DOI: https://doi.org/10.53350/pjmhs221661046

ORIGINAL ARTICLE

Biologically Synthesized Zinc Oxide Nanoparticles and Carbon Tetrachloride as an Anti Cancer Drug: A Review

MUHAMMAD HASEEB BASHARAT[1], MUHAMMAD TARIQ[2], RIAZ MUSTAFA[3], AMAR AKASH[4], HAFIZA HIRA TALIB[5], MUHAMMAD NOUMAN AZIZ[6], ANADIL NOEL[7], ADNAN ZEB[8], MUHAMMAD FAROOQ KHALID[3], FAKHRA SOOMRO[8], QUDSIA MUSHTAQ[9], MEHREEN FATIMA[6]

[1]*Institute of Molecular Biology and Biotechnology, University of Lahore, Pakistan*
[2]*Department of Livestock Management, University of Agriculture Faisalabad, Sub-Campus, Toba-Tek Singh*
[3]*University of Agriculture Faisalabad, Sub-Campus, Toba-Tek Singh*
[4]*Department of Medical Biotechnology, Yeungnam University*
[5]*Department of Chemistry and Biochemistry, University of Windsor*
[6]*Department of Life Science, School of Science, University of Management and Technology, Pakistan*
[7]*University College of medical and dentistry, University of Lahore*
[8]*Department of Zoology, Shah Abdul Latif University Kahirpur Mir's Sindh, Pakistan*
[9]*Department of Zoology, University of Punjab, Lahore, Pakistan*
Corresponding author: Mehreen Fatima, Email: mehreen.fatima@umt.edu.pk

ABSTRACT

Cancer is a life-threatening disease, curing it is one of the primary tasks for scientists around the world. One of the major fields that have exceptional abilities to control cancer is nanotechnology and nano medicines. Zinc oxide nanoparticles have flexible platforms for therapeutic and biomedical practice. There is a vital need to manufacture a new anti-cancerous drug. Zinc oxide nanoparticles have a great potential to act as an anti-cancerous drug. A common effect of zinc nanoparticle and carbon tetrachloride is the primary concern on the liver, biologically synthesized nanoparticles can be used for this cure purpose. This review study aims to explain the effects of synthesized nanoparticles on the rat in the presence of CCl4; Combination of toxic substance with the presence of nanoparticle can give us a better idea on the effectiveness of nanoparticle.

Keywords: Zinc oxide nanoparticles, Liver cirrhosis, Carbon tetrachloride, Liver function

INTRODUCTION

Cancer is a life-threatening disease, curing it is one of the primary tasks for scientists around the world. One of the major fields that have exceptional abilities to control cancer is nanotechnology and Nano medicines. This study aims to study the literature with the effect of nanoparticles on the rat in the presence of CCl4; Combination of toxic substance with the presence of nanoparticle can give us a better idea on the effectiveness of nanoparticle. If nanoparticle has any benefit than it will keep the liver healthy in the presence of CCl4; otherwise the liver will get damage (Callegari et al., 2019).

Cancer is not just a single disease; it is a group of diseases. Cancer can affect any part of body. It can be also termed as a deformity inside our body and cell is a basic entity that shows us the meaning of life. Anything that can survive in the environment, and it can make its own protein is a living thing. Cancer is mainly uncontrolled division of cells, cancerous cells have immortality. Uncontrolled division of these particular types of cells can give rise to a tumor. Cancer occurs due to mutation inside our DNA. These changes could be due to some mutagen, or some other factors. This mutation can be due to insertion, deletion or addition. A tumor can be further divided into two types: Benign tumor: It is a type of tumor that grows at particular part, and it will not spread in other parts of body. Malignant tumor: It is a type of tumor that can spread to another part of body. There are also other types where tumor formation isn't observed. These types are lymphomas, leukemia and myeloma (Mohsen et al., 2018; Quer et al., 2017; Galon et al., 2012).

There are mainly four stages of cancer. These are abnormal cells which may have a potential to convert into cancerous cells. The cancerous cells are present in specific area only. Cancerous cells have a spread towards tissues present nearby and lymph nodes. D) Cancer is present in other body parts now, and it is known as metastasis cancer (Bester, et al., 2011; Parkes 1972).

A cancer is said to be metastasis cancer when it spreads to other part of body from its point of origin. Metastasis happens when cancerous cells leaves the tumor and flow into the blood stream of a person, or a lymphatic system. Now, the cancer can approach any part of body through circulation. It can settle down at any part and grow there. Cancer spread is according to the type of cancer. If a lung cancer spreads towards brain that it would not be called as brain tumor instead we will call it as Metastatic lung cancer (Moris et al., 2019).

Gene controls main portion of cells. Gene is the main commanding unit inside cell which control the type of protein needs to be translated. All genes have different job to perform inside cells. These genes are made up of specific sequence of bases. If there is any type of changing in these bases it will result in the malfunction of protein function which can result in several type of genetic diseases, or a cancer.

These are the type of mutations that are directly due to external harmful factors. These factors can affect body in a very drastic way which can result in a mutation. Following are some major listed factors which can cause mutation. Radioactive radiations, UV light, Tobacco (Zhao et al., 2005).

Germ Line Mutations: This is a type of mutation that can occur in either a sperm or an egg. An affected germ cell once fused with each other can become drastic. Only two cells will give rise to all other cells present inside body. If one of them has some kind of mutation, then mutation will be carried to all over the cells in the body. Although chances of this are rare, but it can occur; furthermore, it will also affect children of that person who have this mutation already (Malkin et al., 1990).

Liver and Liver Cirrhosis: Liver is a large organ in our body that plays very important role in the metabolism process. Blood from digested tract is filtered inside liver. It also metabolizes all medicines that are absorbed in the digestive tract. Liver release bile juice which further help in the process of digestion. Liver also produces some important proteins that are responsible for proper functioning of body (Fukui et al., 2016).

Liver cirrhosis is a serious disease of liver which can even cause death. It happens due to a liver damage. Whenever there is damage in the liver, there is formation of scar tissues. Increase in number of scar tissue can lead towards scarring. Scarring can cause abnormal functioning of liver. Alcohol abusing is one of the common causes of liver cirrhosis because anything that goes inside our digestive tract is filtered by liver. Alcohol is a toxic substance which can cause liver damage Virus can also damage liver which can lead towards liver cirrhosis. Virus damages liver cells to a great extent as they grow inside a cell. Increase in number of virus can decrease healthy liver cells which can be serious for the health. Acetaminophen is commonly used by almost everybody on daily basis. Although it is commonly consumed, but if

someone takes amount more than prescribed amount than it can cause liver damage. There are many such factors that can lead towards liver cirrhosis; even some genetic diseases can also cause liver cirrhosis. (Askgaard et al., 2015).

Nanoparticles are breakthrough of science and technology. Nanoparticles can be used against diseases, inflammations and many other issues linked with them. Nanoparticles are quite small in size and they are calculated in nanometer (nm). Nanoparticles may have different colors depending upon the size. For example, Zinc nanoparticles will have different color when they are at 100nm as compared to nanoparticles present at 50nm. Size also governs the process of melting; it will melt according to the size. Greater size will need greater heat for melting (Loza et al., 2019).

Zinc Oxide Nanoparticles: Nanoparticle that is used here are biologically synthesized Zinc oxide nanoparticles (ZnO). Zinc oxide nanoparticles have several biomedical applications. They are being used for treatments of cancer and bacterial diseases. They are also present in most of sunscreen cream because it can protect skin from UV light to a large extent (Pauzi et al., 2019). Cancer is treated worldwide with chemotherapy and radiotherapy. Both of these treatments have their own benefits, but they can also lead towards many side effects (Shobha et al., 2019). Chemotherapy is a chemical synthesized formula is induced in the body to attack on rapidly growing cells. Cancer as fast growing cell killed by it, the main thing is that it will also affect normal cells inside body that grows rapidly germ cells and hair cells. Radiotherapy is a type of ionizing process in which radio waves are directly supervised to an area where cancer is present. It affects healthy cells around the area which can lead towards other problems. Zinc oxide nanoparticle will target only cancer cells, and help in the induction apoptosis in cancerous cells. It will not affect normal cells to extent chemotherapy and radiotherapy does. These nanoparticles can cause toxicity if proper dose isn't maintained (Pullagurala et al., 2018).

Carbon tetrachloride is a toxic compound, it can cause irritation on skin if comes in contact with it. It can cause irritation even if it is inhaled. In this study, carbon tetrachloride is used to produce or mimic cirrhosis in liver. Repeated administration of carbon tetrachloride for animal model will cause first liver fibrosis that can lead towards liver cirrhosis (Recknagel, 1967).

Although nanoparticles have many advantages, they have lifesaving capabilities. They do spread toxicity inside body which becomes dangerous during the treatment. Zinc oxide nanoparticles are available in different sizes, and it is observed that small sized nanoparticles are much more toxic as compared to the one in larger size. For instance, a nanoparticle in the size of 25nm is more toxic than the nanoparticle size in 100nm. It is observed that smaller zinc oxide nanoparticle of 25nm size can decrease G1 phase of cell cycle, and it can increase S phase and G2 phase of cell cycle; furthermore, smaller size nanoparticles will have more activity as compared to the one which have larger size. Zinc oxide nanoparticles can cause toxicity inside the body and can be dangerous for some vital organs. It gets absorbed inside the liver, kidneys and spleen. Once they are absorbed in a large form there is no turning point. This toxicity may also mimic as liver cirrhosis, but this will only happen if somebody is consuming in large amount of these particles (Padmavathy et al., 2008).

Cancer is a common problem now days. There are treatments available for cancer, but a massive death toll is still there due to this disease. There are signs of progress in medical science when it comes to cancer, but still many people are dying; because of diagnosis is either at the last stage or they cannot handle therapies to treat cancer. The majority of the tumors are resistant to drugs (Chen et al., 2016). An essential need for alternative therapy is the primary goal. Recent studies in the field of nanotechnology can provide an opportunity to end this disease. The combination of nanoparticles and Nano materials can be linked with medicines. It can either kill a cancer cell or highlight the presence of cancer cells in the body. In such a way healthy cells can stay out of danger. Cancer is such an anomaly of the body which is getting uncontrollable these days. It is affecting many people in this world. In the United States, it has surpassed the death by heart disease. There is a great need to discover medicine that can deal with cancer cells and kill them. Chemotherapy and radiotherapy are not the only solution for this as several healthy cells get destroyed in these therapies (Deterding et al., 2015). The death tolls due to heart diseases have dropped, but for cancer, it remained the same. There are a massive number of advancements in the field of nanotechnology which may help in the detection of cancer which includes quantum dot techniques and imaging of cancer. These techniques will help in diagnosis, imaging, and detecting the exact stage of cancer. New therapies formulated with the help of nanotechnology and nano medicine can serve as an alternative to conventional therapies. A probe or a sequence docked with nanoparticle which can directly attach to a cancer cell. There was an idea that Nano robots can work as a therapeutic agent. They can go to nearer to the cells that are affected and repair them. Nanotechnology has a future for a new era in terms of medicines. It is a lock that needs to be opened by individual keys which will give us a new venture for new beginnings (Pinter et al., 2016).

Nanoparticles act as a drug transporter in the field of Nano medicine. Also, they act as a photosensitizer or sonosensitizer (These are the compound that can formulate reactive oxygen species; which will show some wavelength due to excitation). Ligands can be attached to the nano molecule or nanoparticle which can directly link with cell . The advantage of this targeted therapy is; only those cells become a target that is having cancer. Healthy cells are not damaged in this process. Hence, these therapies are quite successful, and they can serve as a cure for cancer (Fukui et al., 2016). The word nanoparticle is coined from the field of nanotechnology. In past few years, there is increase in demand of zinc oxide nanoparticles in the field of medical sciences. They can be synthesized through different type of physical and chemical methods, but the best way to synthesize zinc oxide nanoparticle is by eco-friendly ways. This includes usage of fungi, microbes and bacteria. They are studied these days for their antimicrobial activities. Also, they are widely studied for their anti-cancerous activities. They have a distinct property from that of conventional medicines, they have a tendency to deliver drug to their designated point. A clue of anti-cancerous effect of Zinc oxide nanoparticle can be clearly seen in this research.

Zinc oxide nanoparticles can be synthesized by a set of unique skills. This change gives them a unique character (Mirzaei and Darroudi 2017; Askgaard et al., 2015). Classification of the significant components in the zinc nanoparticles is critical. All properties of nanoparticles should be in understanding before their synthesis. Several different techniques are used to classify these particles based on size and shape. These techniques include x-ray diffraction, electron microscopy, and several other techniques that will help in discovering the size and shape. Even though there are several uses of Zinc oxide nanoparticle, their toxicity is another issue. Their effect was perceived for microbes. Although they have antimicrobial, antiviral, antifungals and anti-cancerous activities, cellular toxicity will remain a significant concern for nanoparticles. They should induce an anti-cancerous effect through reactive oxygen species (ROS), or by inducing cellular apoptosis (Hussain et al., 2018). Besides, Zinc oxide nanoparticles show less toxicity against the normal cells. Their use can also be significant even in drug delivery techniques. This study focuses on the creation and characterization processes of zinc oxide nanoparticles with the help of a plant system (Padmavathy et al., 2008).

Zinc Oxide and its Advancement: Zinc oxide is a part of many skin balms. It can also be found in some antidandruff shampoos as well. Its unique characteristics provide a breakthrough in almost all aspects. Zinc oxide is also present in many sunscreens; because of its ability to absorb a broad spectrum of ultraviolet radiation. The functioning of zinc oxide nanoparticles inside a body is mainly dependent upon its structure. A smaller particle will have more

toxicity, but it will have a fast response against the issue and vice versa. Time of exposure is also a primary concern here because it also governs the effectiveness of zinc oxide. They can cope up with microbes even when they are present in a small concentration. It makes them suitable for the job; because more concentration can cause toxicity which can become dangerous (Fukui et al., 2016).They are pretty much stable when they are exposed to high temperatures and high pressure. Some nanoparticles are also better for the human body. They do not always spread toxicity, but instead, they are absorbed by the body as a source of nutrition. The human body consists of around 2–3 g of zinc, and daily, our body needs at least 10-15 mg. At this moment there is no report of severe toxicity by zinc oxide nanoparticles; however, if someone sniffs a zinc powder, inhale it or ingested than things can get opposite. A person may get a zinc fever and severe coughing (Bomila et al., 2019).

Toxicity of Zinc Oxide: Toxicity of Zinc oxide nanoparticles was determined. A does in different quantities was given to mice. A dosage of 50mg/kg to 5000mg/kg was given to the mice. Mice that had a low dose between 50mg to 500mg per kg did not show any anomaly. Mice that had a dose of almost 5000mg per kg showed signs. The weight of these mice dropped, but the weight of their liver, lungs, spleen, and kidney increased. Also, it increases normal functioning genes that are responsible for zinc uptake in the metabolism (He et al., 2019).

Application of Zinc Oxide: In this study, it was noticeable that the deposition of zinc oxide was found in some vital organs like lungs, liver, spleen, kidneys. There were not any traces of deposition in the brain. Zinc has a vital role in the medicinal industry. It is also a part of most multivitamin tablets. It will get from food, and most of it gets lost in the form of sweat. Additionally, it is a crucial component of bones, teeth, and many proteins that are responsible for proper functioning (Elshama et al., 2018). People who have a genetic disorder and are unable to absorb zinc suffer from acrodermatitis enteropathica. It is a genetic disorder where the skin of a person looks more like the skin of a python. It got the potential to overcome antibiotics; because of its high antimicrobial activity. Bacteria can make resistance against antibiotics, but it is quite tricky for bacteria to make immunity against a nanoparticle. Zinc particles have many applications, and they have high usage in the medical field. Even though they have many usages, they are harmful to a person who got exposed to these particles for a long time (Pauz et al., 2019).

Zinc Oxide in Nano Technology: Nanotechnology mainly consists of particles at the Nano scale. It is quite a difficult task for making particles of such grade inside a laboratory, yet they have a quite significant purpose in the scientific field. A single atom combines with another to make up a molecule. In the same regard cells inside our body are made up of different molecules. We need a brief analysis of the human body at a nanoscale. Although there are instruments available in hospitals that have a use treatment and diagnosis purposes, but there is a vital need for nanotechnology in this regard. Nanotechnology can provide a cheaper solution in this aspect. Devices that can diagnose; moreover, they can provide a therapeutic medicine on the spot. Also, it could be comfortable to wear. Nanoparticles can also enhance radiation therapy for a cancer. One can guide nanoparticles in such a way that they directly act onto a cancerous cell instead of a normal cell (Fukui et al., 2016). There are different uses of zinc oxide at industrial level. Recently it was found that that zinc oxide synthesized by natural ecological cycles. Main problem is to concern in this expected way is zinc oxide toxicity, experimentation methods, environmental and the acceptance of toxicity of zinc nanoparticles. This is the main things that may be helpful to understand the nature of zinc-oxide, their distribution with animals, plants and interaction with pollutants. Zinc oxide nanoparticle has extensive usage. It got applications on a commercial scale. It means that much of the by-product will have zinc particles that will go into the environment. It will further affect the ecosystem and food chain. Performing studies related to the ecotoxicology of nanoparticles is vital. Several in vivo and in vitro studies performed in this regard, and at the end of the day they go into the ecosystem. This data will provide the amount of nanoparticle uptake by soil and plants. An increase in the commercial usage of these nanoparticles can do the destruction of the ecosystem. It is crucial to devise a way that can have a check and balance over this nanoparticle so that it can help our environment in return (Deterding et al., 2015). The combination of nanotechnology and medicine makes up this field of Nano medicine. It is a combination of nanoparticles with biological components. A combination of these components can open up a new venture of science. It can help humanity by eliminating many extracellular and intracellular diseases. In vivo and in vitro studies are possible with this. In the case of in vitro, synthesized particles can help in the detection or presence of specific biological pathogens or anomaly present in the blood. In the case of an in vivo study, these can help in getting the image of a particular anomaly present inside the body. It will directly bind to the targeted cell and fight with the disease. In this procedure, normal cells will be out of any danger, and they will remain healthy. Another application is regenerative medicine that can help in building up cells in one particular place — for example, damaged cells in the spinal cord or nerves. Also, it enhance the growth of cells in the damaged area. (Chen et al., 2016).

CONCLUSION

Zinc oxide nanoparticles have a tendency to induce a release of reactive oxygen species (ROS), and apoptosis inside the cell. It makes zinc oxide nanoparticle a suitable candidate for anticancer and antimicrobial activity. Zinc oxide nanoparticles have a bright future ahead; they can be combined with aptamers to make them target specific. The zinc oxide will lead the nanoparticle directly towards the cancer cell, and keep healthy cells safe. It can overcome the only issue of toxicity is faced in case of nanoparticles. It can be attached with a probe that detects only those cell which got high levels of survivin protein, Zinc oxide nanoparticles can change the future of medicines.

REFERENCES

1. Callegari E, M Domenicali, RC Shankaraiah, L D'Abundo, P Guerriero, F Giannone and M Ferracin (2019). MicroRNA-based prophylaxis in a mouse model of cirrhosis and liver Cancer. Molecular Therapy-Nucleic Acids. 14:239-250.
2. Mohsen H, ESA El-Dahshan, ESM El-Horbaty and ABM Salem (2018). Classification using deep learning neural networks for brain tumors. Future Computing and Informatics Journal. 3(1):68-71.
3. Quer M, V Vander Poorten, RP Takes, CE Silver, CC Boedeker, R de Bree and P Zbären (2017). Surgical options in benign parotid tumors: a proposal for classification. European Archives of Oto-Rhino-Laryngology. 274(11):38253836.
4. Galon J, F Pagès, FM Marincola, HK Angell, M Thurin, A Lugli and F Tatangelo (2012). Cancer classification using the Immunoscore: a worldwide task force. Journal of translational medicine. 10(1):205.
5. Bester AC, M Roniger, YS Oren, MM Im, D Sarni, M Chaoat and B Kerem (2011). Nucleotide deficiency promotes genomic instability in early stages of cancer development. Cell. 145(3):435-446.
6. Parkes, C. M. (1972). Accuracy of predictions of survival in later stages of cancer. Br Med J, 2(5804), 29-31.
7. Moris D, DI Tsilimigras, N Machairas, K Merath, M Cerullo, N Hasemaki and T Pawlik (2019). Laparoscopic synchronous resection of colorectal cancer and liver metastases: A systematic review. Journal of surgical oncology. 119(1):30-39.
8. Zhao R., S Xing, Z Li, X Fu, Q Li, SB Krantz and ZJ Zhao (2005). Identification of an acquired JAK2 mutation in polycythemia vera. Journal of Biological Chemistry. 280(24):22788-22792.
9. Malkin, D, FP Li, LC Strong, JF Fraumeni, CE Nelson, DH Kim and MA Tainsky (1990). Germ line p53 mutations in a familial syndrome of breast cancer, sarcomas, and other neoplasms. Science. 250(4985):1233-1238.
10. Fukui, H Saito, Y Ueno, H Uto, K Obara, I Sakaida and H Tsubouchi (2016). Evidence based clinical practice guidelines for liver cirrhosis. Journal of gastroenterology, 51(7):629-650.

11. Askgaard G, M Grønbæk, MS Kjær, A Tjønneland and JS Tolstrup (2015). Alcohol drinking pattern and risk of alcoholic liver cirrhosis: a prospective cohort study. Journal of hepatology. 62(5):1061-1067.
12. Loza K, Epple M and M Maskos (2019). Stability of Nanoparticle Dispersions and Particle Agglomeration. In Biological Responses to Nanoscale Particles (pp. 85100). Springer, Cham.
13. Pauzi N, NM Zain and NA Yusof (2019). Microwave-Assisted Synthesis for Environmentally ZnO Nanoparticle Synthesis. In Proceedings of the 10th National Technical Seminar on Underwater System Technology 2018. Springer, Singapore. 541-546.
14. Shobha N, N Nanda, AS Giresha, P Manjappa, P Sophiya, KK Dharmappa and BM Nagabhushana (2019). Synthesis and characterization of Zinc oxide nanoparticles utilizing seed source of Ricinus communis and study of its antioxidant, antifungal and anticancer activity. Materials Science and Engineering. 97:842-850.
15. Pullagurala VLR, IO Adisa, S Rawat, B Kim, AC Barrios, IA Medina-Velo and JL Gardea-Torresdey (2018). Finding the conditions for the beneficial use of ZnO nanoparticles towards plants, A review. Environmental pollution.
16. Song YM and MD Chen (2003). Zinc supplementation attenuates thioacetamideinduced liver injury and hyperglycemia in mice. Biological Trace Element Research. 92:173-180.
17. Deterding K, C Höner Zu Siederdissen, K Port, P Solbach, L Sollik, J Kirschner and MP Manns (2015). Improvement of liver function parameters in advanced HCV-associated liver cirrhosis by IFN-free antiviral therapies. Alimentary pharmacology & therapeutics. 42(7):889-901.
18. Pinter M, M Trauner, M Peck-Radosavljevic and W Sieghart (2016). Cancer and liver cirrhosis: implications on prognosis and management. ESMO open. 1(2):e000042.
19. Mirzaei H and M Darroudi (2017). Zinc oxide nanoparticles: Biological synthesis and biomedical applications. Ceramics International. 43(1):907-914.
20. Askgaard G, M Grønbæk, MS Kjær, A Tjønneland and JS Tolstrup (2015). Alcohol drinking pattern and risk of alcoholic liver cirrhosis: a prospective cohort study. Journal of hepatology. 62(5):1061-1067.
21. Hussain Z, JA Khan, H Anwar, N Andleeb, S Murtaza, A Ashar and I Arif (2018). Synthesis, characterization, and pharmacological evaluation of zinc oxide nanoparticles formulation. Toxicology and industrial health. 34(11):753-763.
22. Bomila R, S Suresh and S Srinivasan (2019). Synthesis, characterization and comparative studies of dual doped ZnO nanoparticles for photocatalytic applications. Journal of Materials Science: Materials in Electronics. 30(1):582592.
23. Elshama SS, ME Abdallah and RI Abdel-Karim (2018). Zinc Oxide Nanoparticles: Therapeutic Benefits and Toxicological Hazards. The Open Nanomedicine Journal. 5(1).
24. Pauzi N, NM Zain and NA Yusof (2019). Microwave-Assisted Synthesis for Environmentally ZnO Nanoparticle Synthesis. In Proceedings of the 10th National Technical Seminar on Underwater System Technology 2018. Springer, Singapore. 541-546.
25. Chen G, I Roy, C Yang and PN Prasad (2016). Nanochemistry and nanomedicine for nanoparticle-based diagnostics and therapy. Chemical reviews. 116(5):28262885.