

ABSTRACT

Identification of a novel Anti-Parasitic Compound from Natural Medicinal sources and their effect on *Giardia lamblia*

Giardia lamblia is one of the most frequent protozoan parasite causes giardiasis worldwide. According to WHO reports annually 280 million people have been infected globally. Giardiasis is becoming an increasingly prevalent issue worldwide, particularly in developing country, as it continues to emerge and spread within human populations. In developed countries, the prevalence rate of giardiasis is between 2-5%, while in developing countries ranges from 20-30%. The disease is typically transmitted indirectly through the consumption of food or water that has been contaminated with cysts, or through person-to-person contact, especially among individuals living in unhygienic conditions. However, the present medications for Giardiasis treatment often come with numerous side effects, while the growing problem of drug resistance adds a significant complication. It is required to develop both new drugs and treatment strategies that can enhance therapeutic outcomes and effectively address drug-resistant cases in clinical settings.

Today, medicinal plants are at the forefront of primary healthcare, valued for their accessibility, acceptability, and affordability. With a rich history of use spanning millennia, evidenced by their presence in ancient medical systems like Ayurveda, Unani, and Siddha, medicinal herbs continue to play a crucial role. India, known for its biodiversity, houses over 45,000 plant species, potentially making it the largest producer of medicinal herbs. Among these, the *Andrographis paniculata* (*A. paniculata*) plant shines with its exceptional therapeutic properties, experiencing a surge in demand in recent years. This indigenous herb holds not only economic importance but also serves as a potent remedy, highlighting its significance both economically and medicinally. The pharmacological effects of *A. paniculata* have been studied using both crude extracts and isolated bioactive compounds. While the crude extract showed notable effects, focusing on the major bioactive compound, andrographolide, offers a clearer understanding, especially regarding mechanisms of action. Andrographolide exhibits diverse activities, including anticancer, antidiabetic, anti-inflammatory, and hepatoprotective effects, which could benefit a large population. This study primarily explores the medicinal and pharmacological effects of andrographolide, targeting giardiasis.

In this study, we explored the in-vitro potential of *A. paniculata* (*Ap*) leaf extract and its active compound andrographolide (ADG) as a possible alternative treatment for giardiasis. Natural compounds show promise in the search for more potent anti-giardial agents. After 24 hours of incubation, the test results revealed *Ap* extract and ADG demonstrated an IC_{50} value of 51.26 μ g/ml and 4.99 μ M. We observed a substantial degradation of DNA, alteration in morphology, inhibition in adherence, ROS generation and inhibition of the cell cycle in *Giardia* trophozoites. It also downregulates many genes that are related to pathogenesis. The in vivo results showed a favorable response to ADG treatment at 20 mg/kg body weight in infected mice, with no significant toxicity observed on the intestinal cell line. This encouraging outcome supports the formulation of a new drug development strategy against giardiasis. This approach aims to offer a natural therapeutic solution for giardiasis, minimizing side effects and reducing the risk of drug resistance.

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