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EMERGING NANOTECHNOLOGY-BASED DIAGNOSTICS FOR LEISHMANIASIS AND TRYPANOSOMIASIS

Abstract. In recent decades, there has been a significant increase in interest in nanotechnology, which is considered a potential tool in combating infectious diseases including trypanosomiasis and leishmaniasis. These diseases, caused by protistan parasites, pose a severe threat to the health of humans and animals, especially in low- and middle-income countries. With the emergence of nanotechnological approaches, new perspectives in providing more accurate, rapid, and affordable diagnosis of parasitic infections have become possible. Recent achievements in this field have been aimed at significantly improving diagnostic methods and reducing the burden of infectious diseases on public health in African, Asian, and Latin American countries.

Keywords: nanotechnology, trypanosomiasis, leishmaniasis, infectious disease diagnosis.

Significance of the Research

The results of numerous studies on natural and synthetic nanostructures indicate new opportunities in creating highly sensitive, specific, and cost-effective diagnostic methods, which could be critical to a more successful fight against infectious diseases caused by trypanosomatids.

The statistics on the prevalence of leishmaniasis and trypanosomiasis worldwide vary depending (among other factors) on the region, the effectiveness of the healthcare system, and the availability of diagnostic methods. Leishmaniasis is prevalent in about a hundred countries, primarily in tropical and subtropical regions. According to the World Health Organization (WHO) estimates, approximately 700,000 to 1 million new cases are registered worldwide each year. Most leishmaniasis cases are diagnosed in patients in India, Brazil, Ethiopia, Sudan, and other South America, Africa, and Asia countries. Trypanosomiasis is also widespread in tropical and subtropical regions, mainly in Africa and Latin America. According to the WHO data, more than 10 million people are at risk of African trypanosomiasis in 36 African countries. American trypanosomiasis is mainly restricted to Brazil, where approximately 6-7 million people are infected. In the future, climate change could pose serious risks for spreading leishmaniasis and trypanosomiasis in regions previously considered less susceptible to these diseases.

Despite years of combating, medicine is still losing the battle against trypanosomatids. It is widely acknowledged that precise and accessible diagnostics are crucial in controlling, treating, and preventing the spread of these diseases. Current diagnostic methods for leishmaniasis and trypanosomiasis have several drawbacks. Specifically, some traditional diagnostic techniques, such as blood or tissue microscopy, lack sensitivity, especially in low parasitemia or visceral leishmaniasis cases. This often leads to false-negative results and underestimation of disease prevalence.

Additionally, diagnostic errors may be associated with the limited specificity of particular methods, especially in regions where other diseases with similar clinical symptoms coexist. Some diagnostic procedures, such as polymerase chain reaction (PCR) or immunochemical tests, are considered a "luxury" in resource-limited regions due to the requirement for expensive equipment and specialized personnel training. In regions with limited medical infrastructure, specialized laboratories and equipment are simply inaccessible to the patients [1].

Addressing these issues involves developing and implementing more sensitive, specific, and accessible diagnostic methods. Nanotechnology offers a range of innovative approaches that can significantly improve the diagnosis of trypanosomiasis and leishmaniasis, ultimately leading to more effective control and treatment of these infectious diseases in high-prevalence regions.

Research Objective

This study aimed to analyze established scientific approaches focused on using nanoparticles for creating diagnostic systems to detect leishmaniasis and trypanosomes in biological samples.

Primary Research Materials

The analysis was conducted using open-literature sources and electronic resources, such as Web of Science, PubMed, Scopus, IEEE Xplore, ScienceDirect, Embase, and MEDLINE. The search query used included highly cited articles related to the application of nanoparticles in developing diagnostic systems for trypanosomiasis and leishmaniasis, starting from 2002.

Results

The foundations of nanodiagnostics development for infectious diseases were laid in studies at the beginning of the 2000s [2]. Analysis of literature data shows that there is currently a relatively large arsenal of studied nanoparticles that authors propose to use for creating diagnostic biosensors. As possible platforms for developing more sensitive and specific diagnostic methods for diseases caused by trypanosomatids, it is suggested to use fluorescent nanoparticles, metallic nanoparticles, magnetic nanoparticles, quantum dots, and others [3, 4]. The advantage of such nanosensors is their ability to detect various biological molecules or events at the nanoscale level. Authors of numerous studies highlight several groups of molecules that can serve as recognition bioprobes in nanosensors for diagnosing leishmaniasis and trypanosomiasis. For these purposes, specific antibodies IgM and IgG (to leishmania and trypanosome antigens), oligonucleotides (specifically binding to the DNA or RNA of pathogens), enzymes (lysozyme, peroxidase, or alkaline phosphatase, which can be used in immunochemical assays for detecting antigens), and aptamers (specifically binding to pathogen molecules instead of antibodies) can be used. One example cited in the literature is the development of an electrochemical geosensor based on AuNP-toluidine using *Leishmania*-specific genomic DNA [5].

Several groups of biomarkers can be identified as potential targets for recognition in biosensors. One promising direction in biosensor development is detecting genetic material from *Leishmania* and *Trypanosoma* parasites. The development of oligonucleotide probes implies their hybridization with the DNA or RNA of pathogens. Proteins or glycoproteins produced by *Leishmania* and *Trypanosoma* (for example, LPG and gp63) are also proposed for use as biomarkers. Furthermore, there is interest in certain immune markers (cytokines or antibodies) produced by the host organism in response to the infection. Authors suggest that some products of protein, lipid, and carbohydrate metabolism, produced by both pathogens and host organisms in response to infection, can be applied to assess the presence or activity of infection. One of the proposed approaches for diagnosing leishmaniasis, for instance, involves using gold nanoparticles functionalized with monoclonal antibodies to the antigen of *Leishmania* spp. [6]. These antibodies, localized to the nanoparticles, can specifically bind to parasite antigens in biological sample specimens (blood or tissue). Authors of several studies propose various methods to detect the binding of nanoparticles and biomarkers, including conventional detection methods, such as spectro-photometric and mass spectrometric methods. Notably, changes in the plasmonic resonances of gold nanoparticles or in the intensity of fluorescence of quantum dots may indicate the presence and quantity of bound biomarkers. Such an approach enables the detection of parasites in samples with high sensitivity and specificity, making it promising for the diagnosis of leishmaniasis and trypanosomiasis.

It should also be noted that the combination of the capabilities of nanotechnology and artificial intelligence creates breakthrough prospects for multiplexing as a promising direction in the diagnosis of leishmaniasis and trypanosomiasis, allowing the simultaneous analysis of many biological markers or genes in one sample.

Conclusions

The existing clinical diversity of manifestations in leishmaniasis and trypanosomiasis underscores the diagnostic challenge of these neglected tropical diseases. Nanotechnological approaches to biosensor development hold promise for creating highly specific, sensitive, and cost-effective diagnostic methods, which can contribute to the overall goal of reducing the burden of leishmaniasis and trypanosomiasis.

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