ROLE OF SURFACE FUNCTIONALIZATION OF NANOPARTICLES IN NANO-BIO INTERACTION

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ABSTRACT

With the advent of broad spectrum application of nanoparticles (NPs) in biological domain, there is paramount importance to evaluate nano-bio interaction in more detail. Not only the size and shape of NPs but also the surface capping material plays a pivotal role in cross talk between NPs and biological world. Here the role of surface ligand in determining the stability of NPs in different solvents is discussed especially in case of gold NPs. The toxicity parameters also get changed depending on the capping material present on the surface. In a bioassay it was revealed that NPs of same size and shape but with different surface functionalization interact differently with the surface of the virus called as Bombyx mori *nuclear polyhedrosis virus. So it can be concluded that surface capping agents play a pivotal role in determining the interaction of NPs with biological domain.*

Keywords: Bmnpv, Capping Agent, Dispersion Property, Murine Toxicity, Surface Contour

I. INTRODUCTION

Nanotechnology can be defined as the postulated ability to manufacture objects and structures with atomic precision, specifically atom by atom. Even from the basic research perspective, nanoscience is very much interesting because materials at their nanoscale emerge with unique properties associated with quantized effects and preponderance of surfaces and interfaces. That is why research in the field of nanotechnology is a highly interactive amalgamation of relatively traditional disciplines of physics, chemistry, biology, computer science and engineering. Compared to the bulk counterpart, nanoparticles (NPs) are inherently unstable due to their immense surface-to-volume ratio and the consequent high surface free energy [1]. In general, they have to be stabilized by a matrix which, in the simplest case, may be a mono-molecular coating of organic molecules, such as dodecanethiol coated gold NPs (GNPs). The interaction between the functional group of these molecules and the NP surface passivates the surface energy of the latter, but in the process the entropy may not be maximized. In particular, the organic molecules may be constrained to a smaller set of conformational states than in the bulk [2]. This lowered entropy produces a force which tries to oppose the lowering and acts as driving force for the interaction of the NPs with their surroundings. Therefore, a coated NP, as described above, when applied on cells and tissues, may interact strongly with such systems, leading to some very striking effects. The capping materials mostly define the dispersion property and stability of the NPs synthesized and ultimately dictates the course of nano-bio interaction.

Nowadays NPs are being used in various fields of daily life starting from electronics [3] to food packaging [4], medical diagnostics [5], drug delivery [6] etc. In a nutshell every day we are getting more and more exposed to different NPs. Thus study of interaction of nanomaterials with the biological interface has paramount importance. As the capping molecules play a pivotal role in dictating the overall property of the NPs, the interaction of these surface ligands with the biological interface should be studied carefully. In this article the role of surface capping agents particularly in case of GNPs is highlighted in determining their stability and toxicity in murine model system. Moreover, the nature of interaction of GNPs and few other NPs having different surface capping agents with the polyhedra body of *Bombyx mori* nuclear polyhedrosis virus (BmNPV) is also highlighted here.

II. ROLE OF SURFACE FUNCTIONALIZATION ON DISPERSION PROPERTY AND STABILITY OF GOLD NANOPARTICLES

GNPs were functionalized with different surface capping agents like aspartate (GNPA), bovine serum albumin (BSA), citrate (GNPC) and thiol (GNPT). It was found that change in molar ratio of reactant contents have strong relation with the size of NP produced. But not only the concentration and specificity of reducing material is important but also surface stabilizing material plays pivotal role in determination of their final shape and size. Capping material mostly defines the dispersion of GNPs synthesized. As for example, thiol capping enabled GNPT to disperse in only organic solvent whereas citrate, aspartate and BSA capping made GNPA, GNPB and GNPC soluble in polar solvent [7]. Dispersion of NPs to their respective solvents has strong relation with their interaction to the biological world. Although thiol capping renders interesting catalytic property to GNPs but water dispersible GNPs are more popular for biological usage.

As we are considering interaction at nano-bio domain, the stability study of the synthesized NPs in different buffers and molecules of biological relevance is also immensely important. The stability of GNPs was tested in NaCl solution, phosphate buffer saline (PBS), foetal bovine serum (FBS) of different concentration and at different pH. In this case, it was also found that surface functionality had significant implication. GNPs of nearly similar size but with different surface properties behaved differently with respect to their stability in different solvents. GNPA was found to be most vulnerable in losing stability and thus prone to agglomeration. GNPC was almost stable except in extreme NaCl and PBS concentrations used. GNPB, with long BSA chain was able to maintain normal helicity in all conditions [7].

III. INTERACTION OF NANOPARTICLE WITH SURFACE OF VIRAL POLYHEDRAL

In spite of large amount of initiative including bed disinfectants and plant material based therapeutic approaches to control grasserie disease in silk worm, threat to sericulture industry remained unchecked. In this disease the infected silk worm larvae fails to pupate and thereby cocoon formation is inhibited. Even if the infected larvae successfully pupate, they die thereafter without the completion of life cycle. Thus, an urgent need is being felt for more scientific and targeted management of the sericulture sector. In our study it was found that NPs with proper surface functionalization can prevent BmNPV infection by acting on the surface of the viral polyhedra (Figure 1).

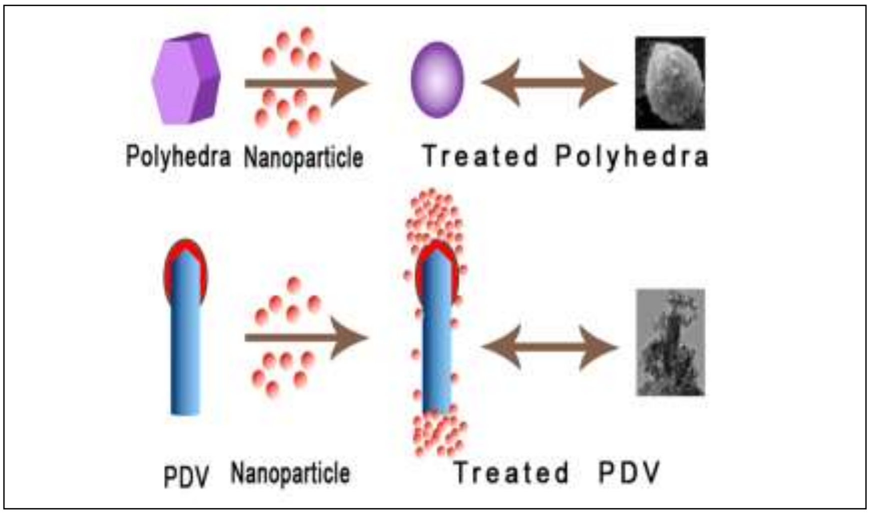

Figure 1. Morphological transition of BmNPV polyhedra caused by nanoparticle treatment.

The interaction of four NPs (with different surface cappings) with BmNPV polyhedra body was screened. Different types of NPs used in this bioassay were GNPA, GNPB, GNPC, hydrophilic, hydrophobic and lipophilically coated silica NPs (SNPs) and zinc oxide NPs (ZNPs), and hydrophilic Alumina NPs in the hexagonal close-packed α structure and cubic γ structure (ANPα and ANPγ respectively). Here it was observed that similar NPs with different surface property interacted with polyhedra body differentially. Lipophilically coated SNP was most effective in distorting the viral surface contour, followed by moderately effective ANP. Though lipophilcally coated SNP caused morphological transition in BmNPV, hydrophilic and hydrophobic SNP was not much effective in this regard (Figure 2). These finding also corroborated our initial results where we found that along with type of nanomaterial surface property also plays a crucial role in nano-bio interaction [8]. SNPL not only deformed viral structure but also controlled the lethal infection both *in vitro* and *in vivo.* Mechanism of action behind antiviral potential of SNPL was different from other approaches taken so far to control grasserie infection. SNPL caused severe distortion to viral morphology with roughening transition of the surface contour and ultimately the polygonal structure was transformed into a nearly spherical one and ultimately it gave the silkworm larvae a prophylactic treatment to the infection [9]. This approach not only protected the infection to a considerable amount but also expanded the life of infected silkworm significantly. But in our SNPL mediated prophylactic approach the larval pupation was in time, cocoon was formed and mature ones emerged thereafter. These adults were able to lay egg form where second generation larvae emerged. Spraying of NPs on mulberry leaves, the primary source of baculovirus polyhedra body through food to the larvae, will render much more reduced infection due to NP mediated inactivation of virus prior to their ingestion. It will not only be an avenue toward NP based approach to sericulture but also viral inactivation in general.

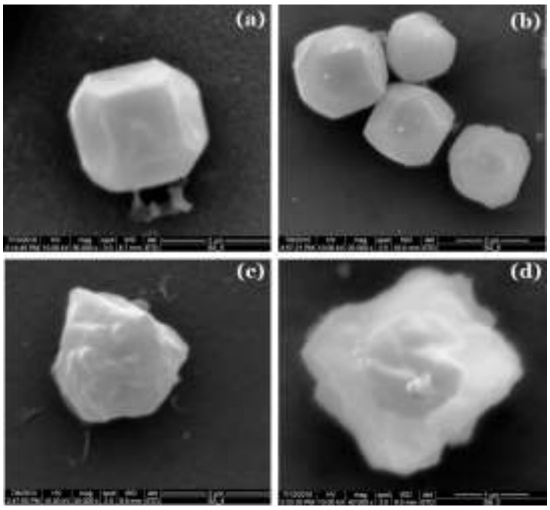

Figure 2. The extent of deformation of BmNPV polyhedra caused by treatment of differently functionalized silica nanoparticles. (a) hydrophilic, (b) hydrophobic and (c) lipophilically coated silica nanoparticle. In all cases BmNPV polyhedra was exposed to these nanoparticles at 7000 ppm of dosage.

IV. NANO-BIO INTERACTION IN TERMS OF TOXICITY

Ultimately the *in vivo* toxicity of differently capped GNPs was examined in murine model system. For many years colloidal gold is being used as elixir of life. But GNP related toxicity which may differ with its surface cappings was never studied thoroughly in mammalian model system. This toxicity study revealed that different GNPs (GNPA, GNPB and GNPC) had differential pattern of interaction with mice health especially to liver and kidney parameters. As for example, *in vivo* assay with very high dosage showed some abnormalities in liver and kidney parameters for GNPA and GNPC treatment, as these two organs are primary repository of any foreign substances. GNPB was found to be non-toxic to these two organs. Results from histopathological parameters were also having correlation with biochemical parameters obtained from treated mice serum sample. Although mice exposed to GNPs did not exhibit any significant alteration in weight of organs, tissue damage or lesions in any of the sections of brain, heart, lungs, spleen, testis and ovary. Mortality or any other deleterious symptoms of any disease was not evident in any cases. Further long term toxicity analysis is needed.

V. CONCLUSION

This study reveals that surface capping material of NPs is an important factor to be considered during nano-bio interaction for their successful implication in different biological applications. Study of interaction of NPs with BmNPV polyhedra in controlling grasserie disease of silk worm will have far reaching implication in NP based novel approach to combat virus inactivation in general. Toxicity and stability analysis of NPs can ensure their suitability and safety aspects in different biological interactions.

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