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Classification and Mechanism of Action of Anti-Parasitic Drugs: A Review Article

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ABSTRACT: The action of antiparasitic drugs is critical in the treatment of infections caused by parasites and that have devastating effects on millions of individuals worldwide. This paper consolidates different research findings on the classification and mechanisms of action of these drugs, highlighting new therapies and natural products. In particular, this special class of heterocyclic compounds, known as Benzimidazoles, has garnered a wide interest in medicinal chemistry due to their broad pharmacological activities. It recognizes the important contribution normally made by these drugs in the treatment of a wide range of different diseases, including cancer, bacterial infection, and parasitic disease. Drug-resistant parasites are now increasingly prevalent and have greatly impeded the management of parasitic infections; thus, there is an increasing demand for new therapeutic approaches. Anti-parasitic metallodrugs have emerged as another auspicious mode of intervention that carefully exploits the unique chemical features of metal ions and their complexes to affect the biological pathways important for the survival of the parasite. In this paper, we will draw up a range of knowledge gaps identified up-to-date and propose future research directions that would enhance the understanding and, what is more important, the efficiency of anti-parasitic therapies.

INTRODUCTION

The development of potent antiparasitic drugs is of importance in winning the war against parasitic diseases that impact millions globally. This review assimilates various research findings that centered on the classification and mode of action of anti-parasitic drugs with particular attention to new treatments and herbal product (Barry et al., 201). Furthermore, the escalating issue of drug resistance to established antiparasitic drugs underscores the need for perpetuity of probing into alternative avenues as well as new chemical entities. The potential repositioning of the same drug for other therapeutic areas, including oncology, speaks to how intertwined drug research is and how much it depends on collaborative studies (Andrews et al., 2012).

Future studies should explore the synergistic interactions between conventional and novel therapies, particularly in the setting of resource limitation when established treatments can fail. Further research into the immunomodulatory effects— especially with compounds derived from helminths— may offer some valuable input toward the development of anti-parasitic treatments that enhance host responses. For all the significant advancements made in benzimidazoles classification and clarification on the mechanisms of their actions, much still remains unknown. One very big area where there is a real gap is in the necessity for proper studies on structure-activity relationships of benzimidazole derivatives. Some research was done on these relationships but there is a need for a more organized approach to pinning down the structural features that could bring about an improvement in therapeutic effectiveness in different applications. The topic of anthelmintic resistance to benzimidazoles, therefore, demands further exploration into molecular mechanisms driving resistance by nematode parasites. Understanding the specific mutations and changes in gene expression may facilitate the design of next-generation benzimidazole derivatives that are more resilient against such challenges (Abdulazeez et al., 2019). Though the value of metal-based drugs is beginning to be realized, significant knowledge gaps remain pertaining to their full mechanistic profiles and long-term efficacy. The available literature tends to focus mainly on individual metal complexes, without much attention to possible synergistic effects that may result from combining different metallodrugs or integrating them with other therapies. Equally important is a study on the environmental impact and biocompatibility of these metallodrugs with specific emphasis on natural ecosystems (Fricker, 2010). Significant progress has been made in the classification and mechanisms of action of trypanocidal drugs with some lacunae that exist known, more importantly to unveil in which ways do natural products act as anti-parasitic agents. This information could be helpful in developing new treatments based on the concept of traditional medicine. Further research should also focus on synthesizing benzimidazoles to achieve new levels of

specificity with their related binding phenomena and thus reduce off-target effects. The study of benzimidazole derivatives in combinational therapy could show a synergistic effect, leading to improved treatments for infectious diseases as well as cancer.

CLASSIFICATION OF ANTI-PARASITIC DRUGS

The anti-parasitics can be broadly classified into different classes based on chemical composition and mechanism of action. Among these, conventional organic compounds such as benzimidazoles (e.g. albendazole and mebendazole) are well known to act against nematodes. The principal mode of action of these drugs is through disrupting the microtubule formation within parasites resulting in eventual cell death (Wyllie et al., 2012). While their broad-spectrum activity is quite remarkable, the emergence of resistance points the way to a better understanding of its mechanisms and exploration of possible new therapeutic uses (Andrews et al., 2012). Conversely, promising candidates for anti-parasitic therapy have arisen in the form of metallodrugs. By taking advantage of the peculiar features of metals and their coordination environments, these compounds can bring new mechanisms of action that might work well through the normal channels of drug resistance (Barry & Sadler, 2013). Furthermore, steps in proteomics and genomics could help better identification of individual molecular targets in parasites, and thus permit new metallodrug treatments.

Moreover, there is growing interest in medicinal plants due to their anti-parasitic properties, especially in regions where there is no standard chemotherapy. The classification of these plants based on their active constituents (terpenoids and phenolics) emphasizes the need for understanding their mode of action. Research on natural products therefore provides a useful avenue toward discovering effective anti-parasitic agents from traditional medicine (Kuete & Efferth, 2010).

The classification of benzimidazoles is majorly based both on the differences in their structures and the bioactivities that they display. In recent studies, these compounds have been placed in some of these subcategories by virtue of their pharmaceutical outcomes, such as antibacterial, anticancer, and antiviral activities. A study on example new trisubstituted benzimidazoles presents significant antibacterial activity against Mycobacterium tuberculosis and hence flags these compounds as prospective anti-tuberculars since they can inhibit the crucial process of the FtsZ protein which is necessary for bacterial cytokinesis (Kumar et al., 2011).

The benzimidazoles are also classified based on their interactions with specific biological targets. For instance, it has been reported that certain benzimidazole derivatives display very strong binding affinity towards the G-quadruplex DNA structures, thereby inhibiting telomerase and promising anti-cancer advantages (Maji et al., 2014). Conversely, compounds that target tubulin polymerization are very vital in furthering both anti-cancer and anthelmintic therapies, underlining the diverse nature of benzimidazoles (Lee et al., 2022). Depending on the metal content, oxidation states, and ligands it incorporates, metallodrugs are classified, all of which dictate their mechanisms against parasites. According to previous work from Barry and Sadler (2013), the choice of both the metal and its ligands can open up new modalities for targeting different parasitic species. For example, this compound, MMV390048, identifies a new class of anti-parasitic compounds by inhibiting phosphatidylinositol 4-kinase (PI4K) of the Plasmodium parasites; thereby, providing a very specific mode by which the compound may interfere with malaria's lifecycle within the erythrocyte (Neafsey et al., 2015). Data on the compound's wide-spread potency against resistant strains bears great impetus to the need for new classes of metallodrugs (Paquet et al., 2017).

Another metal complex to be investigated is, for instance, gold and rhenium that provide more ways of classifying due to mode interactions with important biological targets such as cysteine proteases (Rocamora et al., 2018). These proteases play an essential role in the parasite life cycle; hence, metallodrugs directed against them could disrupt essential biological functions and eventually result in the death of the parasites. This is thereby supporting that classification systems should consider not only the metal ions but also their specific biological targets and the mode of action through which they operate.

MECHANISMS OF ACTIONS

The therapeutic potential of antiparasitic drugs hinges on the mode of action. For instance, fexinidazole is a novel treatment for human African trypanosomiasis that acts through a unique mode of action, being converted into active metabolites specifically directed against the infecting parasite, Trypanosoma brucei (Kuete & Efferth, 2010). Such pharmacological information is necessary to develop treatments that can deal with both conditions of the disease—both the acute and the chronic phase.

It’s possible repurposing for different diseases is based on its efficacy against visceral leishmaniasis (Wyllie et al., 2012). Much knowledge about metabolic routes and modes of action both for fexinidazole and its metabolites would greatly improve the therapeutic uses of this drug. In the category of plant-derived compounds, arecoline, extracted from Areca catechu, proves to possess anti-parasitic effects, thus demanding a detailed study on its pharmacological effects and modes of action (Ehsanian et al., 2011). This present need for an elaborate understanding of natural compound operations aligns with the wider goal of enhancing the arsenal of anti-parasitic drugs available. It is also an established anti-parasitic. Indeed, ivermectin as an antiparasitic has been acknowledged to act as a potentiator of ion channels in mammalian cells, a contribution that has provided very important insights toward its activities that go well beyond its initial and primary intended uses (Chai et al., 2021). This information is necessary to develop new medicines from existing ones, leading to improved treatment against parasitic infections. Further research, especially into the mechanism of autophagy cross-talk with Toxoplasma gondii sensitivity to monensin, underscores the need for wide exploration in the pathways by which anti-parasitic drugs induce cell death in parasites (Mudassar et al., 2020). Revealing these pathways might

present new avenues of therapy and how to overcome populations of parasites that are resistant. The structural disparity and associated biological activities are the major mechanisms for the classification of benzimidazoles. In a study of trisubstituted benzimidazoles as a new class of innovative agents, which are highly active against various strains belonging to Mycobacterium tuberculosis, based their designation as potential new antitubercular agents, due to an ability to impede an important function in FtsZ protein synthesis necessary for bacterial cell division Kumar et al..(2011) .

Derivatives are usually classified based on their interactions with particular biological targets. For instance, some derivatives of benzimidazole have been reported to be excellent binders of the G-quadruplex DNA structure, hence inhibiting the activity of telomerase and possible anticancer effects (Maji et al., 2014). Simultaneously, compound priority in tubulin polymerization falls critical in the development of anti-cancer as well as anthelmintic therapies, underscoring the multifaceted classification of benzimidazoles (Lee et al., 2022). The actions of benzimidazoles are diverse and, to a large extent, dependent on both their composition and the biological targets that influence these effects. Perhaps their most important mechanism comes from inhibiting tubulin polymerization, which naturally can interfere with microtubule dynamics—something very critical to cell division. Such an effect has made benzimidazoles particularly useful as agents in cancer therapy by inducing apoptotic cancer cells (Lee et al., 2022). An important mechanism is the inhibition of the assembly mechanism of FtsZ protein inside the bacterial cell. The ability of some benzimidazoles to enhance GTPase activity plus the disassembly of FtsZ adds a new approach to design novel chemotherapeutics against drug-resistant strains of Mycobacterium tuberculosis (Kumar et al., 2011). This proves to be a key way forward in the battle against the ever-increasing problem of antibiotic resistance among bacterial pathogens.

Moreover, further research was focused on the interactions of benzimidazoles with the HIV-1 capsid protein to prove that they act to inhibit capsid assembly, the important condominiums of HIV life-cycle infection. Understanding these binding modes will enable in the future development and optimization of benzimidazole derivatives for more effective antiviral agents and to solve the problem of drug resistance (Maurer et al., 2013). The mode of action of metallodrugs as antiparasitic agents is very diverse and complicated. One major mechanism through which they develop anti-parasitic properties is by acting as inhibitors of some important enzyme that the parasite cannot live without. For instance, PI4K is inhibited by MMV390048, explaining how lipid metabolism in Plasmodium can be compromised, a highly needed process for the parasite's growth and replication (Paquet et al., 2017). In addition, metallodrugs can induce oxidative stress in the parasites by generating reactive oxygen species that cause damage at the cellular level and eventually kill the cell (Rocamora et al., 2018). The incidence of artemisinin resistance in Plasmodium falciparum research provides a better insight into the prospective methodology that might be adopted to thwart this resistance. Genetic polymorphisms and responses to oxidative stress in the resistant strains can be identified, so scientists can design metallodrugs directed at these adaptive pathways, offering a new approach to drug development. This again highlights how important it is to build lessons from the mechanisms of resistance into future metallodrug design to actually increase its effectiveness (Paquet et al., 2017).

CONCLUSION

In summary, understanding the mode of actions of anti-parasitic drugs is crucial for the development of treatments for parasitic diseases. While conventional compounds are still heavily relied upon, the emergence of metallo drugs and natural products represents an exciting avenue that fully justifies further investigation. This could enhance the ability to improve the health status of populations through better effectiveness and availability of anti-parasitic treatments results from filling present knowledge gaps and pursuing new avenues for research.

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