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REVIEW PAPER OPEN ACCESS

Role of nanoparticles and nano-oxide particles in vaccine development

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Abstract

Nanotechnology is used in vaccine development especially in medical field for diagnosis of many diseases. Different nanoparticles during vaccine formulations designed for their use in promoting of the safe immune response. In order to increase antigen processing, various nanoparticles are used to advance immunity where they might be used as adjuvant. Nanotechnology widely used in medicine for diagnosis by developing nanoparticles of different composition, shapes and sizes. The development of vaccine proves to be very beneficial in the history of controlling diseases. Due to lack of understanding in vivo particular response of various nanoparticles that may operate as delivery system to increase antigen processing. This review provides most recent advances in field of nanovaccinology with the aim of uses of nanoparticles based antigen delivery vehicle and their use in medical field in treating of various diseases. Interaction of nanoparticles with cells of body immune system and their characteristics are discussed. There is need to more understanding of nanoparticles action in immune stimulatory, various delivery modes in addition to their behaviour in vivo and also designing of nanoparticles containing vaccines.

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Introduction

Nanocarrier based delivery systems provide a suitable route of administration of vaccine molecules and enhance cellular uptake thereby resulting in robust innate, humored, cellular as well as mucosal immune responses when compared with unconjugated antigens. This review mainly focuses on the potential use of nano delivery systems as novel vaccine strategies for the induction of innate as well as adaptive immune responses against infectious diseases. In twenty-first Century, infectious diseases have emerged as a serious threat to the health of millions of people across the globe. According to the World Health Organization report for 2016,~3.2 million deaths have occurred due to lower respiratory infections and 1.4 million from tuberculosis alone worldwide. Over the past few decades, many new infectious diseases have emerged and few old diseases reemerged, which were once considered to be no longer a threat to the human being**.** Nanoparticles because of their small size enter into the cell via endocytosis in particular pinocytosis (Treuel *et al.*, 2012). Most important nanoparticles are gold nanonaarriers which are useed in drug delivery systems. In order to increase antigen processing nanoparticles are used and to improve immunity to improve immunity they may be used as adjuvant. Occasionally, inadequate adjuvant action might be the cause of incomplete immunogenicity. Both an antigen and an adjuvant are collectively delivered by means of nanocarriers revealed by some studies (Dunkle *et al.*, 2013).The main purpose of nanocarriers is to ease the directing along with assist in safe approach of adjuvants to APCs (Oyewumi *et al.*, 2010).

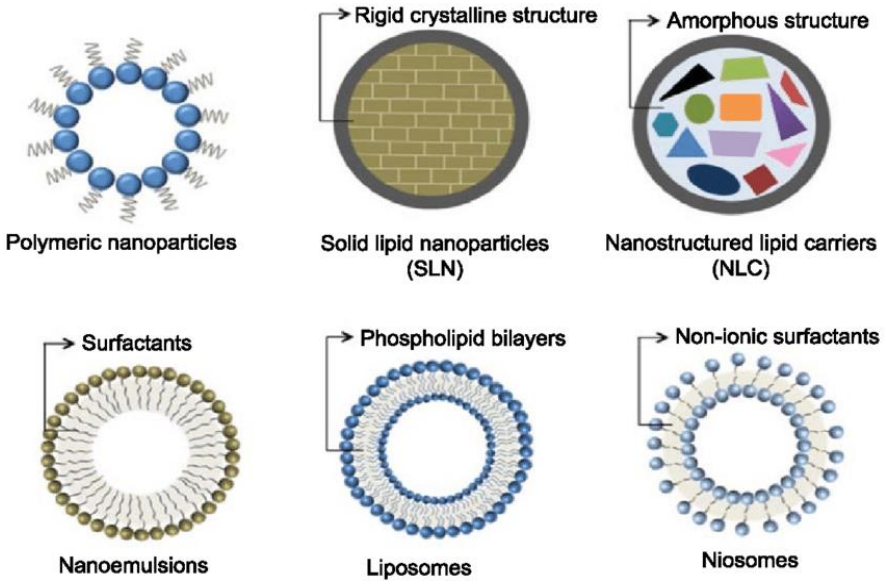

Fig. 1. Different Systems to Deliver Vaccine.

Protein based antigen vaccines are protected degradation by the use of solid nanocarriers (Apostolopoulos *et al.*, 2013). For cell mediated immune responses, before antigen present to naive CTL's, it must be shunted into cytoplasmic major histocompatibility class (MHC-1) pathway. New vaccines are generated continuously to cure different diseases(Lepenies *et al.*, 2013). Nanocarrier based delivery system can protect the vaccines from premature degradation, improve stability, has good adjuvant properties, and also assists in targeted delivery of an immunogenic to the antigen presenting cells (APCs). There are several mechanisms by which vaccines can be delivered to the specific sites using nanocarriers. Vaccine antigens can be encapsulated within the nanocarriers or decorated on their surface. Encapsulation within the nanoparticles (NPs) can protect the antigen from premature protease degradation and elicit sustainable release, whereas the surface adsorption facilitates their interaction with cognate surface receptors such as toll like receptors (TLRs) of APCs .

Different Systems to Deliver Vaccine using nanocarriers

There are different systems to different systems to deliver vaccine using nanocarriers such as liposomes, virus like particles, golden nanotubes, and silver nanopartilcles. When these nanoparticles interact with body parts, these particles show special properties such as biocompatibility, non toxicity and significant interaction with biologically active compounds.

Liposomes

Self-closed vesicle like structures that embedded water in their interior are called liposomes. Antigen is encapsulated within the core of liposomes for delivery (Pinheiro *et al*., 2011). A large variety number of CD-8 T cell responses are produced by vesicles of small unilamellar made up of positive nature of DDA as compared to other large sized many lamellar vesicles (Milicic *et al*., 2012).

Virus like Particles (VLPs)

VLPs are designed by viral proteins present on structure which have characteristic of self-assemblage and imitate the morphology of pathogen. As compared to living viruses they lack contagious genetic material hence they are non-virulent and they do not replicate. VLPs present antigenic epitopes in such an accurate and repeated way that it results in the formation of bonds between B cells immunoglobulin receptors and stimulation B cells (Chackerian *et al*., 2007). Therefore, VLPs are extremely immunogenic and due to their various applications these are involved in vaccination, gene therapy, targeted drug delivery and immune therapy. According to their structure these are divided into two classes, non-enveloped VLPS and enveloped VLPS. Non-enveloped VLPS basically comprises one or more constituent of pathogen which is capable of arranging itself and any host component is not included. This method has been involved in improvement of vaccine against pathogens like RV and HPV (Kushnir *et al*., 2012). Molecules like monophosphoryl lipid A (MPL) are strong adjuvants used in animals and humans (Ishizaka *et al*., 2007). Glucopyranosyl lipid A (GLA), a TLR4 agonist, has been examined as an adjuvant in case of oil in water emulsion vaccine antigen preparation(Schneider *et al*., 2012).Oil in water emulsions comprising of GLA and recombinant hem agglutinin is also used for the treatment of seasonal influenza (Treanor *et al*., 2013). Table 1 shows some delivery types and systems of emulsions.

Table 1. Emulsions composition along with antigen and route of administration.

Delivery system	Composition	Antigen	Route
Emulsions	MF59	Hemagglutinin	Intramuscular
	MF59	Recombinant meningococcal B protein	Intramuscular
	MF59	Recombinant meningococcal B protein	Intramuscular
	W805EC	OVA	Intranasal
	W805EC	OVA	Intranasal
	GLA	Falciparum subunit	Subcutaneous
	GLA-SE	Plasmodium vivax subunit	Subcutaneous

Synthetic Polymer Based Nanodelivery Systems

Various synthetic polymers are involved in the preparation of nanocarriers for the transport of vaccine like polyglutamic acid (g-PGA) Akagi, Polystyrene, Poly d,l-lacticoglycolic acid (PLGA) ,polyethylene glycol (PEG) and poly d,l-lactide-co-glycolide (Akagi *et al*., 2011). PLGA and PLG have been comprehensively studied because they are highly biodegradable and biocompatible. These polymeric nanoparticles capture antigen for transporting it to specific cells or antigens are continuously discharged due to their less biodegradability (Manish *et al*., 2013). PLGA which is involved in transport of antigen is obtained from numerous pathogens like hepatitis B virus (HBV), hepatitis B virus (Demento *et al*., 2012).

Mechanism of action of biodegradable nanoparticles

The delivery of vaccine can be controlled by using antigens encapsulated by biodegradable polymeric nanoparticles and desired immune response can be increased through site specific targeting of antigen to antigen-presenting cells (APCs). Vaccines can be improved through effective deliverance of antigen to APCs (particularly in dendritic cells) and by stimulation of APCs. Release of antigen can be controlled, APCs can be activated and antigens can be

targeted to DC by using nanoparticle-based vaccine delivery systems. Nanoparticles which are manufactured from biocompatible and biodegradable polymers like polyamino acids, polylactide-co-glycolide (PLGA) and polysaccharides transport vaccine more efficiently (Silva *et al.*, 2012).

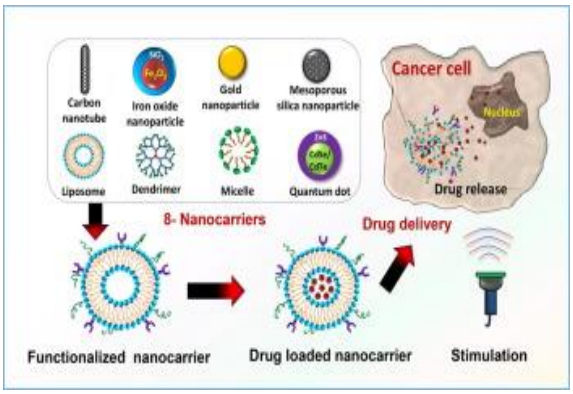

Fig. 2. Synthetic polymers based nanodelivery systems being used in vaccine along with composition antigen and route.

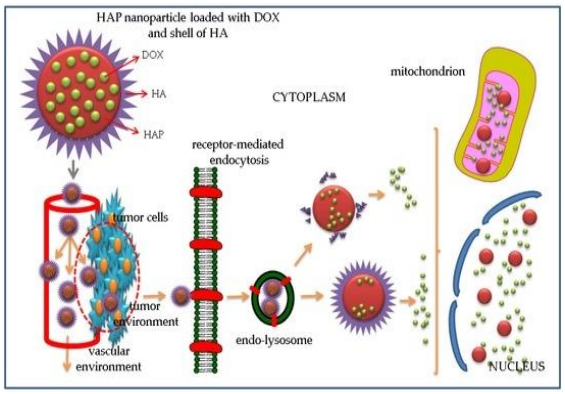

Fig.3. Mechanism of action of biodegradable nanoparticles.

Inorganic Nanodelivery Systems

Several inorganic nanoparticles have been reported to be used in the development of vaccines. The most significant benefit of nanoparticles lies in their firm structure and manageable preparations though they are generally non-biodegradable (Nandedkar *et al.*, 2009).

Gold nanoparticles (AuNPs)

Gold nanoparticles are specifically important to control antibody manufacturing contrary to the platform ingredients. It has previously been defined that subunit vaccines are transported through (AuNPs) lacking the assembly of anti-AuNP antibodies (Chen *et al.*, 2010). By the use of glutamate-immobilized AuNPs the assembly of antibodies was first time studied (Niikura *et al.*, 2013). Eventually, AuNPs are used as antigen transporter for numerous viruses involving influenza and foot-and-mouth disease (Chen et a., 2009).

Silica nanoparticles (SP)

Silica nanoparticles are categorized in two general groups: solid silica nanoparticles (SSN) and mesoporous silica nanoparticles (MSN). Researchers are trying to modify the surface of SP in various ways so they can act as effective transporters of biomolecules and therapeutic drugs. They focus on the importance of using MSN as transporters for vaccines having high surface area. Protein- and DNA based vaccines use MSN as delivery vehicles (Shah *et al.*, 2015). Some studies revealed that vaccine delivery systems consist of Chitosan nanoparticles (Sawaengsak *et al.*, 2014). The intracellular destiny of chitosan nanoparticles encapsulated with HBsAg has been observed (Lugade *et al.*, 2013).

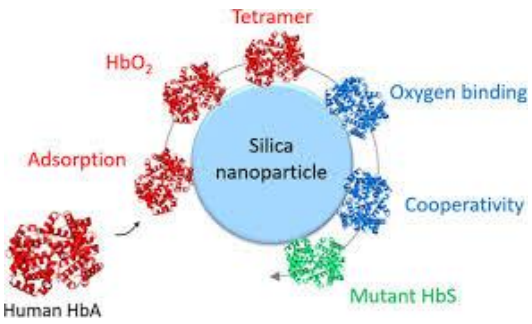

Fig. 4. Biological role of silica nanoparticles.

Pullulan polymer-based nanoscale hydrogels conjugated with cholesyeryl serve as likely vaccine vehicles. BoHc/AClostridium botulinum type A neurotoxin considered as non-hazardous was laden into the nano-gel and was directed intranasally. Retention of BoHc/A in the nasal mucosal layer as supported by the thickness of the nano-gel. BoHc/A was taken up by the mucosal DCsafter elimination from the nano-gel. The antigen-neutralizing serum IgG and antigen specific IgA in the absenteeism of extra mucosal adjuvants were provided at larger scale by the intranasal nano-gel formulations (Gupta *et al.*, 2011).

Conclusion

Advanced drug delivery systems is delivered by nanoparticles Nanoparticles posseses various properties such as small size, comfort surface modifications, target delivery, nanoparticles proficiently transport antigens and capacity to deliver antigens together with adjuvant. However, various applications in advanced nanotechnologies can be planned for carriers at nanoscale dependent vaccine for delivery. These systems to deliver vaccine might be used added largely for to treat various transferrable diseases with special attention to health aspects.

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