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Nanopharmaceuticals as a solution to neglected diseases: Is it possible?

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ABSTRACT

The study of neglected diseases has not received much attention, especially from public and private institutions over the last years, in terms of strong support for developing treatment for these diseases. Support in the form of substantial amounts of private and public investment is greatly needed in this area. Due to the lack of novel drugs for these diseases, nanobiotechnology has appeared as an important new breakthrough for the treatment of neglected diseases. Recently, very few reviews focusing on filiarasis, leishmaniasis, leprosy, malaria, onchocerciasis, schistosomiasis, trypanosomiasis, and tuberculosis, and dengue virus have been published. New developments in nanocarriers have made promising advances in the treatment of several kinds of diseases with less toxicity, high efficacy and improved bioavailability of drugs with extended release and fewer applications. This review deals with the current status of nanobiotechnology in the treatment of neglected diseases and highlights how it provides key tools for exploring new perspectives in the treatment of a wide range of diseases.

Contents

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1. Introduction

1.1. General aspects of neglected diseases

The WHO Special Programme for Research and Training in Tropical Diseases (WHO-TDR) defines a disease of poverty (DoP) as a disease that affects mainly the poor in developing countries, and it is divided into two classes (WHO, 2010a). The first class includes the "big three" DoPs: malaria, HIV/AIDS, and tuberculosis. These diseases have received considerable attention from the community and investment to eradicate them. Around 70% of drug development focuses on these diseases (Ponder, 2012). The other one comprises neglected tropical diseases (NTD). There are seventeen NTD, and these diseases affect populations with little visibility and low political voice. They cause discrimination and stigma and have a strong impact on morbidity and mortality; these diseases are practically neglected by the research community but can be prevented, controlled, and probably eliminated using adequate solutions (WHO, 2010b).

In addition to the "big three" and NTD, BIO Ventures for Global Health, a nonprofit organization that specializes in accelerating research on medicines for developing countries, classifies diseases such as diarrheal diseases, cholera, and typhoid fever as DoP (Ponder, 2012). Policy Cures, another health nonprofit organization, lists 31 neglected diseases. This nonprofit organization considers an illness a disease of poverty if it meets three conditions: the disease strongly affects people in low-income countries; there is a need for different and new products; and the allocation of goods and services is not efficient (Moran et al., 2010). Table 1 lists the DoP identified by WHO, Policy Cures, and BioVentures for Global Health (Woodson, 2014).

A very recent review gives examples of Training in Tropical Diseases (TDR), approaches and contributions to drug discovery research and development (R&D), and the optimization of known treatments against the background of immense changes in the R&D landscape for infectious diseases of poor people (Olliaro et al., 2015).

Between 1975 and 1990, only ten drugs were registered for tropical diseases: benznidazole and nifurtimox for Chagas' disease; pentamidine for human African trypanosomiasis (HAT); oxamniquine and praziquantel for schistosomiasis; ivermectin for onchocerciasis; pyrazinamide, halofantrine and mefloquine for malaria; and albendazole for soil-transmitted nematodes (STNs). It is important to note that all these drugs, except halofantrine, are still in use. All of these drugs were developed 25–40 years ago; however, they continue to be the cornerstones of strategies in disease control.

Drug development between the public and private sector has been rare in the last years, but there are some cases. Mefloquine was studied in collaboration between the United States Army Medical Research and Development Command, La Roche, and TDR.

During the 2000–2011 period, TDR participated actively in the development of three products, including an injectable artemotil [arteether], rectal artesunate for malaria and oral miltefosine for visceral leishmaniasis [VL], and played an important role in contributing to the identification and development of a number of other drugs, such as artesunate-amodiaquine and artesunate-mefloquine for malaria and paromomycin for VL.

Trouiller et al. (2002) reported the development of six products for stage 2 of human African trypanosomiasis, eflornithine for visceral leishmaniasis, liposomal amphotericin B for severe malaria, injectable artemether for uncomplicated malaria, and atovaquone and rifapentine for tuberculosis. TDR provided the coordination and funding for the pivotal clinical trials that supported their registration. Currently, TDR continues to fund research on new targets, screening, identification of leads, and development of new candidates.

The current challenges are completely different from those at TDR's start. Now, there are different players and proportionally more funding than before, and the primarily public or nonprofit organization, devoted to research and the search for new drugs and diagnostics, still requires coordination to optimize resources. This active environment requires new and innovative solutions, but there is a need for continuity and also an adaptation to produce adequate results (Olliaro et al., 2015).

The new trends in the last decades suggest that the most innovative strategy at this time should be the use of nanotechnology in the search of new uses for old pharmaceuticals or new development of innovative and intelligent nanomedicines for neglected diseases.

2. Nanostructures most commonly used in neglected diseases

The relevance of nanostructures in biomedical applications is enormeous. Then, the characteristics and aspects of these nanostructures will be briefly described in this section (Fig. 2).

2.1. Liposomes

Liposomes are sphere-shaped vesicles formed by phospholipid bilayers reported in the mid–60 s that have currently made their way to the market. Currently, they have progressed from conventional vesicles to 'second-generation liposomes', in which long-circulating liposomes are obtained by modulating the lipid composition, size, and charge of the vesicle and functionalized with molecules, such as glycolipids or sialic acid. Liposomes are promising intracellular delivery systems for antisense molecules, ribosomes, proteins and/or peptides, and DNA. Probably the most important function of liposomes is to promote targeting of particular diseased cells within the disease site. Liposomal drugs also exhibit reduced toxicities and retain enhanced efficacy compared with free complements (Akbarzadeh et al., 2013). Examples of liposomal formulation in the treatment of negelted diseases are shown in Table 3.