IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 1, April 2024

Advancements in Vaccine Drug Delivery Systems: A Comprehensive Review

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Abstract: *Vaccine drug delivery systems have undergone significant advancements, revolutionizing the landscape of preventive medicine. This review provides a comprehensive overview of various types of vaccine delivery systems, highlighting their mechanisms, advantages, and applications. Traditional vaccine administration methods, such as intramuscular and subcutaneous injections, are being supplemented by novel approaches aimed at improving efficacy, safety, and patient compliance. These include nanoparticle-based carriers, liposomes, microneedle patches, mucosal delivery systems, and DNA/RNA-based vaccines. Each delivery platform offers distinct advantages, such as targeted antigen delivery, controlled release kinetics, enhanced immunogenicity, and needle-free administration. Moreover, the emergence of mRNA vaccines has garnered significant attention for their potential to rapidly respond to emerging infectious diseases. Additionally, the integration of adjuvants and immunomodulatory agents further enhances the immune response, paving the way for next-generation vaccines. Understanding the diverse landscape of vaccine delivery systems is crucial for optimizing immunization strategies, overcoming existing challenges, and combating infectious diseases more effectively in the future.*

Keywords: Vaccine, Dna, Vaccination, Vaccine Drug Delivery, Immuniazation.

I. INTRODUCTION

The term inoculation and inoculation are derived from Variolae (cow disease), a term given by Edward Jenner for cowp ox. [1] This word comes from the Latin word vacca, meaning cow. The development of the first vaccines against smallp ox (Edward Jenner, 1978) and rabies (Louis Pasteur, 1880) is important in the history of disease prevention. If TH cells are not stimulated, antibodies can be used to remove toxins or fight disease. [1] Many vaccines attack the immune syste m. Immunochemists play an important role in advancing our understanding of the immune system and developing vacci nes to meet these needs. [2] In this article, what exactly vaccines are, how they work in the body, and the cost of vaccin es will be briefly explained. This article will also focus on different types of vaccines and their effective administration. Vaccinations against diseases such as rubella, diphtheria, tetanus, whooping cough, Haemophilus influenza type B (chi ldren), hepatitis B, measles, polio, and tuberculosis are becoming more common. [3] 2. National Vaccination Day
National Vaccination Day is celebrated every year on 16 March in India. It is sometimes referred to as National Immuni zation Day (NID). National Immunization Day was first celebrated on March 16, 1995, when the first oral dose of OPV was administered. Every year, India celebrates National Immunization Day in January to mark the launch of the Pulse Polio Programme. India has been running the Polio Pulse Program since 1995. India has one of the largest Universal Im munization Programs (UIPs) using multiple vaccines. The main aim of the program is to ensure that children under the age of two and pregnant women are fully vaccinated with all vaccines. According to this plan, the cost of vaccination is reduced. [4]
Antibiotics are needed to enter the body to prevent various diseases or to control diseases caused by some diseases. [1] Antibiotics work by strengthening the body's immune system to fight various infections. Vaccines are prepared from pathogenic components that provide protection in small doses of 1 to 3 micrograms to milligrams. Protection lasts long er, from one year to lifetime protection. [5]
How do vaccines work?
Vaccines contain certain types of killed or weakened viruses. When the vaccine is injected into the body, it produces sp ecial cells called antibodies that target the virus. These antibodies work when bacteria attack our body. The body fights

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and kills them by creating certain reactions. These antibodies remain in the body throughout life and provide protection when pathogens enter the body. [6]V. Antibiotic ingredients

Immune-providing ingredients

1. Antigen A small part of a weakened or dead organism that can cause disease. They help our immune system learn ho w to fight infections faster and better. [7]

Example: Flu Virus

2. Adjuvants help our immune system respond more strongly to the vaccine. This increases immunity. [8]

Examples: Aluminum, paraffin oil, squalene, calcium phosphate hydroxide, IL-1, IL-2, IL-

The ingredients ensure the vaccine is safe and longlasting

a) Antibiotics: Antibiotics obtained from external bacteria or fungi. [8]

3. Stabilizers

Stabilizers help the active ingredients in the vaccine continue to work during production, storage and transportation of t he vaccine. They prevent changes in active ingredients. [7]

Example: sugar, gelatin

Components used in the reaction process [9]

1. Cell culture materials

Helps develop antibody antigens

Example: Eggs

2. Sterilizing ingredients (sterilizing) [10]

Eat or kill bacteria and viruses growing on the vaccine.

Example: formaldehyde

4. Antibiotics: Used in the immune system to help prevent the growth of external bacteria and viruses

Example: Neomycin

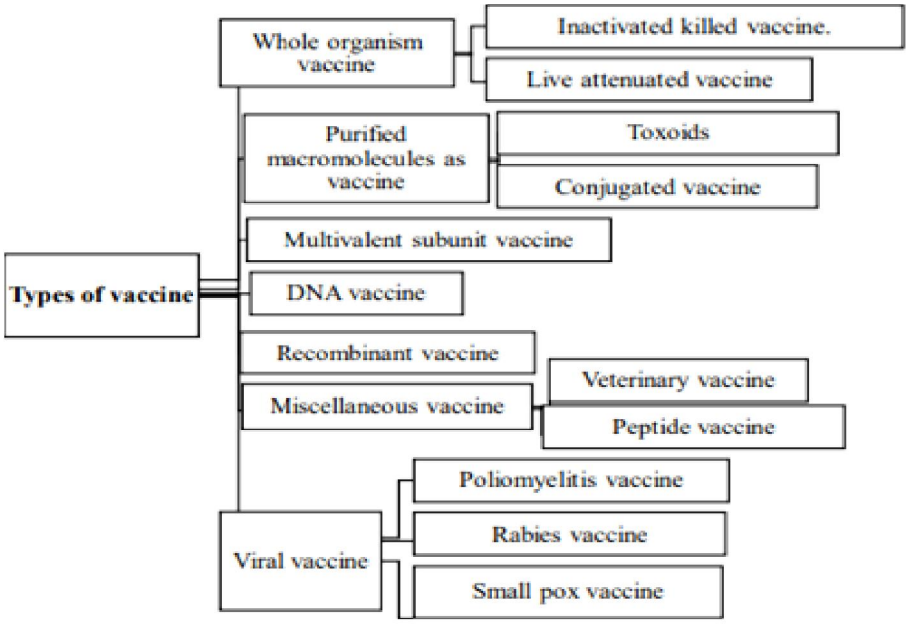

Table no 1 [4]

1. First Generation Vaccines

Inferior and weak vaccines have been identified in the first generation, and important methods are used in their product. Infected viruses, whole viruses or weakened viruses with strong immunity are used to create vaccines. This type of vac cine has the advantage of being able to strongly stimulate the immune system, providing long-

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term protection, easy production, and low production costs (11). However, this generation has some disadvantages, suc h as the effect of diseases due to the use of bad bacteria (live or inactive) and the proliferation of virus virulence in the h ost (12, 13). This type of vaccine is called normal vaccine.

Attenuated vaccine

This type of vaccine, called a live attenuated vaccine, has a large virus, has all the characteristics of a large virus, and is weakened at diagnosis. These antibodies are useful because they can mimic infection, thus leading to effective antibodies and cell protection. Advantages of anti-inflammatory drugs include longterm safety and no need for additional doses (more images) (14). The mechanisms for reducing the number of pathogens may differ depending on the pathogenic factors; For example, in Jenner's approach to smallpox, he used pathogenic bacteria in a different concept that had no known effects on humans. , also available. In addition, the disease can be reduced by tightening the bacteria (adaptation of the cold virus to cold) (16)

Measles, mumps and measles Triple vaccine (MMR) is a well known vaccine. It is a good antidote. It has been available in the United States since 1971 (17). The vaccine contains all 3 viruses, all weakened. All of these strains (measles (Schwarz), mumps (RIT4385), and rubella (Wistar RA27/3)) were obtained from in vitro embryonic or MRC5 human diploid cells, respectively (18). Polio (OPV), influenza, yellow fever and hepatitis A are other vaccines in this group

Inactivated vaccines

The main advantage of inactivated vaccines over attenuated vaccines is the use of inactivated live or killed bacteria, which increases safety and immunity. However, there are some concerns about the return of the features of the disease that caused the disease and the rapid elimination of the disease from the body as there is no growth, which may reduce the effectiveness and efficiency of the vaccine. Comparison with reduced. Hepatitis A antibody is a weak antibody produced using formalin-inactivated hepatitis A virus (type RG-SB) (19). The use of weak vaccines began in the 1940s, with Brazilian researchers pioneering the field (20). The leishmaniasis vaccine is a weak vaccine that has been extensively studied in Iran. A weak vaccine against leishmaniasis was first reported by Mohebali et al. was evaluated by. Iran (21). In a clinical trial conducted in 1998 in Bam, Kerman Province, anti leishmaniasis vaccine (ALM + BCG) was used for personal vaccination against leishmaniasis (22).

Second Generation Vaccines

First generation vaccines are made from live bacteria, bacteria that can return to its natural form, become infected, and e ventually cause disease and pain. Therefore, scientists and researchers developed a second vaccine to solve this problem (23). The basis for this symbol is the expression of immunogens or viruses containing subunit elements, recombinant o r synthetic proteins, nonprotein antigens, and molecules and epitopes from many different species and types of pathoge ns (24). This generation of antibodies include subunit antibodies, conjugated antibodies, and recombinant antibodies. S ubunit antibodies: Viruses, not whole viruses, are used to produce this type of vaccine. The antibody subunit consists of one or more protein peptides or polysaccharides found in pathogenic samples (25). Because the bacteria are part of th e vaccine subunit, they cannot expand, which causes a surprise. They are a viable alternative to traditional vaccines due to their high immunogenicity and low production costs (13)

1.Subunit vaccines

fall into 2 simple things; First, its poison is a toxoid, which is a great antidote. The poison is neutralized using inactive formaldehyde, converted into a non-poisonous form (toxoid), which is then used for injection purposes. Toxoids are similar to toxins and enable the body to fight diseases through antibodies. Tetanus, diphtheria and pertussis toxoid vaccines will be evaluated in this category. The latter consists of polysaccharide capsules that encapsulate the bacteria. Because the antigen (mostly polysaccharide) is bound together by a carrier protein called conjugate (26, 27)

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2. Conjugated vaccine

polysaccharide antigens are large molecules with reverse epitopes that cannot form the antigen directly in this brain, that is, cannot form the drug. It occurs without the participation of T cells and leads to the development of antibodies in small doses and in a short time (28-29). This response does not weaken the immune system and desire against such pathogens (30). Unlike polysaccharide antigens, these proteins are successfully absorbed by the antigen and produce a longlasting response and immunity. In 1929, Avery and Goebel first used proteins to stimulate the body's immunity to polysaccharide antigens. They showed that poor immunity of type 3 Streptococcus pneumoniae polysaccharide antigen in rabbits was ameliorated by binding to the carrier protein. These observations formed the basis for the development of modern conjugate vaccines (31). In 1987, Haemophilus influenza type B (HIB) became the first vaccine licensed for clinical use and was used to protect infants. HIB conjugate prepared from various carrier proteins, including tetanus toxoid, diphtheria toxoid, diphtheria toxin mutants, and outer membrane proteins, causes quantitative and qualitative increases in their immunogenicity (32).may be lost after General planning [38] [39)

3. Recombinant Vaccine

Today, advances in genetic engineering and molecular biology have had a great impact on the development and product ion of vaccines. Specific antigenic bacteria have the ability to trigger strong immune responses. Currently, the sequence of the pathogenic protein antigen can be constructed by combining the genes of the parent antigen and combining them with recombinant DNA technology. Hepatitis B is one of the first and best examples of a synthetic vaccine. Antibodies (HBsAg) formed against the surface of the virus are antibodies and are effective, they have the capacity to produce anti bodies in the body (33)

Other antibody infections are herpes simplex vaccine, rotavirus vaccine and rabies vaccine. antidote. -HPV vaccine

Third Generation Vaccines

The immunogenic potential of plasmids containing genes encoding antigens called antibodies is classified as third generation vaccines and is a valuable method that has been studied by researchers since the early 1990s. This type of vaccine is called by different names such as anti-DNA, anti-RNA and antiplasmid. In 1996, the World Health Organization Immunization Committee designated nucleic acid vaccines, including anti-DNA and anti-RNA vaccines. In addition, the concepts of genetic immunity and DNA immunity are also used for this type of DNA vaccine; This involves direct injection of a plasmid containing the gene-encoding antigen of interest, which is presented in cells with the help of specific promoters. It stimulates the immune system. Therefore, instead of prescribing recombinant drugs required to stimulate the immune system (for example, in hepatitis B), cellular and humoral immunity can be stimulated at various levels by producing the expression of these proteins in the body. Dendritic cells play an important role in providing antibodies to the immune system (34 , 35) against hepatitis, HIV, influenza, and Ebola (36).

Mechanism of Action

To initiate the immune response against an infection, T cells need a variety of signals. The signal is an antipeptide antigen (Ag) that binds to major histocompatibility class II (MHC) and class I displayed on the surface of antigenpresenting cells (APCs). Signal 2, also known as costimulation, works with signal 1 to stimulate the immune system (Figure 1). The second signal involves the binding of CD28 and other receptors of T cells onto costimulatory molecules such as B7-1 (CD80), B72 (CD86), and other ligands expressed by APC. Signal 3 is derived from cytokines and transmitted from APC to T cells that decide to differentiate into effector cells. Signals 2 and 3 are both delivered to T cells by activated cells (DCs). Mature DCs can stimulate the proliferation of T cells and activate the immune system. [37]

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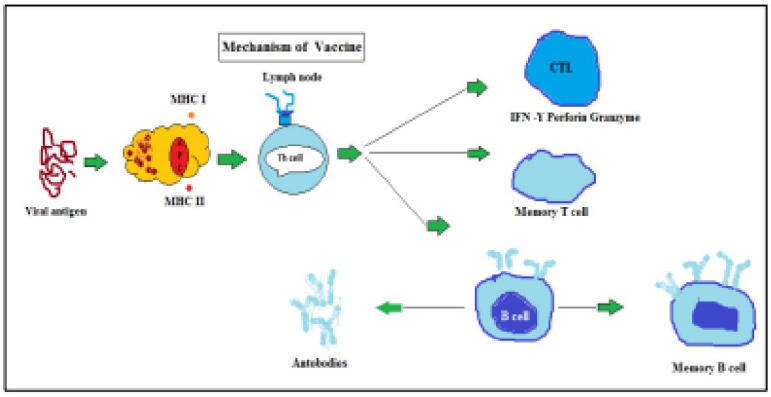


Figure 1 Mechanism of the reaction (37)

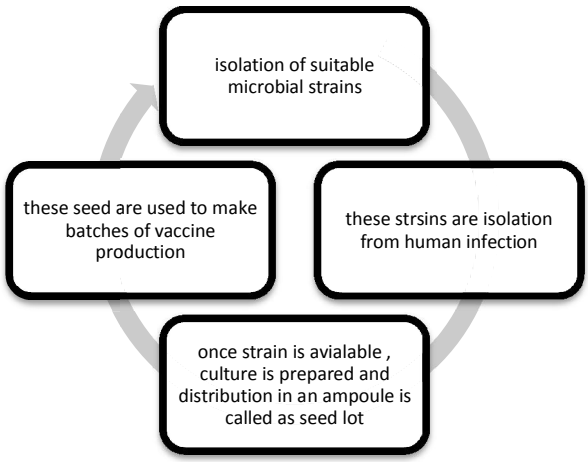
Advantages of the reaction [38]

1. Prevent infection.
2. Provides protection against harmful diseases.
3. Protects chemicals from degradation.
4. Virions are biodegradable, biocompatible and non-toxic.
5. It ensures the transport of the drug into the cytoplasm of target cells. 6. Prevents infectious diseases and infections. 7. Prevention is more expensive than treating patients.
8. It promotes fusion in the endolysosomal pathway.
9. There is no autoimmunity. 10. There is no risk of infection.

Disadvantages of vaccines[38]

1. Shelf life is very short.
2. Vaccines can sometimes cause serious side effects, even in the fetus.
3. Booster shots can be difficult.
4. He may be unhappy or sick.
5. It is not guaranteed to work or provide 100% protection.
6. The ability to have fun.
7. Antigenicity

1. Seed lot system



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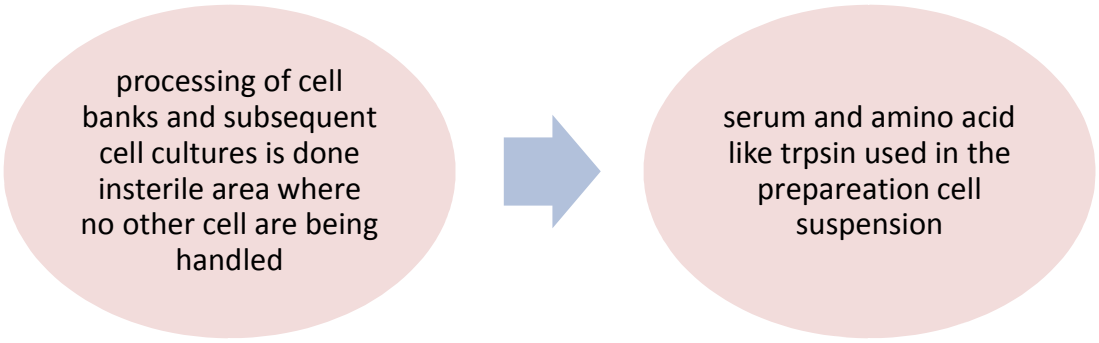
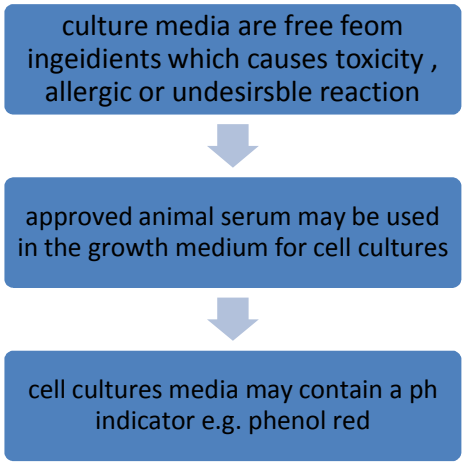
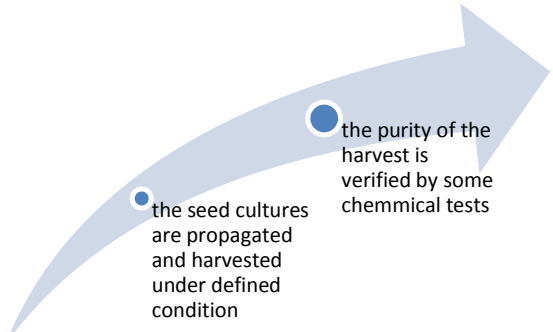
2. Substrate for Propagation Isolation of suitable microbial strains



3. Culture Media



4. Propagation and Harvest



Marketed example of vaccine (40)

Sr no	Manufactured by	Vaccine Marketed	preparation Company	founded	Location
1	Lupin Pvt.Ltd	Pneumococcal vaccine	Pneumovax 23	1968	Pune
2	Panacea Biotech Ltd	Hepatitis B vaccine	Hepatitis B (recombinant) Ecovac Enivac HB	1984	New Delhi

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3	Bharat serum and vaccine Ltd	Hepatitis B (recombinant) vaccine	Heppacine B	1971	Mumbai
4	Serum institute of India	BCG vaccineTetanus vaccine I.P Measles and rubella vaccine Poliomyelitis vaccine I.P	Tubervac Tetanus vaccine MR-VAC Poliovac PFS/SD 1996 Pune	1996	1996

Vaccination Equipment

Automatic Lethal (AD) Syringes and safety boxes AD syringes are used because they are designed to prevent reuse, thus minimizing the risk of human-to human transmission of blood cells. It is the preferred tool for administering vaccines in mass vaccination programs. The risks posed by needles and syringes to healthcare workers and the public can be reduced by the use of sterile containers (socalled safety bins) to collect and dispose of disposable and unused syringes, needles and other equipment. Automatic syringes are now widely available at low costVaccination Equipment

1. Automatic Lethal (AD) Syringes and safety boxes AD syringes are used because they are designed to prevent reuse, thus minimizing the risk of human-to human transmission of blood cells. It is the preferred tool for administering vaccines in mass vaccination programs. The risks posed by needles and syringes to healthcare workers and the public can be reduced by the use of sterile containers (socalled safety bins) to collect and dispose of disposable and unused syringes, needles and other equipment. Automatic syringes are now widely available at low cost. [41]

2. Use of sharps waste disposal technology The reason for using sharps waste disposal techniques is that the risk of stori ng and handling syringes and needles end up in waste will be reduced by: blade selection (i.e. separation, encapsulation or disposal of needles), sterilizing and compressing. After sterilization, the possibility of contamination is reduced and t he storage and transportation process becomes more efficient after compression. [41]

Some technologies are mentioned below:

- Chemical disinfection
- Heat treatment or melting
- Needle destroyer
- Transmission power of plasma melting and small incineration
- Disposable vaccine
- It is a mixture of the main antigen with appropriate material and microsphere components. [42]

The importance of one shot [42]

1. Biodegradation technology
2. Particle size distribution
3. Encapsulation efficiency
4. Treatment of toxic water during production and release
5. Scalable production process
6. Effect of mixing with various additives
7. Effects of Different Control Methods

The size of the microspheres can be controlled by the shear force used during the emulsification step. The presence of e xcipients in the starting composition will change the matrix density and encapsulation efficiency of the microsphere pro duct. [43] For example, DTap (diphtheria-tetanus-pertussis), trivalent IPV (tri-
strain inactivated polio vaccine), MMR (measles-mumps-measles), etc.

Quality of Practice

Sterility test

When testing for bacteria the culture averages 30" to 37"; When testing mushrooms, the culture medium should be at 20 " to 25" for not less than 14 days. However, in live vaccines, the inoculated bacteria are allowed to multiply. [44]

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Combination Vaccines

Development of combination vaccines to protect against various diseases, starting with combining diphtheria, tetanus a nd pertussis (DTP) in a single product; This combination vaccine was first used to immunize infants and children in 194 8. Combination vaccines are a solution to the problem of increasing vaccination. [4]

Advantages of combined reaction [4]

1. There are fewer shots.
2. Minimize injury to the child.
3. Compliance with the vaccination program is higher.
4. The response is better.
5. Get vaccinated immediately.
6. Lower storage space.
7. Allow new vaccines to be introduced into the vaccination schedule.
8. Reduce management costs

II. CONCLUSION

The conclusion regarding vaccine drug delivery methods is that various types exist, each with its advantages and limitations. These include traditional injectable vaccines, oral vaccines, nasal vaccines, and newer technologies like microneedle patches and mRNA vaccines. Each type offers unique benefits such as ease of administration, enhanced immune response, and potential for self-administration. However, factors such as stability, scalability, and cost-effectiveness must be considered when choosing the appropriate delivery method for specific vaccines and populations. Continued research and development are essential to optimize vaccine delivery and ensure widespread immunization coverage.

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Volume 4, Issue 1, April 2024

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