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In vitro toxicity assessment of chitosan oligosaccharide coated iron oxide nanoparticles

Sudeep Shukla[a,*], Alka Jadaun[b], Vikas Arora[c], Raj Kumar Sinha[d], Neha Biyani[e], V.K. Jain[a]

[a] School of Environmental Sciences, Jawaharlal Nehru University, New Delhi 110067, India
[b] School of Biotechnology, Jawaharlal Nehru University, New Delhi 110067, India
[c] Department of Chemistry, Indian Institute of Technology, New Delhi 110016, India
[d] Centre for Biomedical Engineering, Indian Institute of Technology, New Delhi 110016, India
[e] School of Life Sciences, Jawaharlal Nehru University, New Delhi 110067, India

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ABSTRACT

Iron oxide nanoparticles (INPs) have potential biological, biomedical and environmental applications. These applications require surface modification of the iron oxide nanoparticles, which makes it non-toxic, biocompatible, stable and non-agglomerative in natural and biological surroundings. In the present study, iron oxide nanoparticles (INPs) and chitosan oligosaccharide coated iron oxide nanoparticles (CSO-INPs) were synthesized to evaluate the effect of surface coating on the stability and toxicity of nanoparticles. Comparative *in vitro* cytotoxicity of nanoparticles was evaluated in HeLa (human cervix carcinoma), A549 (human lung carcinoma) and Hek293 (human embryonic kidney) cells by using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay along with flow cytometry study for cell viability, membrane integrity, mitochondrial membrane potential (MMP) and reactive oxygen species (ROS) production. Morphological alteration in nanoparticles treated cells was analyzed by Acridine orange/ethidium bromide double staining and electron microscopy. Synthesized nanoparticles were found to be spherical in shape, well dispersed and stable at various pH values, making them suitable for biomedical and environmental applications. The present study also indicates that the chitosan oligosaccharide coating on iron oxide nanoparticles results in the decrease in cellular damage and moderate ROS production, thereby, significantly decreasing the cytotoxic impact of bare iron oxide nanoparticles.

1. Introduction

Nanoscience has emerged as an innovative research field having application in a number of scientific and technological areas, including materials science, electronics, biotechnology and medical sciences [1]. Nanomaterials can be found in more than 1000 consumer products including electronic components, cosmetics, antimicrobial and stain-resistant fabric cleaning products [2,3]. Among the nanostructured materials, metallic nanoparticles in particular, iron oxide nanoparticles have been the focus of intensive research. Magnetic iron oxide nanoparticles have potential applications in various disciplines of science ranging from environmental remediation to biomedical such as magnetic drug targeting, tissue repair, and cell tissue targeting [4].

* Corresponding author. Tel.: +91 9873674030.
E-mail addresses: sudeepshukla@gmail.com, sudeepshukla@rediffmail.com (S. Shukla).

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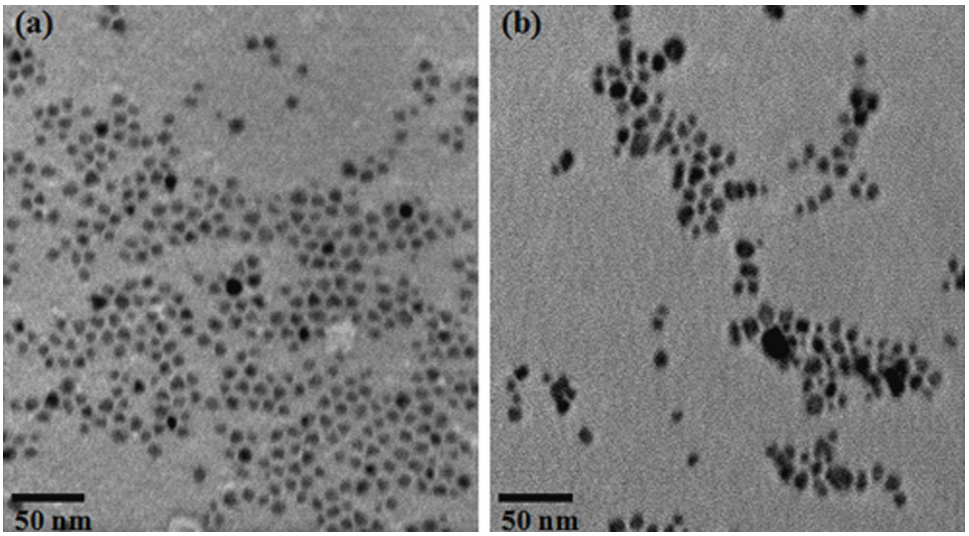

Fig. 1. TEM image of iron oxide nanoparticles (INPs) (a). TEM image of chitosan oligosaccharide coated iron oxide nanoparticles (CSO-INP) (b).

Magnetic iron oxide nanoparticles with a bare surface tend to agglomerate because of strong magnetic attractions among the particles. Stabilizers such as carboxylates, inorganic compounds and polymeric compounds have functional groups to modify these particles and enhance its stability [5,6]. Among the various polymers, chitosan an alkaline product of chitin has been widely examined due to its hydrophilicity, biocompatibility and biodegradability [7,8]. Chemically chitosan is insoluble in water and behaves as a weak base making it inappropriate for biological and environmental applications. On the other hand, chitosan oligosaccharides, which can be produced by degradation of chitosan polymer chain, are water soluble making it suitable for biological and environmental applications [9].

Previous studies have highlighted the potential environmental and health hazards caused by nanomaterials [10–13]. Nanoscale properties such as high surface to volume ratio, high surface energy, and higher surface reactivity may imperil human health through cytotoxic and genotoxic effects [13].

Nanomaterials can enter the human body through dermal absorption, respiratory inhalation, or oral route. Due to their ultrafine size, they are able to move across the olfactory mucosa, alveolar membrane and capillary endothelium. The ability of nanomaterials to cross blood brain barrier enhances its toxicity for the nervous system [14].

There is an urgent need for understanding the potential risks associated with iron oxide nanoparticles along with the range of surface coatings utilized for its functionality [15–17]. Earlier published reports corroborate the probable mechanism of internalization and interaction of iron oxide nanoparticles with various cellular targets mainly mitochondria, nucleus and DNA [18,19].

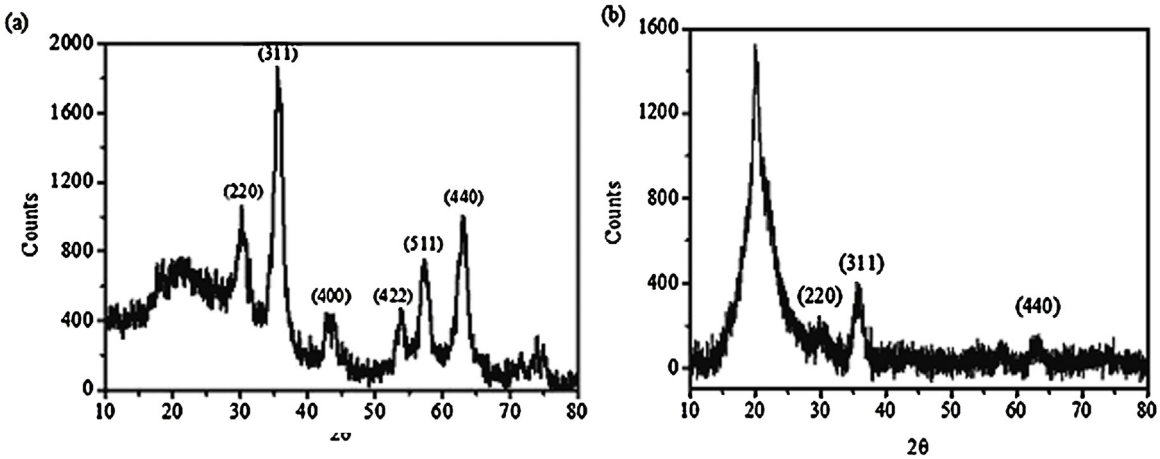

Fig. 2. X-ray diffraction (XRD) pattern of iron oxide nanoparticles (INPs) (a). X-ray diffraction (XRD) pattern of chitosan oligosaccharide coated iron oxide nanoparticles (CSO-INPs) (b).