was formulated with the Algel-IMDG adjuvant, which is an imidazoquinoline class molecule (TLR 7/8 agonist) adsorbed onto Algel(alum). Adjuvant stimulate the immune system to boost the response of the vaccine.[8]

Mechanism of action

The mechanism of action of Covaxin is given below:-[6]



Flow Chart 1: Activation of the immune system by Covaxin vaccine

Clinical Research and Efficacy

Preclinical trial: Preclinical studies in mice, rats, and rabbits have shown sufficient safety profiles and cell-mediated and humoral responses. Live viral challenge protective efficacy studies in hamsters and non-human primates have shown rapid viral clearance from the lower and upper respiratory tracts, and the lack of lung pathology after viral challenge.[9]

Phase 1: In July 2020, a total of 375 participants (18-55 years) were enrolled in the phase 1 trial and generated excellent safety data without any reactogenicity. Covaxin induced binding and neutralizing antibody responses and with the involvement of the Algel-IMDG adjuvant, this is the first inactivated SARS-CoV-2 vaccine that has been reported to induce T helper type 1 (Th-1) biased response. Follow

up data from the phase 1 trials shows that Covaxin produces humoral and cell-mediated immunity at 3 months after the second dose.[8,9]

Phase 2: In September 2020, 380 participants of 12-65 years were enrolled in phase 2 clinical trial. In the phase 2 trial, Covaxin showed satisfactory safety outcomes and enhanced humoral and cell-mediated response.[9]

Phase 3: Between November 2020 and January 2021, 25,798 participants were enrolled in phase 3 trial between the ages of 18-98 years. Covaxin was found to be immunogenic and highly effective against symptomatic and asymptomatic COVID-19 variant associated disease, especially against severe disease in adults.

Covaxin showed an efficacy of 77.8% against symptomatic COVID-19 disease, by evaluation of 130 confirmed cases, with 24 observed in the vaccine group versus 106 in the placebo group. The efficacy against severe symptomatic COVID-19 disease was found to be 93.4%. The efficacy data showed 63.6% protection against asymptomatic COVID-19 disease.

Covaxin neutralizes the Alpha variant (B.1.1.7) first isolated in the UK, Gamma variant (P.1-B.1.1.28), Zeta variant (P.2 - B.1.1.28) first isolated in Brazil, Kappa variant (B.1.617) first isolated in India, Beta variant (B.1.351) and Delta variant (B.1.617.2) first isolated in South Africa and India. Efficacy data showed 65.2% protection against the Delta variant (B.1.617.2) of SARS-CoV-2.[10][11]

Dose, Administration and Storage

0.5 mL of Covaxin is given as an injection into the deltoid muscle of the upper arm. The vaccination series is 2 doses given 4 weeks apart.

It is a vaccine with no sub-zero storage, no reconstruction requirements, and ready to use liquid presentation in multi-dose vials, stable at 2-8°C.[11]

Side effects

Side effects of Covaxin include pain, swelling, redness and itching at the injection site, stiffness in the upper arm, weakness in the injection arm, headache, fever, malaise, weakness, rashes, nausea, vomiting, body ache.

May cause severe allergic reactions. A severe allergic reaction includes difficulty in breathing, swelling of the face and throat, fast heartbeat, rashes all over your body, dizziness and weakness. Serious and unpredicted side effects may occur.

Contraindications

Covaxin should not be administered in individuals who have any history of allergies, bleeding disorder or are on a blood thinner, fever, received another COVID-19 vaccine, any other serious disease or who are immunocompromised, pregnant and breastfeeding. [7]

Post-Vaccination Infection

As per data on 18 May 2021, breakthrough infections of COVID-19 among those who received Covaxin were 23,940 which is about 0.13% of the total vaccinated people. Out of these, 18,427 people became infected after the first dose of vaccine and 5,513 after the second dose. As per provisional data, 1,90,90,274 doses of Covaxin were administered in India till 18 May 2021.[12]

CONCLUSION

Covaxin is an inactivated viral vaccine developed by BBIL in collaboration with ICMR. The efficacy of Covaxin is 77.8% against symptomatic, 63.6% against asymptomatic and 93.4% against severe COVID-19 disease. Vaccines save millions of lives every year from many diseases. Vaccines work by teaching the immune system of the body to recognize and fight against viruses and bacteria. After vaccination, if the body is later exposed to the same bacteria or viruses, the immune cells of the body immediately attack to destroy them and prevent illness. Although no vaccine can provide 100% protection, the approved COVID-19 vaccine can provide a high level of protection against serious illness and death.

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