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Parasitic diseases: Liposomes and polymeric nanoparticles versus lipid nanoparticles ☆

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Abstract

Parasitic diseases such as malaria, leishmaniasis, and trypanosomiasis represent a significant global burden and pose a great challenge to drug discovery and delivery scientists due to their intracellular nature and disseminated locations. Moreover, poor rate of discovery in the anti-parasitic segment seen in last few decades has necessitated effective management of existing drugs by modulating their delivery. The review focuses on the biological and biopharmaceutical issues to be considered in the design of delivery strategy for treating parasitic infections such as malaria, leishmaniasis, and trypanosomiasis. Also, it describes the role of the colloidal carriers liposomes, polymeric nanoparticles, lipid nanoparticles including lipid drug conjugate (LDC) nanoparticles in optimizing the delivery of anti-malarial, anti-leishmanial and anti-trypanosomial agents. Furthermore, the review emphasizes especially the potential of solid lipid nanoparticles (SLN) in the treatment of parasitic infections with the help of recent reports and our own experience.

Keywords: Parasitic diseases; Malaria; Leishmaniasis; Trypanosomiasis; Liposomes; Nanoparticles; Solid lipid nanoparticles (SLNs); Nanostructured lipid carriers (NLCs)

Contents

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1. Introduction

Parasitic diseases are of immense global significance as around 30% of the world's population experiences parasitic infections. Moreover, parasitic infections impose a substantial burden of mortality and morbidity round the globe (Table 1) and more particularly in the developing countries [1,2]. Although a considerable progress has been made in comprehending the cell biology, pharmacogenomics, etiology and pathophysiology of majority of parasitic infections in the last decade, the scenario in the area of therapeutics is disappointing. Despite major research efforts, to date, there exists no effective vaccine against any of the major parasitic infections mainly due to the fact that most of the parasitic diseases do not elicit a pronounced immune response. Hence, anti-parasitic chemotherapy remains to be the only weapon for combating parasitic infections. However, most of the currently existing anti-parasitic agents have been introduced over 50 years ago. Although these agents are effective, most of them are no way close to the modern concept of 'drug' in terms of tolerability, therapeutic regimen, duration of treatment, specificity and patient compliance. The problem of emerging resistance to hitherto effective anti-parasitic agents in the last decade has worsened the scenario [3].

Paradoxically, the rate of new drug development and new drug discovery in the segment of parasitic diseases is very low as compared to the other segments mainly due to the lack of economic incentives in this area. The fact that out of 1223 new drugs brought to market between 1975 and 1996, only 1% of them were introduced for the treatment of tropical diseases such as malaria, leishmaniasis, trypanosomiasis and tuberculosis (which together contributes about 5% of the global disease burden) is sufficient to support the aforementioned statement. The negligence towards parasitic diseases continued till 2000, as only about 0.1% of global investment in health research was devoted to drug discovery for anti-parasitic agents [4].

Table 1
Global burden of parasitic diseases [2]

Disease	Mortality (thousands)	DALYs[a] (thousands)
Malaria	1272	46,486
Leishmaniasis	51	2090
African trypanosomiasis	48	1525
South American trypanosomiasis (Chagas disease)	14	667
Schistosomiasis	15	1702
Lymphatic filariasis	0	5777
Onchocerciasis	0	484

[a] DALYs —disability adjusted life years (the number of healthy years of life lost due to premature death and disability).

However, in recent years, increased awareness of this situation has led to the formation of several not-for-profit product–development partnerships (PDPs) such as the Drugs for Neglected Diseases initiative, The Medicines for Malaria Venture and the Institute for One World Health, along with the WHO Tropical Diseases Research Programme (TDR). Moreover, at present, there are few new chemical entities in preclinical and clinical phases for major parasitic diseases like malaria, leishmaniasis and Chagas disease. But, these efforts could take considerable time to fructify [3,4].

Hence, the best strategy that could be adopted to tackle the aforementioned crisis associated with parasitic diseases is to develop novel delivery systems in order to improve the efficacy, specificity, tolerability and therapeutic index of existing anti-parasitic agents. In this review, we would emphasize on the various attempts that have been made in the development of novel colloidal delivery systems for anti-parasitic agents with focus on 3 major parasitic diseases *viz.* malaria, leishmaniasis and trypanosomiasis. Moreover, we would also discuss the potential of solid lipid nanoparticles (SLN) and modifications thereof (LDC) in the treatment of parasitic diseases.

2. Understanding the biological aspects

Complete information about the localization of the parasite within the host organ, tissue or cells during the acute and chronic phase of the disease must be acquired before one thinks of designing either a novel drug or even a drug delivery system as the main goal of the modern parasitic chemotherapy is to target the drug specifically to the parasite to maximum possible extent in order to minimize the adverse effects arising during the treatment. Additionally, following factors must be given due consideration while designing novel drugs or drug delivery systems

1. Parasite–host cell interaction.
2. Biological barriers to be overcome in order to reach the target organ, tissue or cells.
3. Complete information about the receptors present on the cells infected by the parasite.
4. Changes occurring in the infected cell after the invasion of parasite or with the progression of disease *e.g.* up-regulation of scavenger receptors on macrophages after infection with *Leishmania* [5].
5. Antigens or receptors present on the surface of the parasite.
6. Pathophysiology of the disease.

The information about some of the aforementioned biological aspects with respect to malaria, leishmaniasis and trypanosomiasis are listed in Table 2.