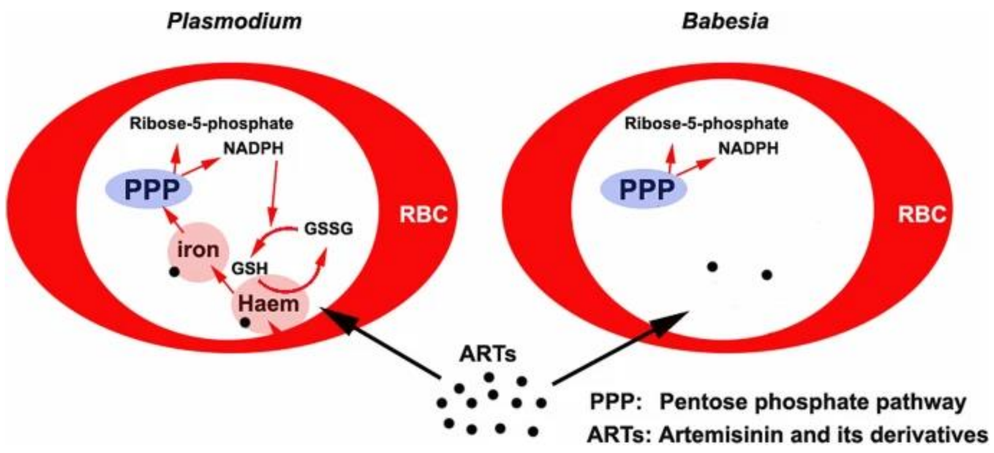
Survey on repurposing of anti-parasitic drugs in babesiosis treatment

Aleksandar Cvetkovski [a], Alfonso T. García-Sosa[b]

[a] University "Goce Delcev" Stip Faculty of medical science Krste Misirkov b.b. P. fax. 201, 2000 Stip Country: Republic of Macedonia

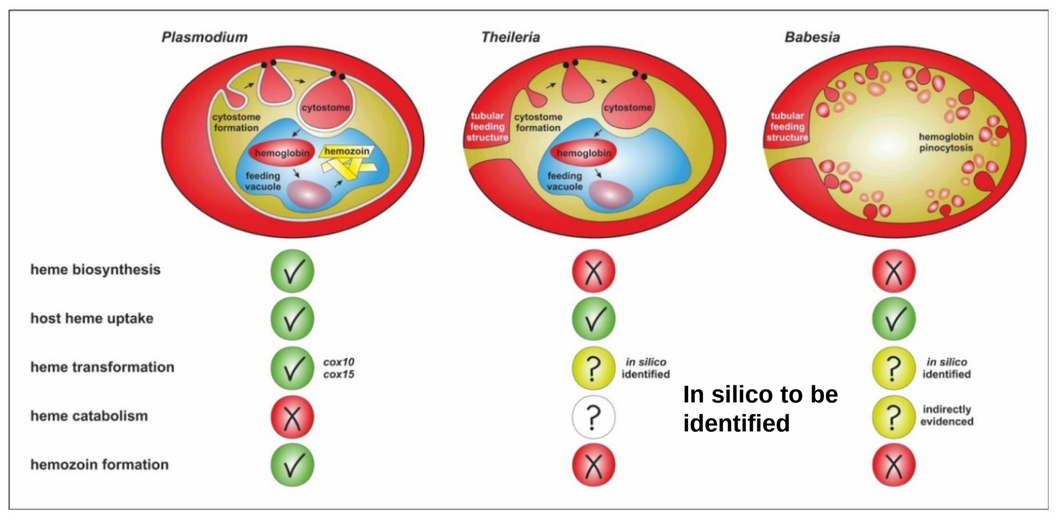
[b]Institute of Chemistry, University of Tartu Ravila 14a 50411Tartu, Estonia

e-mail: aleksandar.cvetkovski@ugd.edu.mk



Si, W., *et al.Parasites Vectors* 16, 193 (2023).

Differences in mechanism of action of arthemisin due to utilization of haem or iron in hemoglobin



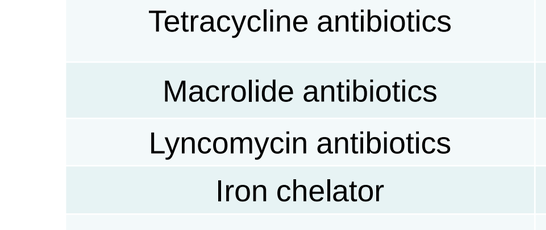
Sojka, D et al. Microorganisms 2022, *10*(8), 1651;

Cellular differences of Plasmodium, Theileria and Babesia trophozoites uptaking and processing host RBC cytosol proteins, including the utilization and detoxification of resulting heme molecules.

Drug group	Compounds	targets	IC_{50}
Naphtoquinone	Atovaquone		93.61 ± 6.01 nM
Aromatic diamidine	Diminazene aceturate, Pentamidine isethionate		88.43 ± 10.94 nM, 102.01 ± 1.80 nM
Artemisinine compounds	Artesunate, Dihydroartemisinine	cytochrome bc_1 complex of the mitochondrial electron transport chain	878.89 ± 27.13 nM 937.50 ± 45.21 nM
Tetracycline antibiotics	Doxycycline hydrochloride Minocycline hydrochloride		30.60 ± 6.77 μM 29.89 ± 0.92 μM
Macrolide antibiotics	Azithromycin	translation machinery in the apicoplast	5.44 ± 0.54 μM
Lyncomycin antibiotics	Clindamycin phosphate	protein synthesis in the apicoplast	108.83 ± 11.18 μM
Iron chelator	Deferocamine mesylate		6.45 ± 3.43 μM
Imidazole antifungals	Clotrimazole Ketoconazole		7.74 ± 2.35 μM 13.58 ± 5.96 μM
Quinoline-containing compounds	Chloroquine diphosphate Quinine hemisulfate	bind to phospholipids and to accumulate in membranous structures, including the parasite plasma membrane, the endoplasmic reticulum, and the mitochondrion, DNA intercalator, purine nucleoside phosphorylase (PfPNP) Sci. Transl. Med. 2019;11	178.65 ± 28.79 μM 2.61 ± 2.75 μM
Nitroimidazole antiprotozoals	Metronidazole		>1000 μM
ACE inhibitors	Fosinopril, prodrug	*B. duncani* fosinopril esterase BdFE1 dipeptidyl carboxypeptidase conversion of fosinopril to its active form fosinoprilat	IC_{50} 42-fold higher than that of the prodrug

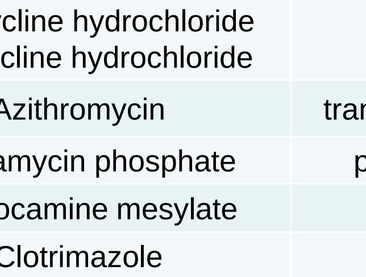
Vet.Parasit. 2023, 324:110055
Asian Pac J Trop Biomed 2015; 5(11): 932–936

Roles of the metal chelator drugs in treatment of babesiosis



Ethylene glycol bis (beta-aminoethylether)-N,N,N,N-tetraacetic acid (EGTA) is a chelating agent capable of binding to positively-charged metal ions, including a Ca2+

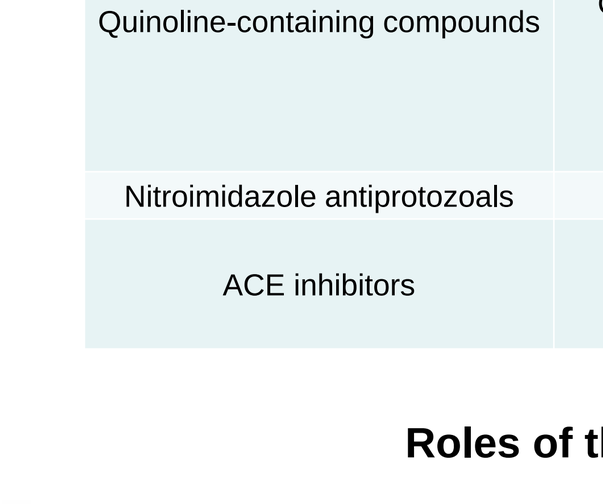
Parasitology (2006), 133, 289–294

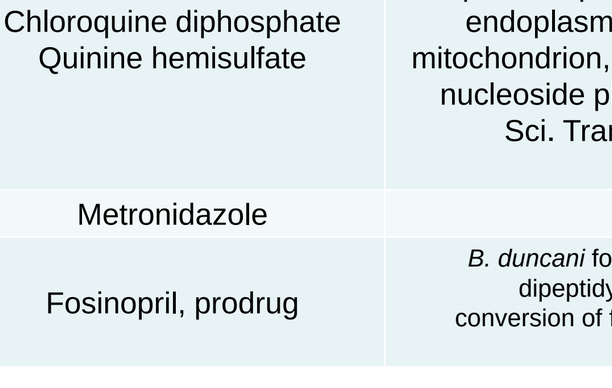


Deferoxamine, iron chelator

Vet. Parasitology 324 (2023) 110055

mitoDFO





J Exp Med. 2016;213(7):1307-1318

(A) Location of atovaquone and ELQ-316 resistance mutations in the Q_o and Q_i sites of the cytochrome (B). Quinol oxidation at the Qo site and ubiquinone reduction takes place at the Qi site of complex III (cytochrome bc1 complex) in the mitochondrial membrane of B. microti. Atovaquone inhibits the Qo site where as ELQs inhibit the Qi site of BmCytb protein (Doggett et al., 2012).

Electrochemical gradient (Δψ) across the inner mitochondrial membrane (IMM) is a driving force for specific experimental targeting of this lipid organelle. It is the interplay of sufficiently lipophilic cations with Δψ electrostatic gradient that allows the uptake and accumulation of molecules in the mitochondrion.This tool offers a wide range of applications, for example, as an imaging probe, a biochemical marker, and, importantly, as a vector for therapeutics.

ACS Infect Dis. 2024 Feb 9; 10(2): 676–687

In Silico Survey and Characterization of Babesia microti Functional and Non-Functional Proteases

Understand the biology and pathogenicity of this parasite and to explore proteases as targets for developing novel therapeutic interventions.
Proteases belonging to the aspartic, cysteine, threonine, serine, and metallopeptidase types encoded by B. microti.

Pathogens 2021, 10, 1457.
https://doi.org/10.3390/pathogens10111457

CA21111 - One Health drugs against parasitic vector borne diseases in Europe and beyond (OneHealthdrugs)