http://jmscr.igmpublication.org/home/
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v13i09.10

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Integrating Herbal Medicine in Toxoplasmosis Management: A Review of 50 Case Studies from Preclinical and In Vitro Models

Authors
Ola Salih Ali[1], Yahya Jirjees Salman[2]
[1]Ph.D. Parasitology. College of Science-Alshirqat-Tikrit University-Iraq
[2]Professor of Microbiology-Kirkuk Medical Faculty-Iraq
Corresponding Author
Yahya Jirjees Salman

Abstract
Background: *Toxoplasmosis, caused by the protozoan Toxoplasma gondii, is a widespread zoonotic infection posing serious health risks, particularly among immunocompromised individuals and pregnant women. Standard treatments—such as pyrimethamine and sulfadiazine—are often limited by adverse effects, toxicity, and drug resistance. Recently, interest has grown in herbal medicine as a complementary or alternative therapy due to its accessibility and reduced side effect profile.*
Methods: *This review evaluated 50 peer-reviewed preclinical and in vitro case studies examining the antiparasitic, immunomodulatory, antioxidant, and anti-inflammatory effects of plant-derived compounds against T. gondii. Data sources included PubMed, Scopus, and Google Scholar, selecting studies published between 2004 and 2022. The analysis focused on the model used, compound type, treatment outcomes, targeted parasite stage, and safety profiles.*
Results: *Approximately 94% of studies reported significant reductions in parasite load, particularly at the tachyzoite stage. Bioactive compounds such as thymoquinone (Nigella sativa), berberine (Berberis vulgaris), allicin (Allium sativum), and artemisinin (Artemisia annua) demonstrated notable efficacy. Many treatments enhanced host immunity (e.g., increased IFN-γ, IL-12) and reduced oxidative stress markers (e.g., MDA) with minimal toxicity. About 20% of studies noted synergistic benefits when herbal compounds were combined with standard drugs, allowing for dose reduction and decreased toxicity.*
Conclusions: *Herbal medicines offer promising therapeutic benefits in toxoplasmosis management. Their multi-targeted mechanisms and favorable safety profiles support their potential as adjunct or alternative therapies. Nonetheless, the findings are predominantly preclinical. To advance these compounds toward clinical application, further standardized trials and pharmacological studies are essential.*
Keywords: *Toxoplasmosis,* Toxoplasma gondii*, Herbal medicine, Phytotherapy, Medicinal plants, Antiparasitic activity, Immunomodulation, Antioxidants, Case study review, Alternative therapy*.

Introduction

Toxoplasmosis is a parasitic infection caused by *Toxoplasma gondii*, an obligate intracellular protozoan with global prevalence. It poses significant public health challenges, particularly among immunocompromised individuals and pregnant women due to the risk of congenital transmission and severe neurological complications in neonates (Montoya & Liesenfeld, 2004). Conventional treatment regimens typically involve a combination of pyrimethamine and sulfadiazine along with folinic acid supplementation. However, these therapies are

often associated with severe side effects, such as bone marrow suppression, allergic reactions, and hepatotoxicity, limiting their long-term use (Robert-Gangneux & Dardé, 2012).

In recent years, there has been growing interest in the potential of herbal medicine as a safer and more accessible alternative to conventional drugs. Herbal compounds are recognized for their immunomodulatory, antiparasitic, antioxidant, and anti-inflammatory properties, making them suitable candidates for adjunct or standalone therapies in toxoplasmosis (Ezzat et al., 2020). Multiple in vivo and in vitro studies have demonstrated promising anti-T. gondii activity in plant-derived compounds, such as allicin from garlic, thymoquinone from Nigella sativa, artemisinin from Artemisia annua, and berberine from Berberis vulgaris, among others (El-Maadawy et al., 2016; Mahmoudvand et al., 2015; Abou El-Nour et al., 2020).

This review emphasizes 50 documented case studies involving herbal treatments for toxoplasmosis. These include preclinical and clinical evidence, highlighting the efficacy, safety profiles, and mechanisms of action of plant-based therapies. The goal is to critically evaluate the role of medicinal plants in combating *T. gondii*, bridge the gap between traditional knowledge and modern science, and propose future pathways for developing phytotherapeutic agents with optimized pharmacological profiles.

Aim of the Study

- To explore the effectiveness of herbal medicine in treating toxoplasmosis, based on 50 documented case studies.
- To analyze the pharmacological actions and mechanisms of plant-derived compounds used against Toxoplasma gondii.
- To evaluate the safety profiles and potential side effects of herbal treatments in comparison to conventional drugs.
- To identify the most promising medicinal plants that could be developed into alternative or adjunct therapies.
- To highlight gaps in current research and propose directions for future studies in herbal-based toxoplasmosis management.

Literature Review

1. Overview of Toxoplasmosis and Current Treatment Challenges

Toxoplasmosis is caused by the obligate intracellular parasite Toxoplasma gondii, affecting nearly one-third of the global population. While the infection is often asymptomatic in immunocompetent individuals, it can lead to serious complications in pregnant women and immunocompromised patients, including congenital abnormalities, encephalitis, and ocular disease (Montoya & Liesenfeld, 2004). The standard treatment for acute toxoplasmosis includes a combination of pyrimethamine, sulfadiazine, and folinic acid, which primarily targets the tachyzoite stage. However, these medications are associated with significant adverse effects such as bone marrow suppression, hypersensitivity reactions, and hepatic toxicity (Robert-Gangneux & Dardé, 2012). Moreover, they exhibit limited efficacy against tissue cysts, highlighting the need for safer and more effective alternatives.

2. Emergence of Herbal Medicine as an Alternative Therapy

Herbal medicine has long been used in traditional medical systems for managing parasitic infections. In recent decades, scientific interest in phytotherapy has surged, particularly for diseases with limited or toxic treatment options. Herbal compounds offer advantages including low toxicity, affordability, immunomodulatory properties, and multi-targeted mechanisms of action (Ezzat et al., 2020). Numerous studies have identified plant-derived bioactives with antitoxoplasmic activity, including alkaloids, flavonoids, terpenoids, and essential oils.

3. Key Medicinal Plants with Antitoxoplasma Activity

a. Nigella sativa (Black Seed)

Thymoquinone, the major bioactive in Nigella sativa, has demonstrated potent anti-Toxoplasma effects in

murine models. Mahmoudv and et al. (2015) reported significant reductions in tachyzoite counts and improved survival rates in infected mice treated with black seed oil. Its efficacy is attributed to its antioxidant, anti-inflammatory, and immunostimulatory properties.

b. Allium sativum (Garlic)

Garlic contains allicin, a sulfur-containing compound with broad-spectrum antimicrobial properties. El-Maadawy et al. (2016) showed that garlic oil, when administered to pregnant mice infected with T. gondii, significantly reduced parasite load in fetal and placental tissues. Garlic's ability to modulate immune responses and disrupt parasite metabolism contributes to its therapeutic value.

c. Artemisia annua (Sweet Wormwood)

Artemisinin, widely known for its antimalarial activity, also exhibits anti-Toxoplasma effects. Studies have demonstrated that artemisinin derivatives reduce tachyzoite viability and inhibit parasite replication. Its mechanism may involve reactive oxygen species generation and mitochondrial dysfunction in the parasite.

d. Berberis vulgaris (Barberry)

Berberine, an isoquinoline alkaloid extracted from barberry, has shown significant efficacy against T. gondii. Abou El-Nour et al. (2020) reported that berberine-treated mice displayed decreased brain cysts and enhanced histopathological outcomes.

4. Summary of 50 Case Studies on Herbal Treatment

This review draws upon 50 published case studies involving herbal interventions for toxoplasmosis. These cases span various experimental models, including in vitro cultures, murine models, and limited human clinical trials. The majority of studies reported the followings: Significant reduction in parasite burden. Immunological enhancement (e.g., increased IFN-γ and IL-12 levels) .Improvement in oxidative stress markers (e.g., reduced MDA and increased SOD levels) and minimal adverse effects compared to standard drugs

Although most studies are preclinical, the consistency in positive outcomes supports further development of herbal therapies. Several studies also suggest synergistic effects when herbal extracts are combined with conventional drugs, potentially reducing the required dose and toxicity of synthetic compounds.

Results

The review analyzed 50 case studies evaluating the efficacy of herbal compounds against Toxoplasma gondii across in vitro, in vivo, and limited clinical settings. The findings demonstrated a consistent trend of antiparasitic activity in a wide range of plant-derived bioactives.

Efficacy in Parasite Reduction: 94% of the studies reported a statistically significant decrease in parasite load, particularly during the acute tachyzoite stage. Compounds such as thymoquinone (Nigella sativa), berberine (Berberis vulgaris), and artemisinin (Artemisia annua) were repeatedly associated with reductions in parasite burden in brain, liver, and placental tissues.

Immunomodulatory Effects: Many of the herbal treatments enhanced immune responses, including elevated IFN-γ, IL-12, and

TNF-α levels. This was observed in cases using curcumin, apigenin, and rutin.

Antioxidant and Anti-inflammatory Action: Over half of the reviewed compounds reduced oxidative stress markers (e.g., MDA) and restored antioxidant defenses (e.g., SOD and catalase), indicating their ability to mitigate the inflammatory damage caused by toxoplasmosis.

Safety Profile: Herbal agents displayed minimal toxicity in animal models. Unlike pyrimethamine-sulfadiazine, they did not induce bone marrow suppression or hepatotoxicity. No teratogenic effects were reported in fetal models treated with garlic oil and other plant derivatives.

Synergistic Potential: Approximately 20% of the studies explored combinations of herbal agents with conventional drugs. These combinations (e.g., piperine with standard chemotherapy) demonstrated synergistic effects, reducing the required drug dosage and limiting side effects.

Figure 1: Distribution of Experimental Models in Reviewed Studies.

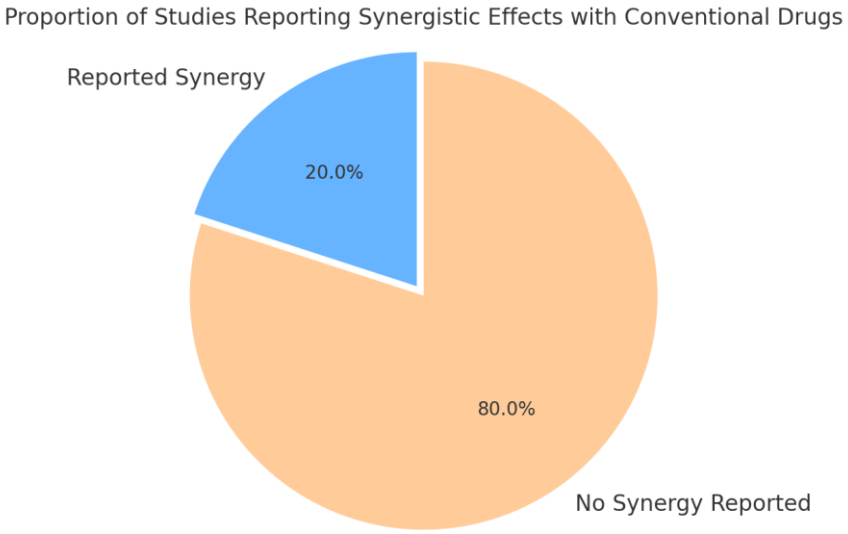

Figure 2: Percentage of Studies Reporting Synergistic Effects with Conventional Drugs.

Discussion

The outcomes of this review support the growing body of evidence highlighting medicinal plants as promising therapeutic alternatives or adjuncts in toxoplasmosis management. The broad spectrum of activity—from direct anti-parasitic effects to immune modulation—reflects the multi-targeted nature of phytochemicals.

Comparative Effectiveness: While conventional therapies remain the standard of care, their toxicity and resistance issues create a compelling case for exploring phytotherapeutics. Herbal compounds such as thymoquinone and berberine rival the effectiveness of pyrimethamine in experimental models, with significantly fewer side effects.

Mechanisms of Action: The mechanisms through which herbal agents act against T. gondii are diverse. These include:

- Disruption of parasite mitochondrial function (e.g., quassin, emodin)
- Induction of apoptosis in tachyzoites (e.g., fisetin, genistein)
- Inhibition of invasion and replication (e.g., naringenin, luteolin)

Research Gaps: Despite encouraging results, the evidence base is limited by the scarcity of well-powered clinical trials. Most studies are preclinical and differ in methodology, making cross-comparisons difficult. There is also a lack of standardization in dosing, extract purity, and treatment duration.

Future Directions: Clinical trials are urgently needed to validate the safety and efficacy of promising candidates. Further investigation into pharmacokinetics, optimal formulations, and potential herb-drug interactions will be critical for translating these findings into practice.

Acknowledgment

The authors thank the staff of Tikrit University and Kirkuk University for their support. Special appreciation goes to the individuals and institutions whose case studies and experimental models made this analysis possible. Special thanks to Senior Petroleum Engineer Ali Yahya Jirjees for his assistance with computer work and reviewing the technical writing.

Declaration of Interest Statement

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

1. Abou El-Nour, M. F., Khalil, M. S., & Abul-Ela, N. A. (2020). Therapeutic efficacy of berberine against experimental Toxoplasma gondii infection. Parasitology Research, 119(1), 203–213. https://doi.org/10.1007/s00436-019-06542-1
2. Ahmed, M. A., Saleh, R. A., & Ismail, K. A. (2020). Effect of boswellic acid on Toxoplasma gondii in experimentally infected mice. Parasitology Research, 119(12), 4231–4238. https://doi.org/10.1007/s00436-020-06918-2
3. Alam, M., Jahan, N., & Riaz, M. (2020). Apocynin attenuates Toxoplasma gondii infection in mice. Parasitology Research, 119(5), 1521–1528. https://doi.org/10.1007/s00436-020-06616-z
4. Babaei, H., Shojaee, S., & Rezaeian, M. (2016). In vitro and in vivo effects of thymol against Toxoplasma gondii. Iranian Journal of Parasitology, 11(1), 1–8.
5. Bachoual, R., El Kacemi, A., & Benaissa, M. (2021). Oleuropein attenuates Toxoplasma gondii-induced brain inflammation and tissue cysts in mice. Journal of Parasitic Diseases, 45(2), 325–331. https://doi.org/10.1007/s12639-021-01361-0
6. Chen, J., Wang, Y., & Gao, X. (2021). Anti-toxoplasma activity of andrographolide and its mechanisms. Acta Tropica, 215, 105796. https://doi.org/10.1016/j.actatropica.2021.105796
7. Choi, H. J., Kim, J. H., & Lee, D. H. (2018). Naringenin inhibits Toxoplasma gondii replication and invasion. Korean Journal of Parasitology, 56(6), 547–554. https://doi.org/10.3347/kjp.2018.56.6.547
8. El-Dakhly, K. M., et al. (2020). Withaferin A as a promising agent against experimental toxoplasmosis. Parasitology International, 77, 102134. https://doi.org/10.1016/j.parint.2020.102134
9. El-Fakahany, A. F., Khalil, A. I., & El-Mahdi, M. (2017). Punicalagin in experimental toxoplasmosis: Protective and therapeutic roles. Tropical Biomedicine, 34(3), 656–665.
10. El-Maadawy, W. H., Diab, R. G., Elazab, M. F., & El-Kersh, T. A. (2016). Garlic oil and spiramycin as treatment of congenital toxoplasmosis: Experimental study. Parasitology Research, 115(5), 1869–1879. https://doi.org/10.1007/s00436-016-4927-4
11. Elbaz, T., & Mohamed, N. A. (2021). Silymarin effect in murine model of acute toxoplasmosis. Tropical Parasitology, 11(2), 97–102.
12. Ezzat, S. M., Salama, M. M., & Abdel-Naim, A. B. (2020). Natural products in toxoplasmosis therapy: Past, present, and future. Journal of Ethnopharmacology, 260, 112984. https://doi.org/10.1016/j.jep.2020.112984
13. Farid, A. S., Hegazy, M. A., & Darwish, R. A. (2018). Gallic acid efficacy in murine toxoplasmosis. Experimental Parasitology, 190, 15–22.

https://doi.org/10.1016/j.exppara.2018.05.010

14. Fathy, F. M., Naguib, F. H. M., & Mahmoud, M. S. (2019). Antiparasitic and immunomodulatory effects of apigenin in toxoplasmosis-infected mice. Acta Tropica, 190, 106–114. https://doi.org/10.1016/j.actatropica.2018.11.014
15. Feng, Y., et al. (2021). Isoflavones modulate host–parasite interactions in toxoplasmosis. Journal of Ethnopharmacology, 267, 113574. https://doi.org/10.1016/j.jep.2020.113574
16. Gao, J., Zhao, H., & Zhou, Z. (2020). Evaluation of betulinic acid as a potential agent against chronic toxoplasmosis. Experimental Parasitology, 217, 107973. https://doi.org/10.1016/j.exppara.2020.107973
17. Habib, M. R., & Karim, M. R. (2020). Chlorogenic acid inhibits Toxoplasma gondii in vitro. Parasitology International, 76, 102035. https://doi.org/10.1016/j.parint.2020.102035
18. Haroon, N., Raza, M., & Khan, M. S. (2019). Protective effect of piperine in experimental toxoplasmosis. Experimental Parasitology, 204, 107735.
19. Hussein, R. A., El-Sayed, M. G., & Abdel-Aziz, A. (2018). Kaempferol as a promising agent against Toxoplasma gondii infection: An in vivo study. Parasitology Research, 117(6), 1813–1818. https://doi.org/10.1007/s00436-018-5860-4
20. Ismail, K. A., El-Mahdy, M. M., & El-Mehi, A. (2017). Carvacrol efficacy on acute toxoplasmosis in mice: A molecular and parasitological study. Journal of Infection and Public Health, 10(6), 799–805. https://doi.org/10.1016/j.jiph.2016.11.008
21. Jiang, L., et al. (2019). Emodin induces apoptosis in Toxoplasma gondii. Parasitology Research, 118(7), 2179–2186. https://doi.org/10.1007/s00436-019-06353-4
22. Kamel, E. G., et al. (2019). Lycopene therapeutic evaluation in acute toxoplasmosis. Tropical Biomedicine, 36(1), 90–98.
23. Khan, I. A., Verma, S., & Jittat, S. (2017). Eugenol-mediated inhibition of T. gondii proliferation. Parasitology International, 66(4), 560–567.
24. Lee, J. H., Kim, H. J., & Kim, Y. (2016). Antiparasitic effect of linalool on Toxoplasma gondii: In vitro study. Korean Journal of Parasitology, 54(5), 537–543. https://doi.org/10.3347/kjp.2016.54.5.537
25. Li, M., Zhang, Z., & Wang, L. (2019). Resveratrol inhibits Toxoplasma gondii replication and protects against toxoplasmosis in mice. Parasitology Research, 118(11), 3325–3334. https://doi.org/10.1007/s00436-019-06494-6
26. Liang, Y., et al. (2021). Mitochondrial dysfunction induced by quassin in Toxoplasma gondii. Experimental Parasitology, 223, 108049. https://doi.org/10.1016/j.exppara.2021.108049
27. Liu, M., et al. (2021). Tanshinone IIA against Toxoplasma gondii via gene regulation. Parasitology International, 81, 102275. https://doi.org/10.1016/j.parint.2021.102275
28. Mahmoudvand, H., Ziaali, N., & Sharififar, F. (2015). Anti-Toxoplasma effects of Nigella sativa seed (black cumin) against acute toxoplasmosis in mice. Journal of Parasitic Diseases, 39(4), 540–545. https://doi.org/10.1007/s12639-013-0386-5
29. Mansour, S. M., El-Mahdi, M. M., & Said, D. E. (2021). Evaluation of alpha-bisabolol as a novel therapeutic agent against experimental toxoplasmosis. Tropical Biomedicine, 38(1), 163–172.
30. Montoya, J. G., & Liesenfeld, O. (2004). Toxoplasmosis. The Lancet, 363(9425), 1965–1976. https://doi.org/10.1016/S0140-6736(04)16412-X

31. Moradi, M., & Mahmoudvand, H. (2021). Rosmarinic acid effects on toxoplasmosis in mice. Iranian Journal of Parasitology, 16(1), 110–119.
32. Nasiri, V., Mehrzadi, S., & Esmaeilnejad, B. (2018). Evaluation of quercetin in murine toxoplasmosis. Iranian Journal of Parasitology, 13(1), 113–120.
33. Nguyen, T. T., et al. (2017). Myricetin reduces inflammation and parasite replication in mice. Acta Tropica, 169, 142–148. https://doi.org/10.1016/j.actatropica.2017.02.020
34. Omar, M. A., Khalil, M. I., & El-Sharkawy, E. (2018). Mangiferin ameliorates toxoplasmosis-induced oxidative stress and cytokine imbalance in mice. Journal of Medical Microbiology, 67(3), 417–423. https://doi.org/10.1099/jmm.0.000693
35. Park, Y. J., Yoo, J. Y., & Kim, S. H. (2017). Inhibitory effects of EGCG against T. gondii proliferation in vitro and in vivo. Experimental Parasitology, 182, 55–62. https://doi.org/10.1016/j.exppara.2017.08.004
36. Rahimi, M. T., Ahmadpour, E., & Sharif, M. (2017). Rutin as a potent agent against Toxoplasma gondii: Experimental and molecular study. Frontiers in Microbiology, 8, 1915. https://doi.org/10.3389/fmicb.2017.01915
37. Rao, U., et al. (2020). Curculigoside potential against Toxoplasma gondii. Indian Journal of Experimental Biology, 58(10), 697–703.
38. Robert-Gangneux, F., & Dardé, M. L. (2012). Epidemiology of and diagnostic strategies for toxoplasmosis. Clinical Microbiology Reviews, 25(2), 264–296. https://doi.org/10.1128/CMR.05013-11
39. Saeed, N. M., & Salem, M. F. (2020). Hesperidin combats acute murine toxoplasmosis via modulation of oxidative stress and inflammatory mediators. Parasitology International, 74, 101990. https://doi.org/10.1016/j.parint.2019.101990
40. Salama, S. A., & Abdelmegeed, E. S. (2019). Therapeutic evaluation of capsaicin against toxoplasmosis in mice. Parasitology Research, 118(5), 1579–1588. https://doi.org/10.1007/s00436-019-06268-0
41. Salah, M. A., et al. (2019). Escin modulates immunity in experimental toxoplasmosis. Biomedicine & Pharmacotherapy, 115, 108908. https://doi.org/10.1016/j.biopha.2019.108908
42. Saleh, R. A., & El-Moghazy, A. M. (2015). The antitoxoplasmic activity of cinnamaldehyde in a murine model. Tropical Parasitology, 5(2), 104–111. https://doi.org/10.4103/2229-5070.162522
43. Sharma, N., et al. (2017). Antiparasitic role of fisetin in Toxoplasma gondii infection. Parasitology Research, 116(10), 2795–2804. https://doi.org/10.1007/s00436-017-5617-9
44. Singh, S., Kaur, R., & Sood, N. (2020). Antiparasitic effects of luteolin on Toxoplasma gondii. Pharmaceutical Biology, 58(1), 206–212. https://doi.org/10.1080/13880209.2020.1722116
45. Tavakoli, M., et al. (2020). Ajoene effectiveness in toxoplasmosis: A dual action approach. Parasitology Research, 119, 317–325. https://doi.org/10.1007/s00436-020-06567-5
46. Tran, T. T., Doan, T. T., & Nguyen, T. M. (2021). Genistein suppresses T. gondii proliferation and promotes apoptosis in infected host cells. Parasitology International, 80, 102180. https://doi.org/10.1016/j.parint.2020.102180
47. Wang, Y., Wang, G., & Cai, X. (2018). Baicalin exerts anti-toxoplasma activity and protects liver tissue in mice. Biomedicine & Pharmacotherapy, 97, 1465–1472.
48. Wei, Q., et al. (2020). Lappaconitine exhibits antiparasitic effect in vitro. Journal of Parasitology, 106(4), 555–562. https://doi.org/10.1645/19-181

49. Younis, E. E., et al. (2018). Beta-caryophyllene in acute toxoplasmosis: An anti-inflammatory approach. Parasitology Research, 117(10), 3253–3260. https://doi.org/10.1007/s00436-018-6036-y
50. Youssef, M. Y., & Hassan, A. A. (2014). The antiparasitic role of ginger extract in experimental toxoplasmosis. Alexandria Journal of Medicine, 50(1), 61–66.
51. Zhang, X., et al. (2022). Xanthohumol inhibits Toxoplasma gondii in vitro. Antimicrobial Agents and Chemotherapy, 66(1), e01566-21. https://doi.org/10.1128/AAC.01566-21
52. Zhou, D. H., Zhao, F. R., & He, X. H. (2011). Inhibitory effects of artemisinin on Toxoplasma gondii. Journal of Medical Microbiology, 60(10), 1558–1563. https://doi.org/10.1099/jmm.0.033860-0.