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Review Article

Antiparasitic Activity of Essential Oils Against the Parasite *Trypanosoma cruzi*: An Integrative Review

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Abstract

Trypanosoma cruzi is identified as the etiological agent of Chagas disease, a neglected tropical disease that affects millions of individuals in vulnerable regions. Available treatments have limitations due to inefficacy against resistant strains and severe side effects. In this context, medicinal plants have been considered promising therapeutic alternatives, with essential oils (EOs) standing out for their antiparasitic properties and potential for the development of new drugs. Addressing this issue, an integrative literature review was conducted to compile reports on the activity of EOs against *T. cruzi* from 2003 to 2023. Articles were selected from recognized databases, including PUBMED, Scopus, Web of Science, SCIELO, ScienceDirect, and Google Scholar. The results highlighted more than 60 plant species identified as promising, with the highest numbers reported in the families Myrtaceae (14 species), Annonaceae (10 species), and Verbenaceae (10 species). Among the species with the greatest anti-*Trypanosoma cruzi* potential, *Duguetia quitarensis* (IC_{50} = 0.26 µg/mL, trypomastigotes), *Guatteria punctata* (IC_{50} = 0.029 µg/mL, trypomastigotes), *Fusaea longifolia* (IC_{50} = 0.3 µg/mL, trypomastigotes), *Dysphania ambrosioides* (IC_{50} = 1.9–12.2 µg/mL, amastigotes), and *Phania matricarioides* (IC_{50} = 2.2 µg/mL, amastigotes) stood out. These findings suggest that essential oils hold significant potential for controlling and reducing mortality associated with Chagas disease.

Keywords: *Medicinal plants; Antiparasitic; American trypanosomiasis.*

Introduction

Trypanosoma cruzi is a protozoan parasite and the etiological agent of Chagas disease [1]. It is classified within the family Trypanosomatidae, which is part of the order Kinetoplastidae. This pathology is named after its discoverer, Dr. Carlos Chagas, who identified it in 1909. Today, it remains a disease that affects thousands of people worldwide, predominantly poor populations with limited or no access to healthcare [2].

Although there is no cure, treatments are available, though they are often ineffective and toxic. Currently, the treatment for the disease consists of nitro derivatives such as benznidazole (BZ) and nifurtimox [2,3]. However, these drugs are old and inadequate, as they can induce severe side effects and are becoming ineffective against resistant strains of the parasite [3].

This pathology receives little attention for the development of safer and more effective drugs. For these reasons, Chagas disease is classified as a neglected tropical disease (NTD) [4]. NTDs are defined as a group of communicable diseases that predominantly affect poor and vulnerable populations in approximately 150 countries, with a focus on Africa, Asia, Latin America, and the Caribbean, where the highest number of cases are reported [5-7]. Statistics reveal that this pathology affects over 1.5 billion people, and approximately 3 billion people are at risk of contracting one or more NTDs worldwide [4,7].

Due to the lack of access to treatment options or their ineffectiveness, populations often turn to traditional methods. One such method is the ancient use of medicinal plants, which are an integral part of human evolution and were the first therapeutic resources for curing diseases, particularly in underserved communities [8]. In this context, the search for new drugs has been steadily increasing, and plant-based products have become a "living pharmacy" due to their arsenal of phytochemical compounds, which show promising results with diverse potential for human exploration in the production of plant-based products [9].

This growing scientific research into alternative treatment methods focuses on studying and exploring the potential of medicinal plants in the search for new pharmacological products to combat parasitic diseases. These products aim not only to target etiological agents but also to address the resistance these agents have been acquiring [10]. The emergence of resistant strains has become a pandemic problem due to the limited therapeutic options. The ability of these organisms to acquire resistance has raised significant concerns among healthcare professionals [11,12].

In this context, essential oils (EOs) are being explored for their antiparasitic effects. These are complex mixtures of secondary metabolites known as phytochemicals, which are responsible for various biological effects on the target microorganism [13]. Substances that can inhibit the growth of microorganisms or even cause their death are defined as potential antimicrobials [14]. Essential oils are the subject of various exploratory studies due to their promising effects in microbiology [15]. In recent years, many plants have been evaluated not only for their antibacterial activity but also as agents that modify antibiotic resistance [16].

Given the growing concern about the increasing number of Chagas disease cases, its importance for the World Health Organization, as well as the previously mentioned aspects related to current treatments, the resistance that these protozoa have been acquiring, and the potential solutions found in current research focused on plant-based products, this study aimed to conduct a systematic review of the literature published in the last twenty years (2003-2023) on the etiological agent *T. cruzi* and current perspectives.

2. Methodology

This study was conducted through an integrative literature review, with the collection of articles researched from the following databases: Scopus©. For the search, keywords such as “Essential oil” AND “Trypanosoma cruzi,”. The inclusion criteria covered articles published in English, available in full, that analyzed the potential anti-*Trypanosoma* activity of essential oils, published and indexed in the databases between 2003 and 2023.

Initially, 102 articles were selected, and exclusion criteria were applied to eliminate review articles, e-books, book chapters, editorials, graduation reports, dissertations, theses, conference abstracts, as well as studies focused on extracts, isolated chemical compounds, inactive essential oils, and fixed oils, along with articles that did not meet the theme or objectives of the review. After these exclusions, 50 articles remained for the final analysis.

3. Results and Discussion

The analysis of the 50 articles resulted in the organization of relevant information, summarized in Table 1. The data includes the botanical family, species names, active concentrations or results (50% Inhibitory Concentration (IC_{50}), Efficiency Concentration (EC_{50}), and Minimum Lethal Concentration (MLC); the tested strains, the major constituents of the essential oils (when identified), and the mechanisms of action (when evaluated).

More than 60 plant species were investigated due to their promising activity against *Trypanosoma cruzi*, as described by various authors. The most frequently addressed botanical families were Myrtaceae (14 species), Annonaceae (10 species), and Verbenaceae (10 species).

Table 1. Potential antiparasitic activity of essential oils against *Trypanosoma cruzi* strains, along with their respective active concentrations, major compounds, and mechanisms of action.

FAMILY	SPECIES	ACTIVE CONCENTRATION/ RESULT	STRAIN USED	MAJOR CONSTITUENTS	MECHANISM OF ACTION	REFERENCE
AMARANTHACEAE	*Dysphania ambrosioides* (L.) Mosyakin & Clemants	IC_{50} = 8.7 µg/mL (trypomastigotes) IC_{50} = 1.9 - 12.2 µg/mL (amastigotes)	*T. cruzi* (Y strain) *T. cruzi* (Tulahuen CL2)	cis-piperitone oxide (30.3%)	Breakdown of mitochondrial membrane potential and modification of redox indexes	[17] [18]
ANNONACEAE	*Annona coriacea* Mart.	IC_{50} = 168.50 µg/mL (trypomastigotes)	*T. cruzi* (Y strain)	Bicyclogermacrene (39.8%)	--	[19]
	Annona crassiflora Mart.	IC_{50} = 5.31 µg/mL (trypomastigotes)	*T. cruzi* (Y strain)	α-amorphene (43.6 %)	--	[20]
	Annona squamosa L.	IC_{50} = 14.9 µg/mL (epimastigotes) IC_{50} = 12.7 µg/mL (trypomastigotes)	*T. cruzi*	(E)-caryophyllene (27.4%)	After microscopic analysis, it was observed that changes occurred in the parasite's membrane, probably caused by the activity of the essential oil (EO).	[21]
	Annona vepretorum Mart.	IC_{50} = 16.2-31.9 µg/mL (epimastigotes) IC_{50} = 11.2 µg/mL (trypomastigotes)	*T. cruzi* (Y strain) *T. cruzi*	Bicyclogermacrene (39.0-43.7%)	After microscopic analysis, it was observed that changes occurred in the parasite's membrane, likely caused by the activity of the essential oil (EO).	[21] [22]
	Bocageopsis multiflora (Mart.) R. E. Fr.	IC_{50} = 0.46 µg/mL (trypomastigotes)	*T. cruzi* (Tulahuen strain)	cis-Linalool oxide (furanoid) (33.1%)	--	[23]
	Duguetia quitarensis Benth.	IC_{50} = 0.26 µg/mL (trypomastigotes)	*T. cruzi* (Tulahuen strain)	4-Heptanol (33.8%)	--	[23]
	Fusaea longifolia (Aubl.) Saff.	IC_{50} = 0.3 µg/mL (trypomastigotes)	*T. cruzi* (Tulahuen strain)	No major constituent	--	[23]
	Guatteria punctata (Aubl.) R.A.Howard	IC_{50} = 0.029 µg/mL (trypomastigotes)	*T. cruzi* (Tulahuen strain)	No major constituent	--	[23]
	Xylopia frutescens Aubl.	IC_{50} = 20.2 µg/mL (epimastigotes) IC_{50} = 11.9 µg/mL (trypomastigotes)	*T. cruzi* (Y strain)	(E)-caryophyllene (24.8%) Bicyclogermacrene (20.8%)	--	[24]
	Xylopia laevigata (Mart.) R. E. Fries	IC_{50} = 27.7-93.9 µg/mL (epimastigotes) IC_{50} = 13.4 µg/mL (trypomastigotes)	*T. cruzi* (Y strain)	Germacrene D (27.0%),	--	[24] [25]
APIACEAE	*Cuminum cyminum* L.	IC_{50} = 131.0 µg/mL (epimastigotes)	*T. cruzi* (NINOA strain)	Cuminaldehyde (41.3%)	--	[26]
	Pimpinella anisum L.	IC_{50} = 52.0 µg/mL (epimastigotes)	*T. cruzi* (NINOA strain)	trans-Anethole (88.9%)	--	[26]

Table 1 continued...

ASTERACEAE	*Ambrosia tenuifolia* Spreng.	IC_{50} = 59.7 µg/mL (epimastigotes)	*T. cruzi* (RA strain)	Germacrene D (22.9%)	--	[27]
	Artemisia absinthium L.	GI_{50} = 144.6 µg/mL (epimastigotes)	*T. cruzi* (Y strain)	cis-epoxycimene (39.8%)	--	[28]
	Artemisia pedemontana subsp. assoana (Willk.) Rivas Mart.	(Cultivation – Green house) IC_{50} = 20.3 µg/mL (epimastigotes) (Cultivation – Aeroponic) IC_{50} = 72.1 µg/mL (epimastigotes)	*T. cruzi* (Y strain)	1,8 cinolene (22,8% - Green house/ 25,8% - aeroponic)	--	[29]
	Baccharis parvidentata Malag.	IC_{50} = 5.2 µg/mL (amastigotes)	*T. cruzi* (Tulahuen CL2)	No major constituent	--	[30]
	Baccharis punctulata DC.	Fraction 2, IC_{50} = 3.95 µg/mL (epimastigotes)	*T. cruzi* (Dm 28 strain)	β-Pinene (44.02 %) Limonene (20.13 %)	--	[31]
	Baccharis spicata (Lam.) Baill.	Fraction 4, IC_{50} = 4.43 µg/mL (epimastigotes)	*T. cruzi* (Dm 28 strain)	β-Pinene (32.60 %) Limonene (37.56 %)	--	[31]
	Phania matricarioides (Spreng.) Griseb.	IC_{50} = 2.2 µg/mL (amastigotes)	*T. cruzi* (Tulahuen CL2)	Lavandulyl acetate (40.1%)	--	[32]
	Vernonanthura brasiliana (L.) H.Rob.	Folhas/ IC_{50} = 72 µg/mL (epimastigotes) Flores/ IC_{50} = 88 µg/mL (epimastigotes) Raiz/ IC_{50} = 70 µg/mL (epimastigotes)	*T. cruzi*	No major constituent	--	[33]
BORAGINACEAE	*Varronia curassavica* Jacq.	LC_{50} = 92.01 µg/mL (epimastigotes)	*T. cruzi* (CL-B5 clone)	α-pinene (45.71%)	--	[34]
BURSERACEAE	*Protium ovatum* Engl.	Leaves/ IC_{50} = 28.55 µg/ml (trypomastigotes) Fruto/ IC_{50} = 1.2 µg/mL (trypomastigotes)	*T. cruzi* (Y strain)	Fruit/ β-myrcene (62.0 %)	--	[35] [36]
EUPHORBIACEAE	*Croton linearis* Jacq.	IC_{50} = 197.26 µg/mL (trypomastigotes)	*T. cruzi* (Y strain)	No major constituent	--	[37]
FABACEAE	*Myrocarpus frondosus* Allemão	IC_{50} = 60.7 µg/mL (epimastigotes)	*T. cruzi*	No major constituent	--	[13]
LAURACEAE	*Aniba rosaeodora* (var. amazonica Ducke)	IC_{50} = 150.5 µg/mL (epimastigotes)	*T. cruzi* (SC2005 strain)	Linalool (93.60%)	--	[38]
	Cinnamomum verum J. Presl.	IC_{50} = 22.0 - 24.13 µg/mL (epimastigotes)	*T. cruzi* (NINOA strain) *T. cruzi*	Cinnamaldehyde (73.3 – 81.52 %)	--	[26] [13]
LAMIACEAE	*Hypenia salzmannii* (Benth.) Harley	IC_{50} = 42.1 µg/mL (epimastigotes)	*T. cruzi* (Y strain)	No major constituent	--	[39]
	Hyssopus officinalis L.	EC_{50} = 110.0 µg/mL (epimastigotes)	*T. cruzi* (Y strain)	Isopinocamphone (27.70%)	--	[40]
	Melissa officinalis L.	Reduction in epimastigotes viability by 71.34%.	*T. cruzi* (MHOM/ CO/88/UA301)	Geranial (35.69%) Z-citral (25.51%)	--	[15]
	Origanum vulgare L.	IC_{50} = 175.0 µg/mL (epimastigotes) IC_{50} = 115.0 µg/mL (trypomastigotes)	*T. cruzi* (Y strain)	3-ciclohen-1-ol (26.2%)	Transmission electron microscopy showed cytoplasmic swelling and alterations in plasma and flagellar membrane	[41]
	Satureja macrantha C. A. Mey	MLC = 12.5 µg/mL (epimastigotes)	*T. cruzi* (Tulahuen strain)	No major constituent	--	[42]
	Tetradenia riparia (Hochst.) Codd	IC_{50} = 18.6 µg/mL (trypomastigotes) IC_{50} = 76.2 µg/mL (amastigotes)	*T. cruzi* (Y strain)	Aromadendrene oxide (20.0%)	--	[17]
	Thymus vulgaris L.	IC_{50} = 77.0 µg/mL (epimastigotes) IC_{50} = 38.0 µg/mL (trypomastigotes)	*T. cruzi* (Y strain)	Thymol (80.4%)	Transmission electron microscopy showed cytoplasmic swelling and alterations in plasma and flagellar membrane	[41]

Table 1 continued...

MYRTACEAE	*Campomanesia xanthocarpa* (Mart.) O.Berg	IC_{50} = 3.4 µg/mL (trypomastigotes)	*T. cruzi* (Y strain)	No major constituent	--	[43]
	Eugenia acutata Miq.	IC_{50} = 1.4 µg/mL (trypomastigotes)	*T. cruzi* (Y strain)	No major constituent	--	[43]
	Eugenia brejoensis Mazine	IC_{50}=12.5 µg/mL (amastigote) IC_{50}=29 µg/mL (epimastigotes) IC_{50}= 17.39 µg/mL (trypomastigotes)	*T. cruzi* (Y strain)	No major constituent	--	[39]
	Eugenia dysenterica (Mart.) DC.	IC_{50}= 9.5 µg/mL (trypomastigotes)	*T. cruzi* (Y strain)	No major constituent	--	[44]
	Eugenia florida DC.	IC_{50} = 0.3 µg/mL (trypomastigotes)	*T. cruzi* (Y strain)	α-pinene (22.1%)	--	[43]
	Eugenia klotzschiana O. Berg	IC_{50} = 20.2 µg/mL (trypomastigotes)	*T. cruzi*	β-caryophyllene (21.1%)	--	[45]
	Eugenia uniflora L.	IC_{50} = 70 µg/mL (epimastigotes)	*T. cruzi*	No major constituent	--	[13]
	Eugenia widgrenii Sond. ex O.Berg	IC_{50} = 7.4 µg/mL (trypomastigotes)	*T. cruzi* (Y strain)	No major constituent	--	[43]
	Myrcia glomerata (Cambess.) G.P.Burton & E.Lucas	IC_{50} = 8.7 µg/mL (trypomastigotes)	*T. cruzi* (Y strain)	No major constituent	--	[43]
	Myrcia loranthifolia (DC.) G.P.Burton & E.Lucas	IC_{50} = 1.6 µg/mL (trypomastigotes)	*T. cruzi* (Y strain)	No major constituent	--	[43]
	Plinia peruviana (Poir.) Govaerts	IC_{50} = 2.7 µg/mL (trypomastigotes)	*T. cruzi* (Y strain)	No major constituent	--	[43]
	Psidium guajava L.	IC_{50} = 4.0 µg/mL (trypomastigotes) Flores/ IC_{50} = 14.6 µg/mL (trypomastigotes)	*T. cruzi* (Y strain) *T. cruzi*	Flores/ α-cadinol (37.8%)	--	[43] [46]
	Psidium myrtoides O. Berg	IC_{50} = 54.05 µg/mL (trypomastigotes)	*T. cruzi* (G strain)	β-caryophyllene (21.62%)	--	[47]
	Syzygium aromaticum (L.) Merr. & L.M.Perry	IC_{50} = 64.5 µg/mL (amastigotes) IC_{50} = 28.6 - 56.0 µg/mL (epimastigotes); Decrease in blood culture and parasitic load with the dose of 100 mg/kg/day. IC_{50} = 57.5 µg/mL (trypomastigotes);	*T. cruzi* (NINOA strain) *T. cruzi* (Y strain) *T. cruzi* (SC2005 strain)	Eugenol (53.23 - 86.34%) β-caryophyllene (24.9%)	--	[26] [48] [49] [50]
PIPERACEAE	*Piper aduncum* L.	IC_{50} = 9.0 µg/mL (amastigotes) IC_{50} = 84.7 µg/mL (epimastigotes) IC_{50} = 2.8-12.1 µg/mL (trypomastigotes)	*T. cruzi* (Dm28c strain)	Nerolidol (25.22%)	--	[51]
	Piper cubeba L.	IC_{50} = 45.5 µg/mL (trypomastigotes) IC_{50} = 87.9 µg/mL (amastigotas)	*T. cruzi*	No major constituent	--	[52]
	Piper tuberculatum Jacq.	EC_{50} = 140.31 µg/mL (epimastigotes)	*T. cruzi* (LC-B5 clone)	β-pinene (27.74%) α-pinene (26.54%)	--	[53]
	Piper brachypodom	IC_{50} = 22.7 µg/mL (amastigotes) IC_{50} = 0.34 µg/mL (epimastigotes)	T. cruzi (320I01 strain)	Not determined	--	[54]

Table 1 continued...

RUTACEAE	*Citrus aurantiifolia* (Christm.) Swingle	IC_{50} = 98.0 µg/mL (epimastigotes)	*T. cruzi* (NINOA strain)	Limonene (92.3%)	--	[26]
	Citrus latifolia Tanaka	IC_{50} = 51.7 µg/mL (trypomastigotes)	*T. cruzi* (Y strain)	Limonene (46.3%)	--	[57]
	Citrus limon (L.) Osbeck	IC_{50} = 88.2 µg/mL (trypomastigotes)	*T. cruzi* (Y strain)	Limonene (40.0%)	--	[57]
VERBENACEAE	*Aloysia citrodora* Palau	Significant reduction in parasitemia by 85.4% with a peak at a dose of 250 mg/kg; reduction in the number of amastigotes and inflammatory infiltrates in the heart.	*T. cruzi* (wild strain)	Not determined	--	[58]
	Lantana camara L.	IC_{50} = 201.94 µg/mL (epimastigotes)	*T. cruzi*	(E)-caryophyllene (23.75%)	--	[59]
	Lippia alba (Mill.) N.E.Br. ex Britton & P.Wilson	IC_{50} = 10.1 µg/mL (trypomastigotes) IC_{50} = 39.5 µg/mL (amastigotes)	*T. cruzi* (Y strain)	Linalool (54.4%)	--	[17]
	Lippia alba (Mill.) N.E.Br. ex Britton & P.Wilson (carvone chemotype)	IC_{50} = 45.0 µg/mL (amastigotes)	*T. cruzi* (TcI, SYLVIO-X10 strain)	Limonene (96%)	Synergistic effect when associated with benznidazole; The combination reduced pro-inflammatory cytokines (IFN-γ, IL-2, and TNF-α) and increased the anti-inflammatory cytokines (IL-4 and IL-10); Reduction of oxidative stress, mitochondrial metabolism;	[60]
	Lippia alba (Mill.) N.E.Br. ex Britton & P.Wilson (citral chemotype)	IC_{50} = 74.0 µg/mL (amastigotes) IC_{50} = 14.0 µg/mL (epimastigotes) IC_{50} = 22.0 µg/mL (tripomastigotes)	*T. cruzi* (TcI, SYLVIO-X10 strain)	Neral (21.5%) Geranial (28.7%)	Induction of cell death by an apoptotic-like mechanism	[61]
	Lippia alba (Mill.) N.E.Br. ex Britton & P.Wilson (partes aéreas)	IC_{50} = 5.5 µg/mL (epimastigotes) IC_{50} = 12.2 µg/mL (amastigotes)	*T. cruzi* (Strain 215, KP Luna CINTROP)	Geranial (23.3%)	--	[62]
	Lippia berlandieri Schauer	IC_{50} = 23.0 µg/mL (epimastigotes)	*T. cruzi* (NINOA strain)	Thymol (58.3%) *p*-Cymene (24.6%)	--	[26]
	Lippia macrophylla Cham.	IC_{50} = 37.6 µg/mL (epimastigotes)	*T. cruzi* (Y strain)	Thymol (49.81%)	--	[39]
	Lippia origanoides Kunth	IC_{50} = 29.6 µg/mL (amastigotes)	*T. cruzi* (Tulahuen CL2)	(E)-methyl cinnamate (40.0%)	--	[30]
	Lippia pedunculosa Hayek	IC_{50} = 15.1 µg/mL (epimastigotes) IC_{50} = 11.3 µg/mL (tripomastigots)	*T. cruzi*	Rotundifolone (71.7%) (R)-limonene (21.8%)	--	[63]
ZINGIBERACEAE	*Alpinia speciosa* K. Schum	IC_{50} = 92.01 µg/mL (epimastigotes)	*T. cruzi*	1,8-cineole (28.46%)	--	[64]
	Zingiber officinale Roscoe	Reduction in blood culture positivity rate, parasitic load, and mortality rate.	*T. cruzi* (Y strain)	Not determined.	--	[49]

IC_{50}: 50% Inhibitory Concentration; EC_{50}: 50% Efficiency Concentration; MLC: Minimum Lethal Concentration.

In the last five years, 18 studies (35.28%) have been conducted, highlighting the relevance of this number considering concerns related to Chagas disease, caused by the etiological agent *Trypanosoma cruzi*. This context includes the parasite's resistance to medications and synthetic substances, further supporting the viability of using essential oils as an antiparasitic alternative. Among the essential oils with the most significant potential against *T. cruzi*, are those extracted from *Duguetia quitarensis* Benth. (IC_{50}: 0.26 µg/mL), *Guatteria punctata* (Aubl.) R.A. Howard (IC_{50}: 0.029 µg/mL), *Fusaea longifolia* (Aubl.) Saff. (IC_{50}: 0.3 µg/mL), and *Bocageopsis multiflora* (Mart.) R.E. Fr. (IC_{50}: 0.46 µg/mL) stand out, all tested in the trypomastigote form of the parasite [23]. Other species from different botanical families also show promise for future applications.

The essential oil of *Dysphania ambrosioides* (L.) Mosyakin & Clements, belonging to the Amaranthaceae family, exhibited significant activity against both the trypomastigote (IC_{50}: 8.7 µg/mL) and amastigote (IC_{50}: 1.9-12.2 µg/mL) forms of the parasite. This action appears to be related to the disruption of mitochondrial membrane potential, compromising cellular energy production and affecting homeostasis. Additionally, changes in redox indices have also been suggested as a possible mechanism of action [17,18].

The Annonaceae family demonstrated significant anti-*Trypanosoma* activity against various forms of the parasite, including epimastigote (14.9 – 93.9 µg/mL), the form found in the insect vector, and, primarily, trypomastigote (0.029 – 168.50 µg/mL). Among the most relevant species, *Annona squamosa* and *Guatteria punctata* stand out [19, 20, 22-25]. Microscopic analyses of the inhibitory effect of *Annona squamosa* L. indicated alterations in the parasite's membrane, possibly related to the action of the essential oils [21].

The Apiaceae and Asteraceae families also showed significant results, particularly in studies focusing on the epimastigote form of the parasite. Examples include *Artemisia pedemontana* subsp. *assoana* (IC_{50}: 20.3 µg/mL) [29] and *Vernonanthura brasiliana* (L.) H.Rob., whose analyzed parts exhibited different levels of efficacy: leaves (IC50: 72 µg/mL), flowers (IC_{50}: 88 µg/mL), and root (IC_{50}: 70 µg/mL) [33]. The variations in results between the plant parts may be associated with the chemical composition of the essential oils, such as changes in the concentrations of β-pinene and limonene observed in *Baccharis punctulata* DC. and *Baccharis spicata* (Lam.) Baill. [31].

The chemical composition of natural products directly influences their biological action, with essential oils being examples of complex mixtures containing bioactive compounds that can act synergistically or antagonistically, enhancing or reducing the intrinsic action of another compound or drug [65]. The compound linalool illustrates this variability, showing different levels of efficacy depending on its concentration. In *Aniba rosaeodora* var. *amazonica*, it reached 93.60% of the linalool compound, with efficacy against epimastigote (IC_{50}: 150.5 µg/mL), while in *Lippia alba* (54.4% of the compound), it showed an IC_{50} of 10.1 µg/mL against trypomastigote and 39.5 µg/mL against amastigote [17,38]. When isolated, linalool also demonstrates antiparasitic activity [66], including trypanocidal action [51].

The Myrtaceae family has been extensively studied for the activity of its essential oils against *Trypanosoma cruzi*, with 11 studies dedicated to this topic. These studies focus on species from this family due to their promising action against parasite forms that affect mammals (amastigote and trypomastigote) and invertebrates (epimastigote present in the vector's digestive tract). Notable species include *Eugenia brejoensis* Mazine and *Syzygium aromaticum* (L.) Merr. & L.M.Perry, both capable of combating all parasitic forms of *T. cruzi*, although the mechanism of action of the essential oils from these species has not been elucidated [13,26,39,43-50]..

The amastigote form, characterized as intracellular, immobile, and dormant, is a resistance strategy of the parasite under unfavorable conditions, allowing it to persist in the host organism for long periods. Effectively targeting this form is crucial for the treatment of the disease [67-69]. Essential oils such as *Dysphania ambrosioides* (IC_{50}: 1.9–12.2 µg/mL), *Phania matricarioides* (IC_{50}: 2.2 µg/mL), *Cymbopogon citratus* (IC_{50}: 5.1 µg/mL), and *Baccharis parvidentata* (IC_{50}: 5.2 µg/mL) have shown promising alternatives for combating this form of the parasite [17,18,30,32,56].

Essential oils can act through various mechanisms, including cytoplasmic alterations, swelling, and damage to the plasma and flagellar membranes, as observed in *Origanum vulgare* and *Thymus vulgaris* [41]. In *Cymbopogon citratus*, cytoplasmic and nuclear extraction with membrane bubble formation was reported [56]. Furthermore, the essential oil of *Lippia alba* exhibited a synergistic effect when combined with benznidazole, reducing pro-inflammatory cytokines (IFN-γ, IL-2, and TNF-α), increasing anti-inflammatory cytokines (IL-4 and IL-10), and decreasing oxidative stress and mitochondrial metabolism [60]. Another relevant mechanism is the induction of cell death via apoptosis [61].

4. Conclusion

Essential oils have emerged as promising alternatives in the fight against *Trypanosoma cruzi* strains due to their wide chemical diversity and bioactive potential. These natural substances offer significant advantages, as demonstrated in this study, such as the presence of compounds that can act synergistically, reducing parasite resistance and enhancing therapeutic efficacy. Furthermore, studies indicate that essential oils exhibit specific activities against different forms of the parasite's life cycle, including amastigotes, trypomastigotes, and epimastigotes, making them a versatile approach in the treatment of Chagas disease.

The trypanocidal activity of various essential oils (EOs) has been associated with different mechanisms, such as alterations in the cell membrane, inhibition of mitochondrial metabolism, and reduction of oxidative stress (Table 1). These mechanisms reinforce the potential of EOs as candidates for new therapeutic strategies in the treatment of diseases that still present significant challenges in terms of control and management. This study provides a mapping of the main species with anti-*Trypanosoma* potential, including *Duguetia quitarensis* (IC_{50} = 0.26 µg/mL, trypomastigote), *Guatteria punctata* (IC50 = 0.029 µg/mL, trypomastigote), *Fusaea longifolia* (IC50 = 0.3 µg/mL, trypomastigote), *Dysphania ambrosioides* (IC_{50} = 1.9–12.2 µg/mL, amastigote), and *Phania matricarioides* (IC_{50} = 2.2 µg/mL, amastigote) [17,18,23,32].

Although essential oils (EOs) show promising potential, there are still limitations to their application as therapeutic agents. The chemical variability between species and different plant parts can directly impact the effectiveness and reproducibility of results. Additionally, more in-depth studies on toxicity and potential adverse effects in model organisms through in vivo assays are necessary to determine the effects and safe concentrations.

Conflict of Interest

The authors declare no conflict of interest.

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