Current Updates in Nanotechnology

Editorial Open Access

Challenges in Antiparasitic Drug Discovery: A Regional Approach

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Original Submission

Received: October 12, 2016
Accepted: October 24, 2016
Published: October 31, 2016

Open Peer Review Status: Editorials, news items, analysis articles, and features do not undergo external peer review.

How to cite this article: Ravetti S, Hergert LY, Sanchez-Bruni SF, Palma SD. Challenges in Antiparasitic Drug Discovery: A Regional Approach. Curr Updates Nanotechnol. (2016) 1: 1.1

The neglected tropical diseases (NTDs), a group of chronic, debilitating, and poverty-promoting parasitic, bacterial, and some viral and fungal infections, represent some of the most common infections of the poorest people living in the Latin American and Caribbean region (LAC) [1-3]. As neglected tropical diseases (NTDs), the World Health Organization (OMS) recognizes 17 major parasitic and related infections.Particularly in tropical regions, parasitic diseases continue to take an enormous toll on human health [4]. Protozoa and helminths cause the major burden.

The helminth infections in LAC include:

- Lymphatic filariasis (LF) caused by infection with the nematodes *Wuchereriabancrofti, Brugiamalayi* and *B. timori*.
- Onchocerciasis (ONCHO) caused by infection with the nematode *Onchocerca volvulus*.
- Schistosomiasis (SCH)
    - SCHi (intestinal schistosomiasis) caused by infection with the trematodes *Schistosomamansoni, S. mekongi, S. japonicum* and *S. intercalatum*,
    - SCHu (urinary schistosomiasis) caused by infection with *S. haematobium*.
- Soil-transmitted helminthiasis (STH) caused by infection with the nematodes *Ascarislumbricoides* (roundworm), *Ancylostomaduodenale* and *Necatoramericanus* (hookworm), and *Trichuristrichiura* (whipworm).

The protozoan infections include:

- Chagas disease. It is one of the highest protozoan infections burden NTDs in LAC caused by *Trypanosoma cruzi* and this infection is between five and ten times greater than malaria [5-8].
- Both cutaneous and visceral forms of leishmaniasis result primarily from zoonotic transmission from either canine or sylvatic reservoir hosts [9-10]. *Leismaniamexicana, L. amazonesis, L. braziliens, L. panamensis, L. peruviana* and *L. guyanensis* are the major species that cause new world zoonotic cutaneous leishmaniasis.

The drugs used in the treatment of these diseases are far from ideal and only a few novel classes of antiparasitic drugs have emerged over the last few decades.

Antiparasitic drug discovery is not primarily oriented by the commercial need to introduce novel compounds. Many antiparasite drugs were first developed for other indications [4,11-12]. Only a few novel classes of antiparasitic drugs have emerged over the last few decades, reflecting the difficulties associated with bringing a safe, effective molecule to market.

Table 1 shows the problems associated with some of the commonly used drugs.

To facilitate the control or elimination of many NTDs there are available critical disease-specific technologies.

Several vaccines for hookworm and other STH infections, as well as for leishmaniasis, onchocerciasis, and schistosomiasis, are in different stages of development [13-18].

The elimination of these diseases will not be possible without additional control mechanisms and other tools including new drugs, vaccines, diagnostics and vector control agents and strategies.

Table 1: Treatment of the major tropical parasitic diseases.

Disease	Drugs or drugs combinated	Disadvantages
Chagas´s disease	Nifurtimox; Benznidazole; Posaconazole; A new prodrug of ravuconazole	Adverse effects In late-stage disease is not effective Not effective as monotherapies: posaconazole and prodrug of ravuconazole
Leishmaniasis	Pentamidine; Pentavalent antimonials; Liposomal amphotericin B; Miltefosine; Paramomycin; Topical creams are currently in clinical trials	Efficacy loss/drug resistance: Pentamidine and antimonials Cost high: liposomal amphotericin B Contraindicated in women of child-bearing age: miltefosine
Onchocerciasis	Ivermectin	Not eliminate adult worms
Lymphatic filariases	Diethylcarbamazine; Ivermectine; Albendazole/Diethylcarbamazine; Albendazole/Ivermectin	Used in combination therapy: albendazole Not eliminate adult worms: ivermectin
Schistosomiasis	Oxamniquine; Praziquantel	Not kill immature worms: praziquantel Only effective against *S. mansoni*

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