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Introduction to Nano-technological Structures and their Potential Therapeutic Uses in Viral Diseases

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Abstract: Nanotechnology from the very beginning has been implicated to be useful in various fields of science, owing to its interdisciplinary dimensions. Various studies around the globe have resulted in a plethora of information regarding the diagnostic and therapeutic potentials of nanotechnology. Different kinds of nano-structures have been produced with unique properties due to their peculiar sizes with propositions in medicine and healthcare. Such nano-scale structures with their prospective geometries are very important in relation to their functionalities. Moreover, modifications on surface of nanoparticles have been impregnated to bring changes that can provide desired effects. Targeted drug therapy by nanoparticles is a subject of recent interest, as it focuses on removing the side effects of certain conventional therapies. Various viral infections have been explored by targeting effects of nanotechnology. Conventional methods, targeting viral infections have certain drawbacks, which can be tackled by nanotechnological approaches. This review focused on the current status of nanoparticles in specific systems that work against viruses, using the conceptual translation of the nano-scale moieties. Different targets for various virology related entities have been exploited and resulted in promising aspects of targeting agents and nano-therapeutics.

Key words: Nanotechnology, Viruses, Nanoparticles, Nano-Carriers, Targeted Drug Delivery

Introduction

Many disciplines having applied benefits are nowadays getting benefits from a field, called "Nanotechnology" which deals with the objects lying in nano-scale, i.e. 1 to 100 nano-meter (nm) ranges. Being multidimensional in nature, this aspect of matter has been exploited in various ways to harness the applications that were not been explored before. Components or substances that have at least one of its features in the above mentioned range are normally studied in this field (Theis et al., 2006). This is one way to define this "new science" but there are other definitions being reported from

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time to time which are slightly different from others, merely based on the formality with which the manipulation of matter is concerned. For example, matter that is artificial or has uniqueness of any kind only due to effect of smaller sizes and nano-meter dimensions are referred as "Nanotechnological structures" (Ferrari, 2005). Main principle of this technology emerged from the studies that showed the materials at smaller sizes are different from the same materials in macroscopic forms, usually in quantum mechanical effects, changing the physicochemical properties significantly (Jenekhe et al., 1997). With these observations, we say that the materials that exhibit unique properties can be investigated for specific interactions that can help in solving mysterious problems underlying important disciplines, e.g. medicine.

Applications of Nanoparticles

One of the early breakthroughs that introduced nanotechnology to world was, when scanning tunneling microscope was first introduced in early 1980s that helped researchers to control individual atoms (Soler et al., 1986). This development further instigated the discovery of important structures like carbon nanotubes (CNTs) (Rao et al., 2001) and quantum dots in nano-scale ranges (Stroh et al., 2005). Tiny vesicles of phospholipids i.e. liposomes (spherical nano-structures), have been introduced in consumer products, for example colorless sunscreens which protect against strong radiations and cosmetics with moisturizing and nurturing properties (Wolf et al., 1995). These discoveries were responsible in taking this field to its limelight in its early phase with researchers working on exploration of further applications of this newborn subject. Later, when more research was conducted, a plethora of fruits came out from different studies around the world, for example: power in batteries was increased, efficiency of solar cells was increased (Wan et al., 2009), amount of mercury released from fluorescent lamps was reduced (Lee et al., 2009) and contamination in food rapidly detected, were made possible (Sozer and Kokini, 2009). Moreover, special composites have been developed to be used in sport items due to properties of strength and light weight, special lenses to be used in optics with scratch less coatings and ceramics for dental and bone implants with properties to fill in the surrounding tissue by tuning (Aronov et al., 2007).

Applications in Medicine

Above mentioned applications paved a way for further investigation of such structures and continued to influence the future applications of this new concept and made a significant impact in various fields including medicine. Liposomes were manipulated to be used in the first drug delivery system in clinical use that exploited the nanoparticles and this concept (Gabizon, 1993). In this system, a chemotherapeutic agent (Doxorubicin) was encapsulated in the spherical liposomes to treat the metastatic breast and ovarian cancer in USA (Peer et al., 2007). Similarly, Paclitaxel was approved in 2005, consisting of an albumin nanoparticle agent that can tolerate the larger dosage of Paclitaxel so that it can extravagate in to the damaged tissue (Ibrahim et al., 2002). Cancer studies around the world have reported the use of several platforms of nanotechnological origin. First case was recorded when liposomes were exploited as vehicles to carry the drug molecules to the diseased site, for example nano-vectors and nano-materials. Nano-vectors, as the name indicate that these are the particles having nano-scale dimensions to encapsulate or attach the potent agent to be used in drug delivery or diagnostic

purposes (Jain, 1998). Nano-materials on the other hand are fabricated materials with desired moieties that are used in same systems in the medicine. Such systems are composed of materials of different origins including carbon nanotubes (Tasciotti et al., 2008) and metals like iron (Winter et al., 2003), gold (Boisselier and Astruc, 2009), silver (Jun et al., 2010) and platinum (Sun et al., 2000). There are other materials that have been explored in such systems including polymers (Jain, 1998), which can either be micelles or dendrimers in nature. Diversity of nanotechnology can be responded from the fact that materials of totally different nature can be used for the same purpose (i.e. medicine) like liposomes (Caplen et al., 1995) and quantum dots (Gao et al., 2004). Furthermore, studies of different kinds have suggested that such nanoparticles must obligate several different shapes in order to implicate their downstream applications. Decuzzi et al, in 2009 have reported those shapes which include spheres, rods, wires, discs, ellipsoids and hemispheres. In 2008 Carmo et al, reported that over 400 different clinical trials are under processing stage that involves nanotechnology at their very core. A few important applications of nanotechnological materials have been enlisted with their importance in **Table 1**, which clearly shows the ascendency of such platforms over the conventional approaches. Some of these applications are reality and some are in early developments and have excessive potential to be realized in near future.

Classes of Nanoparticles for Biomedical imaging, Diagnostics and Therapeutics

Nanoparticles have been distributed into various classes depending upon their nature of origin and physical characteristics and each of which has certain advantages and some limitations according to the context in which these are to be applied. Some of the important classes are shown in Figure 1.

Metal Oxide Nanoparticles

Metal oxide nanoparticles are generally spherical and ferromagnetic, consisting of an iron (Fe) core with a coating, polymeric in nature. Such particles have been reported to be used in different applications of medicine including monitoring of drug delivery, biomedical imaging and cell tracking mechanisms (McCarthy et al., 2007). Iron oxide nanoparticles (FeONPs) are synthesized usually from ferrites which are further composed of magnetite (Fe_2O_3) or magnetite (Fe_3O_4) metal ions. These are often classified according to their effective size and coating properties for example: super-paramagnetic iron oxide (SPIO, >50 nm), mono-crystalline iron oxide, nano-colloid and cross-linked iron oxide (CLIO, 10-50 nm). Such particles have been exploited extensively owing to their use as contrast-enhancing probes for magnetic resonance imaging (MRI) (Longmire et al., 2008). Normally, FeONPs are cleared from blood and are taken up by circulatory cells like monocytes and macrophages which tend to reduce their ability of diagnosis of inflammatory and degenerative disorders (Müller et al., 2008). It happens because such disorders are associated with high macrophage activity, so if better clinical results are required then extensive optimization of different properties of such particles should be studied and performed.

Table 1. Important nanotechnological materials with their applications and importance in medicine.

Materials	Application	Importance
Dendrimers Liposomes Polymers Metallic nanoparticles	Drug delivery	New classes of therapeutics Enhanced therapeutic efficacy Minimized complications associated with available drugs Biologically active new molecular entities
Nano-wires Nanotubes Cantilevers Micro/nano-array Metallic nanoparticles	In vitro diagnostics	Higher sensitivity Lower sample consumption Early detection of infection and tumor Rapid detection of disease biomarkers
Carbon nanotubes Quantum dots Magnetic nanoparticles	In vivo imaging	Targeted imaging using nano-probes Tracking nano-carrier distribution in the body Locating tumors and their margins Mapping sentinel lymph nodes Monitor disease progression Rapid, cheap and precise
Hafnium oxide Gold-based nanoparticles Gold nano-shells/rods Carbon nanotubes Magnetic nanoparticles Nano-crystalline silver	Therapy techniques	Direct therapy Enhanced X-ray therapy Hypothermia induced therapy Antimicrobial therapy
Nano-coatings Nanostructured surfaces	Biomaterials	Biocompatibility Medical implants
Nano-scaled biocellulose	Tissue engineering	Biocompatible scaffolds Spatiotemporal release of biological factors like ECM Implantable tissues

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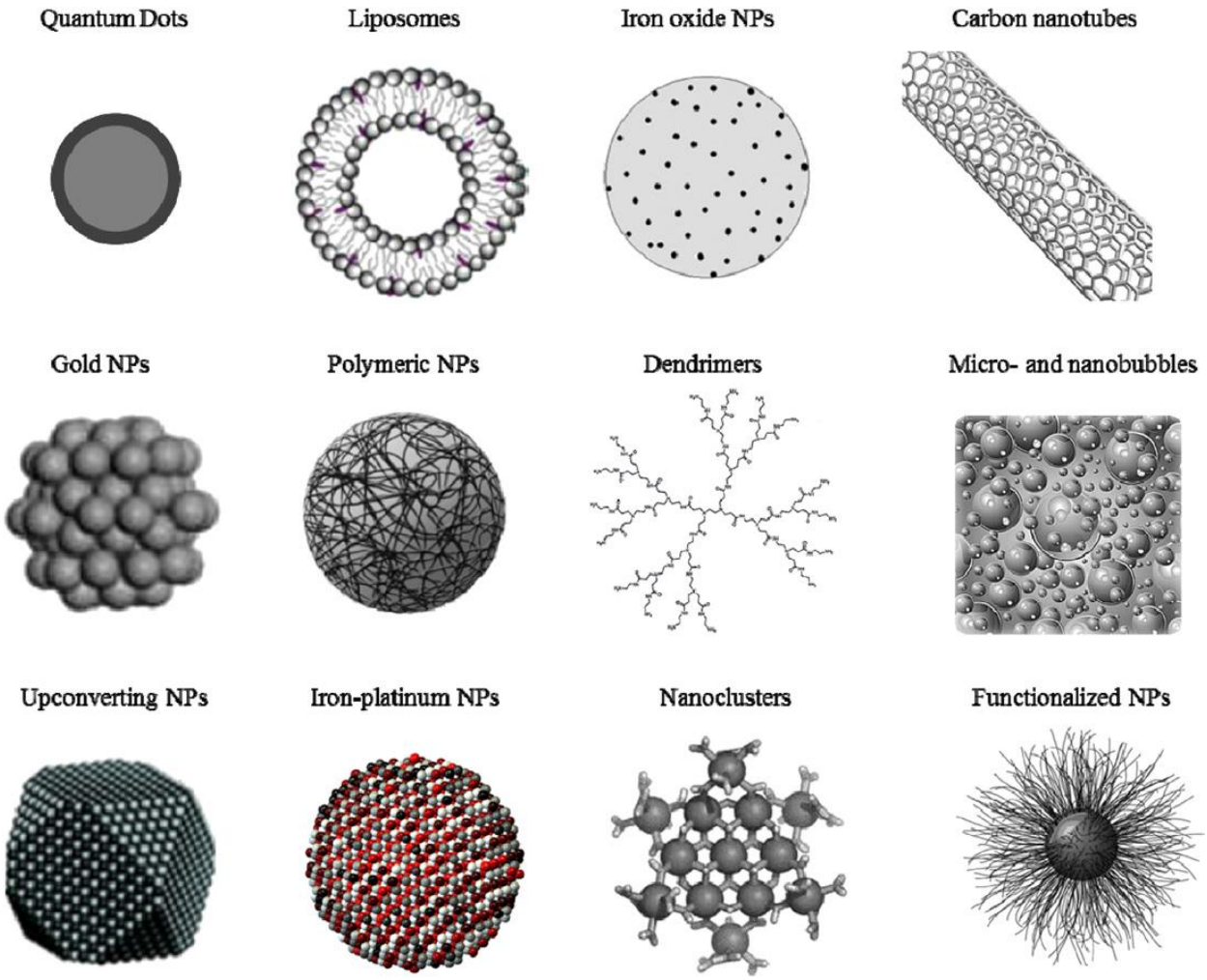

Figure 1. Different classes of nanoparticles; 1-100 nm sized particles with their characteristic texture and shapes are depicted.

Gold Containing Nano-structures

Nanoparticles generated from gold have peculiar geometric symmetries which include nano-rods: a nano-object with rod like symmetry and dimensions of unequal lengths, nano-fibers: rods with flexible nano-dimensions, nano-shells: particles with hollows in between them and nano-cages: shell like structures with porous walls (BSI et al., 2007). Such constructs have been explored for various applications related to biomedicine like imaging, tumor therapy, radiation sensitization, sentinel lymph node mapping and drug delivery (Balogh et al., 2007). Gold nanoparticles have the ability to provide flexibility in the wavelengths of optical absorptions which spread from visible (350 to 750 nm) to near-infrared (700 to 900 nm) (Hu et al., 2009). These particles also have the ability to allow for the photo-thermal ablation of tumors with the help of ultrasound and microwaves (in cases where surgery would be difficult) but require intensive care to reduce the damage to surrounding normal tissue because these

particles can penetrate into skin and other organs to cause irritations, also the accumulation of gold salts can cause severe toxicity inside the body (Fadeel and Garcia-Bennett, 2010).

Quantum Dots

Quantum dots (QDs) are fluorescent semiconductor nano-crystals (range from 5 to 50 nm) which consist of an inorganic core and an organic coating which is biocompatible. These crystals have been used in in vivo imaging and also to monitor biochemical processes (cancer metastasis) (Gao et al., 2004). QDs exhibit higher quantum yield and photo-stability, broadband absorption, narrow emission spectra and conjugation to multivalent ligands as compared to the conventional small molecule fluorophores (Smith et al., 2004). Different studies have reported that near infrared quantum dots when functionalized with small molecules like peptides, proteins or antibodies can detect targets within living animals and forms the basis of in-vivo screening (Cai et al., 2006).

Silica Nanoparticles

Because of the chemical, biological inertness and thermal stability, silica is used as a principle component for biodegradable and biocompatible core-shell hybrid structured nanoparticles (Tan et al., 2004). Various reactions in aqueous systems make these particles compatible with heat-sensitive molecules which are to be incorporated in them in the first place. Silica colloids with charged surfaces are stable at high concentrations and cross linkers (siloxane based) can be used for further modifications. Gold, silver, platinum, and many other metals can be used for making silica-based nano-shells, which can be used as biosensors, biomarkers and detectors (Hirsch et al., 2006). Fluorophore encapsulated silica nanoparticles are being used as optical imaging agents with high fluorescence emission intensity and excellent photo-stability (Cauda et al., 2009).

Molecular Dots

Calcium phosphate nanoparticles (20 to 100 nm) are small and biocompatible with multilayer nano-composites having more rigidity than larger liposomal structures. Calcium phosphate core-shell nanoparticles can be synthesized through a robust and reproducible method based on bio-mineralization of calcium phosphate around precipitated amphiphiles. Nanoparticle formation can also be controlled using ion and surfactant concentrations, pH, ionic strength, and temperature (Kester et al., 2008). These NPs have a lower likelihood of toxicity compared to other types of NPs because of their composition. These are biodegradable for which surface modifications are usually difficult and diagnostic and therapeutic agents can be trapped in these during the process of their synthesis.

Carbon-Based Nanoparticles

Carbon nanotubes are usually of two kinds, i.e. cylindrical single-walled nanotubes (SWNTs) and multi-walled carbon nanotubes (MWNTs) with "buckyballs" (C-60) as their fundamental structure. These are hollow containers (normally 3 to 100 nm in size) that have the ability to accommodate a payload and a wide variety of diagnostic or therapeutic agents. Carbon nanotubes are composed solely of carbon atoms which make them extremely hydrophobic which causes nonspecific binding to plasma proteins. Solublization of these particles is required, which is done by surface modification, including oxidation or conjugation to hydrophilic organic molecules (Tasis et al., 2003). These water soluble nano-structures have potential for biological research by retaining their strength, electrical properties, and thermal conductivities. But for these particles to be used in clinical applications

there are concerns related to their potential toxicity. It is difficult to carry out their surface modifications (Warheit et al., 2004) because recently conducted studies have shown that carbon nano-tubes crossing the cell membrane and retaining for longer periods, can cause cell death and inflammation (Kolosnjaj et al., 2007).

Nano-wires

Nano-wires are metal based semiconductors which are composed of silicon, carbon, and other materials that are widely used as chemical and biological sensors for the high-throughput detection of proteins and DNA (Wang et al., 2005) at cellular level as well as for the potential delivery of targeting agents (drugs) into living cells (Shalek et al., 2010). Single-crystal structured silicon nano-wires (2 to 5 nm) have been reported to prepare both p- and n-type materials, having the ability to perform better than planar silicon microelectronics (Ma et al., 2003). When water soluble coating is applied for in-vivo compatibility, the diameter of these particles increases from 10 to 300 nm so extreme caution is required if the clinical translation is to be considered for application of these structures (Poland et al., 2008).

Biological Nanoparticles

Nano-scale materials which are derived from biological components such as peptides, proteins, enzymes, antibodies, lipoproteins, viruses, and natural polymers are biological NPs. Artificially made NPs have shown undesired responses in in-vivo applications while naturally derived NPs demonstrated high biodegradability and biocompatibility (Lee and Mooney, 2001). Components of extracellular matrices that are mostly considered for tissue derived natural polymers are collagen and hylauronate due to minimal inflammation and can be used as imaging probes if suitable surface modification is done (Castaneda et al., 2008). Similarly NIR fluorophore conjugated proteins, ligands and antibodies have potential to be used as targeting probes for monitoring the therapeutic response (Vollmer et al., 2009). After chemical and physical absorption molecules like albumin, chitosan, dextran and dextrin having long blood half-lives have been evaluated for drug carrying potentials (Langer et al., 1986). However, some problems related to biological polymers can arise due to difficulty in controlling shape and size, degradation and immunogenicity of the NPs (Langer, 1998). These problems can be delimited by chemical cross-linking and chemical modifications but then the materials become artificial in nature.

Polymer Nanospheres

Synthetic polymers such as polylactic acid (PLA), polylactide-co-glycolide (PLGA), polyvinyl alcohol (PVA), polyacrylic acid and polyamino acids etc. are biodegradable in nature and are mostly biocompatible. Therefore, these have been used in the fabrication and processing of nano-spheres that have the potential to be used for the delivery of hydrophobic agents to the target site of the disease (Chan et al., 2009). These polymers can be coated with functional polymers such as PEG, poloxamines, poloxamers, or polysaccharides to produce "smart" polymer nanoparticles functioning in releasing drug molecules only after the action of a specific stimulus (pH, temperature, light, ionic strength, chemical environment) (Dhar et al., 2008).

Dendrimers

Spherical macro-molecular NPs (≤5nm) having highly branched internal structure are dendrimers with terminal groups controlling their interaction with the physiological environment. Dendrimers can encapsulate therapeutic agents either in their interior or on their surface due to their globular structure and internal cavities. Various

dendrimers have been used in diagnostic and therapeutic applications due to their biocompatibility, hydrophilicity, well defined structures easy conjugation with targeting ligands and flexibility (Baker, 2009). Though, production of dendrimers can be expensive as compared to conventional polymers and require complex repetitive steps for synthesis which is difficult to scale-up for production.

Liposomes

Spherical vesicles of lipid bilayer called liposomes have been reported in various occasions when drug delivery systems are studied. These vehicles have the tendency to carry hydrophilic and hydrophobic drugs, diagnostic agents, peptides, antibodies, hormones and other macromolecules after encapsulation by their lipid membranes, because of their large payload capacity and straightforward synthesis characteristics (Caruthers et al., 2006). Their synthesis does not require organic solvents but final products often suffer from poor mechanical stability and burst leakage (Moghimiet al., 1991). However, by introducing inert, biodegradable coatings such as PEG, lipid membranes can be stabilized and then functionalized with various targeting or therapeutic moieties, like peptides, oligonucleotides, and proteins (Langer et al., 1986).

Anti-Viral Approaches Using Nanotechnology

Respiratory Syncytial Virus (RSV)

Respiratory syncytial virus (RSV) is a respiratory pathogen which causes severe diseases like pneumonia and wheezing in human and is responsible for 1 million deaths annually (Thompson, 2003). There is no licensed vaccine currently for RSV. A gold nano-rod (approximately 21 nm to 57 nm in size stabilized by protein ligands) based RSV vaccine has been tested by conjugating viral fusion protein F, as an antigen, with gold nano-rods. Human Dendritic cells were able to phagocytose these dispersed nanoparticles and immune response through Human T cells was induced. This research suggested the use of this vaccine approach in immunization against Human viruses (Stone et al., 2013). DNA chitostan nanoparticles (80-150 nm) are used to deliver RSV antigenic regions cloned into cytomegalovirus vector. These nanoparticles were able to immunize mouse model against RSV with no cytotoxic effects of chitostan nanoparticles up to the concentrations of 400 micro gram per milliliter (Boyoglu et al., 2009).

Virus Based Vectors Delivery

A nano-patch delivery system for the delivery of viral vectors (adenovirus serotype 63 and the poxvirus) encoding malarial antigens has been developed(Pearson et al., 2013). Silicon micro-projections, coated with stabilizing disaccharides trehalose and sucrose protected viral vectors, were injected to murine skin. Animal showed the same immune response as compared to needle based delivery of live vaccine suggesting that this alternative method as advantageous method. Vaccination through nanoparticle based needles has also been reported by (Zaric et al., 2013). Robust clearance of the virus was seen by cytotoxic T lymphocytes as well as micro-needles showed the stable introduction of antigen in the recipient.

Herpes Simplex Virus (HSV)

Herpes simplex virus causes many severe diseases like cold sores, ocular keratitis, retinitis, meningitis and encephalitis. Moreover, it acts as a co receptor for other viruses e.g. respiratory syncytial virus, adeno-associated virus type 2 and human papilloma virus. Tin oxide (SnO_2) nano-wires, diameters hundreds of nm to the µm, are considered as a promising tool for inhibiting the entry of HSV-1 and its subsequent spread to other cells of the host.

These nano-wires interfere with the attachment of virus to the cellular receptor Heparin sulfate (Trigilio et al., 2012).

Influenza Virus

Influenza virus is very dangerous virus which affects 50 million people around the globe every year. Influenza virus A is responsible for pandemics e.g. Spanish flu, the avian flu, swine flu etc. There was a need of developing an approach which could be effective as well as not specific towards a particular strain of influenza since; different variant strains of influenza have been identified recently. Influenza virus spreads through ground and surface water. Conventional methods of disinfection of water have certain drawbacks as they are hazardous to human health (Liga et al., 2011). Porphyrin e.g. Protoporphyrin IX (PPIX) which has strong bactericidal and virucidal potentials has been conjugated with nanomaterial scaffolds known as nanotubes. This conjugate is photoactive and can be used to disinfect water. It has been reported that it can reduce the infection of virus to mammalian cell lines. Moreover, this material can be recovered by filtration leaving no toxic by-products and can be re used multiple times (Banerjee et al., 2012).Influenza A/H1N1 virus is responsible for 5,000 deaths around the world since October 2009 (WHO, 2009). (Chakravarthya et al., 2009) used gold nanoparticles and gold nanotubes for the delivery of ssRNA to activate RIG-I receptor (a pathogen recognition receptor) resulting in the up regulation of interferon and reduction in viral replication and load. Gold nano-rods are biocompatible and excellent delivery vehicles for the delivery of substances due to their surface modification properties (Ding, 2007).

SARS-Coronavirus

SARS-coronavirus or mouse pneumovirus has been treated with protein cage nanoparticle (PCN). PCN is a 12 nm in diameter spherical hollow protein cage made up of 24 identical protein subunits and is derived from Methanococcus jannaschii (a hyperthermophilic archaeon) (Kim et al., 1998). This non infection dependant strategy caused non-specific primary immunity against variety of respiratory viruses (Mail et al., 2009).

Human Papilloma Virus (HPV)

HPV, the most prevalent sexually transmitted disease, is associated with cervical carcinomas with prevalence of 25.2 % in women of 40-49 years of age 32. Vaccine delivery through syringe and needle can cause blood borne diseases and is responsible for 500, 000 deaths annually (Miller and Pisani, 1999; Prüss-Üstün et al., 2005). Nano-patch technology has been used in immunization of HPV. This nano-patch is in the form of short projections/needles with the length of 110 microns. This array sensitizes the immune cells in the dermis and epidermis. It is proved to be very good alternative approach to avoid syringe associated disease and a very good vaccine against cervical cancer causing virus (Corbett et al., 2010).

Herpes Simplex Virus-1

HSV1 is responsible for disease like ocular keratitis, genital disease, labial herpes and encephalitis. During viral infection, it enters the cell by interacting cell surface heparin sulfate molecules with filopodia like structures. Zinc oxide microstructures mimicking these cell surface molecules have been modeled, which trapped the viral particles and inhibited the viral entry into the host cell. This is a novel approach against HPV1 (Mishra et al., 2011).

West Nile virus and Chikungunya Virus

West Nile virus (WNV) and Chikungunya Virus (CHIKV) are viral pathogens which spread through mosquito. Their outbreaks are responsible for fatal diseases in human and have potential to spread all over the world. These viruses pose

severe threats to human populations and are strong targets for vaccine development. Prow et al, used the above mentioned nano-patch technology against these two viruses for immunization purposes in mouse models, suggesting it as a very efficient and cost effective method for immunization (Prow et al., 2010).

Foot and mouth disease virus (FMDV)

FMDV is ssRNA, non-enveloped icosahedral virus which causes foot and mouth disease in animals and is responsible for loss in economy by causing reduced milk production and weight loss in animals (Grubman and Baxt, 2004). A study showed that the dose dependent use of gold nanoparticles as a carrier of vaccine components of FMDV. Gold nanoparticles of size 8-17 nm were found to be most immunogenic with no antibody response against the particles. This approach was completely synthetic i.e. a FMDV resembling protein was synthesized and conjugated with the gold nanoparticles (Chen et al., 2010). FMDV associated peptides conjugated to nano-beads have also shown the development of immunity in sheep (Greenwood et al., 2008).

Cytomegalovirus (CMV)

Arnedo et al. (2004) studied antisense phosphodiester oligonucleotides conjugated with albumin nanoparticles (250 nm) to avoid nuclease degradation of oligonucleotides. Nuclear localization of these oligonucleotides resulted in anti-CMV activity.

Dengue Virus

A novel photo-inactivation therapy has been developed against dengue virus by nanotechnological approach. Zinc phthalocyanine was adsorbed on nanotransducer, which upon activation by light can produce reactive oxygen radicals having virucidal effects. Therapy eradicated virus effectively with minimal cytotoxic effects (Lee et al., 2008).

Adenovirus

Adenovirus is a non-enveloped dsDNA virus associated with ocular, gastrointestinal and respiratory diseases. This virus has high morbidity in immunocompromised patients. Silver nanoparticles have been reported to have virucidal effects on adenovirus. Silver nanoparticles act directly on the viral particle and causes the inhibition of virus resulting in the decrease in DNA(viral) load in the host (Chen et al., 2013).

HIV

Human immunodeficiency virus (HIV) is responsible for acquired immunodeficiency syndrome (AIDS) a sexually transmitted disease. 33 million people are infected with AIDS at this moment around the world (Morris and Lacey, 2010). The situation is getting worse as a promising therapy called highly active antiretroviral therapy (HAART) have also shown the side effects (Hankins and Dybul, 2013). Different prophylactic modalities have been used against HIV. Nano-carriers have offered many benefits which can be useful in overcoming the challenges that are associated with current prophylactic modalities. Different types of nano-architectures have been developed for HIV prophylaxis summarized in **Table 2,** highlighting their specific features (Date and Destache, 2013).

Table 2. Prominent features of different nano-architectures.

Architecture	Features
Dendrimers	Several drug molecules or ligands conjugated to a single dendrimer Augmented interaction of ligand with receptor due to "multivalency" Tailored to achieve desired physicochemical and/or biological properties
Polymeric nanoparticles	Biodegradable or non-biodegradable polymers for desired application Sustained release of encapsulated therapeutic agents Improved chemical, enzymatic and metabolic stability of encapsulated therapeutic agents Amenability for surface modifications
Liposomes	Excellent biocompatibility due to use of phospholipids Ability to encapsulate hydrophilic as well as hydrophobic agents Commercially feasible technologies available for large scale production
SLN/NLC	Low cost biodegradable solid lipids Sustained release of encapsulated therapeutic agents Ability to avoid first pass metabolism by augmenting lymphatic transport
Drug nano-crystals	Drugs transformed to nano-scale using top down/bottom up techniques Significant improvement in solubility/dissolution velocity of hydrophobic drugs Improvement in bioavailability and reduction in intra- and inter-subject variability in pharmacokinetics
Inorganic nanoparticles	Tunable optical and surface characteristics Multiple drug/ligand molecules conjugated to surfaces Ability to function as therapeutic and diagnostic modality after suitable modifications
Nano-fibers	Dimensions similar to fibers present in extracellular matrix Wide applications in regenerative medicine Localized and sustained delivery of therapeutic agents A wide variety of materials can be assembled into nano-fibers

Conclusion

Nanotechnology, an interdisciplinary field comprising the materials at nano-scale has been explored for various purposes exploiting the distinctive features of highly active and stable nanoparticles. These particles arise from distinct origins and have different characteristics as compared to the bulk particles of same origin e.g. surface area to volume ratio. Such properties result in varying interaction abilities of these particles which have been translated into

different application. In medicine, biomedical imaging and diagnostic abilities of such structures have been reported which make use of certain fluorescence properties related to the discrete set of particles. Virology deals with the viral infections and the targets related to such diseases. The biomedical applications of nanotechnology have been widely extrapolated against HIV. Other viruses like Dengue virus, HPV, Adeno virus, HSV, Cytomegalo virus, FMDV and West-nile virus have also been studied in context of potential activity of nano-scale agents in combating these infections. Such studies have resulted in useful information in context of clinical translation of these reported studies. This review focused on the current status of nanoparticles in specific systems that work against viruses using the conceptual translation of the nano-scale moieties. Different targets for various virology related entities have been exploited and resulted in promising aspects of targeting agents and nano-therapeutics. Systems generated through such novel approaches having ability to combat the diseases through targeted mechanisms are not only important but indispensible in future. So we can say that a new era is under way in which building blocks at nano-scale can be tailored to not only fight the diseases but to monitor the therapeutic responses in real time by exploitation of multivalent nano-carrier systems.

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