



Review articles

The systemic study of various vaccines in term of current status of clinical trial, Safety and effectiveness of covid vaccine

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ABSTRACT

Industries leading the experiment and clinical trial of various vaccines to approve effectiveness and safety on humans. Several of them were documentation for a patent, authorization of clinical trial and marketing. In the review study, we provide an overview of Covid-19, types of vaccine and mechanism of action. Consider the reference of the mechanism of actions such as an inactivated vaccine, vector vaccines, DNA and RNA based vaccine and antiviral drugs already entered in (Phase II and III) clinical trials. The systemic study quantified a summary of various vaccines in the form of the present status of clinical trial, safety and effectiveness according to ICH E6 (R2) guidelines. Due to leading adverse interaction with their toxicity study, the inventor may face challenges during the post-marketing clinical trial. The genuine information allows upcoming scientists to improve the quality, and minimize the adverse effects and avoid resistance power for developing newer drugs.

Keywords: SARS-CoV-2 DNA and RNA based vaccine, vector vaccines and clinical trial.

Received – 22/09/2021, Reviewed - 02/10/2021, Revised/ Accepted- 24/11/2021

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INTRODUCTION

Coronavirus is an infectious illness recognized first known case in Wuhan, China in December 2019^[1]. It is brought about by cut off intense respiratory disorder Covid 2 (SARSCoV-2) and side effects will see in gentle to direct conditions like runny nose, migraine, fever, brevity in breathing, chills, hack, and so forth Around 81% people groups endure with gentle to direct manifestations, while 5% individuals can go through basic condition and 14% individuals can endure with severe symptoms^[1]. Covid can be gotten from group of carbonitride^[2] and subfamily of ortho corona virinae in which infection can change through transformations and seen in different variations like alpha, beta, gamma, delta, kappa, zeta, epsilon, Estimated time of arrival, theta, Particle.

Covid-19 Vaccines

The different antibodies like Covovax, BBV154, and to begin the clinical preliminary in February, Walk 2021. Antibody development is important in light of the fact that in second influx of Covid, different people groups can lose their relatives because of Coronavirus contamination.

Worldwide vaccines under clinical trial before vaccination

In India there are 7 vaccines in clinical trials such as: HGC019, BECOV2A, BECOV2B, BECOV2C, BBV154 This vaccine efficacy not added on table because they are in clinical trial

Table1: - Brief information about vaccines & its clinical trials^[4]

Vaccine Name	Sponsor	Mechanism of action	Clinical trials	Efficacy
Covovax	Novavax Inc., Serum Institute of India	Protein subunit vaccine	Phase3 complete	89.3 %
HGC019	Gennova Biopharmaceuticals Ltd., HDT Biotech Corporate, Seattle	mRNA vaccine	Phase 2	-
BECOV2A	Biological E Ltd., Dynavax Technologies Corporation, Baylor College of Medicine in Houston, U.S.	Protein Subunit vaccine	Phase 2	-
BECOV2B	Biological E Ltd., Dynavax Technologies Corporation, Baylor College of Medicine in Houston, U.S.	Protein Subunit vaccine	There is no trials for phases	-
BECOV2C	Biological E Ltd., Dynavax Technologies Corporation, Baylor College of Medicine in Houston, U.S.	Protein Subunit vaccine	Phase 2	-
BBV154	Bharat Biotech International Ltd., American Company Precision virologics, Washington University	Non-replicating viral vector vaccine	Phase1	-
BECOV2D	Biological E Ltd., Dynavax Technologies Corporation, Baylor College of Medicine in Houston, U.S.	Protein Subunit vaccine	Phase 2	90%

Vaccines are used recently for vaccination against Covid-19 in India

There are 7 vaccines in India which is accepted for 18+ people approved by Drug controlled government of India^[11]. About 280,808,336 people are fully vaccinated in India up to 18 October 2021^[9]. The efficacy rate of vaccines signifies the usefulness of

vaccines against Covid-19. According scientist, Covid-19 vaccines have a lesser amount of effectiveness Delta Variants such as Covishield has been seen efficacy rate drops to 65% & Covaxin 61 % [10,12].

Moderna vaccine (mRNA-1273)

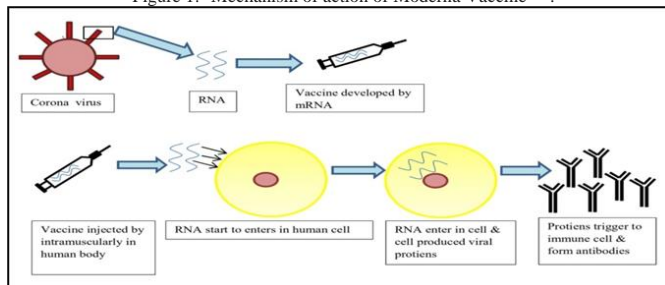
Moderna vaccine developed by Moderna, U.S. National Institute of Allergy & Infectious Diseases (NIAID) & Biomedical Advanced Research & Development Authority. The vaccine is given intramuscularly at 2 dose intervals at least 28 days apart. In India, the Moderna vaccine was approved on 29 June 2021 for eighteen age group people. In the world, nearby 71 countries can accept this vaccine such as Canada, Colombia, Brunei, India Bulgaria, Australia. Storage & Efficacy:-Vaccine will be refrigerated between 2-8° C for up to 30 days & effective as 94.1% against Covid-19. According to the new supply of deal, Moderna price will have Dollar 25.50 per dose[6]. Conferring to the Canadian study, Moderna will be 72% effective from 14 days after the first dose against Covid-19 & its delta Variant. Health workers & older peoples have a greater priority to get vaccinated [7].

Side effects

After vaccination tiredness, headache, nausea, vomiting, fever, headache, pain, redness at the injection site, etc. will be seen [8,9].

Mechanism of action

Figure 1:- Mechanism of action of Moderna Vaccine [10].



Covaxin

Vaccine produced by Bharat Biotech International Limited & National Institute of Virology (NIV) [9]. In India it is approved on 3 Jan 2021 for 18+ age group people. Vaccine kept at 2-8 degree Celsius & dose will be given by intramuscularly at 2 intervals & 2nd dose will be given 4 weeks after first dose. In world, 9 countries approved this vaccine: Iran, Mexico, Nepal, Mauritius, Paraguay, etc. Effectiveness of covaxin vaccine will be 77.8% against Covid-19 virus & worth value of vaccine for government sector will be 150/- per dose and for private sector will be ₹ 1410 in India. The vaccination priority for covaxin in India is to health care workers, front line workers, citizens more than 60 years, citizens more than 45 years of age & then more than 18 years [8].

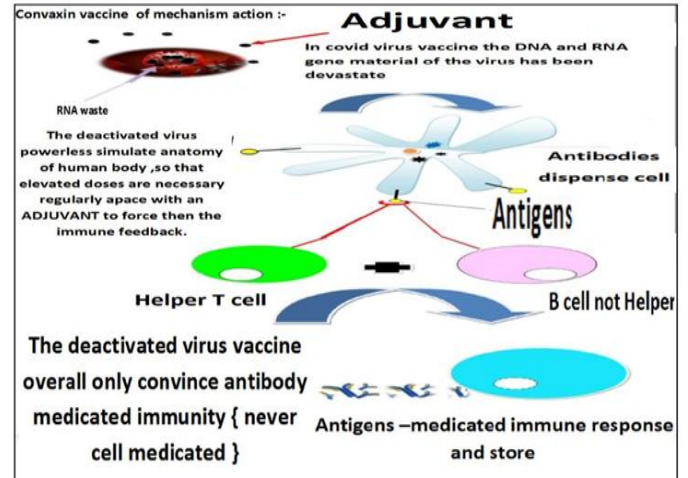
Side effects

After vaccination headache, fever, muscle pain, diarrhea, chills, fatigue severe side effects will be seen.

Mechanism of action

Covaxin is an incapacitated vaccine in which virus genetic material is shattered & acts as dead virus & forms a vaccine. Vaccine injects intramuscularly in human body & it has no potential to replicate in body. Also, use adjuvant such as Alhydroxiqum-II to strong immune response.

Figure 2:- Formation of antibodies [12].

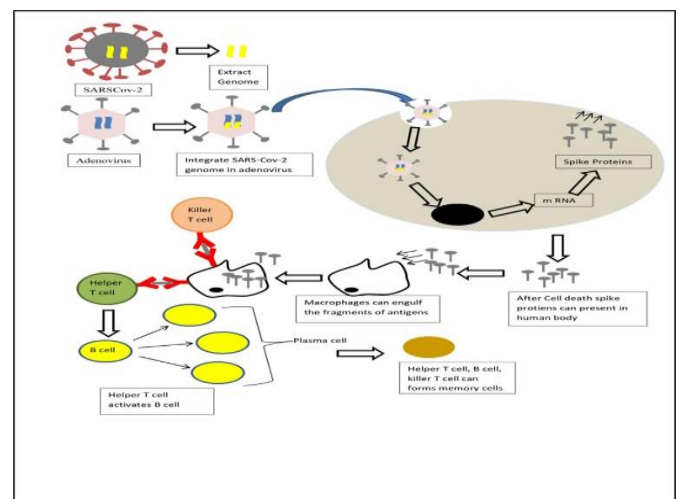


Covishield (AZD1222)

The word “shield” proposes that protection means protection from the Covid-19 virus. The vaccine will be sanctioned in India on 3 Jan 2021 for the age group of 18 above & the vaccine will be manufactured by Astra Zenca & Oxford University & Serum Institute of India. Vaccine dose will be scheduled at an interval of 12-16 weeks from the first dose and 70.42% effective against covid-19. In the world around 121 countries approved Covishield vaccine such as India, Australia, Benin, and Angola.

Mechanism of action

Figure No. 3:- Formation of antibodies of Covishield Vaccine [15]



When vaccine enters in human body, fever, nausea, pain, tenderness at injection site, headache, tiredness, chills, etc. severe side effects will be seen. The price of vaccine in government sector will be 150/- per dose & in private sector will be ₹ 780/- in India and 70.42% effective against covid-19 & stored at 2-8 degree Celsius [12].

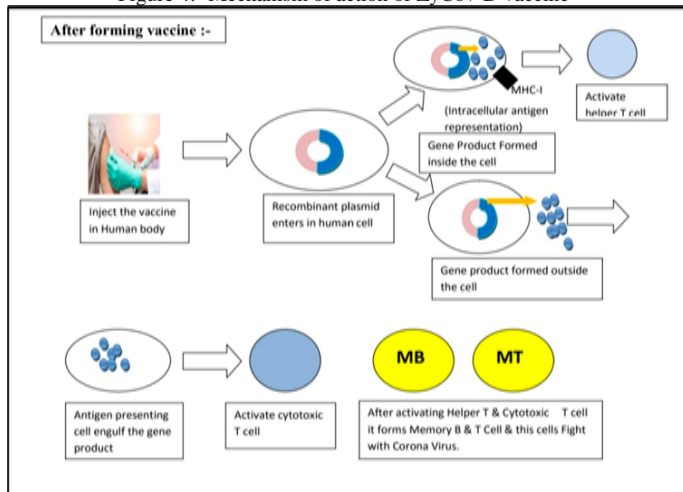
Astrazeneca (AZD1222)

As per the UK study, the AstraZeneca vaccine is extremely effective against the delta variant after the second dose, 33% effective after 1 dose & 88% effective after two doses. Both Covishield and AstraZeneca vaccine formulation is same but different name in country [13,14].

Zycov-D vaccine

This vaccine approved for above 18-year age & 18 year below age group in India. The price of vaccine is not yet announced
Mechanism of action:-

Figure 4:- Mechanism of action of ZyCov-D vaccine



Johnson & Johnson (JNJ-78436735)

These vaccines were developed by the Janssen drug companies of Johnson & Johnson and it was used to treat the viral vector in a single-dose vaccine. The FDA approved vaccine for emergency use authorization for Johnson & Johnson's in 2021 Feb this vaccine stored in normal refrigerator temperatures because it requires only one dose, it easy to distribute in mid of November 2020 vaccine company announced phase 3 clinical trial result using two-dose, its data show provide better protection. It shows 66.9% overall efficacy. The price of the vaccine will be Dollar 25 per dose or Rs 1855. The Johnson & Johnson single-dose vaccine remains stable for two years at -4° F or -20° Celsius & a maximum of three months at a refrigerator at a temperature of 2 to 8°C [13].

Mechanism of action

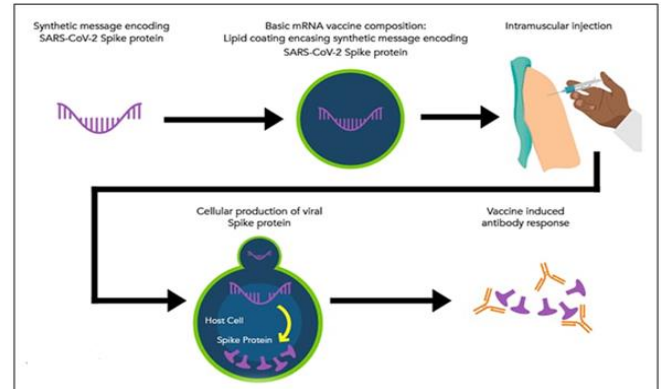
It is a carrier vaccine which have diverse methods compare to mRNA vaccines. It can instruct in human cell by using adenovirus which is harmless to health, it can carry genetic code & yields spike proteins. When cell death occurs, the spike proteins can submerge by macrophages & they can elicits the helper T cell & B cell & destroy the corona virus.

Sputnik-V

Gam-k0VID vaccine was developed by the Gamaleya research institute of epidemiology and microbiology. The Russian department of health registered a vaccine on 11august2021,the world's leading country quickly approached with a vaccine for

emergency use for pandemic critical situation after a best result company developers apply for best vaccine covid-19 after a top-performing company requested the best covid-19 vaccine and WHO presented the vaccine approval list, the top 10 vaccine include the vaccine storage condition require in the vaccine is 2-to-8-degree celcius. It is 91.6% effective against Covid-19. Center Government of India fixes the maximum price of vaccine for private hospitals will be rupees 1145.

Figure 5:- Mechanism of action^[19].



Mechanism of action

Figure 6:- Mechanism of action^[19]

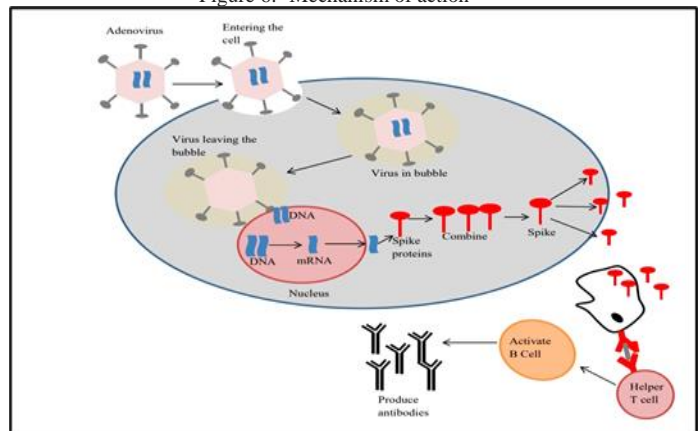
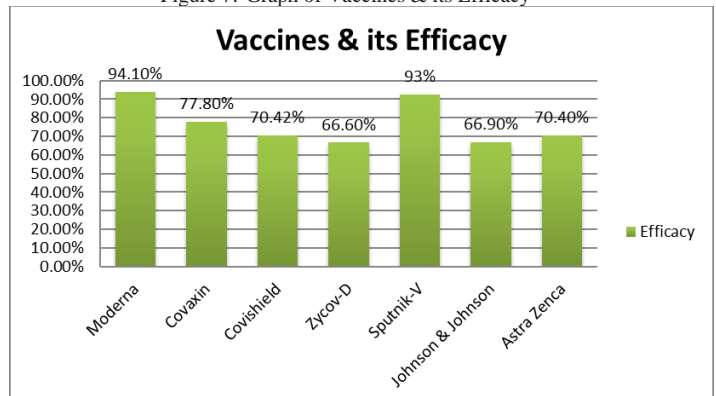


Figure 7:-Graph of Vaccines & its Efficacy



Vaccines under clinical trial & marketed for below 18 age community

In India officials affirmed third wave of corona and he said this wave mostly affected on children below 18 age group some pediatric surgeon studies clinical trial and designed to develop

prescribing information about virus.

In India under 18 age group more vaccine is in the race of trials like,

Covaxin

As we know that Covid-19 vaccine developed by Hyderabad based pharmaceutical company Bharat biotech it's an indigenous anti-Covid 19 giving to children in between 2-6 age group. Thus drug controller of India started trials on children and positive report about immunity develop on children and fight against virus in phase II/III after a successful report are handover to DCGI and moving on next vaccination to grow immunity power in India^[15] If officials say the third wave has hit the country, a trial of the Covaxin vaccine is already taking place at Allms Patna.

Mechanism of action : - The different antibodies like Covovax, BBV154, and to begin the clinical preliminary trial in February, Walk 2021. Antibody development is important of the fact that in second influx of Covid, different people groups can lose their relatives because of Coronavirus contamination^[15].

Zycov-D

Ahmedabad based pharmaceutical company zydus cadilla developed Zycov-D vaccine which have come up for covid-19 pandemic use of vaccination for children in India. This company has applied for licensing permission and it will get it in the next two weeks permission to vaccine trial after a positive result about trials he got approved for emergency use on date 1 July 2021 in between 12-18 age group and the vaccine - 2nd choice of government for children vaccine in India^[19].

Mechanism of action

Zydus Cadila has likewise featured the "quick attachment and play innovation" of ZyCoV-D as something that permits the antibody to "be effectively adjusted to manage transformations in the virus" .A report in the diary 'Nature' says that however researchers have since quite a while ago sought-after immunizations dependent on the DNA stage, a disadvantage has been the insusceptible reaction they have been found to inspire. It takes note of that "notwithstanding being more strong than past DNA immunizations", ZyCoV-D is a three-portion antibody as against the two-portion essential routine that is normal to the greater part of the unmistakable Coronavirus antibodies being utilized as of now, despite the fact that supporter shots are currently being arranged by most pharma majors^[21].

Pfizer

It is already world most famous vaccination in many countries like India, US, EU, UK^[21]. In the second and first wave of covid-19, this vaccine approved by world health organization on an emergency basis for its now aims director also said that Pfizer vaccine not only positive result on adults but will also effective children.

In other country the vaccine already use below 18 age

group for emergency and it tends to be safe vaccine over there in India landmark Pfizer-biotech phase III clinical trials began in late July 2020 and 13 may 2021 DCGI approved for children vaccine in age between 2 to 18 years^[19]

Mechanism of action

Immunizations forestall illnesses that can be perilous, or even lethal. They work with your body's normal guards to securely foster insurance from an infection. An immunization assists your safe framework with delivering antibodies, very much like it would in case you were presented to the infection. Subsequent to getting inoculated, person security from that infection, without getting the sickness.^[19]

Sputnik-v

Also, you must aware vaccination as well sputnik-v vaccine developed by Gamaleya research institute in this vaccine waited for long in India by June end, it will available in Indian market^[20]. It's a first single shot vaccine thus, recently director Gamelya National Research Centre quoted that Sputnik-v vaccine will soon start the clinical trials in India for children according to their age and weight.

Mechanism of action

Sputnik V was the first Covid immunization vaccine to utilize a heterogeneous boosting approach dependent on 2 unique vectors for 2 antibody shots. This methodology produces a more supportable insusceptibility compared with immunizations that utilize a similar conveyance component for the two shots. The security, viability and absence of long-haul antagonistic impacts of adenovirus antibodies have been demonstrated^[18]

CONCLUSION

The flare-up of Covid can influence a world's monetary development and human wellbeing. Various antibodies have an alternate activities viability rate yet have an equivalent plan to annihilate the infection Coronavirus variations can cause a sketchy impact on human wellbeing right now immunizations information can propose that all securely pass immunizations are useful and powerful for generally exhibited Coronavirus infection. For creative thoughts, later scientists can discover in this survey, how does viability will be changed because of sickness variants and likewise help to foster a powerful antibody on different sicknesses as indicated by the premise of their instrument of activities. Corona has made us work harder sharper and faster. India has a novel and faster solution for corona vaccination through Cowin App and Website. To date, 100 Cores Indians are vaccinated and it's a golden mark in the history of this universe. This review emphasis the collaborative and innovative way to treat the global pandemic. A detailed and focused study will be soon published on the effect of the above vaccines on diabetic, hyperlipidemia and immuno compromised patients.

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How to cite this article

Bamb Y R, Bamb P R, Warude B J, Walode S.G, Wagh S N, 2021. The systemic study of various vaccines in term of current status of clinical trial, safety and effectiveness of Covid Vaccine. *Jour. of Med. P'ceutical & Allied. Sci.* V10 - I 6, 2010, P- 3973-3977. doi: 10.22270/jmpas.V10I6.2010