INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA):IJPS00]
Journal Homepage: https://www.ijpsjournal.com

Review Article

Tricabendazole: Emerging Treatment For Human Fascioliasis

Sapna A. Pandey*, Monika Jadhao

Department Of Quality Assurance, Vidyabharati College Of Pharmacy Amravati .Maharashtra 444602

ARTICLE INFO

Received: 28 Feb 2024
Accepted: 02 March 2024
Published: 12 March 2024

Keywords:
Human Fascioliasis, Triclabendazole foodborne disease, Neglected diseases.

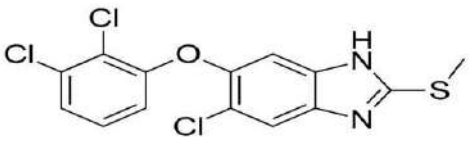
DOI:
10.5281/zenodo.10806040

ABSTRACT

A strong anthelmintic medication for oral use is triclabendazole. Triclofenacle was authorized by the US Food and Drug Administration (FDA) in February 2019 to treat human fascioliasis. We talked about the epidemiology and therapy of human fascioliasis in this review. Every continent that is populated has fascioliasis. It mostly affects domestic animals and is brought on by the trematode parasites Fasciola hepatica and Fasciola gigantica, which have intricate life cycles. Humans contract the disease from drinking contaminated water or eating contaminated food, usually wild aquatic vegetables. Since many symptoms of fascioliasis are non-specific (such as fever, abdominal pain, and anorexia), diagnosis can be challenging. We talked about the mechanism of action, pharmacokinetics, and pharmacodynamics of triclabendazole as well as its side effects. Triclabendazole, a benzimidazole member, is the most advised and successful method of managing.

INTRODUCTION

Triclobendazole (Egaten, Novartis Pharmaceuticals, East Hanover, NJ, USA) was authorized by the US Food and Drug Administration (FDA) in February 2019 for the management of human fascioliasis.1 Through a donation program set up under the direction of the World Health Organization's (WHO) Department of Control of Neglected Tropical Diseases, trimethobenzole has been used in many other parts of the world after receiving permission in Egypt in 1997 and France in 2002. In this article, the history of triclabendazole treatment for human fascioliasis is reviewed, with an emphasis on more recently published research.



TRICLABENDAZOLE
Mol. wt: 359.7 G/MOL
Mol. formula: $C_{14}H_9CL_3N_2OS$

Fig no 1:-Triclobenzazole's chemical formula and structure.

The use of medications is the cornerstone of most successful fasciolosis control methods. One of the

***Corresponding Author:** Sapna A. Pandey
Address: *Department Of Quality Assurance, Vidyabharati College Of Pharmacy Amravati .Maharashtra 444602*.
Email : sapnapandey757@gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

most popular medications used globally to treat fasciolosis is triclabendazole (Fasinex®, Novartis). Given its strong action against adult flukes as well as juvenile flukes as young as one week old, TCBZ is typically the anthelmintic of choice for treating livestock for F. hepatica. The most popular and efficient anthelmintic for treating both immature and mature flukes in animals is TCBZ. Numerous investigations on the use of TCBZ have demonstrated its remarkable efficiency against Fasciola species. But a further investigation has showed that the evidence of TCBZ's extremely low level of efficacies is For the treatment of fascioliasis, triclabendazole is the recommended medication. Nonetheless, reports of TCBZ resistance have surfaced in the literature 19, albeit not all of them may be true instances of resistance, in addition to the evolving pattern of illness. However, as TCBZ is the only medication that has demonstrated great efficiency against the migratory and juvenile stages of infection to yet, any instances of resistance are concerning. Any recent progress achieved in the fight against and management of human and animal fascioliasis may be reversed if patients develop treatment resistance.20,21 Veterinary medicine uses triclabendazole, a flukicidal BZs chemical, extensively because it works very well against both mature and immature stages of the liver fluke, F. hepatica.

The Illness: Fasciolosis

A foodborne trematode infection is known as fascioliasis. Fascioloiasis is a worldwide illness. There have been reports of fasciolosis from 81 countries. One According to the World Health Organization, fascioliasis is a zoonotic illness that is frequently disregarded. Numerous mammals, including people and livestock, are infected by two recognized species of Fasciola: Fasciola hepatica and Fasciola gigantica. It is unknown how many people are infected today. Estimating the number of infected individuals and disease burden is severely hampered by the lack of supporting data from extensive epidemiologic research and the unique characteristics of the fascioliasis distribution. Globally, the estimated number of infected individuals ranged from 2.4 million to 17 million.2,3 These figures, however, are more than 25 years old, and the information needed to calculate them is not given. Expert opinion served as the foundation for Fürst et al.'s more current estimate of 2.6 million illnesses.4 Fasciolasis is a disease that is still relatively new, and reports of its expanding endemic areas suggest that the number of infections worldwide likely exceeds previous estimates. Human fascioliasis is most frequently found in nations like Bolivia, Peru, Cuba, China, Iran, Vietnam, and Egypt where it is usual to consume wild aquatic vegetables or drink contaminated water.2 Human fascioliasis cases have also been documented in several European nations, most notably Turkey, Spain, and France, with sporadic occurrences also documented in the United States.2 Fasciolasis is a disease that can affect people in more than 70 countries; in 2005, the number of cases was estimated to be 2.6 million, with 1.3 million occurring in Latin America and 1.1 million in Africa.5

The parasite's biological cycle and ethology

Liver flukes, or flukes of the genus Fasciola, are the cause of fasciolisis. F. hepatica, which is mostly found in temperate climate regions, and F. gigantica, which is found in tropical locations, are the two species most frequently identified as the causative agents of fasciolosis. Furthermore, in areas where the two species coexist, hybrid forms have been reported. 5, 7 the two unique genetic signals that each species carries have been distinguished using real-time PCR (par) targeting ITS1 renal, ITS2 renal, and 28S renal.7, 9 It is crucial to always use the proper terminology and avoid using F. hepatica and F. gigantica interchangeably because the epidemiological potential of hybridization and introgression

between the two species is still unclear.10 Fasciola spp. have a complicated life cycle with several variants. Molluscs are the typical intermediate hosts that are involved, one or more of them. It has been observed that at least 20 species of the Lymnaeidae family serve as intermediate hosts.11, 12 the asexual larvae multiply.13, 15 times before they eventually infect a final host, which is where sexual reproduction takes place.

Pathogenesis

A number of lesions are caused in the liver parenchyma and the bile ducts as a result of the parasites' migration, penetration, and localization in the bile ducts.15 Seventy-two hours after ingesting metacercaria, the newly encysted juveniles (NEJs) of Fasciola spp. enter the abdominal cavity through the intestinal mucosa. When NEJs reach the liver surface through the peritoneum, they do not exhibit any clinical sinology in animals.16 Because of its physical proximity to the duodenum and the fact that they reach fewer other hepatic lobes, the left hepatic lobe is the destination of most NEJs. These juveniles can occasionally migrate abnormally to other organs, including the lung and the diaphragm, as a result of severe infestations, which can result in fibrous pleurisy and pneumonia. Several pathological processes occur simultaneously within the liver parenchyma, including the migration of juvenile stages that cause necrotic and haemorrhagic lesions, which, in turn, cause inflammatory reactions activating the immune system.47 This response can be found throughout the tortuous migrating trajectory of the parasites, suggesting that the excretion and secretion of these products remain in the tissue, attracting more infiltration of inflammatory cells of an immune nature.48 The biliary phase begins when the parasites enter the bile ducts, where they exert a combined mechanical and chemical action. Through the oral sucker, adult parasites cause mechanical damage while feeding on blood and the liver parenchyma adjacent to the duct. Macerated hepatocytes have been seen within the pharynx and sucker, which can cause minor blood vessel punctures, trauma, isolated duct rupture, and epithelial erosion. Chemical means have been reported to cause bile duct enlargement.49 Praline, an amino acid required for collagen formation by fibroblasts, may also be released in significant amounts by the parasite.50, 51 the adult parasite's two functions result in a considerable hyperplasia of the bile ducts in which the parasites lodge52, and a severe eosinophilia and granulomatous inflammatory response, especially when eggs reach the hepatic parenchyma.51These two phases work together to produce a sequence of lesions in the liver parenchyma, and the severity of these lesions is closely proportional to the infectious dose; a high dosage results in more acute, severe, and potentially deadly lesions. Yet, further research on sheep51 and goats has also demonstrated that, when administered in modest, repeated doses (trickle infections), the liver damage was more severe than when the same number of metacercariae were employed in a single treatment. The immune system's reaction to the initial infection and several stages are crucial in the development of fasciolosis.49 these results imply that liver damage may have its origins in the mechanical and enzymatic activities of the parasite. Therefore, concurrent infection and the immune response or healing when food or drink is tainted with infectious parasite forms—typically wild watercress, or Nasturtium officinal—or grass that has metacercariae embedded in it, the parasite is transferred to its ultimate host. The existence of intermediary hosts, which are molluscs belonging to the family Lymnaeidae, genus Linnaean, is necessary for the parasite cycle.53 Fascioliasis is usually asymptomatic in humans, yet it can occasionally cause vague symptoms including fever, nausea, diarrhoea, and abdominal pain that

could be indicative of a chronic or acute infection.53

DIAGNOSIS

Because many of the disease's clinical signs, such as gastrointestinal symptoms and eosinophilia, are non-specific, fascioliasis can be difficult to diagnose.18 A combination of clinical symptomatology, laboratory assessments, imaging (usually computed tomography or ultrasound), serological testing or coprology antigen testing, and the identification of Fasciola spp. are used to make the diagnosis. eggs in excrement or duodenal aspirates, utilizing the Kato-Katz technique, for instance.19 Although it can lead to a definitive diagnosis, the detection of eggs from Fasciola spp. is thought to be possible only in cases of chronic disease (where adult flukes are present in the biliary tract). Acute fascioliasis is still more difficult to diagnose.20, 21 even though serology and imaging may be more sensitive and specific than in chronic disease.17

Overseeing

Human fascioliasis is treated with anthelminthic to kill the flukes, along with symptomatic medication to relieve abdominal pain and possibly antispasmodic medication to treat biliary colic, which may arise from the accumulation of dead or dying flukes in the biliary ducts, obstructing drainage.57

Triclabendazole

Treatment for persistent fasciolosis involves the administration of trimetzolide, an oral anthelmintic drug. Trimetazole administration is generally well tolerated, albeit it may induce upset stomach. Tricloabendazole (6-chloro-5-(2, 3-dichlorophenoxy)-2-(methylation)-1H benzimidazole) is a Benzimidazole derivative with impolitic characteristics. It was initially developed and marketed as Fascine by Ciba to treat fascioliasis in domestic livestock, and it has been used in veterinary medicine since 1983.22

Among the benzimidazoles, triclabendazole is distinct since it has a very selective action against Fasciola spp. and little to no activity against nematodes, custodies, or other treaties 5. In collaboration with the World Health Organization (WHO), Novartis subsequently developed it for human use after it was initially designed to treat fascioliasis in domestic livestock. Furthermore, it demonstrated a substantial suppression of the motility of the parasite and of growth-related enzymes, which led to growth arrest and eventually death. All stages of the parasite, including the eggs, were shown to be resistant to its antiphrastic activities.7 Since 1983, veterinarians have been using carbendazole regularly to treat fascioliasis; nevertheless, it is now authorized for use in humans as well.

The mode of action of triclocarbamazole

Triclabendazole is a BZs derivative and, by analogy with what is known about other BZs drugs, it would be anticipated that TCBZ might bind to the β-tubulin molecule and so disrupt microtubule-based processes. Evidence in support of this idea has come from morphological studies on the tegument, vitellaria and testis, following treatment with the active sulphide metabolite. For example, there is inhibition of mitosis in the vitalize and spermatogenic cells; disturbance of the transport mechanisms in the tegument, a trematode's outer layer, which results in the tegument's entire destruction after gradually more severe injury to the tegmental surface.23 It has also been noted that the tegmental syncytium lacks tubulin immune-staining. These findings imply that the microtubules have vanished, which would impede the transfer of secretory bodies from the cell bodies to the tegmental surface. The significant morphological abnormalities seen could be explained by the disruption of this mechanism, which is essential for maintaining the integrity of the surface membrane.24 Years of research have not yet revealed the exact

mechanism of action of TCBZ. TCBZ is a derivative of BZ, and all the information presently available about gastrointestinal roundworms suggests that BZ anthelmintic attach to α and β-tubulins inside the parasite's cells, interfering with essential functions including feeding and digestion. The tegument, vitellaria, and testis of the fluke were the subject of several morphological investigations investigating the effects of TCBZ and its active metabolites on F. hepatica. All three tissues displayed notable indications of Ultra structural disruption, which is consistent with the inhibition of microtubule-based activities.25

The pharmacodynamics and pharmacokinetic aspects

Triclabendazole is a narrow-spectrum anthelminthic that works against Paragonimus species as well as Fasciola (F. hepatica and F. gigantica). It works well against Fasciola species during the whole infection cycle.26,27 Triclobenzazole's mode of action is still unclear and could involve a number of targets, such as acetylate cyclase activity or microtubule-based mechanisms that disrupt the tegument.28 Pharmacokinetic studies have mostly depended on the measurement of the sulphoxide metabolite's plasma concentrations since it appears to have a more powerful but delayed effect on parasite motility than triclabendazole itself.29 It is likely that the drug functions primarily through this metabolite, which is highly prevalent in human plasma. The pharmacokinetic characteristics of patients with fascioliasis and healthy volunteers were comparable.30 similar outcomes were seen in both of the open-label, non-randomized trials comparing administration of the medication to patients with fascioliasis under fed and fasting conditions. The investigations were conducted in Europe and Peru, respectively (unpublished data, Novartis). The parent compound exhibited rapid absorption with a tmax of two to three hours, indicating the time to reach the maximum serum concentration. When the sulphoxide metabolite was fed, its median tmax and mean maximum serum concentration (Cmax) rose from 15.8 μmol/L (fasting) to 38.6 μmol/L (fed condition) and from 2 to 4 hours (fasting). Eating caused an overall increase in the sulphoxide metabolite's AUC of nearly 2.2 times.31 the average half-life of the sulphoxide metabolite's elimination from plasma in the fed state is around 11 hours. It was suggested that triclabendazole be taken with food as a result of the drug's increased exposure under fed conditions. Human excretion studies have not been carried out; nonetheless, in animals, the medication is primarily eliminated through the biliary tract in the faeces (about 90%), together with the sulphoxide and the sulphone metabolite. A dose taken orally excretes less than 10% in the urine.32 Clinical trials and post-marketing safety data (unpublished data, Novartis) did not reveal any substantial safety concerns pertaining to drug-drug interactions. The injection of triclabendazole in a single dose may be the cause of this.

Safety and effectiveness research on humans

Using a range of dosages and regimens in a vast geographic area, the treatment of human fasciolias with trimethoprim and trimethoprim has been studied for nearly 30 years. Although one placebo-controlled trial using nitazoxanide for fascioliasis has been undertaken, the majority of studies were not comparable due to the lack of effective alternative treatments and the ethical objections to using placebo controls.36 Two very recent investigations contrasted artemisinin derivatives with triclabendazole.33,-35 Fasciolosis vaccines.

Vaccines against Fasciolosis: A Recap

Even if there has been a lot of work in identifying potential vaccine molecules to lower fasciolosis in cattle, one may argue that the product is still not at the level of efficacy required to go on sale. A major issue that has to be addressed is the immunological suppression/modulation by fasciolids, which

prevents the development of protective T helper (Th)1 immune responses and is accountable for the lack of immunity observed in animals infected both naturally and in trials.37–45 This is because a strong regulatory/Th2 type immune response arises during an infection, effectively suppressing the host's Th1 responses.37 However, a number of studies have shown that after catching Fasciola, animals acquire immunity, and that rats, sheep, or cattle can be madeinstances of triclabendazole resistance in humans In recent years, fascioliasis has emerged as a major zoonotic disease, with an increase in the number of human cases, and it is a serious health problem in a number of countries. TCBZ is also the drug of choice for treating fasciolosis in humans and it is conceivable that TCBZ-resistant fluke populations, selected in livestock, could pose a zoonotic risk to human health, especially in areas such as Peru and Bolivia, where there is a high incidence of human infections.55 The first incidence of TCBZ treatment failure in humans was reported in a livestock farmer in the Netherlands, with further recent reports of four cases from Chile, one case from Turkey, and seven cases from Peru. Clearly, TCBZ-resistant zoonotic infections are a serious emerging issue.56

Use by humans after initial creation and certification

The use of triclabendazole in the treatment of human fascioliasis has been the subject of numerous case reports, case studies, and research published in a variety of nations since the first human investigations. Patients who are elderly or who have renal or hepatic impairment have not been specifically studied in the therapy data, however it does include information on treating adults, adolescents, and children. Neither the usage of it during lactation nor pregnancy has been researched. Clinical studies include two randomised trials: one compares triclabendazole with artesunate in 100 patients in Vietnam30, and the other compares two doses of triclabendazole in 84 pediatric patients in Peru. Other studies include 33 a study with 90 pediatric patients in Bolivia, 34 a study with 134 patients in Egypt, 35 a study with 165 patients in Iran 36, and a trial with.

Alternative therapies

Most anthelminthics, such as praziquantel, albendazole and metronidazole, show little efficacy in fascioliasis.57,58 Emetine has been reported to be effective,59 but the use of emetine (and dehydroemetine) is limited by safety issues, principally cardiotoxicity.39 Prior to the development of triclabendazole, bithionol was widely used,60 but it requires a lengthy treatment course, is associated with tolerability issues64 and cure rates vary considerably.51–63 Bithionol is no longer commercially available. Other compounds that have shown some efficacy but have not been investigated further are metronidazole55 and nitazoxanide.65-68 Artemisinin derivatives have also been investigated in human fascioliasis, but efficacy was not optimal and/or required rescue with triclabendazole.69, 70

Studies on human efficacy and safety.

Triclabendazole treatment of human fascioliasis has been studied over a period of almost 30 year using a variety of doses and regimens in a wide range of geographic areas. Most studies were non-comparative, giventhe lack of effective alternative treatments and that use of placebo controls would not be considered ethically acceptable (although one placebo controlled study with nitazoxanide in fascioliasis has been conducted).71 Two relatively recent studies compared triclabendazole with artemisinin derivatives. 69, 70

CONCLUSION

Although reports of human fascioliasis have been made on every continent that is populated, the disease is most prevalent in a few areas, most notably in Peru, Bolivia, Egypt, Iran, and Vietnam. Even though fascioliasis is found all over the world, there were few treatment choices available

before triclabendazole was developed. This is still the case because no other medication has shown comparable or sufficient efficacy against fascioliasis. Triclobenzazone is a very successful treatment for human fascioliasis, according to research conducted in the 1990s by the WHO in association with Ciba, studies conducted by the Egyptian government, and later published studies, case series, and case reports. A single dose of 10 mg/kg administered postprandially was found to be generally successful in the early investigations; nevertheless, patients needed to be monitored to confirm any improvement in their clinical condition. Two further doses of 10 mg/kg can be administered 12–24 hours apart if the initial 10 mg/kg dose does not work as intended. The current WHO recommendations are based on these research, which served as the foundation for regulatory approvals in France in 2002 and Egypt in 1997. The US FDA's latest approval helps to heal a Clinical trials on both acute and chronic forms of fascioliasis and F. hepatica and F. gigantea infections have demonstrated the effectiveness of trimethoprim-sulfamethoxide.72-75 The majority of adverse events (AEs) were likely caused by the ejection of dead or dying flukes from the biliary tract, but the treatment with trimethobenzole was typically well tolerated. It is reasonable to assume that, given its widespread use in veterinary medicine, resistance to triclabendazole in diseases affecting cattle is well-established; nevertheless, resistance in human fascioliasis appears to be uncommon and intermittent.

REFERENCES

1. US Food and Drug Administration. Drug Trials Snapshots: EGATEN. https://www.fda.gov/drugs/drug-trials-snapshots-egaten [accessed 29 April 2019]
2. Mas-Coma S, Bargues MD, Valero MA. Human fascioliasis infec tion sources, their diversity, incidence factors, analytical meth OD and prevention measures. Parasitology. 2018; 145(13 Special Issue):1665–1699.
3. Mas-Coma S, Bargues MD, Valero MA. Diagnosis of human fascioliasiby stool and blood techniques: update for the present global scenario.Parasitology. 2014; 141(14):1918–1946.
4. Mas-Coma S, Valero MA, Bargues MD. Chapter 2. Fasciola, lymnaeids and human fascioliasis, with a global overview on diseasetransmission, epidemiology, evolutionary genetics, molecular epidemiology and control. Adv Parasitol. 2009; 69:41–146.
5. Agatsuma T, Arakawa Y, Iwagami M, Honzako Y, Cahyaningsih U, Kang SY, et al. Molecular evidence of natural hybridization between Fasciola hepatica and F. gigantica. Parasitol Int. (2000) 49:231–8. Doi: 10.1016/S1383-5769(00)00051-9
6. Lotfy WM, Brant SV, DeJong RJ, Le TH, Demiaszkiewicz A, Rajapakse RP, et al. Evolutionary origins, diversification, and biogeography of liver flukes (Digenea, Fasciolidae). Am J Trop Med Hyg? (2008) 79:248–55. Doi: 10.4269/ajtmh.2008.79.248
7. Marcilla A, Bargues MD, Mas-Coma S. A PCR-RFLP assay for the distinction between Fasciola hepatica and Fasciola gigantica. Mol Cell Probes. (2002) 16:327 33. Doi: 10.1006/mcpr.2002.0429
8. AlasaadS,Soriguer RC,Abu-MadiM,ElBehairyA,JowersMJ,BañosPD,etal .A TaqMan real-time PCR-based assay for the identification of Fasciola spp. Vet Parasitol. (2011) 179:266–71. Doi: 10.1016/j.vetpar.2011.01.059
9. Calvani NED, Ichikawa-Seki M, Bush RD, Khounsy S, Šlapeta J. Which species is in the faeces at a time of global livestock movements: single nucleotide polymorphism genotyping assays for the differentiation of

Fasciola spp. Int J Parasitol. (2020) 50:91 101. Doi: 10.1016/j.ijpara.2019.12.002
10. Calvani NED, Šlapeta J. Fasciola gigantica and Fasciola Hybrids in Southeast Asia. In: Dalton, JP, editor. Fasciolosis 2nd edn. Cambridge: CABI Publishing (2022). p. 423–60. Doi: 10.1079/9781789246162.0013
11. Torgerson P, Claxton J. Epidemiology and control. In: Dalton JP, editor. Fasciolosis. Wallingford: CAB International (1999). p. 113–49.
12. Correa AC, Escobar JS, Durand P, Renaud F, David P, Jarne P, et al. Bridging gaps in the molecular phylogeny of the Lymnaeidae (Gastropoda: Pulmonata), vectors of Fascioliasis. BMC Evol Biol. (2010) 10:381. Doi: 10.1186/1471-2148-10-381
13. Wilson RA, Pullin R, Denison J. An investigation of the mechanism of infection by digenetic trematodes: the penetration of the miracidium of Fasciola hepatica into its snail host Lymnaea truncatula. Parasitology. (1971) 63:491 506. Doi: 10.1017/S003118200008001X
14. Thomas AP. The natural history of the liver-fluke and the prevention of rot. J R Agric Soc. (1883) 19:276–305.
15. ThomasAP.Thelifehistory of the liver-fluke (Fasciola hepatica). Q J Microsc Sci. (1883) 23:99–133. Doi: 10.1242/jcs.s2-23.89.99Dawes B, Hughes DL. Fascioliasis: the invasive stages of Fasciola hepatica in mammalian hosts. Adv Parasitol. (1964) 2:97 168. Doi: 10.1016/S0065-308X (08)60587-4
16. Dow C, Ross JG, Todd JR. The histopathology of Fasciola hepatica infections in sheep. Parasitology. (1968) 58:129–35. Doi: 10.1017/S0031182000073480 29. Boray JC. Experimental fascioliasis in Australia. Adv Parasitol. (1969) 7:95 210. Doi: 10.1016/S0065-308X (08)60435-2
17. Marcos LA, Terashima A, Gotuzzo E. Update on hepatobiliary flukes: fascioliasis, opisthorchiasis and clonorchiasis. Curr Opin Infect Dis. 2008; 21(5):523–530.
18. Cabada MM, White AC Jr. New developments in epidemiology, diagnosis, and treatment of fascioliasis. Curr Opin Infect Dis. 2012; 25(5):518–522.
19. Katz N, Chaves A, Pellegrino J. A simple device for quantitative stool thick-smear technique in Schistosomiasis mansoni. Rev Inst Med Trop Sao Paulo. 1972; 14(6):397–400.
20. Marcos LA, Tagle M, Terashima A et al. Natural history, clinicoradi ologic correlates, and response to triclabendazole in acute massive fascioliasis. AmJTropMedHyg.2008; 78(2):222–227.
21. 21 FICA A, Dabanch J, Farias C et al. Acute fascioliasis—clinical and epidemiological features of four patients in Chile. Clin Microbiol Infect. 2012; 18(1):91–96.
22. McCarthy JS, Moore TA. Drugs for helminths. In: Bennet JE, Dolin R, Blaser MJ, editors. Mandell, Douglas, and Bennett's principles and practice of infectious diseases, 8th edn. Vol. 1. Philadelphia: Saun ders; 2015, p. 519–27.e3.
23. Fairweather I (2005) Triclabendazole: new skills to unravel an old (ish) enigma. J Helminthol 79: 227-234.
24. Robinson MW, Trudgett A, Hoey EM, Fairweather I (2002) Triclabendazole resistant Fasciola hepatica: beta-tubulin and response to in vitro treatment with triclabendazole. Parasitology 124: 325-338.
25. 6. Fairweather I (2009) Triclabendazole progress report, 2005-2009: an advancement of learning? J Helminthol 83: 139.
26. Keiser J, Engels D, Büscher G et al. Triclabendazole for the treat ment of

fascioliasis and paragonimiasis. Expert Opin Investig Drugs. 2005; 14(12):1513–1526.
27. Fairweather I. Triclabendazole progress report, 2005–2009: an advancement of learning? J Helminthol. 2009; 83(2):139–150.
28. Kelley JM, Elliott TP, Beddoe T et al. Current threat of triclabendazole resistance in Fasciola hepatica. Trends Parasitol. 2016; 32(6):458–469.
29. Stitt AW, Fairweather I. The effect of the sulphoxide metabo lite of triclabendazole (Fasinex®) on the tegument of mature and immature stages of the liver fluke, Fasciola hepatica. Parasitology. 1994; 108(5):555–567.
30. el-Tantawy WH, Salem HF, Mohammed Safwat NAS. Effect of fas cioliasis on the pharmacokinetic parameters of triclabendazole in humansubjects. Pharm World Sci. 2007; 29(3):190–198.
31. Lecaillon JB, Godbillon J, Campestrini J et al. Effect of food on the bioavailability of triclabendazole in patients with fascioliasis. Br J Clin Pharmacol. 1998; 45(6):601–604.
32. Hennessy DR, Lacey E, Steel JW et al. The kinetics of triclabendazole disposition in sheep. J Vet Pharmacol Ther. 1987; 10(1):64–72.
33. HienTT, TruongNT, MinhNHetal.Arandomizedcontrolledpilotstudy of artesunate versus triclabendazole for human fascioliasis in central Vietnam. AmJTropMedHyg.2008; 78(3):388–392.
34. Keiser J, Sayed H, el-Ghanam M et al. Efficacy and safety of artemether in the treatment of chronic fascioliasis in Egypt: exploratory phase-2 trials. PLoS Negl Trop Dis. 2011; 5(9):e1285.
35. HienTT, TruongNT, MinhNHetal.Arandomizedcontrolledpilotstudy of artesunate versus triclabendazole for human fascioliasis in central Vietnam. AmJTropMedHyg.2008; 78(3):388–392.
36. Humansubjects. Pharm World Sci. 2007; 29(3):190–198. 29 Favennec L, Jave Ortiz J, Gargala G et al. Double-blind, randomized, placebo-controlled study of nitazoxanide in the treatment of fascio liasis in adults and children from northern Peru. Aliment Pharmacol Ther. 2003; 17(2):265–270.
37. Cwiklinski, K.; O'Neill, S.M.; Donnelly, S.; Dalton, J.P. A prospective view ofanimal and human Fasciolosis. Parasite Immunol. 2016, 38, 558–568. [CrossRef][PubMed]
38. Molina-Hernández, V.; Mulcahy, G.; Pérez, J.; Martínez-Moreno, Á.; Donnelly, S.; O'Neill, S.M.; Dalton, J.P.; Cwiklinski, K. Fasciola hepatica vaccine: We may not be there yet but we're on the right road. Vet. Parasitol. 2015, 208, 101–111. [CrossRef] [PubMed]
39. 39 Flynn, R.J.; Musah-Eroje, M. Evasion of host immunity during Fasciola hepatica infection. Methods Mol. Biol. 2020, 2137, 107–115. [CrossRef] [PubMed]
40. 40. Vaccines 2020, 8, 553 11 of 15 7. 8. 9. Cwiklinski, K.; Jewhurst, H.; McVeigh, P.; Barbour, T.; Maule, A.G.; Tort, J.; O'Neill, S.M.; Robinson, M.W.; Donnelly, S.; Dalton, J.P. Infection by the helminth parasite Fasciola hepatica requires rapid regulation of metabolic, virulence, and invasive factors to adjust to its mammalian host. Mol. Cell. Proteom. 2018, 17, 792–809. [CrossRef]
41. 41. Dalton, J.P.; Robinson, M.W.; Mulcahy, G.; O'Neill, S.M.; Donnelly, S. Immunomodulatory molecules of Fasciola hepatica: Candidates for both vaccine and immunotherapeutic development. Vet. Parasitol. 2013, 195, 272–285. [CrossRef] [PubMed]
42. 42. Rodríguez, E.; Noya, V.; Cervi, L.; Chiribao, M.L.; Brossard, N.; Chiale, C.;

Carmona, C.; Giacomini, C.; Freire, T. Glycans from Fasciola hepatica modulate the host immune response and TLR-induced maturation of dendritic cells. PLoS Negl. Trop. Dis. 2015, 9, e0004234. [CrossRef]

43. 43. Sulaiman, A.A.; Zolnierczyk, K.; Japa, O.; Owen, J.P.; Maddison, B.C.; Emes, R.D.; Hodgkinson, J.E.; Gough, K.C.; Flynn, R.J. A trematode parasite derived growth factor binds and exerts influences on host immune functions via host cytokine receptor complexes. PLoS Pathog. 2016, 12, e1005991. [CrossRef]
44. 44. Liu, Q.; Huang, S.Y.; Yue, D.M.; Wang, J.L.; Wang, Y.; Li, X.; Zhu, X.Q. Proteomic analysis of Fasciola hepatica excretory and secretory products (FhESPs) involved in interacting with host PBMCs and cytokines by shotgun LC-MS/MS. Parasitol. Res. 2017, 116, 627–635. [CrossRef]
45. 45. Musah-Eroje, M.; Flynn, R.J. Fasciola hepatica, TGF-and host mimicry: The enemy within. Curr. Opin. Microbiol. 2018, 46, 80–85. [CrossRef]
46. 46. Sripa, B.; Jumnainsong, A.; Tangkawattana, S.; Haswell, M.R. Immune response to Opisthorchis viverrini infection and its role in pathology. Adv. Parasitol. 2018, 102, 73–95. [CrossRef]
47. 47. Zafra R, Pérez-Écija RA, Buffoni L, Moreno P, Bautista MJ, Martínez-Moreno A, et al. Early and late peritoneal and hepatic changes in goats immunized with recombinant cathepsin L1 and infected with Fasciola hepatica. J Comp Pathol. (2013) 148:373–84. Doi: 10.1016/j.jcpa.2012.08.007
48. 48. Molina-Hernández V, Mulcahy G, Pérez J, Martínez-Moreno Á, and Donnelly S, and O'Neill SM, et al. Fasciola hepatica vaccine: we may not be there yet but we're on the right road. Vet Parasitol. (2015) 208:101–11. Doi: 10.1016/j.vetpar.2015.01.004
49. 49. LopezP, TuñonMJ, GonzalezP, DiezN, BravoAM, Gonzalez-GallegoJ.Ductular proliferation and hepatic secretory function in experimental fascioliasis. Exp Parasitol. (1993) 77:36–42. Doi: 10.1006/expr.1993.1058
50. 50. Isseroff H, Sawma JT, Reino D. Fascioliasis: role of proline in bile duct hyperplasia. Science. (1977) 198:1157–9. Doi: 10.1126/science.929191
51. 51. Modavi S, Isseroff H. Fasciola hepatica: collagen deposition and other histopathology in the rat host's bile duct caused by the parasite and by proline infusion. Exp Parasitol. (1984) 58:239–44. Doi: 10.1016/0014-4894(84)90040-7
52. 51. Pérez J, Ortega J, Moreno T, Morrondo P, López-Sández C, Martínez-Moreno A. Pathological and immunohistochemical study of the liver and hepatic lymph nodes of sheep chronically reinfected with Fasciola hepatica, with or without triclabendazole treatment. J Comp Pathol. (2002) 127:30–6. Doi: 10.1053/jcpa.2002.0561
53. 52. Zafra R, Pérez-Écija RA, Buffoni L, Pacheco IL, Martínez-Moreno A, LaCourse EJ, et al. Early hepatic and peritoneal changes and immuneresponseingoatsvaccinated with a recombinant glutathione transferase sigma class and challenged with Fasciola hepatica. Res Vet Sci. (2013) 94:602–9. Doi: 10.1016/j.rvsc.2012.10.026
54. 53. Cabada MM, White AC Jr. New developments in epidemiology, diagnosis, and treatment of fascioliasis. Curr Opin Infect Dis. (2012) 25:518–22. Doi: 10.1097/QCO.0b013e3283567b7e
55. 54. Nyindo M, Lukambagire AH. Fascioliasis: an ongoing zoonotic trematode infection. Biomed Res Int. (2015) 2015:786195. Doi: 10.1155/2015/786195

56. Sripa, B.; Jumnainsong, A.; Tangkawattana, S.; Haswell, M.R. Immune response to Opisthorchis viverrini infection and its role in pathology. Adv. Parasitol. 2018, 102, 73–95.
57. Young, N.D.; Gasser, R.B. Opisthorchis viverrini draft genome-biomedical implications and future avenues. Adv. Parasitol. 2018, 101, 125–148.
58. MillánJC, MullR, FreiseSetal.Theefficacyandtolerabilityoftriclaben dazole in Cuban patients with latent and chronic Fasciola hepatica infection. Am J Trop Med Hyg? 2000; 63(5–6):264–269.
59. World Health Organization. Report of the who informal meeting on use of triclabendazole in fascioliasis control. https://www.who. int/neglected_diseases/preventive_chemotherapy/WHO_CDS_NTD_ PCT_2007.1.pdf [accessed 30 April 2019].
60. Hardman EW, Jones RLH, Davies AH. Fascioliasis—a large outbreak. Br Med J. 1970; 3:502–505.
61. Arjona R, Riancho JA, Aguado JM et al. Fascioliasis in developed countries: a review of classic and aberrant forms of the disease. Medicine (Baltimore). 1995; 74(1):13–23.
62. Farid Z, Kamal M, Woody J. Treatment of acute toxaemic fascioliasis. Trans R Soc Trop Med Hyg. 1988; 82(2):299.
63. Bassiouny HK, Soliman NK, el-Daly SM, Badr NM. Human fascioliasis in Egypt: effect of infection and efficacy of bithionol treatment. JTrop MedHyg. 1991; 94(5):333–337.
64. Yazgan-Aksoy D, Kerimo˘ glu U, Oto a et al. Fasciola hepatica infection: clinical and computerized tomographic findings of ten patients. Turk J Gastroenterol. 2006; 17(1):40–45. 55 Mansour-Ghanaei F, Shafaghi A, Fallah M. The effect of metronidazole in treating human fascioliasis. Med Sci Monit. 2003; 9(10): 127–130.
65. Arjona R, Riancho JA, Aguado JM et al. Fascioliasis in developed countries: a review of classic and aberrant forms of the disease. Medicine (Baltimore). 1995; 74(1):13–23.
66. Favennec L, Jave Ortiz J, Gargala G et al. Double-blind, randomized, placebo-controlled study of nitazoxanide in the treatment of fascio liasis in adults and children from northern Peru. Aliment Pharmacol Ther. 2003; 17(2):265–270.
67. Rossignol JF, Abaza H, Friedman H. Successful treatment of human fascioliasis with nitazoxanide. Trans R Soc Trop Med Hyg. 1998; 92(1):103–104.
68. Zumaquero-RíosJL, Sarracent-PérezJ, Rojas-GarcíaR.Fascioliasisand intestinal parasitosesaffectingschoolchildreninAtlixco, PueblaState, Mexico: epidemiology and treatment with nitazoxanide. PLoS Negl Trop Dis. 2013; 7(11):e2553.
69. Lukambagire AH, Mchaile DN, Nyindo M. Diagnosis of human fascio liasis in Arusha region, northern Tanzania by microscopy and clinical manifestations in patients. BMC Infect Dis. 2015; 15:578.
70. Hien TT, TruongNT, MinhNHetal.Arandomizedcontrolledpilotstudy of artesunate versus triclabendazole for human fascioliasis in central Vietnam. AmJTropMedHyg.2008; 78(3):388–392.
71. Keiser J, Sayed H, el-Ghanam M et al. Efficacy and safety of artemether in the treatment of chronic fascioliasis in Egypt: exploratory phase-2 trials. PLoS Negl Trop Dis. 2011; 5(9):e1285.
72. Humansubjects. Pharm World Sci. 2007; 29(3):190–198. 29 Favennec L, Jave Ortiz J, Gargala G et al. Double-blind, randomized, placebo-controlled study of nitazoxanide in the treatment of fascio liasis in adults and

children from northern Peru. Aliment Pharmacol Ther. 2003; 17(2):265–270.

73. Maco V, Marcos L, Delgado J et al. Efficacy and tolerability of two single-day regimens of triclabendazole for fascioliasis in Peruvian children. Rev Soc Bras Med Trop. 2015;48(4):445–453.
74. Villegas F, Angles R, Barrientos R et al. Administration of triclabenda zoleis safeandeffectiveincontrollingfascioliasis inanendemiccom munity of the Bolivian Altiplano. PLoS Negl Trop Dis. 2012;6(8):e1720.
75. el-Morshedy H, Farghaly A, Sharaf S et al. Triclabendazole in the treatment of human fascioliasis: a community-based study. East Mediterr Health J. 1999;5(5):888–894.
76. Talaie H, Emami H, Yadegarinia D et al. Randomized trial of a single, double and triple dose of 10 mg/kg of a human formulation of tri clabendazole in patients with fascioliasis. Clin Exp Pharmacol Physiol. 2004;31(11):777–782.

HOW TO CITE: Sapna A. Pandey, Monika Jadhao, Tricabendazole: Emerging Treatment For Human Fascioliasis, Int. J. of Pharm. Sci., 2024, Vol 2, Issue 3, 322-333. https://doi.org/10.5281/zenodo.10806040