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NANOTECHNOLOGY IN ONCOLOGY: THE POTENTIAL OF NANOPARTICLES IN THE ADMINISTRATION OF ANTINEOPLASTIC DRUGS

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Abstract: Nanoparticles are agglomerated molecules on the nanometer scale, which are used in nanotechnology because of their unique structure, enabling the delivery of medicinal substances. They have their own characteristics, such as physicochemical qualities, greater pharmacological bioavailability and the option for researchers to pre-architect their structures for a specific interaction. The aim of this work was to demonstrate through a literature review the main types of nanoparticles currently used to deliver drugs to target cells and to explain how they have the potential to be used in cancer treatment in the future. Conventional cancer treatment has faced challenges in effectively targeting chemotherapy drugs inside cancer cells, often resulting in collateral damage to patients. In this context, nanoparticles have emerged as a promising alternative, as they have demonstrated significant results in the targeted delivery of drugs to the interior of target cells, due to their ability to penetrate the plasma membrane. However, studies also indicate potential harmful effects associated with nanoparticles, especially in prolonged exposure, which can cause toxicity to both the human body and the environment. Therefore, further research is needed, both in vivo and in vitro, to better understand the long-term consequences of this technology. Furthermore, more in-depth investigations into the biology of cancer on the nanometric scale are essential to improve the precision and safety of using nanoparticles as a therapeutic alternative in cancer treatment.
Keywords: Nanomedicine, Nanotechnology; Nanoparticles; Cancer Treatment.

INTRODUCTION

Cancer has haunted humanity for millennia, an example of which is the discovery of a hominid with osteosarcoma, dating back more than 1.7 million years, found in the Swartkrans cave in South Africa (ODES et al., 2016).

Understanding this concept, it is important to understand that cancer is not a new enemy in contemporary society. Cancer currently represents a significant challenge for public health worldwide. An example of this is the forecast provided by the American Cancer Society, which estimates that there will be 1,958,310 new cases of cancer and 609,820 deaths from cancer in the United States in 2023 (SIEGEL MPH et al., 2023). According to the same authors, cancer is a disease with a high mortality rate, and it is on the rise among the world's populations. How can nanoparticles be used and innovated to improve the delivery of chemotherapy drugs to cancer cells and reduce side effects for patients undergoing treatment?

Cancer treatment has become fundamental to patient survival. However, the therapeutic approaches available can be ineffective in certain cases (AMREDDY et al., 2018). An example of this, according to the same authors, is the administration of chemotherapy drugs to cancer cells, which does not always result in a satisfactory response due to the resistance of the tumors, the uneven distribution of the drug in the tissues and significant side effects. These challenges highlight the need to develop new therapeutic strategies, such as the use of nanotechnology, making treatment more effective and safer for patients.

New approaches have been explored and developed, such as the administration of intelligent nanoparticles to transport drugs into cancer cells (SUN et al., 2023). Representing a promising potential within nanomedicine, according to the same authors, this technology has the ability to respond to endogenous and exogenous stimuli from the body's cells, such as the pH and temperature of the selected area.

The study of nanoparticles in the delivery of drugs in the fight against cancer is of extreme scientific relevance (GAVAS; QUAZI; KARPIŃSKI, 2021). According to the same authors, nanoparticles, with sizes ranging from 1 to 100 nm, have been widely used in cancer treatment due to their specific advantages, such as high biocompatibility, low toxicity, greater stability, enhanced permeability, prolonged retention effect and ability to precisely target cells. Its impact reaches various sectors, from medical to industrial. Through its applicability in various sectors, it has demonstrated innovative results compared to those usually used.

With the advance of nanotechnology, it has become possible to develop highly specific and precise nanoparticles, capable of responding to minimal biological, physical and chemical stimuli in the human body (MITCHELL et al., 2020). The authors highlighted the relevance of advanced precision nanoparticle designs, with the potential to enhance therapies by overcoming heterogeneous barriers in the human body. These nanoparticles contribute to the optimization of clinical results, promoting more favorable outcomes for patients. In this way, this technology allows cell penetration and the controlled release of drugs directly inside the target cells, reducing the side effects associated with the use of drugs in high concentrations (AL-THANI et al., 2024). As a result, there has been a significant improvement in the clinical condition of hospitalized patients.

Considering the relevance of nanoparticles in healthcare, this study was conducted with the aim of presenting the main nanoparticles currently used in the targeted delivery of drugs to target cells, as well as exploring the potential of this technology for future cancer treatments. The research was based on an in-depth review of academic articles and scientific publications related to the use of nanoparticles in cancer treatment.

NANOPARTICLE DYNAMICS: PROPERTIES AND ABSORPTION

Nanomedicine, a specialized field of nanotechnology applied to medicine, uses tools and materials on a nanometer scale (one billionth of a meter) to help diagnose, prevent and treat diseases. In therapeutic oncology, this approach has emerged as an innovative proposal to increase the precision of treatments, improve the transportation of chemotherapy drugs and reduce both the side effects and toxicity associated with these drugs (FAN et al., 2023; IRACHE, 2008; RIZZO et al., 2013).

Nanoparticles are molecules with nanometric dimensions, measuring between 1 nm and 1000 nm, and can have a metallic, inorganic, organic and biological composition (ASSIS et al., 2012; JOVČEVSKA; MUYLDERMANS, 2019). Due to their unique physicochemical characteristics (figure 1) and their possibility of being structurally manipulated with the addition of external factors, they can play a major role within targeted drug delivery in cancer (JAIN, 2010; SELMANI; KOVAČEVIĆ; BOHINC, 2022).

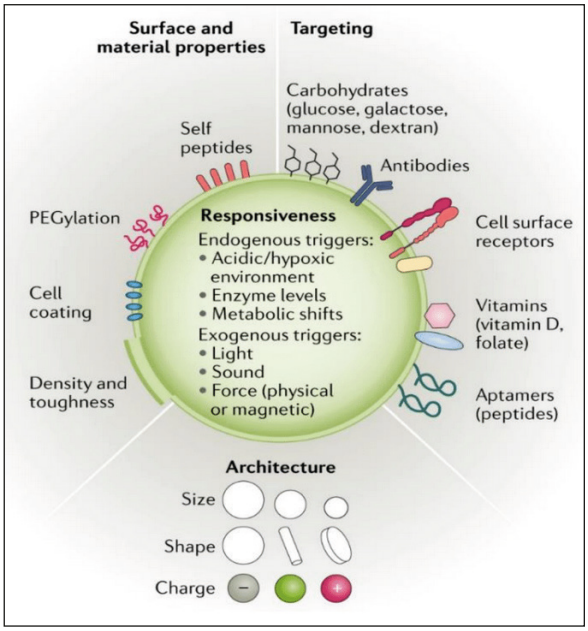

Figure1 - Surface properties of nanoparticles (MITCHELL et al., 2020)

According to the literature (LIU et al., 2018; RUAN et al., 2015; ZHENG et al., 2022), we can synthesize drug delivery with nanoparticles in three steps: the nanoparticles reach the cancer by vascular transport, cross the tumor blood vessel wall and penetrate the stroma for drug release.

The cellular absorption of nanoparticles depends directly on their uptake or penetration of the plasma membrane, with several routes for their entry, these mechanisms can be separated into two groups: via endocytosis and via direct cellular entry (DONAHUE; ACAR; WILHELM, 2019). According to the same authors, in the endocytosis route, nanoparticles interact with plasma membrane structures (proteins, lipids, recognition receptors and others), allowing the cell to trap the NPs inside membrane vesicles into the cell interior, where the chosen drug will be released. In the direct cell entry route, nanoparticles can cross the plasma membrane due to their biological, chemical and physical characteristics, without the need to form vesicles (DONAHUE; ACAR; WILHELM, 2019)

Figure 2 shows the process of nanoparticle entry into the cell, highlighting the endocytosis route (figure 2a) and direct cell entry through the plasma membrane (figure 2b). In this mechanism, the nanoparticles initially interact with the plasma membrane, either by recognizing specific ligands or by electrostatic interaction, depending on their functionalization and composition. These vesicles allow the particles to be transported intracellularly to specific organelles, such as endosomes or lysosomes, where they can release their therapeutic content in a controlled manner. This process is fundamental to the effectiveness of nanoparticles in biomedical applications, such as the targeted delivery of antineoplastic drugs, guaranteeing selectivity and reducing systemic adverse effects.

In order for this nanoparticle to penetrate the cell membrane of cancer cells and escape the human immune system, it is necessary to pre-engineer the nanoparticle structures (JAIN, 2010). Therefore, in order to achieve a reduction in adverse effects, greater therapeutic precision and efficient drug delivery, it is essential to identify and select the most suitable nanoparticles for cancer treatment. This choice must take into account specific nanoparticle properties, such as biocompatibility, stability, functionalization capacity, and drug transport and release efficiency in tumour cells. In addition, the selection should be guided by characteristics of the tumor microenvironment, ensuring greater selectivity and efficacy in combating cancer cells, while minimizing impacts on healthy tissues (DRISTANT et al., 2023).

According to the authors Dristant et al. (DRISTANT et al., 2023)(, various nanoparticles NPs) can be used in cancer therapy. Thus, several NPs have been designed for drug delivery and controlled release of therapeutic reagents in cancer patients. Some of the main nanocarriers used are: polymer-based nanocarriers, biomimetic-based nanocarriers, inorganic-based nanocarriers and other types under development (SUN et al., 2023).

LIPOSOMES

Liposomes are vesicular nanoparticles with a lipid composition and spherical shape, characterized by structures made up of one or more phospholipid bilayers surrounding an aqueous core. This organization gives them amphipathic properties, allowing them to incorporate both hydrophilic and lipophilic drugs. Due to their structural similarity to the cell membrane, liposomes have a high capacity for interaction and fusion with target cells, facilitating the intracellular delivery of drugs. This characteristic makes them an effective tool for drug delivery, increasing bioavailabili-

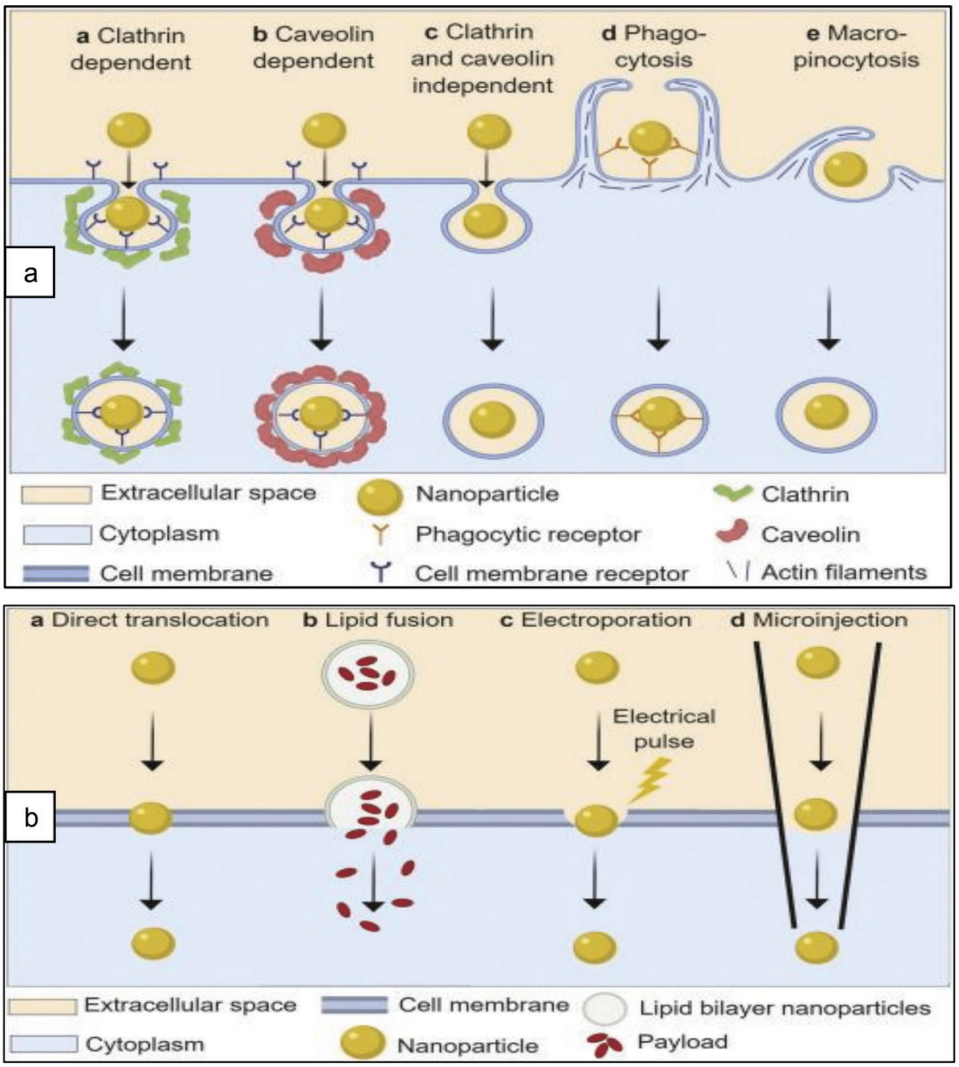

Figure2 : a) Schematic of the cellular entry of nanoparticles into the cell membrane via endocytosis; b) Schematic of the direct cellular entry of nanoparticles into the cell membrane. (DONAHUE; ACAR; WILHELM, 2019)

ty and therapeutic efficiency (KARANDIKAR et al., 2017; NGUYEN; GUPTA; NGUYEN, 2022; SUN et al., 2023).

With technological advances, various methodologies have been developed for the synthesis of liposomes, allowing the production of optimized structures for different therapeutic applications. According to the literature (OTAKE et al., 2006; SUN et al., 2023), the innovative technologies used to manufacture liposomes are: supercritical fluid technologies, supercritical anti-solvent techniques and supercritical reverse phase evaporation techniques. Each method has specific advantages, such as greater control of particle size, efficient encapsulation of drugs or scalability for industrial production. These approaches have made it possible to customize liposomes according to the desired characteristics, such as lipid composition, electrical charge and functionalization with specific ligands, expanding their potential for clinical application.

One of the promising applications of liposomes is in the treatment of colorectal cancer (CRC). This type of cancer is characterized by its solid composition, being coated by a biological barrier composed of endothelial cells, perivascular cells and extracellular matrix,

which hinders the direct penetration of drugs. This barrier requires high doses of drugs to reach the tumor, which often results in significant adverse effects for the patient (SHAZLEEN IBRAHIM et al., 2024). According to the same authors, liposomes, due to their high biocompatibility, low immunogenicity and biodegradability, present an effective and safe alternative. Their structural properties allow them to act in a targeted manner on target cells, facilitating the delivery of drugs inside the tumor and reducing the need for high doses. This minimizes the side effects associated with conventional treatment and offers a more efficient and less invasive therapeutic approach.

Despite their promising structural properties, many nanoparticles, including liposomes, are still in the scientific research stages before being released for clinical use. However, some liposomes already approved and available for clinical application include Doxil and Myocet (KRISHNAMURTHY et al., 2015; ZHANG et al., 2008), both of which have been widely studied and used in the treatment of various types of cancer. These formulations represent significant advances in drug delivery, especially due to their ability to improve therapeutic efficiency and reduce the adverse effects associated with conventional treatments.

POLYMERIC NANOPARTICLES

According to the literature (BHASARKAR; BAL, 2021; PELTONEN; SINGHAL; HIRVONEN, 2020; SURIYA PRABHA et al., 2020), polymeric nanoparticles (PNPs) are nanometric structures produced from natural and synthetic polymers with colloidal organic materials. PNPs can be grouped into two groups, nanocapsules and nanospheres, each with a different purpose and morphology (DRISTANT et al., 2023; ZIELINSKA et al., 2020).

Nanocapsules are drug release systems with an oily core in which the drug particles are dissolved, and the control of drug release is determined by the pores present in the polymer coatings that make up their structure. In contrast, nanospheres have a structure made up of a polymeric network that acts as a matrix. This matrix allows the absorption and molecular distribution of substances, and the release of the drug is directly related to the concentration of the polymer used in its manufacture. Both structures have unique characteristics that make them promising for specific therapeutic applications (AHMED; ARIAN; KHAN, 2022; DRISTANT et al., 2023; ZIELINSKA et al., 2020). It is important to note that the drug selected by healthcare professionals can be adsorbed onto the surface of both the polymeric structures mentioned, both in nanocapsules and nanospheres. This adsorption capacity expands the possibilities for controlling the release of the drug, contributing to greater therapeutic efficiency and a potential reduction in adverse effects (MADEJ; KUROWSKA; STRZALKA-MROZIK, 2022; ZHANG et al., 2022; ZIELINSKA et al., 2020).

Currently, the synthesis and preparation of polymeric nanoparticles (PNPs) involves the application of various techniques, including emulsion polymerization, solvent evaporation, salting-out, dialysis and technologies based on supercritical fluids (MASOOD, 2016; SUN et al., 2023). These approaches make it possible to obtain PNPs with specific characteristics, tailored to therapeutic needs and the desired properties for biomedical applications.

Oliveria et al. (OLIVEIRA et al., 2023) state that the applicability of this nanometric technology has been used in various health scenarios, due to its biodegradability, targeted delivery and increased half-life, making it an alternative option in the treatment of cancer. A practical example of the applica-

tion of polymeric nanoparticles can be seen in the treatment of brain diseases. Due to their small size and the specific interaction between ligands and receptors, these particles are able to effectively overcome the blood-brain barrier (BBB), which usually constitutes a significant obstacle to the administration of drugs to the central nervous system (MADEJ; KUROWSKA; STRZALKA-MROZIK, 2022; MAHMOUD; ALAMRI; MCCONVILLE, 2020).

Studies indicate that some polymeric nanoparticles (PNPs) have already been approved for clinical use, such as Adagen, Genexol PM, Eligard and Copaxone (KRISHNAMURTHY et al., 2015; ZHANG et al., 2008).

GOLD NANOPARTICLES

As described by several authors (CHEN; FENG, 2022; MAHATO, 2017; SUN et al., 2023), gold nanoparticles (AuNPs) are metallic particles composed of gold, with dimensions on the nanometer scale, generally ranging from 1 to 100 nm.

According to the authors Hammani et al. (HAMMAMI et al., 2021), the observation of gold nanoparticles (AuNPs) dates back to 1857, when the scientist Michael Faraday noticed that these inorganic structures emitted a red-colored light. This phenomenon is related to their nanometric size, as the wavelength of the light interacts in a specific way with the particles. AuNPs absorb light in the blue-green spectrum (~450 nm) and reflect light in the red spectrum (~700 nm), due to their ability to resonate with light of longer wavelengths. This optical characteristic allows gold nanoparticles to be used to signal specific target tissues, providing a valuable tool in targeted therapies, with adjustable optical properties during their manufacture (HAMMAMI et al., 2021; MEIR; POPOVTZER, 2018)

In addition, gold nanoparticles (AuNPs) have a number of advantageous characteristics in drug delivery, including: Biocompatibility: They are well tolerated by the body, minimizing adverse reactions; Formation of stable chemical bonds (S and N): Allows efficient conjugation of drugs, antibodies or other therapeutic molecules, ensuring the stability of the payload; Physical stability: Maintains the integrity of the particles during transport and release of the drug; Electronic and optical properties: Their adjustable optical characteristics, due to the phenomenon of plasmon resonance, allow them to be used in imaging and photothermal therapies; Facilitated synthesis: AuNPs can be produced using simple and efficient methods, which favors their large-scale application; Oral administration: Gold nanoparticles can be administered by non-invasive routes, such as orally, facilitating adherence to treatment; Efficient penetration into cancer cells: Their structure allows effective penetration into tumor cells, favoring direct delivery of the drug to the areas of interest (BAI et al., 2020; HUSSAIN, 2015; SIDDIQUE; CHOW, 2020). These properties make gold nanoparticles promising for clinical application, especially in cancer treatment and targeted therapies. Gold nanoparticles (AuNPs) can be classified into several groups based on their morphology, each offering different advantages for therapeutic and diagnostic application. Some examples include: Nanospheres: These are the simplest forms of AuNPs, with a spherical structure. They are widely used due to their easy synthesis and good dispersion properties; Nanoconchas: They have a hollow, shell-like structure that can be used to load and release drugs in a controlled manner, taking advantage of their internal cavity; Nanobastons: They have an elongated, anisotropic shape with unique optical properties, such as greater light absorption, which makes them useful in photothermal therapies, in which light is used to heat and destroy tumor cells; Nanogaiolas: They feature a porous structure

that can be used to store therapeutic molecules or contrast agents. These particles offer a large surface area and are effective for releasing drugs in a targeted manner (ACHARYA; MITRA; CHOLKAR, 2017). Each of these forms has specific characteristics that make them more suitable for different applications in the treatment of diseases, such as cancer, and in improving diagnostic imaging techniques.

Gold nanoparticles are synthesized by biological and physicochemical action (SCHRÖFEL et al., 2014; SINGH et al., 2018). The synthesis of AuNPs involves a variety of techniques, the main ones employed being: colloidal method, galvanic substitution, site--exchange reaction and biosynthesis (SIDDIQUE; CHOW, 2020; SINGH et al., 2018).

Due to their unique characteristics, AuNPs are being used as a promising platform for drug transportation (CHEN et al., 2007; SINGH et al., 2018). The use of methotrexate (MTX) conjugated to gold nanoparticles (AuNPs) has shown promising results, both in vitro and in vivo, in the treatment of cancer. As stated by Singh et al. (SINGH et al., 2018), "methotrexate (MTX), which has been used to treat cancer for decades, after conjugation with gold nanoparticles, showed greater cytotoxicity in several tumor cell lines compared to free MTX". This increase in therapeutic efficacy can be attributed to the ability of gold nanoparticles to target the drug directly to the tumor site, improving the concentration of the drug in the target cells and reducing the dispersion of the drug in healthy tissues. This effect results in greater local cytotoxicity for cancer cells, which increases the effectiveness of the treatment and reduces side effects, compared to the use of free MTX. In addition, conjugation with nanoparticles allows the drug to be delivered more efficiently, promoting controlled and localized release, with less need for high doses of the drug, thus minimizing systemic adverse effects (CHEN et al., 2007; SINGH et al., 2018).

FUTURE PROJECTIONS

Nanoparticles (NPs) and nanomaterials are being continuously developed and improved to overcome the limitations of conventional cancer treatments. Their unique characteristics, such as intracellular navigation, biocompatibility, the ability to architect their structure in a personalized way, enhanced pharmacokinetics, selectivity in tissue penetration and highly efficient drug delivery systems, offer great potential in nanomedicine. These properties allow nanoparticles to become a promising platform for drug delivery, providing precision in directing drugs to target cells, minimizing side effects on healthy tissues and increasing treatment efficacy. In addition, nanoparticles can be designed for controlled release of active substances, ensuring an optimized dosage over time, which can result in a better therapeutic response and a reduction in the adverse effects typical of conventional therapies. In the long term, these innovations are expected to transform cancer treatment by providing more effective, safe and personalized therapies (MITCHELL et al., 2020; YUSUF et al., 2023).

A wide variety of nanoparticles are currently being researched and improved for future therapeutic applications, especially in the field of nanomedicine. These nanoparticles offer unique characteristics that can be exploited to optimize drug delivery and overcome the limitations of conventional treatments. The main nanoparticles under study include: Micelles: spherical structures formed by surfactants that can encapsulate hydrophobic drugs and improve their solubility; Dendrimers: particles with a branched structure that can be used to release drugs in a controlled and specific way; Polymeric nanoparticles: compounds formed by polymers that allow the controlled release of drugs and increase biocompatibility; Liposomes: lipid vesicles that can encapsulate therapeutic substances, improving their

delivery and reducing side effects; Protein nanoparticles: proteins modified to create drug delivery systems with greater selectivity; Cell membrane nanoparticles: particles that mimic cell membranes and can improve the delivery of drugs directly to target cells; Mesoporous silica nanoparticles: structures with nanometer-sized pores that allow for the controlled release of drugs; Gold nanoparticles: metallic particles with optical properties and biocompatibility, used in targeted therapies and diagnostics; Iron oxide nanoparticles: widely used in medical imaging and hyperthermia therapies, as well as being biocompatible; Quantum dots: semiconductor nanoparticles that have fluorescent properties, used in diagnostics and imaging therapies; Carbon nanotubes: Cylindrical structures with unique electrical conduction properties, used in drug delivery and bioimaging therapies; Black phosphorus (BP): two-dimensional material that can be used for phototherapy and controlled release therapy; Metal-organic framework (MOF): composed of metal and organic ligands that have a high capacity for loading and releasing drugs (SUN et al., 2023). Figure 3: shows an illustrative diagram of nanoparticles used in nanotechnology, the image shows different types of nanoparticles.

According to the literature, these nanoparticles are being intensively studied and improved to ensure that they can be applied efficiently and safely in the treatment of diseases such as cancer and other conditions. The continued development of these technologies could revolutionize medicine, offering more specific, effective treatments with fewer adverse effects.

Although nanoparticles and nanomaterials have a wide range of therapeutic advantages, such as better drug delivery, greater selectivity and reduced side effects, it is essential to consider the possible risks and adverse effects associated with their use. Increased scientific concern about the safety of these materials reflects the need to understand how they interact with biological systems and what the potential impact is on human health and the environment. In studies carried out (CHOI; OH; CHOY, 2009; FU et al., 2014; GATOO et al., 2014; KERFAHI et al., 2015; SOHN et al., 2015; YUSUF et al., 2023), nanoparticles showed potential toxic side effects for organisms and the environment.

(YUSUF , 2023) et al.point out that the toxicity of carbon nanotubes can negatively impact the bacterial diversity of the soil, suggesting potential environmental risks associated with the use of these materials. Furthermore, as pointed out by Kerfahi et al. (KERFAHI et al., 2015), carbon nanotubes have the ability to induce oxidative stress, which can result in damage to the plasma membrane and cause inflammation in human lung carcinoma cell lines (A549). These findings highlight the need for an in-depth study of the biological and environmental effects of carbon nanoparticles, considering their potential impacts on human health and ecosystems.

Furthermore, another significant challenge in the use of nanoparticles is their recognition as foreign substances by the immune system (ERNST et al., 2021; YUSUF et al., 2023). When nanoparticles enter the body, they can be identified as unnatural bodies, triggering an immune response. This response can include phagocytosis by immune system cells, such as macrophages, or activation of other immune pathways, such as the release of pro-inflammatory cytokines. This recognition can compromise the effectiveness of the treatment, as the nanoparticles can be quickly removed from the body, reducing their ability to deliver the drug to the target tissue. In addition, an exacerbated immune response can cause adverse effects such as inflammation and systemic toxicity, compromising the safety of nanotechnology-based treatments.

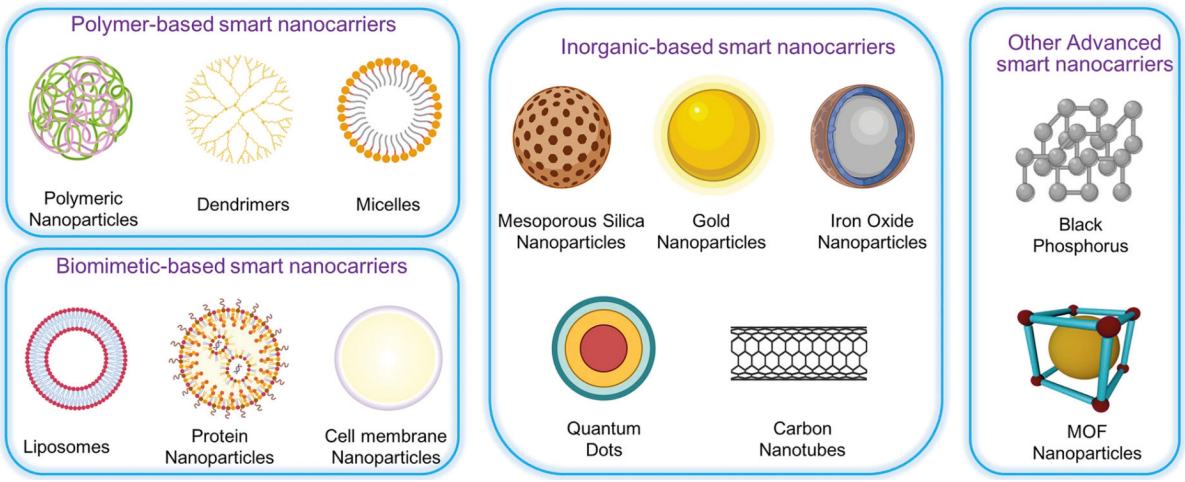

Figure 3 - Schematic drawing of nanoparticles used in nanotechnology (SUN et al., 2023).

Therefore, the development of biocompatible nanomaterials and the modulation of their properties to avoid or minimize the immune response are key points in the evolution of nanomedicine.

According to the authors Ernst et al. (ERNST et al., 2021), the interaction of nanoparticles with the immune system depends on various factors such as: structural surface, size, composition, shape, surface charge and others

Therefore, further studies are needed to assess the cytotoxicity of nanoparticles and their potential toxic effects on both organisms and the environment. Although nanoparticles show promising results as a platform for targeted delivery of drugs to target cells, a thorough understanding of their safety and biocompatibility is essential to ensure that there is no collateral damage. The toxicity of nanoparticles can affect not only patients, but also ecosystems and human health in the long term. It is therefore essential that more research is carried out, not only to assess the effectiveness of these nanoparticles in cancer treatment, but also to understand their potential impacts.

CONCLUSION

Nanoparticles (NPs) represent a significant innovation in the field of nanotechnology, generating great interest and being the subject of intense research due to their ability to act as a promising platform for the targeted delivery of chemotherapeutic drugs. This study has highlighted the potential of NPs as a viable alternative in the treatment of cancer, offering distinct physicochemical characteristics, flexibility in the architecture of their structures and the possibility of developing hybrid nanoparticles, among other advantages. However, it is essential to recognize that, like any emerging technology, nanoparticles (NPs) also raise concerns about potential adverse effects on the human body and the environment. In view of this, it is imperative that further research is carried out to better understand the risks and benefits associated with the long-term use of these technologies. In addition, it is essential to further investigate the interaction of NPs with cancer biology at the nanometric level, in order to gain a more comprehensive understanding of the mechanisms involved and the potential therapeutic implications. Thus, it is hoped that the advancement of knowledge in this field will contribute to a more effective integration of nanoparticles as a safe and efficient alternative in the therapeutic arsenal against cancer.

REFERENCES

ACHARYA, G.; MITRA, A. K.; CHOLKAR, K. Nanosystems for Diagnostic Imaging, Biodetectors, and Biosensors. **Emerging Nanotechnologies for Diagnostics, Drug Delivery and Medical Devices**, p. 217–248, 1 jan. 2017.

AHMED, A.; ARIAN, M. F.; KHAN, M. Q. Nanomaterials recycling standards. **Nanomaterials Recycling**, p. 249–268, 1 jan. 2022.

AL-THANI, A. N. et al. Nanoparticles in cancer theragnostic and drug delivery: A comprehensive review. **Life Sciences**, v. 352, p. 122899, 1 set. 2024.

AMREDDY, N. et al. Recent Advances in Nanoparticle-Based Cancer Drug and Gene Delivery. **Advances in Cancer Research**, v. 137, p. 115–170, 1 jan. 2018.

ASSIS, L. M. DE et al. Revisão: características de nanopartículas e potenciais aplicações em alimentos. **Brazilian Journal of Food Technology**, v. 15, n. 2, p. 99–109, 24 abr. 2012.

BAI, X. et al. The Basic Properties of Gold Nanoparticles and their Applications in Tumor Diagnosis and Treatment. **International Journal of Molecular Sciences 2020, Vol. 21, Page 2480**, v. 21, n. 7, p. 2480, 3 abr. 2020.

BHASARKAR, J. B.; BAL, D. K. Nanomaterial-based advanced oxidation processes for degradation of waste pollutants. **Handbook of Nanomaterials for Wastewater Treatment: Fundamentals and Scale up Issues**, p. 811–831, 1 jan. 2021.

CHEN, Y.; FENG, X. Gold nanoparticles for skin drug delivery. **International Journal of Pharmaceutics**, v. 625, p. 122122, 25 set. 2022.

CHEN, Y. H. et al. Methotrexate conjugated to gold nanoparticles inhibits tumor growth in a syngeneic lung tumor model. **Molecular Pharmaceutics**, v. 4, n. 5, p. 713–722, set. 2007.

CHOI, S. J.; OH, J. M.; CHOY, J. H. Toxicological effects of inorganic nanoparticles on human lung cancer A549 cells. **Journal of Inorganic Biochemistry**, v. 103, n. 3, p. 463–471, 1 mar. 2009.

DONAHUE, N. D.; ACAR, H.; WILHELM, S. Concepts of nanoparticle cellular uptake, intracellular trafficking, and kinetics in nanomedicine. **Advanced Drug Delivery Reviews**, v. 143, p. 68–96, 15 mar. 2019.

DRISTANT, U. et al. An Overview of Polymeric Nanoparticles-Based Drug Delivery System in Cancer Treatment. **Technology in Cancer Research and Treatment**, v. 22, 1 jan. 2023.

ERNST, L. M. et al. The Interactions between Nanoparticles and the Innate Immune System from a Nanotechnologist Perspective. **Nanomaterials 2021, Vol. 11, Page 2991**, v. 11, n. 11, p. 2991, 6 nov. 2021.

FAN, D. et al. Nanomedicine in cancer therapy. **Signal Transduction and Targeted Therapy 2023 8:1**, v. 8, n. 1, p. 1–34, 7 ago. 2023.

FU, P. P. et al. Mechanisms of nanotoxicity: Generation of reactive oxygen species. **Journal of Food and Drug Analysis**, v. 22, n. 1, p. 64–75, 1 mar. 2014.

GATOO, M. A. et al. Physicochemical properties of nanomaterials: Implication in associated toxic manifestations. **BioMed Research International**, v. 2014, 2014.

GAVAS, S.; QUAZI, S.; KARPIŃSKI, T. M. Nanoparticles for Cancer Therapy: Current Progress and Challenges. **Nanoscale Research Letters 2021 16:1**, v. 16, n. 1, p. 1–21, 5 dez. 2021.

HAMMAMI, I. et al. Gold nanoparticles: Synthesis properties and applications. **Journal of King Saud University - Science**, v. 33, n. 7, p. 101560, 1 out. 2021.

HUSSAIN, T. Gold Nanoparticles:A Boon to Drug Delivery System Gold nanoparticles: a boon to drug delivery system Manuscript details Abstract. **Article in South Indian Journal of Biological Sciences**, n. 3, p. 1, 2015.

IRACHE, J. M. Nanomedicina: nanopartículas con aplicaciones médicas. **Anales del Sistema Sanitario de Navarra**, v. 31, n. 1, p. 7–10, 2008.

JAIN, K. K. Advances in the field of nanooncology. **BMC Medicine**, v. 8, n. 1, p. 83, 13 dez. 2010.

JOVČEVSKA, I.; MUYLDERMANS, S. The Therapeutic Potential of Nanobodies. **BioDrugs 2019 34:1**, v. 34, n. 1, p. 11–26, 4 nov. 2019.

KARANDIKAR, S. et al. Nanovaccines for oral delivery-formulation strategies and challenges. **Nanostructures for Oral Medicine**, p. 263–293, 1 jan. 2017.

KERFAHI, D. et al. Effects of Functionalized and Raw Multi-Walled Carbon Nanotubes on Soil Bacterial Community Composition. **PLOS ONE**, v. 10, n. 3, p. e0123042, 31 mar. 2015.

KRISHNAMURTHY, S. et al. Lipid-coated polymeric nanoparticles for cancer drug delivery. **Biomaterials Science**, v. 3, n. 7, p. 923–936, 16 jun. 2015.

LIU, R. et al. Theranostic size-reducible and no donor conjugated gold nanocluster fabricated hyaluronic acid nanoparticle with optimal size for combinational treatment of breast cancer and lung metastasis. **Journal of controlled release : official journal of the Controlled Release Society**, v. 278, p. 127–139, 28 maio 2018.

MADEJ, M.; KUROWSKA, N.; STRZALKA-MROZIK, B. Polymeric Nanoparticles—Tools in a Drug Delivery System in Selected Cancer Therapies. **Applied Sciences 2022, Vol. 12, Page 9479**, v. 12, n. 19, p. 9479, 21 set. 2022.

MAHATO, R. Multifunctional Micro- and Nanoparticles. **Emerging Nanotechnologies for Diagnostics, Drug Delivery and Medical Devices**, p. 21–43, 1 jan. 2017.

MAHMOUD, B. S.; ALAMRI, A. H.; MCCONVILLE, C. Polymeric Nanoparticles for the Treatment of Malignant Gliomas. **Cancers 2020, Vol. 12, Page 175**, v. 12, n. 1, p. 175, 10 jan. 2020.

MASOOD, F. Polymeric nanoparticles for targeted drug delivery system for cancer therapy. **Materials Science and Engineering: C**, v. 60, p. 569–578, 1 mar. 2016.

MEIR, R.; POPOVTZER, R. Cell tracking using gold nanoparticles and computed tomography imaging. **Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology**, v. 10, n. 2, p. e1480, 1 mar. 2018.

MITCHELL, M. J. et al. Engineering precision nanoparticles for drug delivery. **Nature Reviews Drug Discovery 2020 20:2**, v. 20, n. 2, p. 101–124, 4 dez. 2020.

NGUYEN, H. L.; GUPTA, R. K.; NGUYEN, T. A. Nanoencapsulation of tyrosine kinase inhibitors for oncological therapeutics. **Smart Nanomaterials for Bioencapsulation**, p. 251–267, 1 jan. 2022.

ODES, E. J. et al. Earliest hominin cancer: 1.7-million-year-old osteosarcoma from Swartkrans Cave, South Africa. **South African Journal of Science**, v. 112, n. 7/8, p. 5–5, 28 jul. 2016.

OLIVEIRA, C. R. et al. Polymeric Nanoparticles for the Treatment of Prostate Cancer- Technological Prospecting and Critical Analysis. **Recent patents on nanotechnology**, v. 17, n. 1, p. 8–14, 1 fev. 2023.

OTAKE, K. et al. Preparation of liposomes using an improved supercritical reverse phase evaporation method. **Langmuir**, v. 22, n. 6, p. 2543–2550, 14 mar. 2006.

PELTONEN, L.; SINGHAL, M.; HIRVONEN, J. Principles of nanosized drug delivery systems. **Nanoengineered Biomaterials for Advanced Drug Delivery**, p. 3–25, 1 jan. 2020.

RIZZO, L. Y. et al. Recent progress in nanomedicine: therapeutic, diagnostic and theranostic applications. **Current Opinion in Biotechnology**, v. 24, n. 6, p. 1159–1166, 1 dez. 2013.

RUAN, S. et al. Matrix metalloproteinase-sensitive size-shrinkable nanoparticles for deep tumor penetration and pH triggered doxorubicin release. **Biomaterials**, v. 60, p. 100–110, 1 ago. 2015.

SCHRÖFEL, A. et al. Applications of biosynthesized metallic nanoparticles - a review. **Acta biomaterialia**, v. 10, n. 10, p. 4023–4042, 1 out. 2014.

SELMANI, A.; KOVAČEVIĆ, D.; BOHINC, K. Nanoparticles: From synthesis to applications and beyond. **Advances in Colloid and Interface Science**, v. 303, p. 102640, 1 maio 2022.

SHAZLEEN IBRAHIM, I. et al. Engineered liposomes mediated approach for targeted colorectal cancer drug Delivery: A review. **International Journal of Pharmaceutics**, v. 651, p. 123735, 15 fev. 2024.

SIDDIQUE, S.; CHOW, J. C. L. Gold Nanoparticles for Drug Delivery and Cancer Therapy. **Applied Sciences 2020, Vol. 10, Page 3824**, v. 10, n. 11, p. 3824, 31 maio 2020.

SIEGEL MPH, R. L. et al. Cancer statistics, 2023. **CA: A Cancer Journal for Clinicians**, v. 73, n. 1, p. 17–48, 1 jan. 2023.

SINGH, H. et al. Development of superparamagnetic iron oxide nanoparticles via direct conjugation with ginsenosides and its in-vitro study. **Journal of photochemistry and photobiology. B, Biology**, v. 185, p. 100–110, 1 ago. 2018a.

SINGH, P. et al. Gold Nanoparticles in Diagnostics and Therapeutics for Human Cancer. **International Journal of Molecular Sciences 2018, Vol. 19, Page 1979**, v. 19, n. 7, p. 1979, 6 jul. 2018b.

SINGH, P. et al. In vitro anti-inflammatory activity of spherical silver nanoparticles and monodisperse hexagonal gold nanoparticles by fruit extract of Prunus serrulata: a green synthetic approach. **Artificial Cells, Nanomedicine, and Biotechnology**, v. 46, n. 8, p. 2022–2032, 17 nov. 2018c.

SOHN, E. K. et al. Acute toxicity comparison of single-walled carbon nanotubes in various freshwater organisms. **BioMed Research International**, v. 2015, 14 jan. 2015.

SUN, L. et al. Smart nanoparticles for cancer therapy. **Signal Transduction and Targeted Therapy 2023 8:1**, v. 8, n. 1, p. 1–28, 3 nov. 2023.

SURIYA PRABHA, A. et al. Recent advances in the study of toxicity of polymer-based nanomaterials. **Nanotoxicity: Prevention and Antibacterial Applications of Nanomaterials**, p. 143–165, 1 jan. 2020.

YUSUF, A. et al. Nanoparticles as Drug Delivery Systems: A Review of the Implication of Nanoparticles' Physicochemical Properties on Responses in Biological Systems. **Polymers 2023, Vol. 15, Page 1596**, v. 15, n. 7, p. 1596, 23 mar. 2023.

ZHANG, G. M. et al. Advanced Polymeric Nanoagents for Oral Cancer Theranostics: A Mini Review. **Frontiers in Chemistry**, v. 10, p. 927595, 14 jun. 2022.

ZHANG, L. et al. Nanoparticles in Medicine: Therapeutic Applications and Developments. **Clinical Pharmacology & Therapeutics**, v. 83, n. 5, p. 761–769, 1 maio 2008.

ZHENG, K. et al. K. Zheng et al. Gold-nanoparticle-based multistage drug delivery system for antitumor therapy. **Drug Delivery**, v. 29, n. 1, p. 3186–3196, 31 dez. 2022.

ZIELINSKA, A. et al. Polymeric Nanoparticles: Production, Characterization, Toxicology and Ecotoxicology. **Molecules 2020, Vol. 25, Page 3731**, v. 25, n. 16, p. 3731, 15 ago. 2020.