International Journal of Scientific Research in Science and Technology
Print ISSN: 2395-6011 | Online ISSN: 2395-602X (www.ijsrst.com)
doi : https://doi.org/10.32628/IJSRST

Antineoplastic effect of Nanoparticles in Dalton's Lymphoma Ascites (DLA) with Emphasis on Mechanisms of Action - A Review

V. Keerthika, Nisha A R, Arya Mohan
Department of Veterinary Pharmacology and Toxicology College of Veterinary and Animal Sciences, Mannuthy, Kerala, India

Article Info
Volume 7, Issue 6
Page Number: 61-65
Publication Issue :
November-December-2020

Article History
Accepted : 01 Nov 2020
Published : 10 Nov 2020

ABSTRACT

Cancer, one of the most deadly disease, having chemotherapy, radiotherapy, and surgery as the therapeutic approaches. To increase the selectivity and potency of the approaches used, nanoparticles (NPs) play a major role in the cancer therapeutics. Also, they play a major role in the diagnostic part. Phytochemical derived nanoparticles are gaining importance for a fruitful result in the treatment of neoplasms. This new approach offers selective toxicity to cancerous cells with minimal collateral damage to the non-malignant cells. The purpose of using NPs is by the reason of permeation and retention effect which achieves specific targeting on tumor cells. The mechanism of NPs, evading the cells of cancer involves diversified activities.

Keywords: Nanoparticles, Phytochemical, Selective Toxicity

I. INTRODUCTION

Of the 14 million new cancer cases diagnosed worldwide, slightly more than 1 million are from India. Tobacco use, diseases, and other preventable causes are linked with many cancer cases in India (Mallath *et al.*, 2014). Similarly, in India, 700,000 cancer deaths have occurred out of 8 million cancer deaths worldwide. According to IARC's predictions, GLOBOCAN estimates that India's cancer burden will almost double in the next 20 years (Ferlay *et al.*, 2015). The incidence and mortality of cancer is growing rapidly around the world, particularly in low- and middle-income countries. There is an overwhelming need for cancer prevention actions to be embraced and enforced by the countries (Ferlay *et al.*, 2019). Dietary shifts, tobacco use, alcohol, radiation effects, and toxins are the causes of cancer (Ali *et al.*, 2011). Chemotherapy, radiotherapy, and chemically derived medications are among the latest therapies.

Treatments such as chemotherapy will bring patients under a great deal of pressure and harm their health further. Therefore, there is an emphasis on using alternative medicines and therapies against cancer. Research has therefore been conducted to examine the possible properties and uses of terrestrial plant extracts for the preparation of possible nanomaterial-based disease drugs. (Sivaraj *et al.*, 2014).

The goal of this paper is to take an overview of existing compounds extracted from plants that have

therapeutic anti-cancer properties and their combination with nanoparticles. It also views the various mechanism involved in the destruction of DLA cells by the nanoparticles.

NANOPARTICLE

Nanoparticles are classified in the 10-1000 nm range as particulate dispersions or solid particles with a size. A nanoparticle matrix is dissolved, trapped, encapsulated or bound to the drug. (Brigger *et al.*, 2012).

GREEN SYNTHESIS OF NANOPARTICLE

At the moment, as an alternative to conventional approaches, the synthesis of nanoparticles using biological agents was becoming more desirable. Biosynthesis of nanoparticles included the use of bacteria, fungi, actinomycetes, yeast, and algae and plants using an environmentally friendly, green-chemistry-based approach. The synthesis of nanoparticles based on plant extracts provided an eco-friendly, safe, non-toxic and inexpensive method of manufacturing nanoparticles of various shapes, sizes and morphologies.

The following steps were involved in the green synthesis of nanoparticles as described by Patil and Kim, 2017.

The plant extract was prepared from the desired portion of the plant containing anticancer potential. The extract was then combined with a specified concentration of metal salt solution and held at room temperature. The color change was observed for the indication of nanoparticle formation.

CHARACTERIZATION

Many approaches had been used for the characterization of nanoparticles. However, for nanoparticle synthesis, the first qualitative indication was the color shift of the reaction solution. For silver NPs, the characteristic color shift was from yellow to brown (Poinern ,2014) and yellow to deep red or purple for gold NPs (Lee *et al.*, 2016; Malik *et al.*, 2014) due to surface plasmon vibration. Ultraviolet-visible (UV-vis) spectrophotometer, dynamic light scattering (DLS), scanning electron microscopy (SEM), transmission electron microscopy (TEM), energy dispersive x-ray spectroscopy (EDX), X-ray powder diffraction (XRD) , fourier transform infrared spectroscopy (FT-IR), atomic force microscopy (AFM), particle size analysis were the usually used techniques for nanoparticle characterization (Patil and Kim, 2017).

REQUISITE FOR NANOPARTICLES

Recent interest had been focused on the development of nano scale delivery vehicles capable of regulating the release, directly inside cancer cells. Studies had shown that the use of medicinal plants for the development of nanoparticles might be cost efficient and eco-friendly (Gu *et al.*, 2007). Nanoparticles were engineered to securely hit their target and precisely release their cargo at the disease site, thus enhancing the bioavailability of the drug's tissue. By merely accumulating and becoming stuck in tumors (passive targeting), nanoparticles were provided with the benefit of targeting cancer. The phenomenon, caused by leaky vessels and weak lymphatic drainage, known as the enhanced permeation and retention effect and had been used to describe why macromolecules and nanoparticles were present in tumors at higher ratios, compared to normal tissues (Wang and Thanou, 2010).

DALTONS LYMPHOMA ASCITES (DLA) CELLS

Dalton's lymphoma had been a successful model system, with reproducible biological end points such as local growth and predictable survival time. As an interesting model for cancer research, Dalton's lymphoma was commonly used, because of its utility in the pre-clinical method for testing experimental or known drugs in the treatment of different cancers. It

was a T-cell transplantable lymphoma of spontaneous origin in the murine host thymus. It provided a convenient model system to research the effects within a short period of time. The development of tumor would start immediately and actively, after transplanting DL ascites cells into the abdominal cavity of healthy recipient mice. Typically, the recipient or transformed mice might live for up to around 3 weeks (Koiri *et al.*, 2017).

ANTINEOPLASTIC ACTIVITY OF NANOPARTICLES(NPs)- MECHANISM

The mechanism on which the nanoparticles elicited their antineoplastic activity could be due to the ability of nanoparticles to induce apoptosis , surface properties of cancer cells and nanoparticles, nanoparticle induced leakiness, production of reactive oxygen species, activating the caspase cascade of apoptosis in the cancer cells.

ABILITY OF NPs TO INDUCE APOPTOSIS

Normally , cancer cells had the property to escape the apoptotic mechanism provoked by the immune system. The NPs could prevent the escape of cancer cells from apoptosis and induced the death of the cancer cells. Additionally, NPs revealed a significant P53 independent apoptosis. (Sriram *et al.*,2010).

SURFACE PHENOMENON OF NPs AND CANCER CELLS

The surface charge of the cancer cell was negative owing to the unique metabolic process, which produced the lactate. They had the high rate of glycolysis, thereby making the cancer cell pH, acidic. The NP's charge would be positive. The lactate enabled strong binding affinity with nano particles (Gong *et al.*,2015).

NANOPARTICLE INDUCED LEAKINESS

The need for oxygen and nutrients would increase, as the tumor grew rapidly, leading to irregularly shaped blood vessels with leaky gap junctions. This faulty vessel wall would allow extravasation of NPs from circulation into the tumor tissue. Owing to poor lymphatic drainage, retention of NPs might occur rather than being filtered. This could improve the effectiveness of anticancer treatment. (Setyawati *et al.*, 2017).

PRODUCTION OF REACTIVE OXYGEN SPECIES (ROS)

In the cancer cells, NPs had a direct impact on intracellular space and increased the development of ROS followed by decrease in the mitochondrial membrane potential. This could cause DNA fragmentation, preceded by cancer cell death (Parida *et al.*, 2014).

ACTIVATION OF CASPASE CASCADE OF APOPTOSIS

The nanoparticles got internalized in the cancerous cells by the process of endocytosis. It could be followed by the generation of ROS and would cause dysfunction of mitochondria. This further brought about the caspase cascade mechanism, resulted in DNA damage and cell death (Tiloke *et al.*, 2016).

ANTINEOPLASTIC MECHANISM OF NANOPARTICLES ON DLA CELLS

Continuous diffusion of nanoparticles through cells contributed to the prolonged activation of channels of calcium. Higher mitochondrial levels of calcium promoted the release of apoptogenic factors such as Cytochrome C and other factors that would cause apoptosis. Apoptosis might be initiated by these factors that are released into the cytosol. This increase in calcium concentration occurred within 48 hours of the nanoparticles action.

Nanoparticles caused a genetic mutation, which inhibited the expression of proteins and its gene expression. This, in turn reduced the expression of

anti-apoptotic genes like *Bcl-2*. It gradually expressed the apoptotic genes like *Caspase*, *Bax* (Kavya *et al*., 2013).

CHALLENGES FACED IN CANCER NANOTHERAPY

There are many problems in the field, and the possible danger of anti-tumor therapies remains controversial. Potential chronic and acute toxic effects are the most important concerns. Adsorption or electrostatic interactions can bind nanoparticles to the surface of the cells, thereby causing cell damage. In contrast, the US Food and Drug Administration has licensed only a few types of materials and very few have been approved as an antitumor agent to enter in phase 3 clinical trials. It suggests that NPs need to be understood more thoroughly prior to their possible use in cancer therapy. Hence, it is important to intensively analyze the long term toxicity of NPs to living systems (Huang *et al*., 2017).

II. CONCLUSION

Cancer therapy is the most fascinating aspect of clinical outcomes for researchers. In the recent years. The application of nanotechnology in the field of cancer treatment has seen an exponential growth. This sort of advanced and experimental approach like nanomaterial based phytochemical delivery can resolve the effect of toxicity from the drugs. Additionally, it can achieve a targeted delivery system.

III. FUTURE PROSPECTIVES

There is a possibility that methods to nullify nanoparticles induced toxicity would be a fruitful opportunity to boost the armamentarium of cancer therapy. The transition of nanotechnology to standard clinical practice would require a multidisciplinary approach guided by clinical, ethical and social perceptions. It can be anticipated that in the very future, humans will benefit greatly from nanotechnology and NPs, especially in tumor therapy, in view of the important research results dedicated to this field.

IV. REFERENCES

[1]. Ali, I., Wani, W.A. and Saleem, K., 2011. Cancer scenario in India with future perspectives. Cancer therapy. 8: 56-70.

[2]. Brigger, I., Dubernet, C. and Couvreur, P., 2012. Nanoparticles in cancer therapy and diagnosis. Adv. drug dlv. Rev. 64: 24-36.

[3]. Ferlay, J., Colombet, M., Soerjomataram, I., Mathers, C., Parkin, D.M., Piñeros, M., Znaor, A. and Bray, F., 2019. Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods. Int. J. cancer. 144: 1941-1953.

[4]. Ferlay, J., Soerjomataram, I., Dikshit, R., Eser, S., Mathers, C., Rebelo, M., Parkin, D.M., Forman, D. and Bray, F., 2015. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int. J. cancer. 136: .E359-E386.

[5]. Gong, N., Chen, S., Jin, S., Zhang, J., Wang, P.C. and Liang, X.J., 2015. Effects of the physicochemical properties of gold nanostructures on cellular internalization. Regen. Biomater. 2: 273-280.

[6]. Gu, F.X., Karnik, R., Wang, A.Z., Alexis, F., Levy-Nissenbaum, E., Hong, S., Langer, R.S. and Farokhzad, O.C., 2007. Targeted nanoparticles for cancer therapy. Nano today, 2: 14-21.

[7]. Huang, Y., Fan, C.Q., Dong, H., Wang, S.M., Yang, X.C. and Yang, S.M., 2017. Current applications and future prospects of nano materials in tumor therapy. Intl. J. nanomed. 12: 1815.

[8]. Kavya, J., Amsaveni, G., Nagalakshmi, M., Girigoswami, K., Murugesan, R. and Girigoswami, A., 2013. Silver Nanoparticles Induced Lowering of BCl2/Bax Causes Dalton's Lymphoma Tumour Cell Death in Mice. J. Bionanosci. 7: 276-281.

[9]. Koiri, R.K., Mehrotra, A. and Trigun, S.K., 2017. Dalton's lymphoma as a murine model for understanding the progression and development of T-Cell lymphoma and its role in drug discovery. Int. J. Immunother. Cancer Res. 3: 001-006.

[10]. Lee, S.Y., Krishnamurthy, S., Cho, C.W. and Yun, Y.S., 2016. Biosynthesis of gold nanoparticles using Ocimum sanctum extracts by solvents with different polarity. ACS Sustain. Chem. Engng. 4: 2651-2659.

[11]. Malik, P., Shankar, R., Malik, V., Sharma, N. and Mukherjee, T.K., 2014. Green chemistry based benign routes for nanoparticle synthesis. J. Nanoparticles. 2014: 01-14.

[12]. Mallath, M.K., Taylor, D.G., Badwe, R.A., Rath, G.K., Shanta, V., Pramesh, C.S., Digumarti, R., Sebastian, P., Borthakur, B.B., Kalwar, A. and Kapoor, S., 2014. The growing burden of cancer in India: epidemiology and social context. Lancet Onc. 15: 205-212.

[13]. Parida, U.K., Biswal, S.K. and Bindhani, B.K., 2014. Green synthesis and characterization of gold nanoparticles: study of its biological mechanism in human SUDHL-4 cell line. Adv. Biol. Chem. 4: 360.

[14]. Patil, M.P. and Kim, G.D., 2017. Eco-friendly approach for nanoparticles synthesis and mechanism behind antibacterial activity of silver and anticancer activity of gold nanoparticles. Appl. Microbiol. Biotech. 101: 79-92.

[15]. Poinern, G.E.J., 2014. A laboratory course in nanoscience and nanotechnology. CRC Press: 230.

[16]. Setyawati, M.I., Tay, C.Y., Bay, B.H. and Leong, D.T., 2017. Gold nanoparticles induced endothelial leakiness depends on particle size and endothelial cell origin. ACS nano, 11: 5020-5030.

[17]. Sivaraj, R., Rahman, P.K., Rajiv, P., Narendhran, S. and Venckatesh, R., 2014. Biosynthesis and characterization of Acalypha indica mediated copper oxide nanoparticles and evaluation of its antimicrobial and anticancer activity. Mol. Biomol. Spectroscopy. 129: 255-258.

[18]. Sriram, M.I., Kanth, S.B.M., Kalishwaralal, K. and Gurunathan, S., 2010. Antitumor activity of silver nanoparticles in Dalton's lymphoma ascites tumor model. Intl. J. nanomed. 5: 753.

[19]. Tiloke, C., Phulukdaree, A., Anand, K., Gengan, R.M. and Chuturgoon, A.A., 2016. Moringa oleifera gold nanoparticles modulate oncogenes, tumor suppressor genes, and caspase-9 splice variants in a549 cells. J. Cell. Biochem. 117: 2302-2314.

[20]. Wang, M. and Thanou, M., 2010. Targeting nanoparticles to cancer. Pharmacol. Res. 62: 90-99.

Cite this article as :

V. Keerthika, Nisha A R, Arya Mohan, "Antineoplastic effect of Nanoparticles in Dalton's Lymphoma Ascites (DLA) with Emphasis on Mechanisms of Action - A review", International Journal of Scientific Research in Science and Technology (IJSRST), Online ISSN : 2395-602X, Print ISSN : 2395-6011, Volume 7 Issue 6, pp. 61-65, November-December 2020.
Journal URL : http://ijsrst.com/IJSRST20763