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Review Article

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Role of metal and metal oxide nanoparticles as diagnostic and therapeutic tools for highly prevalent viral infections

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Abstract

Nanotechnology is increasingly playing important roles in various fields including virology. The emerging use of metal or metal oxide nanoparticles in virus targeting formulations shows the promise of improved diagnostic or therapeutic ability of the agents while uniquely enhancing the prospects of targeted drug delivery. Although a number of nanoparticles varying in composition, size, shape, and surface properties have been approved for human use, the candidates being tested or approved for clinical diagnosis and treatment of viral infections are relatively less in number. Challenges remain in this domain due to a lack of essential knowledge regarding the in vivo comportment of nanoparticles during viral infections. This review provides a broad overview of recent advances in diagnostic, prophylactic and therapeutic applications of metal and metal oxide nanoparticles in human immunodeficiency virus, hepatitis virus, influenza virus and herpes virus infections. Types of nanoparticles commonly used and their broad applications have been explained in this review.

Key words: Nanoparticle; Metal and metal oxide; Virus

Nanomaterials have attracted enormous interest in field of targeted therapeutics and diagnostics in the past decade.[1,2] As the nanoparticles typically span in the size range of 10-500 nm, their interactions with mammalian cells can be programmed based on the particle size and functional requirement. In addition to more conventional polymeric nanoparticles, metal and metal oxide nanoparticles can also play a major role in detection,[2] and external control over drug delivery.[3] Over the past two decades, various nanoparticles and drug delivery models have been designed and implemented to treat cancers,[3,4] offset diabetes,[5] control bacterial infections via antimicrobial coatings,[6] cross the blood brain barrier,[7] and form vaccines.[8]

Nanomaterials offer a plethora of opportunities in the field of medicine owing to the unique quantum mechanical properties exhibited in their size range. The market share of these medical innovations based on nanotechnology has grown approximately 20 times in the past decade. The emergence of commercially available quantum nanodots, superparamagnetic nanoparticles and nanopolymeric suspensions has given previously unavailable tools to scientists who did not have sophisticated laboratories to produce the same. This has not only increased the use of nanomaterials in biological sciences, but has seen the birth of new fields of study such as nanovaccinology and nanobiotechnology.

The role of nanotechnology in virology, in particular, has been increasing exponentially in the past decade (Figure 1). In diagnostic, prophylactic and therapeutic approaches, nanoparticles have been used for imaging purposes,[9] and/or as drug carrying adjuvant to enhance virucidal properties.[10] Virucidal nanoparticles and drug delivery models have been used mainly for the fighting human immunodeficiency virus (HIV), hepatitis (type A, B, C and E) and herpes simplex virus (HSV-1 and HSV-2). The use of nanoparticles for virucidal outcomes is still under investigation and has not been approved for clinical or pre-clinical trials.

In this review, we provide an overview of recent advances made in the broad area of virology with specific focus on the use of metal and metal oxide nanoparticles. We first survey the advances made in the general field of nanomaterials for virology followed by their specific use in fighting HIV, hepatitis and herpesvirus infections.

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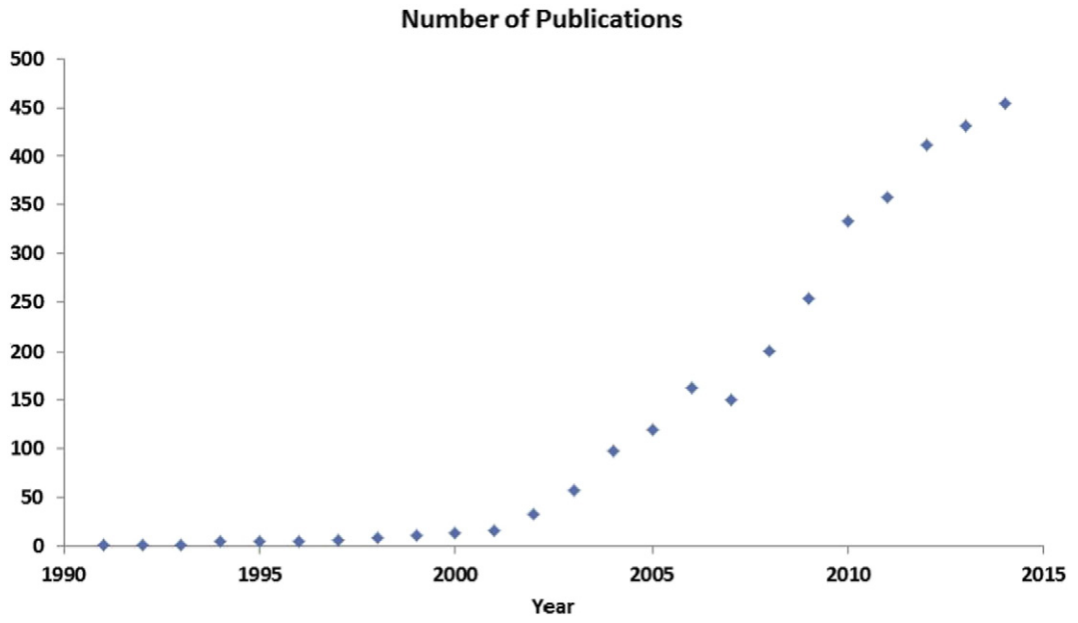

Figure 1. Number of publications returned using the search terms "nanoparticle* and virus*" from Scopus (http://www.scopus.com/; results for a search conducted on 19 October 2015).

Each of them would be further sub-divided to highlight their usage in detection, and treatment of viral diseases.

Use of nanoparticles in virology

A broad survey of literature revealed that majority of the published studies which use nanomaterials were focused on detecting/and/or treating HIV, followed by hepatitis (A, B and C) virus, influenza virus and herpes simplex virus (1 and 2). A few other studies have also been conducted in the areas of detection and treatment of human papilloma virus, human rotavirus and Japanese encephalitis virus. Further, it is interesting to note that the majority of studies use polymeric systems such as polyethylene glycol (PEG),[11] poly-lactic-co-glycolic acid (PLGA),[12] and liposomes[8] for the drug delivery systems. While the use of metal nanoparticles has been strictly restricted to gold and silver, metal oxide nanoparticles such as iron oxide (magnetite), zinc oxide (ZnO), and titanium dioxide (TiO_2) have been used in the past studies as well. Although many reports relating to the use of virus like particles (VLPs)[13] and nano-DNA vaccines[8] have been discussed, this review will limit to the study of metal and metal oxide nanoparticles used in virological studies. A broad Scopus search for the terms 'Virus' and 'nanoparticles' showed numerous studies published since 1990s (Figure 1).

Studies on HIV

Detection

Traditionally HIV has been detected using enzyme linked immunosorbent assay (ELISA). This remains to be the gold standard for the detection of HIV in a clinical scenario. Over the past decade, various enhancements have been made to this process in order to increase the efficiency several fold. The more prominent detection process involves the use of polymerase chain reaction (PCR) for enhancing viral DNA in a given sample and hence pertaining to the detection of the same.

With the advent of nanotechnology, detection mechanism of HIV has been modified using various nanomaterials. One of the simplest methods for detection of viruses involves the measurement of aggregation (and resultant color change) in gold nanoparticles attached to viruses (Figure 2). Xiansong et al[14] used gold magnetic particles functionalized with antibodies against the HIV capsid protein p24 and gold nanoparticles functionalized with both oligonucleotide barcodes and antibodies against a non-overlapping region of the cognate p24. Using this, they improved the real time immuno-PCR amplification process for the detection of HIV. Limit of detection of this model was as low as 100 copies of p24 antigens which show that real-time immune-PCR through nanoparticle based barcode amplification offers an disruptive approach to p24 detection and quantification, thus may potentially shorten the window of HIV-I diagnosis. Using a similar bio-barcode based method. Kim et al[15] evaluated the efficiency of this technique at the Chicago component of the multicenter AIDS cohort study. The results indicated that the bio-barcode-amplification method was superior to the conventional ELISA assay for the detection of HIV-1 p24 Gag protein in plasma with a breadth of coverage for diverse HIV-1 subtypes. Although bio-barcode based methods have further been used by many other groups with greater efficiency, the use of gold nanoparticles remains to be the common link in these processes.[16–18]

In a novel study, Mahmoud et al,[19,20] exploited the chemical interaction between HIV-1 protease and pepstatin for the detection and subsequent evaluation of its inhibitors. A ferrocene tagged, gold nanoparticle coated single walled nanotube (SWNT/AuNP) was used as the electrode in an electrochemical impedance spectroscopy technique for this purpose. Later the same group