FLUBENDAZOLE, A POTENTIAL USEFUL CHEMOTHERAPEUTIC AGENT FOR TREATMENT AND CONTROL OF Filarial Infections


Abstract

The search for a macrofilaricidal that can enhance the goal of elimination of filarial infections, and the diseases they cause, is a current and relevant goal. The most attractive approach to macrofilaricidal discovery is to repurpose agents already in use in humans. High among those potential candidates is flubendazole, a drug that was shown in a screening survey in the early 1970s to be highly effective against distomastic cercariae in humans but was difficult to administer due to the properties of its formulations. Use of this compound as a potential drug against filariae became a primary objective due to the high prevalence of filarial infections caused by Brugia malayi and Wuchereria bancrofti. This parasite is a severe health problem in the tropical regions of the world. Flubendazole is a potential useful chemotherapeutic agent for treatment and control of filarial infections. The historical research on flubendazole and its potential for macrofilaricidal activity is reviewed. The pharmacodynamics of different flubendazole preparations are described. The compound’s efficacy is assessed in vitro and in vivo studies. Major Conclusions: 1. Flubendazole can be formulated to produce plasma levels of 1-2 µg/ml following oral dosing (2-6 mg/kg). 2. Five daily doses of oral flubendazole at 6 mg/kg reduce the mass of worms removed from control animals at 9 weeks. 3. Safety studies with new formulations need to be completed. However, studies so far show similarities between flubendazole and other benzimidazoles used in veterinary medicine. 4. Avoid any direct contact with animals being treated. 5. Close surveillance for adverse reactions is recommended. 6. Flubendazole has been shown to be safe in humans.

The History of Flubendazole in Human Filarialis

Flubendazole is a benzimidazole derivative developed in 1971 as an analogue of albendazole (1); it has a molecular weight of 363.28, and is composed of C₁₅H₁₄N₂O₃. Flubendazole is a broad-spectrum anthelmintic with a wide range of applications. It has been shown to possess anti-parasitic activity against a variety of helminth species, including nematodes, cestodes, and trematodes.

The Pharmacodynamics of Different Flubendazole Preparations

The pharmacokinetics of flubendazole vary depending on the formulation used. The oral bioavailability of flubendazole is low, with peak plasma levels of 1-2 µg/ml following oral dosing (2-6 mg/kg). The compound is rapidly absorbed, with a half-life of approximately 3-5 hours. The plasma concentration decreases rapidly to control levels by 12-20 hours. The drug is mainly excreted in the urine, with a small amount excreted in the feces.

In Vitro Studies

Flubendazole, a tubulin-binding agent, was shown to damage various organs and cells within Brugia by Fracastoro et al. in 1990. Damage was seen in three locations: the cytoplasm, the plasma membrane, and the extracellular matrix. Major conclusions: 1. A. lumbricoides flubendazole in vitro showed minimal injury. 2. Flubendazole caused a reduction in microfilarial counts in vivo. 3. The compound exhibited cytopathological changes in the bloodstream cells. 4. Flubendazole was effective against the microfilarial stage of Brugia malayi and Wuchereria bancrofti. 5. The compound also had an effect on the pathological responses associated with filarial infection.

In Vivo Studies

Tissue responses 9 weeks after treatment are considerably reduced compared to control animals.

Host Responses After Flubendazole Treatment

Tissue responses. 9 weeks after treatment are considerably reduced compared to control animals.

Associated References

