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THE BIONANOTECHNOLOGY OF QUANTUM DOTS APPLIED IN HEALTHCARE

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ABSTRACT

This article addresses the applications of quantum dots in the health area, focusing on the applications of graphene and carbon dots. It also presents the explanation of what quantum dots are, and the motivation for using this technology in health. For this approach, research was carried out with sever-al authors, in order to present to the reader the importance of further studies of this nanotechnology so that in the future it can be applied in the health network. It should be noted that only a portion of the studies already published on quantum dots and the health area have been addressed.

Keywords: Graphene quantum dots. Carbon quantum dots. Healthcare. Bionanotechnology.

1 INTRODUCTION

In the mid-1930s, the French physicist Herbert Frohlich theoretically discussed the existence of nanoparticles that we now know as quantum dots. Decades later, three scientists proved that these quantum dots were real and received the 2023 Nobel Prize in chemistry [1]. The evolution of this field began in the 1980s with studies on the quantum size effects in colloidal nanoparticles. In the 2000s, significant advances occurred, including the synthesis of quantum dots in glass matrices by Ekimov and the development of optimized synthesis methods by Bawendi. Around 2005, quantum dots showed promise in biomedical imaging due to improvements in brightness, stability, and tunable properties, as well as the development of biocompatible dots. By 2010, research had advanced notably, with the integration of quantum dots into LED screens to improve color accuracy and energy efficiency, as well as their use in electronics such as smartphones, tablets, monitors, and TVs. In the 2020s, there was a substantial increase in the use of quantum dots in renewable energy, such as more efficient solar cells and greater energy capture and conversion, as well as in catalysis, nanomedicine, and high-speed communication [2]. Quantum dots are small crystals composed of a specific number of atoms confined in a tiny region, resulting in changes in the energy levels of the electrons. These quantum dots have interesting optical and electronic properties, emitting photons of a specific frequency when there are electronic changes in energy levels, which generates coloration. The size of the particles influences their coloration, with larger particles absorbing electromagnetic waves tending towards the red [1]. Quantum confinement refers to the fact that the smaller the size of the material, the greater the confinement of charge carriers (electrons and holes), resulting in higher energy in the forbidden band. Due to these properties, quantum dots have great technological potential in various areas, including biomedical imaging, LED screens, solar energy, catalysis, and nanomedicine. What was analyzed in the research is that the smaller the size of the material, the greater the confinement of the charge carriers, and thus a higher energy is in the prohibited band.

A. Carbon quantum dots

In 2004, while manipulating carbon nanotubes in order to carry out a purification process, the quantum dot of carbon was accidentally obtained. This material is based on carbon, has photoluminescence, quasi-spherical characteristics and has a zero dimension [4]. Since its discovery, numerous researches have been carried out, and from them it has been observed that this material is endowed with advantages, such as: Low toxicity, stable, it is considered low cost and abundant [4]. Carbon quantum dots (CQDs) are hydrophilic due to the presence of amino, carboxyl and hydroxyl functional groups. For the photoluminescence mechanism there are still doubts about its operation, and because of this there is no single explanation. Among these explanations are the factor of surface groups, size and even the presence of fluorescent molecules, so it is noted that there is not only a common understanding of this issue, but several explanations. Because it is a quantum point, in general, it can be understood that fluorescence comes from electronic excitations and exchange of its ground state.

B. Graphene quantum dots

Graphene is a material that is an allotropic form of carbon, with a two-dimensional structure and a thickness of a single atom. This material is a highly valued due to it is thermal, electronic, mechanical properties, and chemical stability. When a portion of graphene is small enough to be influenced by the quantum confinement effect, it becomes a semiconductor, exhibiting special properties. Graphene quantum dots (GQDs) are sheets of graphene with isolated nanometric dimensions smaller than 100 nanometers (nm). Due to their quantum confinement, GQDs generate intense photoluminescence, which is also influenced by edge effects. They belong to the group of graphene nanomaterials [5]. GQDs have low toxicity, stable dispersions in water due to hydrophobic interactions, rapid interaction with chemical species, stable optical properties, and high sensitivity to analytical responses. These advantages are notable when compared to semiconductor quantum dots. Several factors can influence the photoluminescence of GQDs, including structural defects, the presence of oxygen-containing groups, and doping elements. However, there are uncertainties about the exact photoluminescence mechanism of GQDs, leading to multiple theories [6]. GQDs can emit a range of colors from ultraviolet to red when interacting with ultraviolet (UV) light. Various methods exist for preparing and synthesizing this material, though they are not the focus of this discussion. Studies have shown that GQDs can potentially transport drugs, with their size allowing easy penetration into the lipid layer without causing damage, facilitating drug delivery. Quantum dots, including GQDs, are nanomaterials with significant applications and can impact various fields, particularly healthcare. Their impact on health will be discussed further, and they also offer economic advantages, beneficial for the health system [7]. Thus, it is noted that quantum dots are nanomaterials of great applications and that they can promote a significant impact in several areas, including the health area. Its impact on health is broad and will be analyzed in further discussion, in addition to this material has economic advantages, which is positive for the health system.

C. Market

The market growth for quantum dots predicted from 2024 to 2029 is detailed in the report available by Mordor's Intelligence, a technical website for industrial growth and investment information, in this document several scenarios are considered for the applications of dots, in which possible biomedical applications are mentioned. The market as a complex currently holds about 5 billion dollars, concentrating the largest investment and expansion in the regions of Asia and Oceania. However, the report highlights the quantum applications related to imaging improvements, and their implementations in the market, in addition to their probabilistic applications such as biosensors and pathogenicity detectors, but does not corroborate for the applications related to drugs and treatment due to the toxicity effects of the compounds, which still have an experimental and investigative state.

D. Biological applications of quantum dots

CQDs are mostly relevant for biological applications due to their organic relationship based on the element carbon, which not only composes molecular structures, but is also intrinsically related to biological structures such as peptides, cells and tissues. Cells are complex structures composed of several mechanisms, which perform the most diverse and complex functions, from the absorption of water, to their replication for tissue renewal or defense against invading organisms. Because they have the most diverse differentiations in organisms, they can be identified by means of more precise markers, that is, if they are made of more permeable materials or even more compatible with the environment. Quantum dots are valuable as biomarkers because they emit photoluminescent signals, which help detect mutations (like carcinomas) and metabolic issues. They are also useful in treatments by aiding biological structures in defending or restructuring their metabolic activities after damage from microorganisms, injuries, or other factors. Targeted therapies aim to use low-toxicity materials, such as carbon-based quantum dots, to ensure drugs are dispersed or absorbed only by specific organs, tissues, or areas needing treatment. To achieve less invasive and more effective treatments, health sciences continuously research more precise materials and methods, requiring detailed examinations of organs, tissues, and their gradual, stable functions. Consequently, the greatest prominence and market expansion are those related to image resolution through quantum dots and their light emissions, enabling the visualization of the areas where the disturbances occur, so that their nanometric structure facilitates the identification of reactions and activities related to pathogenicities.

2 MATERIAL & METHODS

To understand the vastness of quantum dots and their applications in the biomedical sciences, a multifaceted methodology composed of multiple steps was adopted. First, a thorough review of the scientific literature related to quantum dots was conducted. This review has ranged from the theoretical beginnings discussed by Herbert Frohlich to the most recent discoveries and applications, which are presented in articles. A variety of sources, including papers, technical reports, and other relevant publications, were consulted to gain a comprehensive understanding of the development and evolution of this area of study. In addition, previous studies conducted by renowned scientists such as Ekimov and Bawendi were analyzed, and then sought to understand the advances and discoveries that contributed to the current knowledge about quantum dots. This analysis allowed us to identify the distinctive properties of quantum dots, especially carbon dots. Data collection played a key role in our methodology. Relevant information on applications in different sectors and market trends was gathered, with a greater focus on the areas of health. Ethical and safety considerations have been care-fully weighed throughout our research, especially with re-gard to the use of quantum dots in biomedical engineering. The challenges and ethical concerns related to the use of nano-technological materials in biomedical and therapeutic ap-plications were discussed, in accordance with international conventions on bioethics and animal welfare. Finally, a comprehensive market analysis was conducted, examining the growth trends, highlighted application areas, and eco-nomic and business considerations related to quantum dots. This methodology allowed a detailed and comprehensive analysis of quantum dots, from their theoretical bases to their practical applications, considering ethical, security and market aspects. The results and discussions obtained pro-vided valuable insights into the potential of these materials in several areas, including health and technology.

3 RESULTS & DISCUSSION

Quantum dots have several applications and advantages, particularly in the health area. Research has demonstrated the potential of these materials in bioimaging. In one study, carbon quantum dots (CQDs) were prepared and used to label cancer cells from the human breast region, with human epithelial cells as controls. Upon excitation at a certain wavelength, the cells exhibited photoluminescence, showing that CQDs are more biocompatible and have 80% higher cell retention. This retention was observed using common fluorescence microscope. Further tests confirmed that CQDs were internalized into the cells via endocytosis. The study concluded that CQDs are promising for biological applications due to their low cost and non-toxic nature, indicating a significant potential impact in healthcare. It is concluded in this article that CQDs are interesting due to their low cost, they have a non-toxic character, demonstrating that they do not have problems for biological applications, demonstrating that their use will have a great impact [8]. Work was done to develop methods of analysis using graphene quantum dots, and these quantum dots would have the effect of a photoluminescent probe with the objective of determining a drug for cardiac patients. Graphene quantum dots were produced from aqueous dispersions and prepared by glutathione and citric acid pyrolysis, this dispersion generated GQDs functionalized with amino groups. In addition, analyses were also performed with or without the presence or absence of

Fe^{3+}. These GQDs were used in the study as probes to determine the use of the medication, the results obtained were significant and with this it was observed that regardless of whether or not there was Fe^{3+}, but that it is possible to use these probes to measure the medication. In addition, it was also observed that these probes have a competitive ad-vantage in relation to others already used, this differential is the fact that no toxic reagent is used [6]. In 2018, a comprehensive study examined the use of graphene quantum dots (GQDs) as an analytical probe. This study included observations of medication effects on six cardiac patients and analyses involving histamines and kanamycin sulfate. For histamines, the study evaluated photoluminescent scattering reactions, while for kanamycin sulfate, gold nanoparticles were used to measure the photoluminescence effect associated with the GQDs. The probe for the cardiac medication showed promising results, proving competitive with existing methods. For the histamine probe, mediators in an aqueous system were required, and a good correlation with Fe^{3+} for histamine analysis was observed. Finally, the kanamycin probe successfully determined concentrations in samples fortified with yellow fever and pharmaceutical formulations. Therefore, it is possible to observe in this work a good use of GQDs for the analysis of certain substances [5]. In 2019 it published studies and analyses referring to as-says using quantum dots for biomedical purposes, however, only in vitro and ex vivo studies were included, due to the difficulties of bioethical approval related to long term toxicity associated with their administration. The study reaffirms the relevance of the applications of these methods for more assertive and specialized treatments, focused on the permeability and affinity of the tissues under treatment, making them a suitable tool for personalized treatments [9]. In 2020, a study was carried out using the graphene quantum dot for the treatment of leukemia, the quantum dots in this case would be in charge of loading chemotherapy drugs, in order to reduce the toxic effects of the treatment. In this study, carbodiimide was functionalized so that it could later be conjugated to the drug imatinib. This drug was intended to be synthesized and conjugated to the GQDs, and this procedure was successfully performed by the study. It was possible to observe that this conjugate was able to induce the death of leukemia cells, and presented lower toxicity to healthy cells when compared to the use of the drug Imatinib alone. This work was able to demonstrate that drug carriers made from carbon nanoparticles have been effective in the treatment of cancer. In addition, they are less toxic, which is positive for the patient under treatment [7]. In addition to technical and scientific issues, it is critical to consider the ethical and safety implications associated with Quantum Dots studies in biomedical engineering. The bioethics conventions related to the studies in question are the Universal Declaration on Bioethics and Human Rights - UNESCO 2005, Oviedo Convention (Convention for the Protection of Human Rights and the Dignity of the Human Being with regard to the Applications of Biology and Medi-cine): - Council of Europe in 1997 and the Declaration of Helsinki, in which the need to inform patients about the risks of the research to which they are being submitted are highlighted, the freedom in relation to the aggressiveness of the compounds or activities to be performed. There are also conventions that cover animal welfare and protection, as well as the feasibility and authorization of their use in research, some of which are: European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes of 1986, Guide to the Care and Use of Laboratory Animals, Directive 2010/63/EU on the Protection of Animals Used for Scientific Purposes and Principles of the Three R's. These documents discuss the implications of the well-being of individuals for the results and preservation of life in corroboration with the advancement of scientific research, predicting limits for pain, sleep deprivation, food, habitat area and other topics.

4 CONCLUSION

Quantum dots have been shown to have a high capacity for use in the health environment, in addition to their exploration capacity is still great, with this it is understood that over time this material will have greater use in the health area than it currently has. Through this article, it was demonstrated that the material is biocompatible, low cost and great applicability, these points are advantages that make this material have great potential for use in the health system. As a suggestion for future work, it was observed that there is a need for studies of this material for application in other exams such as cardiac examinations, since there is a significant number of individuals who are affected by heart diseases, eventually using this material together with an image analysis device, it is possible to obtain clearer and better-defined images.

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