ISSN: 2155-9597
Journal of Bacteriology & Parasitology

OPEN ACCESS Freely available online

Commentary

Mechanisms of Drug Resistance in Parasites and Strategies to Overcome Resistance

Eliza Gong*

Department of Parasitology and Vector Biology, Imperial College London, London, UK

DESCRIPTION

Drug resistance in parasites poses a significant challenge to the treatment and control of parasitic diseases worldwide. Parasites have developed various mechanisms to resist the effects of antiparasitic drugs, limiting treatment options and contributing to treatment failures. Understanding these mechanisms and developing effective strategies to overcome resistance are critical for combating parasitic infections and improving patient outcomes.

Mechanisms of drug resistance in parasites

Target modification: One of the primary mechanisms of drug resistance in parasites involves modifications to the drug target molecules. Parasites can alter the structure or expression of target proteins, such as enzymes or receptors, thereby reducing drug binding affinity or efficacy. For example, mutations in the Dihydrofolate Reductase (DHFR) gene of *Plasmodium* spp. reduce the binding affinity of antifolate drugs like pyrimethamine and sulfadoxine, leading to resistance in malaria parasites.

Efflux pumps: Parasites can develop resistance by increasing the efflux of drugs from their intracellular compartments. This is achieved through the upregulation of efflux pump proteins embedded in the parasite's cell membrane. These pumps actively transport drugs out of the cell, maintaining lower intracellular drug concentrations that are insufficient to exert therapeutic effects. Efflux pump-mediated resistance is observed in various parasites, including *Plasmodium* spp. and *Leishmania* spp., against multiple classes of antiparasitic drugs.

Drug metabolism and detoxification: Parasites can metabolize or detoxify drugs through enzymatic pathways, rendering them inactive or less toxic to the parasite. This metabolic resistance mechanism often involves the upregulation of detoxification enzymes, such as cytochrome P450 monooxygenases and glutathione S-transferases, which catalyze the biotransformation and elimination of drugs from the parasite's cytoplasm. This mechanism is particularly prominent in helminth parasites, such as *Schistosoma* spp., which exhibit high metabolic diversity and can metabolize a wide range of drugs.

Reduced drug uptake: Some parasites develop resistance by reducing the uptake of drugs into their cells. This can occur through alterations in membrane transport proteins or changes in membrane permeability, effectively limiting the amount of drug that enters the parasite. Reduced drug uptake has been observed in protozoan parasites like Trypanosoma brucei, the causative agent of African trypanosomiasis, which develops resistance to trypanocidal drugs like suramin and pentamidine.

Altered metabolic pathways: Parasites may adapt to drug pressure by bypassing or circumventing the metabolic pathways targeted by antiparasitic drugs. By developing alternative metabolic routes or acquiring compensatory mutations in metabolic enzymes, parasites can maintain essential biological functions despite drug exposure. This adaptive mechanism allows parasites to survive and proliferate in the presence of drugs that would otherwise inhibit their growth. An example is the resistance of *Plasmodium* spp. to atovaquone, a drug targeting the parasite's mitochondrial electron transport chain, through mutations in the cytochrome b gene.

Strategies to overcome drug resistance in parasites

Combination therapy: Combination therapy involves administering two or more drugs with different mechanisms of action simultaneously or sequentially. This approach reduces the likelihood of parasites developing resistance to multiple drugs simultaneously and enhances treatment efficacy by targeting different stages of the parasite lifecycle. For example, Artemisinin-based Combination Therapies (ACTs) are widely used to treat malaria and help delay the emergence of resistance by targeting both the blood and liver stages of *Plasmodium* spp.

Correspondence to: Eliza Gong, Department of Parasitology and Vector Biology, Imperial College London, London, UK, E-mail: gong_eliza@imperial.a.c.uk

Received: 25-Jun-2024, Manuscript No. JBP-24-26230; **Editor assigned:** 27-Jun-2024, Pre QC No. JBP-24-26230 (PQ); **Reviewed:** 11-July-2024, QC No. JBP-24-26230; **Revised:** 18-Jul-2024, Manuscript No. JBP-24-26230 (R); **Published:** 25-Jul-2024, DOI: 10.35248/2155-9597.24. S27.107.

Citation: Gong E (2024) Mechanisms of Drug Resistance in Parasites and Strategies to Overcome Resistance. J Bacteriol Parasitol. S27:107.

Drug repurposing: Drug repurposing involves identifying new therapeutic uses for existing drugs that were originally developed for other indications. By screening libraries of approved drugs or investigational compounds against parasites, researchers can identify candidates with antiparasitic activity and potential efficacy against drug-resistant strains. Drug repurposing accelerates the drug development process and expands the therapeutic options available for treating parasitic infections.

Development of novel drug targets: Research efforts focus on identifying and validating novel drug targets in parasites that are essential for their survival and growth. By targeting unique biological pathways or metabolic processes specific to parasites, researchers can develop new classes of drugs with reduced cross-resistance to existing therapies. Advances in genomics, proteomics, and high-throughput screening technologies facilitate the discovery and validation of novel drug targets in parasitic organisms.

Adaptive therapy and drug cycling: Adaptive therapy involves adjusting drug treatment regimens based on real-time monitoring of parasite susceptibility and treatment responses. This approach aims to maintain a sublethal drug concentration that suppresses parasite growth without exerting strong selection pressure for resistance. Drug cycling involves periodically alternating between different drug regimens to prevent the emergence and spread of drug-resistant parasites while preserving treatment efficacy.

Enhancing drug delivery and formulations: Improving drug delivery systems and formulations can enhance drug efficacy, bioavailability, and pharmacokinetics, thereby optimizing treatment outcomes against drug-resistant parasites. Nanotechnology-based drug delivery systems, sustained-release formulations, and combination products improve drug stability, tissue penetration, and patient compliance, particularly in resource-limited settings where adherence to treatment regimens is challenging.

Challenges and future directions

Overcoming drug resistance in parasites requires a multidisciplinary approach integrating basic research, drug discovery, clinical trials, and public health interventions. Challenges include the complex genetic and biochemical mechanisms underlying resistance, variability in parasite susceptibility among geographic regions, and the need for sustainable funding and global cooperation in drug development.

Future research directions include advancing genomic surveillance of drug-resistant parasites, exploring host-parasite interactions influencing drug efficacy, and integrating innovative technologies for rapid diagnostics and personalized treatment regimens. Collaborative efforts between academia, industry, and public health agencies are essential for developing and deploying next-generation therapies that mitigate the impact of drug resistance on global health.

CONCLUSION

In conclusion, understanding the mechanisms of drug resistance in parasites and implementing effective strategies to overcome resistance are imperative for addressing the global burden of parasitic diseases. By employing combination therapies, repurposing existing drugs, developing novel drug targets, and enhancing drug delivery systems, researchers can innovate therapeutic approaches and sustain the effectiveness of antiparasitic treatments in diverse epidemiological settings. Continued investment in research and innovation is important for achieving sustainable control and elimination of drug-resistant parasites, ultimately improving health outcomes for affected populations worldwide.