Nanobiotechnology And Its Application in Vaccine Delivery

Abstract:

The term "nanobiotechnology" refers to the use of nanotechnology in biological fields. Nanotechnology is a multidisciplinary area that is currently recruiting approaches, technologies, and capabilities from traditional and advanced engineering, physics, chemistry, and biology. Vaccination has made a huge difference in human health. Despite advances in this area, there is no effective vaccine for a large number of diseases, and some of the available ones do not offer long-term immunity. Numerous studies have been conducted recently to determine the feasibility of using nanostructures as an effective method for vaccine delivery, and the initial findings have been encouraging. So, in the present review, we will address which types of nanoparticles are appropriate for vaccination delivery and reveal and discuss the significance of virus-like particles (VLPs), liposomes, polymeric-based nanoparticles Polyanhydride-based nanoparticles for vaccine delivery. It is crucial to understand their size, shape, charge, porosity, and hydrophobic properties. In conclusion, nanotechnology will help to have a brief understanding of nanotechnology in the delivery of vaccines. So, it could also motivate new strategies for human disease prevention or treatment.

Keywords: Nanobiotechnology, Nanoparticle (NP), Vaccine delivery, Virus-like particle, Polyanhydride-based nanoparticles, liposomes.

1. Introduction:

Nanotechnology is one of the most exciting fields of science and technology in the twenty-first century. It is the capacity to apply nanoscience theory to practical applications through the observation, measurement, manipulation, assembly, control, and manufacture of matter on the nanometer scale [1]. In the United States, the National Nanotechnology Initiative (NNI) defines nanotechnology as "a science, engineering, and technology conducted at the nanoscale (1 to 100 nm), where novel phenomena allow novel applications in a variety of fields, ranging from chemistry, physics, and biology to medicine, engineering, and electronics" [2].

Food and drug administration (FDA) approval is needed for therapeutic authorization of nanotechnology applications and significant regulatory issues in nanotechnology-based products. As a result, the word "nanobiotechnology" was created [3].

Nanobiotechnology is known to be the only combination of biotechnology and nanotechnology that enables the real-world application of classical microtechnology to a molecular biological approach. This technique enables the fabrication of atomic or molecular-scale machines by mimicking or integrating biological systems or developing miniature tools for studying or modulating a biological system's various properties on a molecular level [4].

Researchers in the field of nanomedicine have been increasingly examining the relationship between the ability of various nano-systems and viral vectors to transport genes and their high infectivity. Researchers in nanomedicine have investigated the molecular dynamics of vectors in order to build delivery systems that can be used in several applications [5], [6]. Since nanoparticles (NPs) and viruses operate on the same level, the nanotechnology procedure is highly effective in the delivery of vaccines and immunosuppressants [7].

The creation of vaccines is one of medicine's most important accomplishments [8]. Traditional vaccination approaches, such as the introduction of live or killed pathogens, create a poor immune response and do not fully eliminate the viral load; thus, nanoparticles attract attention in recent years due to their various attractive characteristics for vaccine production[9], [10]. Generally, nanostructures play two key roles in the manufacturing of vaccines. First, they are

included in vaccines' delivery; second, they could enhance immune responses because of their intrinsic adjuvant [11]–[14]. Nanostructure materials are classified into three main groups, based on the dimensions of the structural elements: nanofibers (one-dimensional), nanotubes (two-dimensional), and nanoparticles (three-dimensional)[15].

Of nanostructure materials, nanoparticles are the most used ones in vaccine studies. Vaccine-associated nanoparticles come in a variety of forms, including virus-like particles (VLPs), polyanhydride-based nanoparticles, and liposomes polymeric-based nanoparticles. [16].

In the present review, we will address which types of nanoparticles are appropriate for vaccination delivery and reveal and discuss the significance of virus-like particles (VLPs), Polyanhydride-based nanoparticles, and liposomes polymeric-based nanoparticles for vaccine delivery. It is crucial to understand their size, shape, charge, porosity, and hydrophobic properties.

2. Nanobiotechnology

Scientists are still looking for natural inspiration for their studies. On earth, the bulk of the organic structures are nanoscale. A researcher can obtain in-lab findings to use all the biological theories in the processing, characterization methods, and formulating of the nanoscale's biomolecules and devices using biological systems in chemistry, physics, nanotechnology, and engineering principles. A new invention recognized as nanobiotechnology has been developed using such findings [17].

By definition, nanobiotechnology is a multi-strategy system that involves nanotechnology and biotechnology to optimize therapeutic agents' effects, such as targeted delivery of therapeutics through nanoparticles [18], [19]. In developing and implementing many useful tools for studying life, integrating these two technologies, i.e., nanobiotechnology, may play a significant role.

Diseased or inflamed tissues can produce a range of targeted nanotechnological products according to the pathophysiological conditions and anatomic changes. This is an advantage of nanobiotechnology (Figure 1) as follows. Drug targeting can be done by manipulating the specific pathophysiological characteristics of injured tissue [20]. Numerous nanoproducts can be generated at amounts high than those found in conventional drugs [21]. Via improved distribution and retaining, enhanced vascular permeability combined with reduced lymph

drainage in tumors enhances the effect of nano-systems in tumors or inflamed tissues[22]. Nano-systems have the ability to localize themselves selectively within inflamed tissues [23]. The loading of drugs onto nanoparticles changes cell and tissue distribution and results in many selective deliveries of bioactive substances, thus increasing therapeutic effectiveness and minimizing side effects [24], [25].

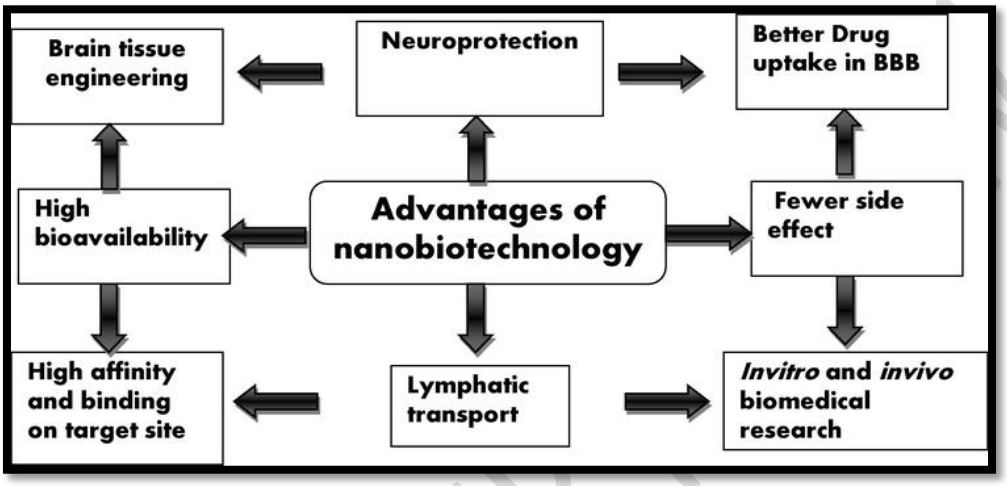

Figure 1: Nanobiotechnology Advantages [26].

Several nanobiotechnology clinical applications are currently under investigation, including medical caring such as improved diagnosis, treatment and prevention, targeted therapy and drug delivery and tissue engineering. There are also clinical trials of some new, promising products (Figure 2)[27]. For instance, a method based on nanoparticles has been established that combines both treatment and imaging modalities for the diagnosis of cancer [28]–[30]. The initial generation of nanoparticle-based therapy used lipid systems such as liposomes and micelles, which have since been accepted by the FDA [31]. Liposomes and micelles may be loaded with inorganic nanoparticles such as gold or magnetic nanoparticles. These characteristics have resulted in an increased application of various inorganic nanoparticles for drug delivery, imaging, and therapeutic purposes [32]–[34]. Nanostructures remain in the blood circulatory system for an extended period of time, allowing for the controlled release of formed drugs at the prescribed dose. As a result, they result in fewer plasma variations and have less harmful effects. Due to their nanoscale size, these structures penetrate the tissue system, facilitating the drug's easy absorption by cells, enabling effective drug delivery, and ensuring action at the desired site. The absorption of nanostructures by cells is significantly greater than that of large particles with

a diameter of between one and ten micrometers [35]. As a result, they work in concert to treat diseased tissue more effectively and with less or minimal health risks.

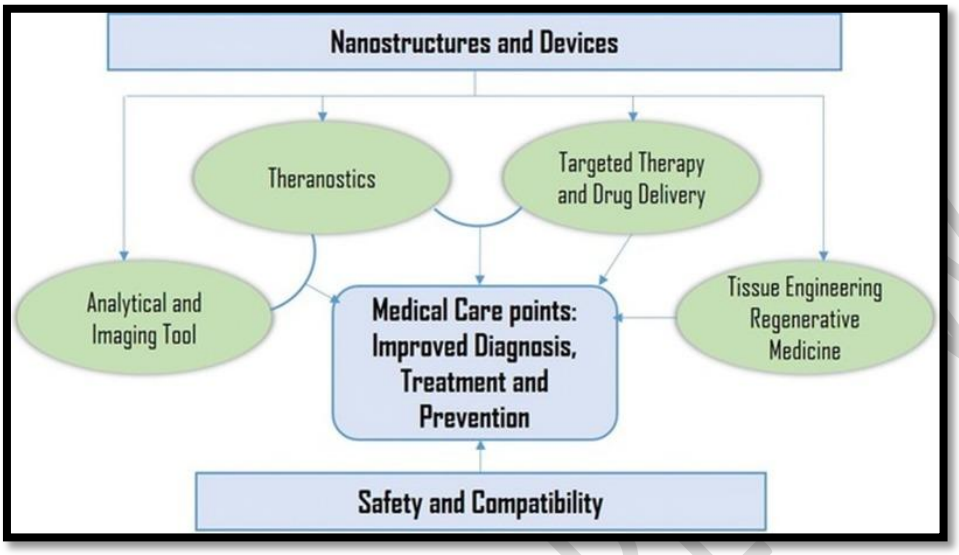

Figure 2: Application and goals of Nanobiotechnology [27].

Clinical nanotechnology's most important use in the foreseeable future will likely be in pharmaceutical production. Drug delivery research is now progressing from the micro to the nanoscale. Nanoparticles (NPs) as drugs or drug components allow novel methods for controlled release, targeted delivery, and bioavailability enhancement [8].

Furthermore, nanomaterials are divided into three major groups: metal or metallic, organic, and all mixtures, that is, metals and nanometals commonly known as semi-conducting molecules. The outer surfaces of the NPs are adorned with natural, pseudo-natural, or biorecognition substances to identify and improve bioavailability. It is essential to understand their synthesis and delivery mechanisms or even their use as a diagnostic tool in order to plan and design a drug delivery system. During the formulation, the properties considered surface-to-volume, shape, and size ratios could easily cross the biological barriers [36].

Globally, researchers are now concentrating their efforts on developing new polymers and testing complex polymer-drug combinations. For example, nanocapsules have been synthesized from monomers or by performing a simple nano deposition of a polymer [8]. At present, nanocapsules are synthesized using liposomes and albumin. Nanopores would be used to monitor the drug's release profile in the implantable drug delivery system. Additionally, nanomaterials

have a variety of applications in medical sciences, such as nanomedicine, which alter their physical properties and novel properties. This is extremely beneficial for molecular-level care and diagnosis. Nanomaterials are designed in a specific way to communicate with molecules, monitor motion at the molecular level, and transport diagnostic and therapeutic agents. Thus, nanomaterials can be easily designed to achieve the scale, shape, surface properties, composition, and structure necessary for various uses [9, 10].

3. Nanotechnology Expands Vaccine Design Possibilities

Infectious diseases are just the tip of the iceberg in terms of the economic burden on developed nations, owing to pathogen resistance to antibiotics and a shortage of vaccines. Vaccines have become a significant concern in recent decades, with attention focusing on scientific issues like vaccine production, adjuvant, and delivery system development. In recent decades, vaccines were formulated using live or killed species such as influenza, smallpox, BCG, and some subunits like Hepatitis B. Under immunosuppressive circumstances, attenuated vaccines run the risk of regaining pathogenicity [37]. The production of risk-free subunit vaccines in conjunction with appropriate delivery systems is viewed as a critical need for eliciting desired cell and humoral immune responses against infectious diseases. The use of NPs as a delivery mechanism for vaccines has gained increased attention in recent decades as a means of increasing vaccine efficacy [38].

NPs have been used in vaccine formulations more than any other kind of nanomaterial. The nanoparticles used for vaccine delivery usually consist of three components: the material (s) from which the NP is constructed, which may include natural polymers, synthetic polymers, inorganic substances, lipids, and so on; the immunogen or immunomodulatory agent, which may include antigens, DNA vaccines, RNA, or cytokines; and finally, the targeting and immunostimulatory ligands added to the particle surface [39]–[41].

The uptake of NPs is determined by their physicochemical properties, including their size and surface charge. Size has a major effect on absorption, and the impressive size range of nanoparticles is another aspect that can increase vaccine material distribution. The size of the particle has a major effect on the process of absorption, with smaller particles (200 nm) being internalized via clathrin-mediated endocytosis and larger particles (500 nm) being internalized via caveolae-mediated endocytosis [42]. Moreover, nanocarriers' nanoscale dimensions allow for

more efficient lymphatic drainage into the lymphoid organs where antigen uptake and processing can occur [43].

4. Importance of nanoparticle-based vaccine delivery platforms

The use of nanotechnology in vaccines design provides some significant advantages that can be used to further build upon what is presently accessible in the field. More to improve nanoscale systems' usefulness, studies have extensively drawn inspiration from nature [44].

Up to now, different forms of NPs have been used for protein delivery into cells, consisting of gold, dendrimers, micelles, carbon, polymers, and liposomes. All can enhance cytokine production and antibody reactions [45]–[48] (Figure 3).

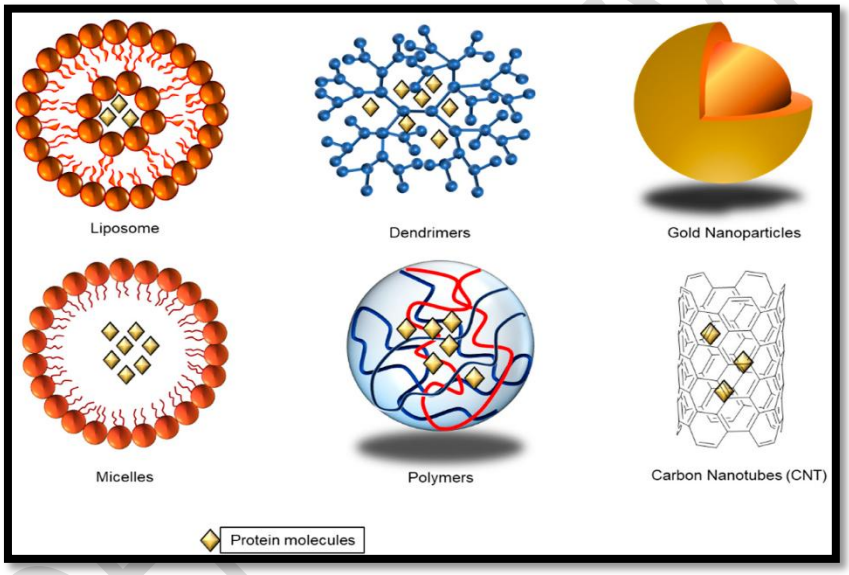

Figure 3: Different forms of nanoparticles have been used for protein delivery into cells [49].

The NP material composition has important roles in transport, cellular uptake, and intracellular trafficking of the NPs and their biodegradability and biocompatibility. Numerous vaccines have been evaluated on various forms of NPs. In comparison to unconjugated antigens, nano carrier-based delivery systems allow the application of vaccine molecules and enhance cellular uptake, leading to vigorous immune responses [50].

Some of the known nano-immune stimulators that have been used to deliver antigens to give protection against different diseases are virus-like particles (VLPs)[51], polymeric NPs (chitosan) [52], [53], liposomes [54], and inorganic NPs [55], [56] (Figure 4 and Table 1).

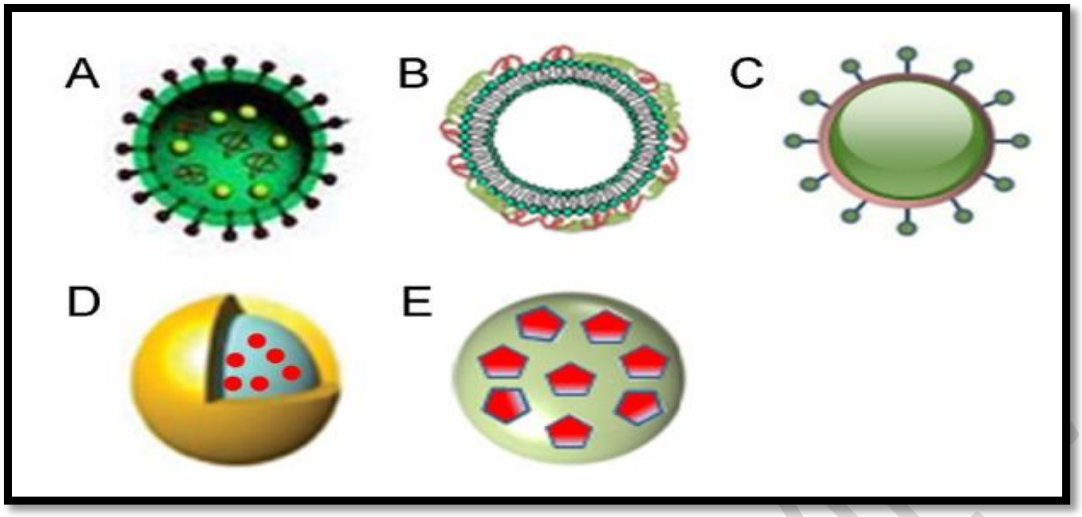

Figure 4: Nano-immuno stimulators such as virus-like nanoparticles (VLPs) (A), liposomes (B), ligand labeled (C), drug loaded polymer (D), and Non-degradable (E) [50].

Subunit vaccines utilize an antigen derived from a component of the pathogen, such as an individual protein. These vaccines are appealing due to their improved protection due to their inability to return to a virulent state and their absence of toxins from the original pathogenic organism. Consequently, actively generating huge amounts of antigen in well-defined quantities through recombinant methods is particularly attractive [8], [57]. The vaccine antigen is either encapsulated inside the NP or is coated on its surface (Figure 5). By encapsulating antigenic content, NPs allow the delivery of antigens that otherwise might dissolve rapidly or trigger a targeted immune response. Antigens conjugated to NPs can be introduced to immune systems in a manner comparable to how they would be exposed by a pathogen, eliciting a similar reaction [7].

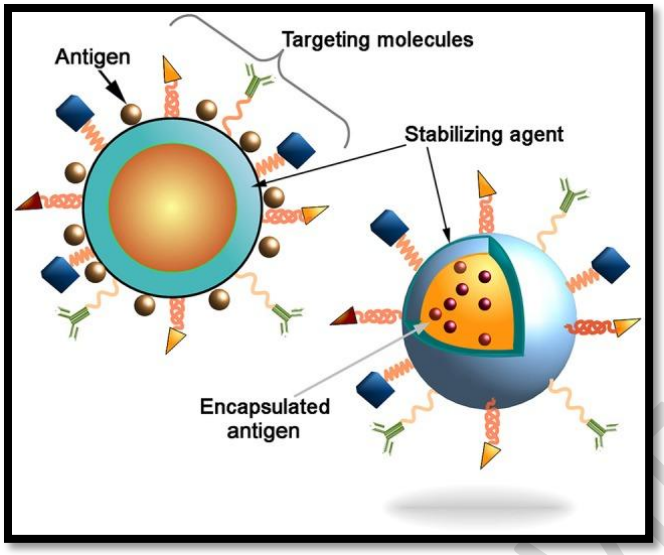

Figure 5: Diagram showing antigen conjugated to the nanoparticles' surface or encapsulated inside the particles' center [58].

NP-based platforms may be used for multiple antigen combinations or for antigen-assistant compounds to enhance antigen uptake and simultaneous activation of presenting antigen cells leading to innate immune reaction [59], [60].

Along with promoting drug delivery, NPs can directly inhibit virus receptor binding and cell entry. Ting et al. demonstrated that 1.6 nm cationic carbon dots (CDs) synthesized from curcumin could inhibit viral entry into the porcine epidemic diarrhea virus, a coronavirus model [61].

Table 1: Antigens delivered through nanocarriers in vaccine research for the treatment of various diseases.

Nanocarrier used	Size range	Antigen	Disease	Reference
virus like particles (VLPs)	15–30 nm	Capsid protein	Norwalk virus infection	[62], [63]
		Influenza virus structural protein	Influenza	[64], [65]
		Nucleocapsid protein	Hepatitis	[66]
Chitosan Nanoparticle	10-1000 nm	DNA encoding T cell epitopes of Esat-6 and FL. Mycobacterium lipids	Tuberculosis	[52], [53]
			Tuberculosis	[67]
Liposomes	≤500 nm	Polysaccharides	Pneumonia	[68]
		Bacterial toxic and parasitic protein	Cholera and Malaria	[69]
		Mycobacterium fusion protein		[70], [71]
Gold Nanoparticles	5-400 nm	Viral protein	Foot and mouth disease	[72], [73]
		Membrane protein	Influenza	[74], [75]
		Viral protein	Swine transmissible gastroenteritis virus (TGEV) coronavirus	[76]
Poly (D, L-lactic-co-glycolic acid) nanospheres	100–200 nm	Antigenic protein	Anthrax	[77]
Oil in water Nanoemulsion	200–400 nm	Antigenic protein	Cystic fibrosis	[78]
MF59 (example of nanoemulsion)	150–200 nm	Bacterial toxic protein	Cholera	[79]

5. Nanotechnology-Based Antigen Delivery Systems

Considerable research has been conducted in recent years on vaccine delivery systems based on nanoparticles, as they provide a plethora of opportunities for vaccine creation. Some of the nanocarrier systems that have been used in the production of vaccines are briefly listed below.

5.1. Virus-like particles (VLPs) in Vaccine Delivery

The existence of virus-like particles has encouraged investigators to value vaccine creation as a bionanotechnology platform for treating various viral diseases that are notoriously difficult to treat after detection, whereas dramatically reducing manufacturing time and expense [80].

Several attempts to produce plain or chimeric NPs with scaffolds from various sources were identified following the advent of NPs in the 1970s [81]. VLPs are the first to be researched, owing to their simplicity of development and potential to elicit robust immune responses [82], [83]. In the sera of Down syndrome, leukemia, and hepatitis patients, these structures were first found in 1968. However, they remained vague in biological origin, although antigenic sites on these particles' surfaces are seen [84].

VLPs are nanoscale protein structures ranging in size from 30 to 90 nm that is formed by the self-assembly of viral capsid proteins. They lack nucleic acid genome or lipid envelope spikes, which renders them non-infectious and secure for therapeutic use [83], [85].

VLPs are categorized into two broad categories depending on the existence or absence of lipid envelopes and the appearance of single-layered, two-layered, or multi-layered proteins. VLPs can be classified into many categories depending on their biophysical properties. Capsid proteins can be organized into layers. Additionally, other single-layer VLPs can contain multiple structural proteins. Although single-protein VLPs has a relatively simple structure, multi-protein VLPs have many different structural elements, including the existence of multiple capsid layers (Figure 6a). Other VLPs, such as those derived from HIV-1 and influenza virus, contain a lipid layer containing viral surface antigens covering the capsid structure, resembling the lipid envelope observed on infectious virus particles in nature (Figure 6b) [86], [87]. Unenveloped VLPs are further graded as VLPs for single and multi-capsid protein and as VLPs for single, dual, and three layers. Single capsid VLP structure like Human Papillomavirus (HPV) VLP vaccine comprises the most basic unenveloped model available in VLP [88].

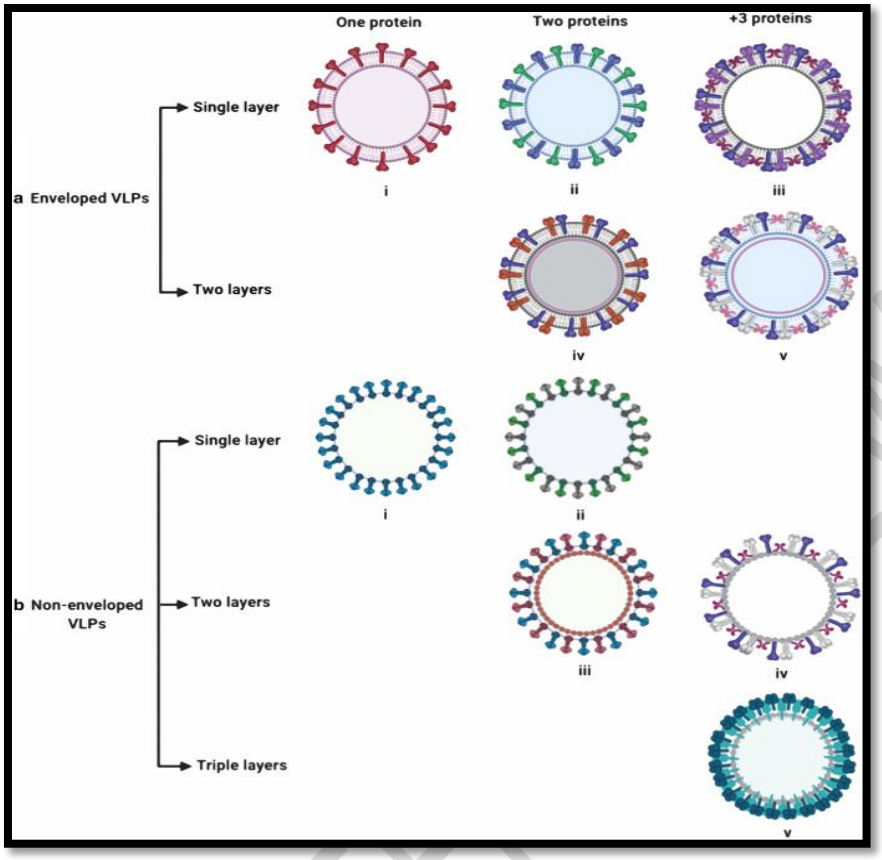

Figure 6: Classification of various VLPs structure [88].

The VLP generic method generally consists of three main sections. The upstream (production) treatment, the downstream (purification), and the formulation. The first stage is to clone the structural viral genes of concern for VLP. Next, in prokaryotic or eukaryotic expression systems, viral structural proteins with self-assembling abilities are expressed. After cell location and harvest, a clarification step is implemented to protect the elimination of cell debris and aggregates [89], [90]. More purification steps are required to produce more intact and purified VLPs, including chromatography of the ion exchange and ultra-centrifugation [89]. Polishing can be used to extract the residual host proteins and nucleic acids for an end-stage purification. Sterile filtration and formulations are done to achieve a clean, efficient, and effective product at the end of a VLP vaccine [90].

The laboratory will produce VLPs with recombinant viral proteins expressed in a number of different systems of expression, including prokaryote cells [91], yeast[92], and insect cell lines

[93]. VLPs may also be generated by assembling structural protein from a range of viruses, whereas VLPs are generally produced by protein(s) of one virus type [91].

With the exception of viruses, VLPs do not contain any viral RNA, which makes them non-replicating and non-infectious. However, prior to release, viral integrase genes are removed to prevent the packed genome from integrating into the host cell and/or recombination with the live or defective virus in an infected person. Extra proteins may be expressed on VLPs by fusing them to the molecule or producing several antigens [94].

A variety of uses, including infectious diseases vaccination and even cancer, have verified that VLPs are used. VLPs have also been applied in the manufacture of vaccines against drug abuse [95].

The discovery and successful commercialization of the hepatitis B virus surface antigen and the HPV capsid protein as commercial vaccines against hepatitis B [96] and HPV[97]-induced cervical cancer, respectively, sparked interest in new VLPs. Numerous VLP-based vaccine candidates have recently entered various stages of clinical trials with the goal of developing VLP-based vaccines for medical and veterinary applications in the future [82], [98].

Notably, tiny unenveloped VLPs (size 25–40 nanometers) penetrate stronger tissue barriers and invade lymph nodes. VLPs with a diameter greater than 100 nanometers normally accumulate at the injection site and penetrate the lymph nodes sparingly. Additionally, nanoparticles tend to be more suitable for cell targeting than microparticles. [99].

5.2.Liposome-based NPs in Vaccine Delivery:

Alec Bangham discovered them in 1960 at the University of Cambridge's Babraham Institute. They are composed of a single or several concentric lipid bilayers enclosing an aqueous compartment (Figure 7) [100]. Liposomes are spherical vesicles, typically of 50–450 nm size, composed of phospholipids and steroids [101]. Liposomes are the second most prevalent NP type and, under special provisions, automatically assemble in water. They are made up of lipids with a hydrophilic head and hydrophobic tail that supports inner- and outer hydrophilic membranes, bilayer lamellar lipids, or multilayered vesicles in cells [102]. Liposomes appear to be a nearly perfect pharmaceutical carrier because they have the same morphology as cell membranes and have different substances incorporated into it. They are respected for their biological and

technical benefits as the ideal delivery mechanisms for both in vitro and in vivo bioactive compounds and are recognized as the best-selling drug carrier system ever established [103].

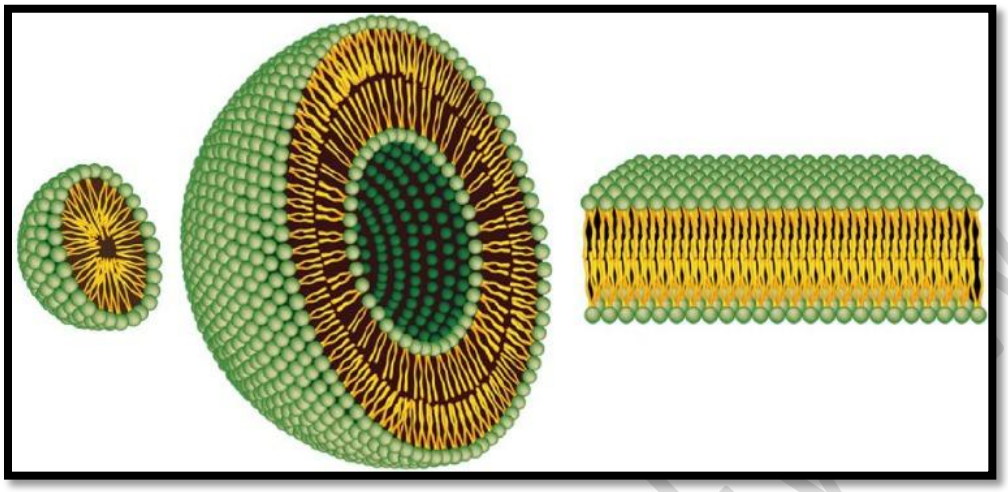

Figure 7: Representation of the steric organization of a micelle (left), a liposome (center), and a lipid bilayer (right) [104].

Liposomes can be divided into sizes (e.g., small, medium-sized, or large) and lamellarity in the form of uni-, oligo-, and multilamellar vesicles according to a preparation process such as reverse-phase evaporation vesicles or vesicular extrusion. The shape of unilamellar (ULV) or multilamellar (MLV) vesicles depends on the synthesis and the post-formation processing used to prepare them (for information, see the section on the 'Methods for liposome preparation'). Since the ULVs are made of a large aquatic center, they are ideal for hydrophilic drug embodiments since they contain a lipid bilayer 50–250. MLVs, however, are preferred to enter lipid-soluble drugs (two or more concentric bilayers arranged like an onion skin of 1–5 mc) [105].

The preparation of liposomes is done using several multiple techniques. The thin-film hydration or Bangham method is amongst the most commonly utilized techniques for liposome-production preparation. This approach includes lipid degradation in an organic solvent, solvent evaporation, and aqueous distribution of the film obtained. In the aqueous medium (for hydrophilic drugs) or lipid film, the drug may be captured in the (for lipophilic drugs). Even so, the water-soluble drugs' encapsulation performance is poor (5% – 15%). This approach also generates huge and non-homogeneous MLVs requiring sonification or emulsion in homogeneous small ULVs [106],

[107]. The reversed-phase evaporation process provided lipid hydration directly from an organic solvent and aqueous MLV and ULV suspension together [108], [109].

Liposomal vaccines are sufficiently effective to cause an inherent and efficient immune response. They can have both immunomodulatory and vaccine antigen supplies [110].

Liposomal vaccines were the first to elicit an innate immune response. Creature of pro-inflammatory molecules and activation of Antigen Presenting Cells and the immune-modulatory molecules, including chemokines and cytokines, are the product of innate immune reaction [111]. Toll-Like Receptors, Non-Toll-Like Receptors, and C-type Lectin Receptors are the three types of innate activators. All of these receptors are capable of recognizing a variety of microbial nucleic acids and components of bacterial cell walls. Following activation of the innate immune response, the adaptive immune response is triggered [112].

Liposomes are an effective method of delivering vaccines. However, there are a few additional considerations to consider when delivering liposomal vaccines [113]. Factors such as antigen nature, route of administration, immune system, type of immune response, the structure of the phospholipid, a particular size, lamellarity, attachments of the antigen, surface load, bilayer fluidity, and temperature. The key step of transformation temperature should be higher during liposomal vaccines preparation [114], [115].

Wesley used DNA-loaded cationic liposomes as a vaccine against malarial proteins in 2017. DNA-encoded vaccines are more effective than transgenic vaccines since transgenic vaccines produce a delayed immune response [116], [117]. Wesley combined naked and liposome-encapsulated DNA vaccines. Liposome-dependent approach induced a successful humoral immune response against Plasmodium falciparum rhoptry antigen dependent on Plasmodium vivax and Plasmodium falciparum titers. It was established that liposomal DNA vaccines are more effective than transgenic vaccines [116]. That when highly specific antibodies are needed, recombinant vaccines cannot be generated. Cationic liposomes (typically with a particle diameter of 200–1000 nm depending on the formulation) are used to encapsulate the antigens. They continue to accumulate antigens and release them into immune cells for an extended period. Their productivity is enhanced by their positive charge and lipid composition [118].

5.3. Polyanhydride-based NPs in Vaccine Delivery

Biodegradable polymers possess a variety of favorable properties that have resulted in their use as drug and protein vectors over the last two decades. Biocompatibility, continuous-release, and tunable release kinetics are a few of these characteristics [119]. Particle-based vaccine delivery vehicles derived from synthetic or natural polymers have many benefits over conventional formulas; not the least of that is their broad ability to adapt [120]. New vaccine formulations should strive to be effective, affordable, stable, and mimic pathogenic infection. Vaccines based on polymers can mimic infection in a variety of ways. First, they may serve as a depot, allowing them to survive long enough to elicit adaptive immune responses. Second, they can ensure efficient antigen-adjuvant co-delivery to dendritic cells, effectively priming naive T-cell responses. Thirdly, the size of micro- and nanoparticles is often comparable to that of various bacterial and viral pathogens [121]. As a result, biodegradable nanoparticles have garnered considerable interest in the design of vaccines.

A class of synthetic polymers with interesting properties is a biodegradable amphiphilic polyanhydride (PAs), which is used to support vaccine vectors. They can easily metabolize and degrade by-products non-toxic. Polyanhydride is a functionalized polymer with continuous release and erosion of the surface properties (Figure 8) [122]. Carboxylic acids are metabolites of polyanhydride. These are biologically compatible, non-mutagenic and FDA-approved. Polyanhydrides have many benefits compared to other synthetic polymers, for example, high immune responses and antigenic stability [123].

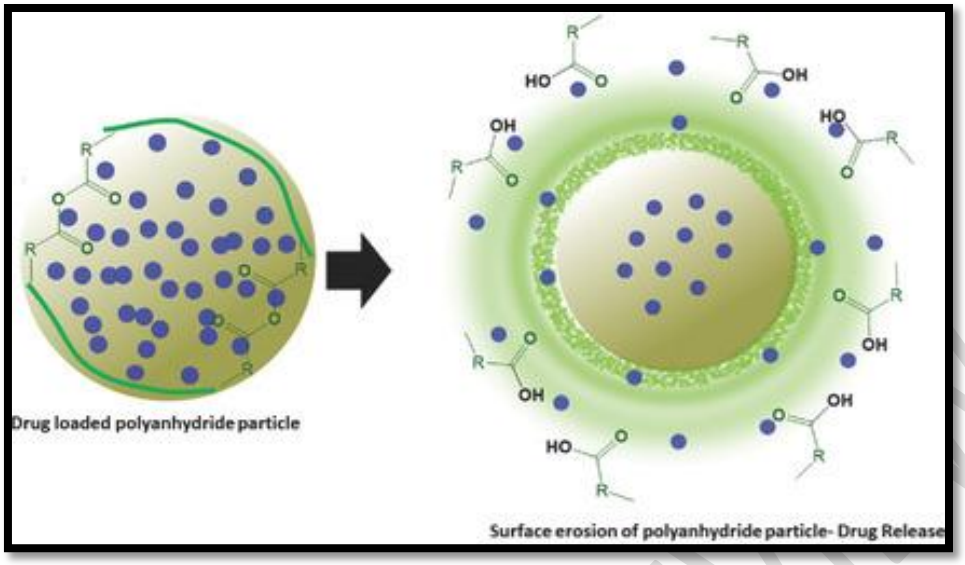

Figure 8: Biodegradable amphiphilic polyanhydrides [124].

The use of 1,8-bis (p-carboxyphenoxy)-3,6-dioxaoctane microparticles (CPTEG) and 1,6-bis (P-carboxyphenoxy) hexane (CPH) was shown to stabilize structural integration of encapsulated antigen and to provide continuous protein releases [122]. Various methods, including melt condensation, ring opener polymerization, condensation interfaces, dehydrochlorination and dehydrative couplers, have been formulated by polyanhydrides [125].

Amphiphilic polyanhydride nanoparticles exhibit pathogenic mimicry and the capacity to activate dendritic cells. Polyanhydride nanoparticles show optimum cytokine release and internalization by dendritic cells due to their hydrophobicity. Amphiphilic polyanhydride nanoparticles are more effective at preserving the antigen's functional integrity. Previous studies have established the flexibility and superiority of amphiphilic nanoparticles as long-term vaccine delivery carriers [125]. In comparison to uncoated nanoparticles, mice orally immunized with mannosamine or flagellin-coated bio-adhesive polyanhydride nanoparticles elicited a more sustained and stable humoral, cellular, and mucosal immune response and expressed high levels of immunoglobins [126].

Conclusion

Nanobiotechnology is the twenty-first century's modern frontier. Its implementations in traditional medicine have demonstrated a significant effect. Nanomedical research enables accessibility to novel nanomaterials and nanotechnologies, which enables us to construct and

create extremely effective drug delivery systems with enhanced therapeutic and decreased toxicity. There have been enormous advancements in the field of nanotechnology and its implementation in biomedicine, specifically in vaccine delivery systems, over the last few years. Nanoparticles often enhance the immunogenicity of fragile antigens, and this technique has a number of advantages over traditional adjuvant methods, including directed vaccine delivery, continuous-release, and several others. We summarize that some of the nanoparticles are suitable for vaccine delivery and address the importance of virus-like particles (VLPs), liposomes, polymeric-based nanoparticles, and polyanhydride-based nanoparticles for vaccine delivery. For widespread use of nanoparticles, scientists must continue to work on improving nanoparticles' performance in vaccine delivery systems. We anticipate that more nanoparticle-based "drug delivery systems" will become commercially available shortly.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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