ORIGINAL RESEARCH PAPER

Physics

BIODISTRIBUTION AND TOXICITY ASSESSMENT OF CURCUMIN COATED MAGNETIC NANOPARTICLES (IN VIVO STUDY)

KEY WORDS: magnetic nanoparticles, biodistribution, toxicity.

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ABSTRACT

This work aims to study in vivo biodistribution of green synthesized magnetic nanoparticles and assess their toxicity on different body organs. Because of their unique magnetic properties, curcumin coated magnetic nanoparticles (Cur- MNPs) have extensive applications in various biomedical aspects. For in vivo studies, Single Dose Administration has designed as a treatment protocol. In order to assess the biodistribution and toxicity of Cur- MNPs, many experiments have been conducted using atomic absorption spectroscopy to measure iron content in different organs (liver and brain) as well as serum biochemical analysis to assess the performance of the many body organs (liver).

INTRODUCTION

Nanoscience is one of the most important researches in modern science. Increasing application of Nanostructure materials in medicine will bring remarkable advances in diagnostics, prevention and treatment of prevalent diseases. Perspectives of nanotechnology and nanostructured materials in medical applications include Analytical Tools (AT), Nano Imaging (NI), Nanomaterial and Nanodevices (NM/ND), Modern Clinical Therapeutics (MCT) and Drug Delivery Systems (DDS), Regulatory and Toxicological Issues (RTI) –[1; 2].

Medical advances of nanoscience and nanotechnology is depended on accurate knowledge of magnetic properties of nanoscale materials. Investigation indicates that the magnetic properties in nano scale fundamentally different form their bulk ones. So, nanosized biomagnetic nanoparticles (ranges from 1 to 100 nm) have attracted core focus of researchers in the biotechnological fields to their importance. Magnetic materials are essential components of modern technology with applications ranging from recording media to medical imaging. Magnetic nanomaterials (MNPs), those with at least one dimension below 1um, are proving to be equally versatile with unique applications and properties. Magnetic nanoparticles have been studied for applications including biomedical imaging, medical diagnostics and magnetic memory devices. One important magnetic property on the nanoscale is superparamagnetism which can lead to particles with much higher magnet susceptibilities than in traditional paramagnets. Because of the widespread applications MNPs in biotechnology, biomedical, material science, engineering, and environmental areas, much attention has been paid to the synthesis of different kinds of MNPs[3; 4].

Chemically synthesized nanomaterials possess special properties such as high surface area, higher mechanical, electrical and imaging properties –[5]. Due to these characteristics, they are being used for various applications. Certain metal particles such as zinc, cadmium, cobalt, nickel, and silver are reported to be toxic and not recommended to use for biomedical applications, whereas iron oxide and titanium are less toxic to cells[6; 7]. Among various nanoparticles, iron oxide particles such as magnetite and hematite gained much importance due to their superparamagnetic property [8]. The applications of magnetic nanoparticles include magnetic resonance imaging, hyperthermia, drug delivery, macromolecular labeling and removal of heavy metals, etc.[9].

MATERIALS AND METHOD

Nitric acid (HNO3), ketamine/xylazine (KX), hydrochloric acid (HCl), polyethersulfone (PES) and phosphate buffered saline (PBS) were purchased from (Sigma- Aldrich, USA). BioMid Diagnostic kits for (alanine aminotransferase (ALT), & aspartate aminotransferase (AST)) were purchased from (BioMed Diagnostic, Singapore). Magnetic iron oxide nanoparticles coated with curcumin (Cur-MNPs) were obtained from King Abdulaziz University, Jeddah, Saudi Arabia.

The animals were allocated into 4 groups (5 mice/ group). Control mice group (N= 5) were received PBS (100 µl), while reminder 3 groups (N= 5) were intravenously injected with Cur-MNPs suspended in normal saline solution at a dose of 8 mg /kg (Cur-MNPs) via the tail vein using a mouse restrainer. After injection of Cur-MNPs, clinical signs were carefully observed during the period of the study. Mice were anesthetized using KX mixture (87/13 mg/kg) and then sacrificed at different time points following administration (3 days ,7 days,10 days) to analyze the tissue distribution and perform toxicity studies.

To study the biodistribution of Cur-MNPs, the content of iron in different body organs (liver and brain) was studied by using the atomic absorption spectroscopy (AAS) (Analytik Jena, Jena, Germany). The studied organs were collected at different time points administration (as mentioned above) as well as the control group and kept freezing at –80 °C. The organs were weighted and digested overnight with 2 ml of 70% HNO3: 36% HCl (1:1 v/v) at 70 °C. The solution was diluted with deionized water to a final volume of 10 ml and filtered through 0.2 µm PES filter. The samples were analyzed using AAS.

For biochemical analysis, serum blood samples in all experimental groups were collected to measure the level of ALT and AST which are indicating to the liver function.

RESUTS AND DISCUSSION

Atomic Absorption Spectroscopy (AAS)

The group of 3 days showed a significant increase of iron content in liver comparing with the control group. While the other groups (7 &10 days) showed non- significant changes in the iron content comparing with the control group, Figure 1.

A large number of Cur-MNPs were collected by mononuclear macrophages in the liver after being injected intravenously [10; 11].

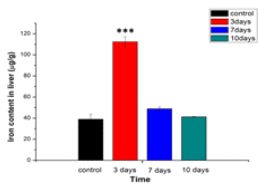

Figure 1. The biodistribution of iron in liver throughout the selected times.

All parameters are expressed as average ± SE (n = 5). *** Extremely significant at p < 0.001. The statistical significant differences were determined using one-way ANOVA.

There was a non-significant change of iron content in brain of groups (7 days and 10 days) comparing with the control group. On the other hand, there was a significant increase of iron content in brain (3 days) comparing with their control group, Figure 2.

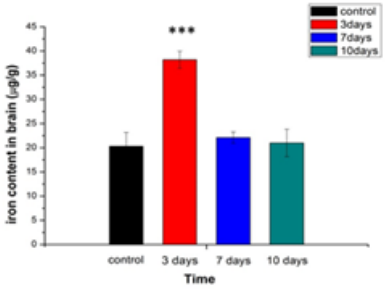

Figure 2. The biodistribution of iron in brain throughout the selected times.

All parameters are expressed as average ± SE (n = 5). *** Extremely significant at p < 0.001. The statistical significant differences were determined using one-way ANOVA.

There is a significant difference between brain iron content of the experimental and control group. This indicated the successful penetration of Cur- MNPs across blood–brain barrier (BBB).

Fortunately, Cur- MNPs can be utilized as drug nanocarrier that can easily overcome the physiologic limitations of drug transport by brain barrier – .

Biochemical Analysis

At the end of treatment, Serum biochemical analysis was performed to assess the toxicity of the administrated dose of Cur MNPs on mice biochemical parameters. ALT and AST remained unchanged indicating no toxic effects on liver function, Figures 3 and 4.

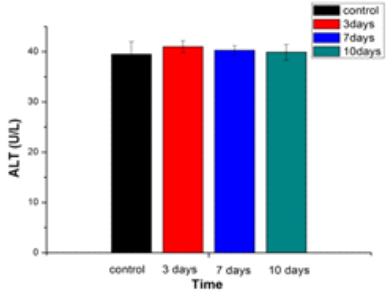

Figure 3. The changes in serum concentration of ALT in mice at different time intervals after single dose of Cur-MNPs.

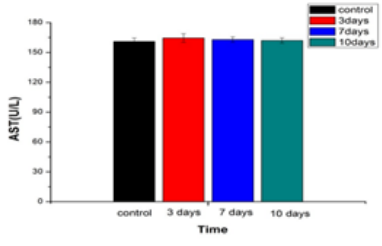

Figure 4. The changes in serum concentration of AST in mice at different time intervals after single dose of Cur-MNPs.

CONCLUSION

Cur-MNPs were mostly taken up in the liver, so their curative effect could be more pronounced for liver tumors. Cur-MNPs can successfully penetrate the blood–brain barrier, so they might be used as drug carriers to overcome the limitations of such physiological barriers. Cur-MNPs as "All in One" nanoplate form are safe enough to be used in diagnosis and therapy.

REFERENCES:

1. Afghahi, S., & Shokuhfar, A. (2014). Two step synthesis, electromagnetic and microwave absorbing properties of FeCo@ C core–shell nanostructure. Journal of Magnetism and Magnetic Materials, 370, 37-44.
2. RezazadehNochehdehi, A., Sandri, M., & Mohammadzadeh, A. (2015). Bio magnetic Nano Particles (BMNPs) used for cancer treatment via Hyperthermia method. Paper presented at the World Congress on Medical Physics and Biomedical Engineering, June 7-12, 2015, Toronto, Canada.
3. Maurer, T. (2007). Physics Application of Biomaterials. J Physics Letter, 1, 30-38.
4. Buurma, A., Blake, G., Palstra, T., & Umut, A. (2016). Multi ferric Materials: Physics and Properties. J Reference Module in Materials Science and Materials Engineering, 1-7.
5. Colvin, V. (2003). The potential environmental impact of engineered nanomaterials Nat Biotechnol 21: 1166–1170. Find this article online.
6. Berry, C. C., & Curtis, A. S. (2003). Functionalisation of magnetic nanoparticles for applications in biomedicine. Journal of physics D: Applied physics, 36(13), R198.
7. Hofmann, A., Thierbach, S., Semisch, A., Hartwig, A., Taupitz, M., Rühl, E., & Graf, C. (2010). Highly monodisperse water-dispersable iron oxide nanoparticles for biomedical applications. Journal of Materials Chemistry, 20(36), 7842-7853.
8. Huber, D. L. (2005). Synthesis, properties, and applications of iron nanoparticles. Small, 1(5), 482-501.
9. Zhang, C., Liu, T., Gao, J., Su, Y., & Shi, C. (2010). Recent development and application of magnetic nanoparticles for cell labeling and imaging. Mini reviews in medicinal chemistry, 10(3), 194-203.
10. Saito, M., Matsuura, T., Nagatsuma, K., Tanaka, K., Maehashi, H., Shimizu, K., . . . Tajiri, H. (2007). The functional interrelationship between gap junctions and fenestrae in endothelial cells of the liver organoid. Journal of Membrane Biology, 217(1-3), 115-121.
11. Wang, J., Chen, Y., Chen, B., Ding, J., Xia, G., Gao, C., . . . Li, X. (2010). Pharmacokinetic parameters and tissue distribution of magnetic Fe3O4 nanoparticles in mice. International journal of nanomedicine, 5, 861.
12. Leonard, F., Kulkarni, R. K., Brandes, G., Nelson, J., & Cameron, J. J. (1966). Synthesis and degradation of poly(alkyl -cyanoacrylate). . J Appl Polym Sci, 10(2), 259–272.