

Gold Nanoparticles and its use to Treat Cancer in Liver Cirrhosis: A Review

BERGEES KHAN¹, MUHAMMAD WASIQUE SHAHID², SAFDAR SAEED³, QUDSIA MUSHTAQ⁴, UZAIR ISHTIAQ⁵, SANA FAROOQ⁶, TABISH ARIF⁷, AMJAD MAQSOOD⁸, HASSAN RAZA⁷, SIMRA ARIF⁷, FATIMA KHALID⁹, MARIA¹⁰, AYESHA AMEEN¹¹, MEHREEN FATIMA⁷

¹Institute of Molecular Biology and Biotechnology, University of Lahore, Pakistan

²Department of Science and Technology, Virtual university of Rawalpindi, Pakistan

³Consultant Urologist, DHQ hospital Rajanpur

⁴Department of Zoology, University of Punjab, Lahore, Pakistan

⁵Department of Quality Control, Paktex Industries, Kamoke, Pakistan

⁶School of Science, Engineering and Environment, University of Salford, UK

⁷Departments of Life Sciences, University of Management and Technology, Lahore, Pakistan

⁸Department of Chemistry, Faculty of Sciences, University of Central Punjab, Lahore, Pakistan

⁹School of Biochemistry and Biotechnology, University of Punjab, Pakistan

¹⁰Biochemistry section, Institute of Chemical Sciences, University of Peshwar, Pakistan

¹¹Office of research Innovation and Commercialization, University of Management and Technology, Lahore, Pakistan

Corresponding Author: Ayesha Ameen, Email: ayesha.ameen@umt.edu.pk

ABSTRACT

Gold Nano particles have been use as an anti-cancer in nanotechnology and many other beneficial effects have been reported. In this study, Gold nanoparticles use is discussed as therapeutic effect in the liver. Gold nanoparticles have a considerable advantage due to their size, shape, and ease of transmission. They can be used widely in pharmaceutical industries. They exhibit many different dimensions which include two dimensions and three dimensions. They have a unique set of features that manage their usage against microbes, and cancer. There are not enough studies performed on the shape and size of gold nanoparticles. It was essential to conduct a study on the shape and size of these nanoparticles for different cells and cell lines. Gold nanoparticles are very actively use in the cancer treatment. Moreover, they can bind many drugs, Cancer that relates third cause of death worldwide is liver cirrhosis.

Keywords: Liver cirrhosis, Cancer, Nanoparticles, Cell lines

INTRUDUCTION

Cancer that relates third cause of death worldwide is liver cirrhosis. Genome of liver cancer in hug amount sequenced globally that leads high frequency gene/mutations (Nakagawa et al., 2019). The liver organ under the rib cage and below the right lung is one of the largest organs in the body the function of the liver is to removing toxins from the body and it is crucial to survival. Liver cancer is that type of cancers that starts in the liver or develops outside on the surface of organ and spread to the all - area. The fact of liver cancer has very low survival rate and major factor are includes alcohol intake and become a main reason of liver cirrhosis. Alcohol usually consumed with meals every day or often (Zimmermann et al., 2019). Secondly, type 2 diabetes indicates serious liver disease like liver failure needs to be liver transplantation and causes liver cirrhosis. Third and last factor of liver cancer is hepatitis (A, B, C) named by viruses gradually can major cause of liver cancer.

Liver is one of the largest organs present in the abdomen of a human being. In a healthy adult liver weight is around 1.5kg. Liver produces bile juice which gets stored in the gall bladder. This fluid travels all the way from the gall bladder through bile duct and helps in the digestion of food. Liver is the only organ in body that have a capacity to regenerate, this capacity is so intense that even a 70% damage liver tissues can fix themselves within a time period of few weeks; however, if the injury is continuous than this lead to a condition known as liver fibrosis. In case of liver fibrosis the tissue of liver gets accumulated by extra cellular matrix which may lead towards severe changes in structure and function of a liver. CLD is one of the major concerns worldwide; with this condition a normal liver can get damage to critical levels. A damaged liver will produce a condition known as liver cirrhosis (Bartneck et al., 2014). There are diseases in which liver is chronically affected; these diseases are known as CLD or chronic liver diseases. Now, we all know that liver have a capacity to regenerate and fix up the part of the liver that has been damage. Several cells are involved in this process. There are several different factors involved towards the liver damage, liver damage can be due to some disease, virus or by some medicine. It can further lead towards liver fibrosis which can lead liver condition towards liver cirrhosis and liver

cancer. Chronic infection in liver can result in the liver fibrosis. It is mainly due to a disease like hepatitis, which includes jaundice, hepatitis B and hepatitis C can damage liver to a great extent. People who consume a lot of amount of alcohol can leads towards a fatty liver which can result in liver damage. Many cases of liver cancer worldwide are because of alcohol abusive usage. There are some medicines which can cause liver damage, for instance, metronidazole usage for a long period of time or paracetamol/acetaminophen usage for a long period of time can cause CLD. There are no medicines available in the market as such which can act as liver anti-fibrosis (Rechberger et al., 2003). Many therapies are done in this regard, but they are failed to give an accurate concentration involved in this process to avoid or cure liver diseases. Therapies that include nanoparticle had much better effect as compared to other conventional therapies; Nanotechnology is a vast field that is growing at a very rapid scale. These days' nanoparticles are conjugated somehow with biological compounds or a drug that can go to a specific part of a body. Nanoparticle has suitable and quite astonishing support for drug delivery system. In past few years nanotechnology and medical sciences joined hands together in many studies for the cure of several different liver diseases (Giannitrapani et al., 2014; Sperling et al., 2008).

Angiogenesis play a key role in providing oxygen and nutrients for tumor cells. Hallmark in cancer cell cannot grow without blood supply 106 cells are mass of ~2mm. Moreover, in the cancer therapy proteins and peptides, aptamers are very effective approach (Mashreghi et al., 2018).

Benign Tumors: A benign tumor can originate at any part of body and grows slowly. Generally localized, small in size and appears like warts, colon polyps, etc. It acts like similar to other cells and it can be easily removed with the help of surgery (Mohsen et al., 2018; Quer et al., 2017).

Malignant Tumors: They remain at one place for some time, once the conditions are satisfactory for them they can spread to other parts of body by metastasis. They can go into the blood stream, and spread towards surrounding tissues which becomes quite difficult to treat (Galon et al., 2012).

Cancer Metastasis: It is a process in which cancer cells spread to other part of body. Once cancer cells goes into the blood stream of

lymphatic system it can lead towards other parts of body. Mostly patients with that cancer die as result of tumor spreading to other organs. However, no medical care to stop death that associate with metastatic cancer (Farnsworth et al., 2018).

Tumor Angiogenesis: Angiogenesis play a key role in providing oxygen and nutrients for tumor cells. Hallmark in cancer cell cannot grow without blood supply 10⁶ cells are mass of ~2mm. Moreover, in the cancer therapy proteins and peptides, aptamers are very effective approach (Mashreghi et al., 2018).

Genetics of Cancer: According to the study of cancer it can be checked at genetic level. We can even check the origination of cancer. The genetics of cancer is a field of its own. Paternal and maternal genetics can also tell another story on the cancer. It includes breast cancer, ovarian cancer, prostate cancer, colon or rectum and other cancers. Genetic testing is now available (Lengauer et al., 1998).

Oncogenes: The Genes associates with cancer are oncogenes that are overproducing genes, or they are in highly active form. Mutation of genes can be dangerous, and even if one allele of a gene mutates than there is a risk of a cancer (Bishop 1991).

Inherited Mutations: There are some hereditary mutation pass through germ line. They pass from parents to their children. Around ten percent of all type of cancers falls into this category (Malkin et al., 1990).

Radiation Mutations: Some cancer radiation mutation is caused by Ultraviolet radiation, ionizing radiation (Gamma and x-rays, particle radiation), Electromagnetic radiation (power lines, cell phones) (Dubrova et al., 2000).

Carbon Tetrachloride: The molecular formula of carbon tetrachloride is CCl₄, and it got a molecular weight of 153.811g/mol. Melting point- 9°F (NTP, 1992). CCl₄ is stable chlorinated hydrocarbon. Carbon tetrachloride is clear; colorless the chemical uses as dry cleaning agent, refrigerant, oils and fats. The side effects of CCl₄ are to degenerate of liver and kidney by inhalation of its vapors and central nervous system also depress, Carbon tetrachloride anticipated in being carcinogenic which is proved by animal model (Recknagel 1967).

Nanotechnology is a field of science that deals with nanoparticle, these particle have great impact in future, from the usage of nanoparticles in chipsets of computers to the vast science of medicines. Nanotechnology is not fielded that is behind in any aspect. Nanoparticles can be revolutionary for the industries that will work with them. Nanoparticles are used in the field of medicines which have a great benefit on the future of medicines. They can be used in the drug delivery methods, or they can be attached with some probe. So, that it can reach towards a desired place. They can be used for the bio imaging. They have great benefits in oncology as well. Nanoparticles are proven to act as an anticancer. It can open new endeavors for the mankind. According to the American society for testing and materials (ASTM), nanoparticles are defined as the particles that exist at the size of 10-100nm and they have a two or three dimensional shape (Jain et al., 2012).

Global production of nanoparticles (ENPs) is increasing due to industrial applications by shown adverse biological effects (Rashidi et al., 2019). Due their tunable, chemical, biological properties nanomaterial gained prestige in technology. Nanoparticles categorized on the bases of the shape, size, composition and origin. Nano particles can be produce naturally such like Nano-organisms, viruses, Nano bacteria, algae, fungi, yeast and bacterial spores (Jeevanandam et al., 2018). Nanoparticle deliver system has many advantages as compared to other drug delivery systems. The therapeutic agent is protected by nanoparticle to a great extent, and when it comes to nucleic acid or other sensitive material it protects them from inactivation. Nanoparticles can be incorporated by a great ease with hydrophilic or hydrophobic therapeutic agents. The effectiveness of a drug improved as it is directed towards one place only which reduces toxicity and side effects happening due to a particular drug. The administration is can be through various passages which includes

intravenous or by oral cavity. The targeting is specific for one tissue

Gold is an element and it is represented in the periodic table by a symbol: AU. It is derived from the Latin word "Aurum". It has an atomic number of 79. Nanotechnology is a science that is growing day by day. It is rapidly spreading around the world. Nanoparticles manufactured with the help of nanotechnology have significant usage. Gold nanoparticles have a considerable advantage due to their size, shape, and ease of transmission. They can be used widely in pharmaceutical industries. They exhibit many different dimensions which include two dimensions and three dimensions. They have a unique set of features that manage their usage against microbes, and cancer. There are not enough studies performed on the shape and size of gold nanoparticles. It was essential to conduct a study on the shape and size of these nanoparticles for different cells and cell lines. Gold nanoparticles are very actively use in the cancer treatment. Gold nanoparticles have quite small size, and because of that it can penetrate to the tumor site with a great ease and continue its action; moreover, they can bind many drugs, protein and the can target cancer cells actively. They are biocompatible: Gold nanoparticles preparations can be toxic in the both system like in vivo and in vitro. Gold nanoparticles provide best contrast then standard agents because of high atomic number its can absorb kilo voltage of x-rays radiations. They produce sound when they are excited with the help of light, it can produce heat that can be used for tumor in cancer and that is called photo thermal therapy (Jain et al., 2012).

Gold Nano Particles and Cancer: Cancer is very dangerous to the cancerous patients. Now, it's going to prove that modern technology of gold nanoparticles is effective and cancers are going to be curable. The main reason is to overcome and cure is the particles produce heat due to high atomic number, and lead to treatment of tumors (Mekheimer et al., 2018). Gold nanoparticles are one of the most extensively studied material and have large number of the protocol is available to synthesis gold nanoparticles (Au NPs). In recent years gold nanotechnology rapidly progressed in molecular field (Carnovale et al., 2016). Cancer is very serious health issue worldwide. After hug effort now find a competent strategy in cancer which is against cancer diseases and only limited result and success has been obtained. Our common treatments of cancer are therapies and surgery, radiotherapy and chemotherapy these are considerable progress in recent years as advance technology because of limited treatment and consequence side effects often fail to fully satisfactory results from cancer and no one can provide drawbacks. When new modalities combined with certain treatment the effects of that is more enhanced and result is better. According to the new trend development in oncology field, The mono therapy shifts towards combination therapy in order occurred among different treatments (Beik et al., 2019). As far as surgery of cancer cells is concerned then large number of cells should be removed by surgery, the removable tumor can also leave some of the cells behind, and these cells can further grow back into a cancer. The cells that are left behind are known as residues. Gold nanoparticles comes into play here, detecting one residual cell isn't easy, they can only be detected when they are present in the form of clusters, gold nanoparticles can even detect a single residual cell left behind after the surgery. In such a way gold nanoparticle have two uses here. Firstly, it can detect residues of cancer cells that are left behind. Secondly, we can integrate some medicine with this nanoparticle which can kill these residual cells. In some situations, there is a point when cancer cells are present on the vital organs which cannot be operated. If they are operated than chances for the survival of patient becomes rare. This type of cancer can easily be treated with the help of gold nanoparticles. The main advantage here is that these processes destroy cancer cells only and a healthy cell does not get any harm. In case of radiotherapy or chemotherapy things are opposite as cancer cells are destroyed as well as other healthy cells are also destroyed (Ghosh et al., 2008).

CONCLUSION

Among the unique and novel nanoparticles, the gold nano particles have special attention because of their unique biological and physicochemical properties. Therefore, it is lead to their use of nanoparticles in the science field. The central point of this study is to use of gold nanoparticles in the liver cancer and optimized the effect of CCl₄ which is very affected in liver and the tumor also appears on the surface of the spleen and kidney. There are number of study in the case of liver cancer and gold nanoparticles.

REFERENCES

- Nakagawa H, M Fujita and A Fujimoto (2019, April). Genome sequencing analysis of liver cancer for precision medicine. In *Seminars in cancer biology* Academic Press. 55:120-127
- Zimmermann A, F Darstein, M Hoppe-Lotichius, G Toenges, A Lautem, F Abel and H Lang (2019). Cirrhosis risk score of the donor organ predicts early fibrosis progression after liver transplantation. *Journal of gastrointestinal and liver diseases: JGLD*. 281:53-61.
- Bartneck M, KT Warzecha and F Tacke (2014). Therapeutic targeting of liver inflammation and fibrosis by nanomedicine. *Hepatobiliary surgery and nutrition*. 3(6): 364
- Rechberger W, A Hohenau, A Leitner, JR Krenn, B Lamprecht and FR Aussenegg (2003). Optical properties of two interacting gold nanoparticles. *Optics communications*. 220(1-3):137-141
- Giannitrapani L, M Soresi, ML Bondi, G Montalto and M Cervello (2014). Nanotechnology applications for the therapy of liver fibrosis. *World Journal of Gastroenterology: WJG*. 20(23):7242
- Sperling RA, Gil PR, Zhang F, Zanella M and Parak WJ (2008). Biological applications of gold nanoparticles. *Chemical Society Reviews*. 37(9):1896190
- Sperling RA, Gil PR, Zhang F, Zanella M and Parak WJ (2008). Biological applications of gold nanoparticles. *Chemical Society Reviews*. 37(9):18961908.
- Mashreghi M, H Azarpara, MR Bazaz, A Jafari, A Masoudifar, H Mirzaei and MR Jaafari (2018). Angiogenesis biomarkers and their targeting ligands as potential targets for tumor angiogenesis. *Journal of cellular physiology*. 233(4):29492965
- 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
- Galon J, F Pagès, FM Marincola, HK Angell, M Thurin, A Lugli and F Tangelolo (2012). Cancer classification using the Immunoscore: a worldwide task force. *Journal of translational medicine*. 10(1):20
- Farnsworth RH, MG Achen and SA Stacker (2018). The evolving role of lymphatics in cancer metastasis. *Current opinion in immunology*. 53:64-73.
- Mashreghi M, H Azarpara, MR Bazaz, A Jafari, A Masoudifar, H Mirzaei and MR Jaafari (2018). Angiogenesis biomarkers and their targeting ligands as potential targets for tumor angiogenesis. *Journal of cellular physiology*. 233(4):2949296
- Lengauer C, KW Kinzler and B Vogelstein (1998). Genetic instabilities in human cancers. *Nature*. 396(6712):64
- Bishop JM (1991). Molecular themes in oncogenesis. *Cell*. 64(2):235-248
- Malkin, D., Li, F. P., Strong, L. C., Fraumeni, J. F., Nelson, C. E., Kim, D. H., ... & Tainsky, M. A. (1990). Germ line p53 mutations in a familial syndrome of breast cancer, sarcomas, and other neoplasms. *Science*, 250(4985), 1233-1238.
- Dubrova YE, M Plumb, B Gutierrez, E Boulton and AJ Jeffreys (2000). Genome stability: Trans generational mutation by radiation. *Nature*. 405(6782):37
- Recknagel RO (1967). Carbon tetrachloride hepatotoxicity. *Pharmacological Reviews*. 19(2):145-20
- Jain S, DG Hirst and JM O'sullivan (2012). Gold nanoparticles as novel agents for cancer therapy. *The British journal of radiology*. 85(1010):101-113.
- Rashidi S, N Karimi, O Mahian and JA Esfahani (2019). A concise review on the role of nanoparticles upon the productivity of solar desalination systems. *Journal of Thermal Analysis and Calorimetry*. 135(2):1145-1159
- Jeevanandam J, A Barhoum, YS Chan, A Dufresne amd MK Danquah (2018). Review on nanoparticles and nanostructured materials: history, sources, toxicity and regulations. *Beilstein journal of nanotechnology*. 9(1):1050-1074
- Ghosh P, G Han, M De, CK Kim and VM Rotello (2008). Gold nanoparticles in delivery applications. *Advanced drug delivery reviews*. 60(11):1307-1315