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AN STUDY ON CYTOTOXICITY OF NANOPARTICLES

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Abstract

Prior to their application in medicine, nanoparticles must be biocompatible and non-toxic. Because they are so small, nanoparticles can enter the body fast and go through a number of different pathways to reach the organs that are intended to be their targets. A range of parameters, including as size, charge, shape, chemistry, and modifications, might influence a nanoparticle's cytotoxicity. In order to assess the toxicity of nanoparticles, this article provides a succinct overview of many in vitro cytotoxicity experiments. Nanoparticle cytotoxicity is a result of their higher surface area to volume ratio. Increased oxidative stress, cellular dysfunction, and ultimately cell death could result from this increased surface area to volume ratio. A wide variety of nanoparticles are covered in this review, including those that are most frequently utilized in biological research as well as those composed of metal and carbon.

Keywords; Nanoparticles, Cytotoxicity, biocompatible.

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1. Introduction

Silver nanoparticles, or Ag-NPs, are the talk of the town and have the biggest potential impact when compared to other non-materials. As a result, they are currently going through a period of high demand [1]. Ag-NPs have shown useful in a wide range of industries, such as biotechnology, pharmacology, magnetic fields, engineering, medical devices, and environmental cleaning [2]. Ag-NPs have acquired popularity in a wide range of industries, including but not limited to the textile, food, consumer goods, and medical industries, among others, because of their potent antibacterial action in both solution and component form [3].

Ag-NPs are in great demand across a wide range of sectors due to the fact that, in comparison to bulk materials, they possess different physical and chemical features as well as the potential to inhibit bacterial growth. For example, since Ag-NPs have a larger surface area to volume ratio than bulk particles, they are better able to interact with fluid components of the lung lining such as serum, saliva, and mucus [4]. Bulk particles, on the other hand, have a smaller ratio of surface area to volume. However, the robust oxidative activity of Ag-NPs results in the production of silver ions, which are known to have a broad range of deleterious effects on biological systems, including cytotoxicity, genotoxicity, immunological reactions, and death of cells [5-8]. Colloidal Ag+ that has been activated for medicinal or other reasons could have an effect, either directly or indirectly, on the health of human beings [9]. Because of the increasing usage of Ag-NPs, the concentration of Ag+ in soil has grown by 22.7 ppm, while the increase in the concentration of Ag+ in water has been measured at 0.76 ppm [9, 10]. Unanswered problems include whether or whether Ag-NPs can be safely

synthesised, as well as the mechanism by which they function as a disinfectant in the environment. It is still unclear the mechanisms by which Ag-NPs exert their cytotoxicity or the degree to which they may impact human physiology in either the short or long term [11, 12]. There may be cause for worry due to a lack of understanding about the ways in which nanoparticles interact with biological systems [13, 14].

2. Evaluations of Potential Cytotoxicity

Researching a drug's effects on cells in culture is often the first step in figuring out how those effects will manifest in living organisms. In comparison to research on animals, testing on
cells are more useful, less expensive, and less questionable from an ethical standpoint. When considering cytotoxicity, it is essential to take into account the fact that cell cultures are sensitive to changes in their surrounding environment, including temperature, pH, and the quantity of nutrients and waste products. Due to the fact that nanoparticles may adsorb dyes and are redox active, it is essential that the cytotoxicity test be used in the correct manner. It is advised that many tests be performed in order to get accurate findings. An easy method for determining cytotoxicity is to examine changes in the cellular or nuclear morphology of the cells using bright-field microscopy. This method was used by Fiorito et al. [15] in order to determine the level of cytotoxicity shown by single-walled carbon nanotubes (SWNTs). A frequent site for the dye to be stored is inside the lysosomes of the cell. The differential absorption of neutral red by living cells as compared to non-living cells, followed by the subsequent release of the dye, is the basis for the capacity to differentiate between the two. An evaluation of the cytotoxicity may be accomplished by the use of spectrophotometric examination of neutral red absorption at varying concentrations. [16] The neutral red test was used in two separate studies examining the cytotoxicity of carbon nanotubes. These studies were conducted by Flahaut et al. and Monterio-Riviere et al. (17, 18] Only cells with broken membranes are able to be penetrated by the diazo dye trypan blue, which is why it is only able to selectively stain dead cells blue while leaving living cells colourless. The use of light microscopy is helpful in evaluating the level of cell death that has occurred.[19] This test was used by Bottini et al. and Goodman et al. in order to evaluate the cytotoxicity of gold nanoparticles and SWNTs, respectively.[20, 21]. When excited at 495 nm, calcein AM and ethidium homodimer both display distinctive fluorescence signatures at 515 and 635 nm, respectively.[22] As a third method for determining cytotoxicity, lactate dehydrogenase (LDH) release monitoring has been used in a number of studies that have made use of carbon nanoparticles. [23-25,] During this experiment, LDH is released from injured cells, where it oxidises lactate to pyruvate. This, in turn, stimulates the conversion of tetrazolium salt INT to formazan, a water-soluble molecule that absorbs light at 490 nm. Tetrazolium salts may be used as a tool for measuring mitochondrial activity [26] because to the fact that mitochondrial dehydrogenase enzymes are capable of severing the tetrazolium ring. The quantity of lactate dehydrogenase (LDH) that is secreted is directly proportional to the number of cells that have been damaged or lysed. Because these enzymes are only found in the most effective, living mitochondria, the process can only take place in cells that are still alive. There is a "comet" structure to DNA damage, with healthy DNA positioned at the "head" of the cell and damaged DNA fragments departing via the "tail" of the cell. When gels are analysed using the DNA-specific dye propidium iodide, the quantity of DNA found in the tail has an inversely proportional relationship to the degree of DNA damage that is found.[27-31]

3. The cytotoxicity of PLGA nano formulations is the third point.

3.1 Experiments using culture dishes

PLGA nanoparticles that have been conjugated with specific targeted ligands that supply specific active compounds have been shown to be effective against cells in the brain, lung, colon, belly, gastric, liver, ovary, cervix, prostate, uterine, pancreas, skin, umbilical vein endothelial, oesophagus, bladder, head, neck, and kidney. This has been demonstrated through scientific research.

3.1.1 Brain

When compared to the other drug carriers that were investigated (3.1.1 Brain Magnetic silica), the PLGA nanoparticles that were loaded with doxorubicin and paclitaxel had the most effective fatal impact (IC50 = 0.13 g mL1.32) against the U-87 brain cancer cells. In
this work, the primary targets of transferrin were found to be overexpressed transferrin receptors in brain capillary endothelium and glioma cells. Using concentrated ligands increased the bioavailability of drug-loaded nanoparticles. [32]

3.1.2 Breast

When aromatase inhibitors were used to treat SKBR-3 breast cancer cells, the lipid-coated PLGA nanoparticles containing 7-(4′-amino) phenylthio-1,4-androstadiene-3,17-dione (7-APTADD) proved to be the most effective treatment. [33]

3.1.3 Lung

Nanoparticles loaded with paclitaxel and modified with arginine-glycine-aspartic acid (RGD) peptide had the most significant fatal impact against H1975 lung cancer cells lines (IC50 = 0.0017 g mL1.34). This was determined by measuring the IC50 value. Because of the properties of RGD, the PTX-PLGA-CSNP-RGD nanoparticles demonstrated enhanced absorption. [34]

3.1.4 Liver

To stabilise PLGA nanoparticles, it is now common practise to make use of TPGS, which is a waste product that results from the production of vitamin E. Peptide-conjugated LFC131 nanoparticles were taken up by HepG2 cells three times more effectively than uncentered nanoparticles, and LFC131 was able to overcome multi-drug resistance [35] owing to its activity as a P-glycoprotein inhibitor. Peptide-conjugated LFC131 nanoparticles were taken up by HepG2 cells three times more efficiently than uncentered nanoparticles. After 24 hours of treatment, CX-EPNP shown a good anti-

proliferative activity against HepG2 cells, with an IC50 of 0.78 g mL1 and an IC50 of 0.38 g mL1 after 48 hours of therapy, respectively. [36]

3.1.5 Ovary

The possibility of using PLGA nanoparticles to deliver paclitaxel to ovarian cancer stem cells (OCSCs) emerged as a result of this research. It was possible to produce PLGA nanoparticles loaded with paclitaxel by evaporating the emulsion solvent, and then it was possible to conjugate these nanoparticles with folic acid (FA), which is a highly concentrated ligand. According to the results of the cytotoxicity test, FA-conjugated nanoparticles had an IC50 of 0.00075 g mL.[37], and FRs are indicators that may be over-expressed in human cancer cells, including ovarian cancer cells.

3.1.6 The Endothelium of the Umbilical Vein

An in vitro investigation was conducted in which human umbilical vein endothelial cells (HUVECs) were treated with poly (-amino ester)-synthesized, reversible pullulan-conjugated PLGA nanoparticles loaded with either paclitaxel or combretastatin A4. Pullulan-conjugated PLGA nanoparticles were shown to have a high level of cytotoxic activity in HUVECs, as shown by their IC50 values of less than 0.0396 and 0.0118 g mL1, respectively.[38] In HUVECs, the polysaccharide spine of pullulan has an unusually strong affinity for the asialoglycoprotein receptor (ASGPR).

3.1.7 Organ Systems, the Kidney

We were able to achieve targeted delivery of doxorubicin to the COS-7 kidney fibroblast-like cell line by building folate-focused and discount-precipitated PLGA nanoparticles. This allowed us to more effectively treat the cancer. To create PLGA nanoparticles with a concentration of folate, a monolayer of soybean lecithin was covered with a layer of monomethoxy-poly (ethylene glycol)-S-S-hexadecyl (mPEG-S-S-C16) before the coating was applied. The poor environment (high awareness of glutathione) of cancer cells [39-42] makes the disulfide bonds (-S-S-) in the outer layer of mPEG-S-S-C16 highly degradable. This makes it possible for drugs to be released at the location of the tumour. In FR-risky COS-7 cells, there was not a discernible difference in the level of cytotoxicity between center-centered and non-cantered PLGA nanoparticles. This demonstrates that FR-mediated endocytosis was necessary for folate-targeted PLGA nanoparticles to be absorbed by mobile organisms.[43]

3.2 Cytotoxicity and Body Dimensions

According to the cytotoxicity results, the anti-proliferative impact of PLGA nanoparticles might be noticed as early as three hours and as late as 240 hours after exposure to the nanoparticles. The average size of PLGA nanoparticles ranged from 58 to 407 nm, although the size might be anywhere in between. It was seen that the IC50 of cytotoxicity rose as particle size grew, which suggests that smaller nanoparticles induced lower IC50 values and better cytotoxicity efficiency. This was shown to be the case when comparing larger particles to smaller nanoparticles. Despite the fact that the length of the encapsulated particles grew following the addition of corona components such as hyaluronic acid, the distribution of the medication did not become any more efficient.[44-46]

3.3 Cytotoxicity and zeta potential

The zeta potential value provides an accurate definition of the surface charge of a particle. It would seem that the absolute zeta capability is directly linked to the cytotoxicity efficacy of PLGA nanoparticles, and it has been observed that nanoparticles with a zeta potential of 20 mV or less are suitably stable. When it comes to the creation of a drug delivery system, having nanoparticles that are both robust and have a constant zeta potential is beneficial.[47-50]

4. Conclusion and future perspectives

In this review, NPs used in biomedicine including, carbon nanotubes, graphene, gold NPs, silver NPs, iron oxide NPs, iron-platinum NPs, and QDs and their cytotoxicity mechanisms have been discussed. Generally, the large surface of NPs renders them unique physicochemical properties for use as therapeutic, diagnostic, and delivery agents in biomedicine. Biocompatibility, solubility, non-toxicity, and chemical stability, are major factors for the applicability of NPs in biomedicine. Various studies have revealed that copper nanoparticles can be synthesized by chemical, physical, and biological routes. The physical and chemical methods are time-consuming and tedious. Moreover, some chemical methods include use of hazardous chemicals, which may exert adverse effects to the user. Therefore, ecofriendly, easy, and rapid methods are needed. Biological synthesis is an effort in this direction. Studies on bioactivities of copper nanoparticles proved their effectiveness against the wide range of pathogenic bacteria, fungi, algae, and viruses. Similarly, it has also been reported to possess anti-parasitic and anti-cancer activities. Since the salts of metallic copper are cheaper than those of silver, overall technology is cost-effective; and therefore, copper nanoparticles can be used as one of the cheap alternatives to silver nanoparticles.

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