

In vitro antiplasmodial activity of selected plants from the Colombian North Coast with low cytotoxicity

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Abstract

Background: Plants are an important option in the treatment of malaria, especially in endemic regions, and are a less expensive and more accessible alternative with a lower risk of toxicity. Colombia has a great diversity of plants, and evaluation of natural extracts could result in the discovery of new compounds for the development of antimalarial drugs. The purpose of this work was to evaluate the *in vitro* antiplasmodial activity and the cytotoxicity of plant extracts from the Colombian North Coast against *Plasmodium falciparum*.

Materials and Methods: The antiplasmodial activity of 12 plant species from the Colombian North Coast that are used in traditional medicine was evaluated through *in vitro* cultures of *P. falciparum*, and the cytotoxicity of extracts of these species to human cells was determined. Plant extracts with high antiplasmodial activity were subjected to preliminary phytochemical screening.

Results: Extracts from five plants had promising antiplasmodial activity. Specifically, *Bursera simaruba* (Burseraceae) (bark), *Guazuma ulmifolia* Lam. (Malvaceae) (whole plant), *Murraya exotica* L. (Rutaceae) (leaves), *Hippomane mancinella* L. (Euphorbiaceae) (seeds), and *Capparis odoratissima* Jacq. (Capparaceae) (leaves). Extracts presented 50% inhibitory concentration values between 1 and 9 µg/ml. Compared to no extract, these active plant extracts did not show cytotoxic effects on mononuclear cells or hemolytic activity in healthy human erythrocytes.

Conclusions: The results obtained from this *in vitro* study of antiplasmodial activity suggest that active plant extracts from the Colombian North Coast are promising for future bioassay-guided fractionation to allow the isolation of active compounds and to elucidate their mechanism of action against *Plasmodium* spp.

Keywords: Antiplasmodial activity, cytotoxicity, malaria, plant extracts, *Plasmodium falciparum*

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INTRODUCTION

Approximately 80% of the world's population depends on drugs extracted from plants for their basic health needs.

Compounds derived from plants have been central in the development of antimalarial treatments, and two such compounds emerged from South America. Quinine, an active ingredient from the bark of the Cinchona tree,

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became the first compound with antimalarial activity and led to the design of chloroquine, one of the most widely used antimalarial agents until recently.^[1]

Likewise, lapachol, a naphthoquinone used in the 19th century for the treatment of fever in South America, was isolated for the first time from *Tabebuia avellanedae* Lorentz ex Griseb. (Bignoniaceae). Later, after chemical optimization, atovaquone was obtained, and it is currently used in association with proguanil for malaria prophylaxis and treatment.^[2,3]

Traditional remedies are an integral part of Colombian culture. Various studies of the ethnopharmacology and use of popular medicine among the population of the Atlantic Coast of Colombia, specifically in the state of Bolívar, have reported many perspectives in the search for new drugs based on local uses of medicinal plants.^[4]

To date, there is no registered and effective vaccine that can be applied to the population as a preventive measure to control or eradicate malaria. Therefore, chemotherapy continues to be the main measure to combat the disease, and due to increasing drug resistance, the discovery of new therapeutic options is necessary.^[5]

In this work, the *in vitro* antiplasmodial activity of 12 plants from the Colombian North Coast used in traditional medicine was evaluated. The results obtained from this study suggest that the extracts tested are promising for future biodirected assays that could allow the isolation of active compounds to further unravel their mechanism of action against *Plasmodium*.

MATERIALS AND METHODS

Selection and collection of plant material

Plant species from the North Coast of Colombia used as traditional medicine were studied.^[4,6] Twelve species were selected via a bibliographic database review in which

they had no or few previous reports of antimalarial activity [Table 1]. Voucher specimens were collected and numbered during the interviews, with prior permission obtained by the University of Cartagena through the regional autonomous corporation of Canal Del Dique. Specimen identification was carried out by comparison with authentic samples. The vouchers were deposited in the botanical garden in Cartagena and the Herbarium of the National University of Colombia (COL).

Preparation of plant extracts

Vegetable samples were dried for 2 days at 40°C in an oven with air circulation. After this period, the plant material was ground by mechanical methods using a blade mill. Extracts of the different organs of the plants were obtained by continuous maceration of 100 g of pulverized material in 96% ethanol (relation 1:4 of plant material) at 25°C, as previously described in other studies.^[7] The extraction was repeated until the plant material was exhausted; after this time, the extracts were filtered and concentrated under reduced pressure in a rotary evaporator. Finally, after weighing, the obtained extracts were dissolved with the smallest possible volume of dimethyl sulfoxide (DMSO) and then diluted as required in culture medium (RPMI 1640) to prepare different concentrations of the extracts for biological assays. The final DMSO concentration was never >0.05% to avoid carry-over (solvent) effects.^[8]

In vitro culture of *Plasmodium falciparum*

Two different strains of *Plasmodium falciparum* were used, the chloroquine sensitive (3D7) and chloroquine resistant (Dd2). A detailed description of the culture and synchronization methods used has been reported previously.^[9]

In vitro antiplasmodial activity of the plant extracts

A microfluorimetric DNA-based assay was used to monitor *P. falciparum* (strain 3D7 and Dd2) growth inhibition at different concentrations of the plant extracts.^[10] Synchronized

Table 1: Plant species from the Colombian North Coast selected for the *in vitro* study of antiplasmodial activity

Scientific name	Common local name	Family	Voucher number
<i>Bursera graveolens</i> Kunth. (Burseraceae)	Caraña	Burseraceae	[JBC 5115]
<i>Bursera simaruba</i> L. (Burseraceae)	Almácigo	Burseraceae	[JBC 5115]
<i>Cardiospermum grandiflorum</i> Sw. (Sapindaceae)	Topo-topo	Sapindaceae	[JBC 1452]
<i>Capparis odoratissima</i> Jacq. (Capparaceae)	Olivo	Capparidaceae	[JBC 1492]
<i>Chenopodium ambrosioides</i> L. (Amaranthaceae)	Paico, Hierba santa	Chenopodiaceae	[JBC 4005]
<i>Coccoloba uvifera</i> (L.) L. (Polygonaceae)	Uvita de playa	Polygonaceae	[JBC 4593]
<i>Guaiacum officinale</i> L. (Zygophyllaceae)	Guayacán	Zygophyllaceae	[JBC 2507]
<i>Guazuma ulmifolia</i> Lam. (Malvaceae)	Guácimo	Sterculiaceae	[JBC 4539]
<i>Gustavia superba</i> (Kunth) O. Berg (Lecythidaceae)	Membrillo	Lecythidaceae	[JBC 1382]
<i>Hippomane mancinella</i> L. (Euphorbiaceae)	Manzanillo	Euphorbiaceae	[JBC 2478]
<i>Hyptis Capitata</i> Jacq. (Lamiaceae)	Botón negro	Lamiaceae	[JBC 1389]
<i>Murraya exotica</i> L. (Rutaceae)	Azahar de la India	Rutaceae	[COL 538418]

rings from stock cultures were used to test serial dilutions of plant extracts (100 µg/mL to 0.01 µg/mL) in 96-well culture microplates to obtain 2% hematocrit and 1% parasitemia. Subsequently, the parasite was allowed to grow for 48 h in 5% CO₂ at 37°C. After incubation, the microplates were centrifuged at 600 × g for 10 min, and the contents were resuspended in saponin (0.15%, w/v in phosphate-buffered saline [PBS]) to lyse the erythrocytes and release the malaria parasites. To eliminate all traces of hemoglobin, the pellet was washed by the addition of 200 µL of PBS followed by centrifugation at 600 × g. The washing step was repeated twice to ensure the complete removal of hemoglobin. Finally, the pellets were resuspended in 100 µL of PBS and mixed with 100 µL of PicoGreen (Invitrogen-P7589).^[11] Plates were incubated for 30–60 min in the dark, and the fluorescence intensity was measured at 485-nm excitation and 528-nm emission. Each test also included an untreated control, and chloroquine was used as the reference drug. Growth inhibition was calculated as previously described.^[10] Three independent experiments were performed in triplicate to determine the antiplasmodial activity of each extract. The 50% inhibitory concentration (IC₅₀) values of plant extracts against *Plasmodium* growth were determined using SigmaPlot software.

In vitro cytotoxicity test of the plant extracts on human peripheral blood mononuclear cells

The cytotoxic activity of plant extracts against human peripheral blood mononuclear cells (PBMCs) was evaluated by the trypan blue dye exclusion method.^[12] The dye exclusion test was used to determine the number of viable cells present in a cell suspension. These cells were obtained from the blood of healthy donors using Histopaque (Sigma-Aldrich-1077). A total of 6 × 10⁵ cells per well were mixed in triplicate for each tested concentration of the plant extracts (range: 1000–0.01 µg/mL) and controls in RPMI 1640 supplemented with 10% fetal bovine serum and 1% penicillin-streptomycin for a total volume of 200 µL in 96-well microplates. Cells were immediately incubated for 48 h at 37°C in a humid atmosphere with 5% CO₂.^[13] At the end of incubation, 100 µL of trypan blue dye was added to 100 µL of cell suspension. Then, viable cells were counted for each replicate at each extract concentration and for the controls. Three independent experiments were performed in triplicate to determine the cytotoxicity of each extract. The 50% lethal concentration (LC₅₀) values of the plant extracts in PBMCs were determined using SigmaPlot software.

Hemolysis assay of plant extracts

The potential hemolytic effects of those plant extracts with promising antiplasmodial activity were investigated

by incubating them with healthy human erythrocytes in 96-well microplates and determining the absorbance at 540 nm, which corresponds to the released hemoglobin in the supernatants.

For these tests, erythrocytes at 2% hematocrit were incubated with different concentrations of the plant extracts (1–100 µg/mL). A 2% hematocrit control solution was prepared in distilled water (100% relative hemolysis) as previously described.^[14] The results are expressed as a percentage of relative hemolysis compared to that of the 100% hemolysis control.

Morphology of the *Plasmodium falciparum* cultures after treatment with the plant extracts

The morphologies of the parasites (*P. falciparum* strain Dd2) from each culture at different concentrations of the plant extracts (described in the previous section) were evaluated by microscopic analysis of thin blood smears stained with Wright's stain after incubation. Stage-specific development was assessed by examining a minimum of 1000 parasitized cells on each smear for the differential counting of rings, trophozoites, schizonts, and pyknotic forms whose developmental stages could not be established. The fraction in each group was calculated as a percentage of the total parasitized cells. Parasitemia was measured by counting 1000 red cells and is reported as the percent of parasitized erythrocytes.^[15] Smears from plant extract-free cultures were used as a control.

Phytochemical screening

Plant extracts with favorable antiplasmodial activity were subjected to a preliminary phytochemical screen in order to detect the presence (or absence) of alkaloids, flavonoids, tannins, coumarins, saponins, triterpenes, sterols, quinones, and cardiac glycosides, as previously described in other studies.^[16]

RESULTS

In vitro antiplasmodial and cytotoxic activity of the plant extracts studied

The *in vitro* antiplasmodial activity of 12 plant extracts from the North Coast of Colombia was evaluated for the 3D7 and Dd2 strains of *P. falciparum*. The results are described in detail in Table 2.

According to the WHO guidelines, antiplasmodial activity is classified as follows: high activity at IC₅₀ <5 µg/mL, good activity at 5–10 µg/mL, moderate activity at 11–50 µg/mL, and inactive at >50 µg/mL.^[17,18]

The selectivity index (SI) of each extract is also presented in Table 2. The SI is defined as the ratio of the LC₅₀ value in PBMCs to the IC₅₀ value against *P. falciparum*.^[8]

Table 2: Antiplasmodial activity and cytotoxicity values of selected plant extracts from the North Coast of Colombia

Scientific name	Plant part used [*]	IC ₅₀ [†] Dd2 strain (µg/mL)	IC ₅₀ [†] 3D7 strain (µg/mL)	Antiplasmodial activity	Cytotoxicity LC ₅₀ [‡] (µg/mL)	SI [§] (Dd2)	SI [§] (3D7)
<i>Bursera simaruba</i>	Bark	1.2±0.16	1.7±0.43	High	369.4±17.2	307.8	217.3
<i>Guazuma ulmifolia</i>	Whole plant	3±1.40	3.4±0.61	High	272.9±15.4	91.0	80.3
<i>Murraya exotica</i>	Leaves	3.1±0.21	2.8±0.15	High	351.6±3.5	113.4	125.6
<i>Hippomane mancinella</i>	Seed	4.4±1.30	5.1±0.70	High	186.8±1.7	42.5	36.6
<i>Capparis odoratissima</i>	Leaves	8.8±0.84	7.6±1.28	Good	298.8±13.3	34.0	39.3
<i>Hyptis capitata</i>	Leaves	14.1±2.13	13.2±1.93	Moderate	312.4±12.6	22.2	23.7
<i>Guaiacum officinale</i>	Leaves	15.7±3.20	16.1±2.10	Moderate	301.6±5.3	19.2	18.7
<i>Gustavia superba</i>	Leaves	19.9±0.40	21.4±0.36	Moderate	254.3±4.2	12.8	11.9
<i>Bursera graveolens</i>	Bark	26.9±0.56	25.3±1.33	Moderate	298.3±8.7	11.1	11.8
<i>Coccoloba uvifera</i>	Whole plant	29.6±4.70	31.1±5.20	Moderate	278.6±11.8	9.4	9.0
<i>Cardiospermum grandiflorum</i>	Leaves	181.8±7.53	172.6±8.12	Inactive	321.5±2.2	1.8	1.9
<i>Chenopodium ambrosioides</i>	Leaves	198.7±6.50	189.2±7.31	Inactive	290.1±15.5	1.5	1.5
Control (chloroquine)	-	0.05±0.018	0.007±0.01	High	-	-	-

^{*}Crude ethanol extracts were used for each part of the plant, [†]IC₅₀: 50% lethal concentration against *Plasmodium falciparum*. The IC₅₀ values are expressed as the mean±SD of three different determinations per experiment, [‡]LC₅₀: 50% lethal concentration in human peripheral blood mononuclear cells. The LC₅₀ values are expressed as the mean±SD of three different determinations per experiment, [§]SI=LC₅₀/IC₅₀. IC₅₀: 50% inhibitory concentration, SD: Standard deviation, LC50: 50% lethal concentration, SI: Selectivity index

These results highlighted five extracts with high to good antiplasmodial activity [Table 2]: *B. simaruba* (bark), *G. ulmifolia* (whole plant), *M. exotica* (leaves), *H. mancinella* (seeds), and *Capparis odoratissima* (leaves).

Human PBMCs exhibited high survival rates when exposed to the extracts at 100–0.01 µg/mL. The LC₅₀ values were above 100 µg/mL and much higher than the IC₅₀ values against *P. falciparum*, indicating lower cytotoxicity than the control without treatment. The SI of the plant extracts was assessed and demonstrated specific antiplasmodial activity rather than toxicity to PBMCs since most of the indices were ≥2.

Hemolytic effects of the active plant extracts

To evaluate the effects of the active extracts on the structural integrity of erythrocytes, the hemoglobin concentration was determined in samples of red blood cells incubated with each extract with high antiplasmodial activity (*B. simaruba*, *G. ulmifolia*, *M. exotica*, *H. mancinella*, and *C. odoratissima*) for 48 h at 37°C. Compared with the control treatment without extract, none of the extract treatments showed hemolytic activity against healthy erythrocytes, as shown in Table 3, which suggests low toxicity for the extracts against erythrocytes.

Phenotypic effects of the active plant extracts on the intraerythrocytic stages of *Plasmodium falciparum*

The effects on the morphology of the intraerythrocytic stages of the parasite (*P. falciparum* strain Dd2) were determined by microscopic visualization of smears from sediments of the microcultures exposed to 100, 10, and 1 µg/mL active plant extracts. In this analysis, we found variations in the proportion of *P. falciparum* forms compared to that of the untreated control [Figure 1]. Pyknotic forms, a morphological sign of cell death consisting of the retraction of the nucleus

Table 3: Percentage of hemolysis in erythrocytes treated with the active extracts from the Colombian North Coast*

Plant extracts	Concentration (µg/mL)	Percentage hemolysis
<i>Bursera simaruba</i>	1	5.5±0.25
	10	5.0±0.22
	100	5.9±1.93
<i>Guazuma ulmifolia</i>	1	5.5±0.19
	10	5.7±0.38
	100	5.7±0.25
<i>Murraya exotica</i>	1	5.7±0.29
	10	5.0±0.27
	100	5.7±0.42
<i>Hippomane mancinella</i>	1	5.2±0.83
	10	5.7±1.51
	100	5.5±0.55
<i>Capparis odoratissima</i>	1	5.8±0.34
	10	5.8±0.34
	100	5.7±0.23
Control without treatment	-	5.7±0.23
positive control	-	100

*Erythrocytes were incubated with each extract at concentrations of 1, 10, and 100 µg/mL at 37°C for 48 h. Each data point represents the mean±SD of two independent experiments performed in triplicate against a positive control (100% hemolysis) and a control without treatment. The percentage of hemolysis generated by the extracts relative to that of the control (without extract) did not show statistically significant differences ($P>0.05$). SD: Standard deviation

with condensation of the parasite's chromatin in the form of a solid mass, were frequently observed at all three concentrations of the five active extracts studied [Figure 2].

Other modifications to the structures of the parasitic stages, specifically alterations in the normal shape of the rings, were observed, such as dysmorphism, delayed maturation of trophozoites, and the presence of forms with an increased size of the parasitophorous vacuole [Figures 1 and 2]. These morphological alterations were seen more frequently at 10 and 1 µg/mL [Figures 1 and 2]. Chloroquine treatment did not generate these alterations

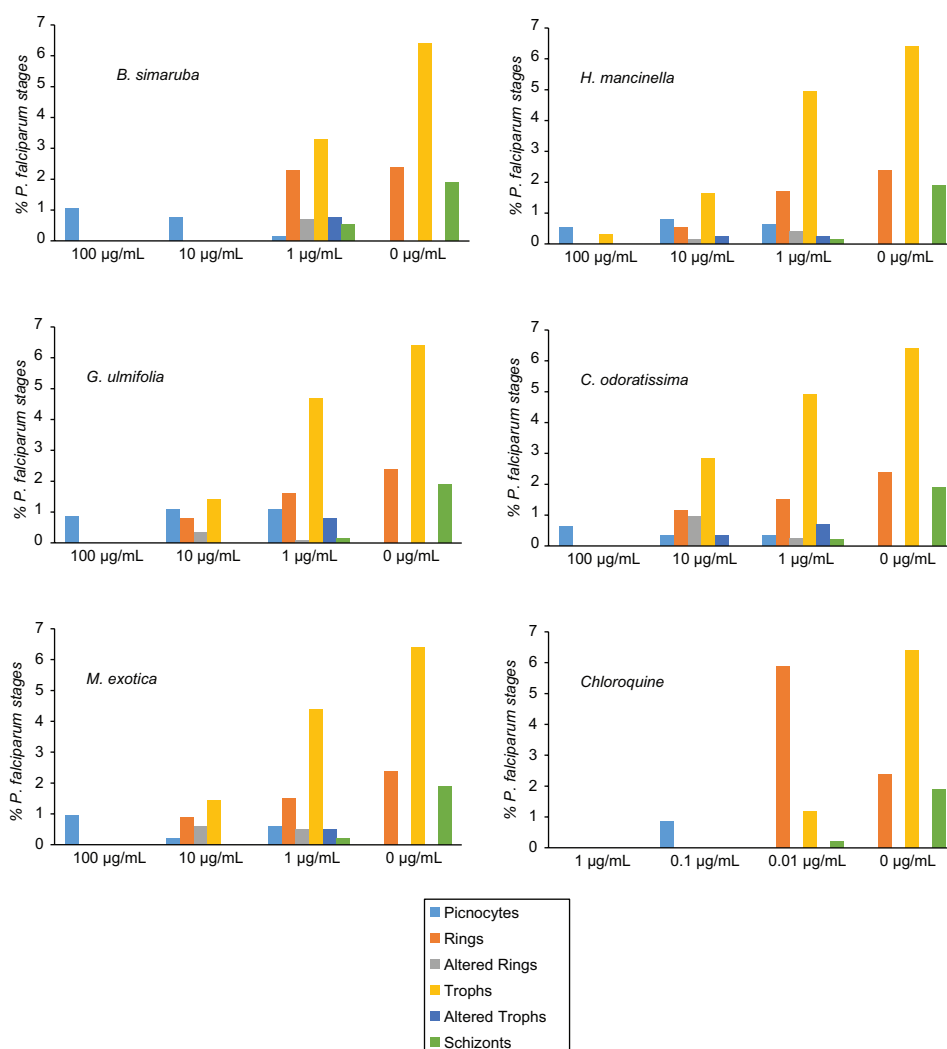


Figure 1: Percentage of intraerythrocytic *Plasmodium falciparum* strain Dd2 stages in the presence of active plant extracts from the North Coast of Colombia. The percentages of each parasitic stage and the morphological alterations observed (rings, trophozoites, schizonts, and pyknotic forms) after treatment with different concentrations of the active extracts (*Bursera simaruba*, *Guazuma ulmifolia*, *Murraya exotica*, *Hippomane mancinella*, and *Capparis odoratissima*) are shown

[Figures 1 and 2]. Accordingly, we suggest that the active extracts inhibit the maturation of the parasite.

On the other hand, the percentage of rings decreased at higher concentrations of the active plant extracts, suggesting that these extracts inhibited the invasive cycle of the parasite; moreover, in all extracts, a low percentage of schizonts was observed at the three concentrations tested [Figure 1]. All these morphological alterations indicate that these active extracts, when tested at concentrations close to their IC_{50} values, cause important phenotypic changes during the parasite life cycle.

Phytochemical screening

Chemical identification tests were applied to the extracts of the selected species that displayed antiplasmodial activity, and they show the presence of several families of

secondary metabolites. Table 4 shows the results of this phytochemical screen.

DISCUSSION

The acceleration of the increase in the resistance of parasites against available antimalarial drugs has become one of the greatest difficulties for the control and eradication of malaria. The development of new therapeutic alternatives that meet the requirements of rapid efficacy, minimal toxicity, and low cost is essential and in great need worldwide to counteract this disease.^[19] Primary screenings for the antimalarial activity of plant species can generate basic information that allows the selection of potential extracts and determination of their composition of secondary metabolites and biological activity against the parasites.^[20]

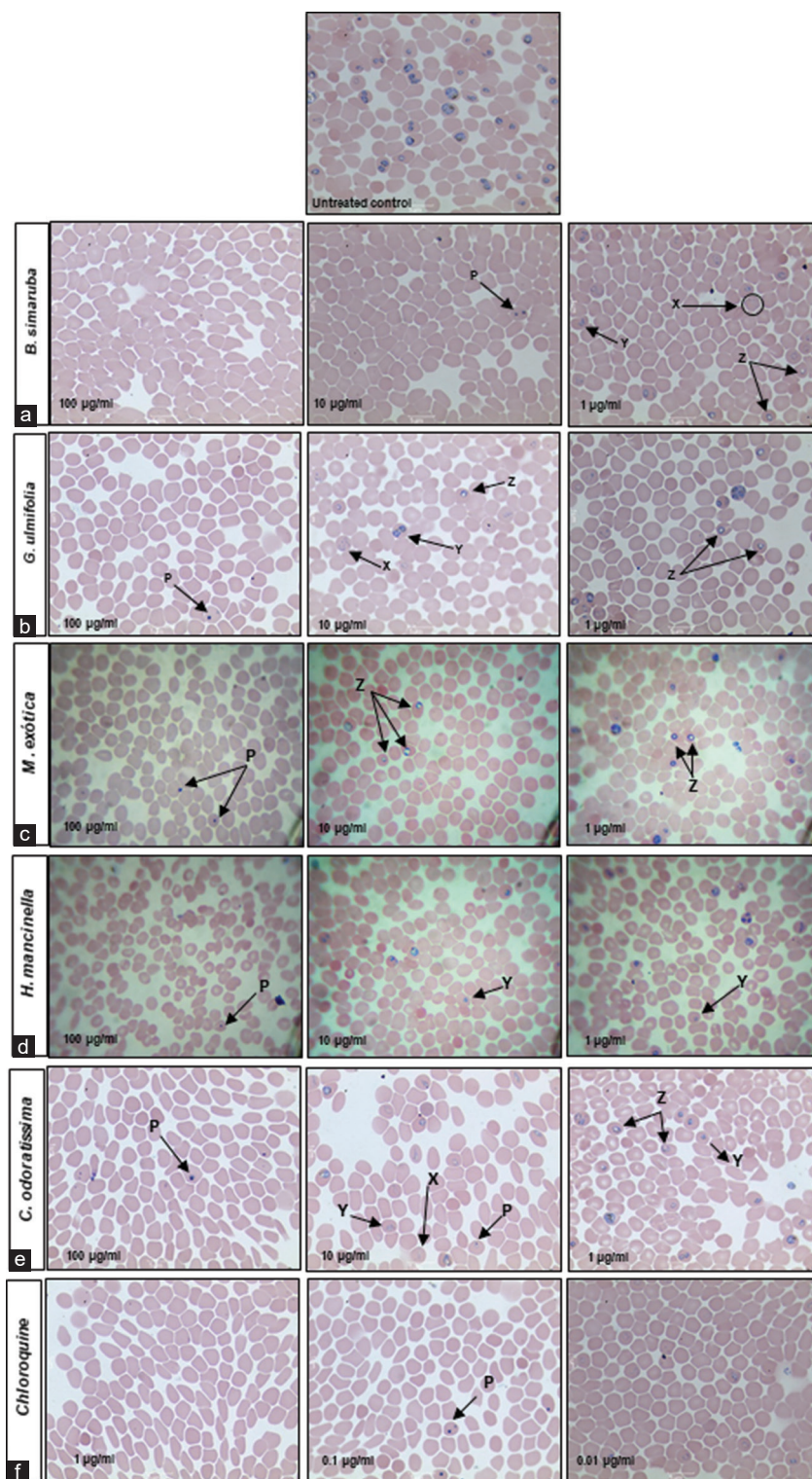


Figure 2: Effects of the active extracts from the Colombian North Coast plants on the development of the parasite. *Plasmodium falciparum* strain Dd2 cultures incubated for 48 h compared to the untreated control cultures. Active extracts: (a) *Bursera simaruba*, (b) *Guazuma ulmifolia*, (c) *Murraya exotica*, (d) *Hippomane mancinella*, (e) *Capparis odoratissima* in the concentration range 1.0–100 µg/mL, and (f) chloroquine (range 0.01–1 µg/mL). The following morphological changes can be observed: pyknotic forms (P), alterations in the normal shape of rings (x), forms with delayed maturation of trophozoites (Y), and increases in the size of the parasitophorous vacuole (Z)

In this study, five plant extracts were found to have promising activity in inhibiting the development of

P. falciparum in vitro. The selected species are representative of the Colombian North Coast and are used in traditional

Table 4: Phytochemical screen of the plant species from the Colombian North Coast active against cultures of *Plasmodium falciparum*

Plant species	Secondary metabolite							
	Alkaloids	Coumarins	Tannins	CG	Flavonoids	Saponins	Triterpenes/steroids	Quinones
<i>Bursera simaruba</i>	+	-	-	-	+	+	+	+
<i>Guazuma ulmifolia</i>	-	+	+	-	+	-	+	-
<i>Murraya exótica</i>	+	+	-	-	+	+	+	-
<i>Hippomane mancinella</i>	+	+	+	+	+	-	-	-
<i>Capparis odoratissima</i>	+	+	-	-	-	-	+	-

+: Present, -: Not Detected, CG: cardiotoxic glycosides

medicine in the region; these species have been part of a chemical study to identify secondary metabolites, and to date, there are few reports on their actions as antimalarial plants [Table 5].

The five species that were active for antiplasmodial activity were *B. simaruba* (bark), *G. ulmifolia* (whole plant), *M. exótica* (leaves), *H. mancinella* (seeds), and *C. odoratissima* (leaves), which presented IC₅₀ values <10 µg/mL for the 3D7 and Dd2 strains of *P. falciparum*. The IC₅₀ values were always similar for both strains. Chloroquine exhibited an IC₅₀ of 0.05 µg/mL against strain Dd2 (chloroquine resistant) and 0.007 µg/mL against strain 3D7 (chloroquine sensitive). The comparable IC₅₀ values for active plant extracts found in chloroquine-resistant and sensitive strains suggest that these extracts may affect plasmodial processes different to those targeted by chloroquine. The extract of *B. simaruba* stands out with the lowest IC₅₀ value of 1.2 µg/mL for the Dd2 strain and 1.7 µg/mL for the 3D7 strain.

The phenotypic effects of the five active extracts on the intraerythrocytic stages of *P. falciparum* strain Dd2 generated mostly the presence of the pyknotic form of the parasite at the maximum concentration tested and a small proportion of the ring forms and schizonts during the incubation period, which indicates that the parasite is not capable of completing the intraerythrocytic cycle, which probably affects the invasive stage of new erythrocytes. At concentrations close to the IC₅₀ values of the active extracts, there were modifications to the structure of the parasitic form, such as delayed maturation of trophozoites and stages with a larger parasitophorous vacuole. These alterations have already been associated with compounds with powerful antimalarial activity.^[36]

The alterations observed in the stages of the parasite incubated with the active plant extracts suggest that they could share similar mechanisms of action, possibly due to the common presence of secondary metabolites such as alkaloids and triterpenes/steroids. This hypothesis might be supported by a previous research, e.g., ten triterpenoid compounds with antimalarial activity (IC₅₀ of 6–7 µM)

Table 5: Traditional uses and scientific studies that demonstrate the medicinal properties of the five species of plants from the Colombian North Coast with promising antimalarial activity

Scientific name	Traditional uses	Biological and pharmacological activities
<i>Bursera simaruba</i>	Gastrointestinal and respiratory diseases, skin rashes, anti-inflammatory, urinary infections ^[21,22]	Anti-inflammatory, ^[23] antimicrobial, ^[24] antioxidant, ^[25] anti-herpesvirus, ^[26] antihypertensive ^[27]
<i>Guazuma ulmifolia</i>	Inflammation, coughs, malaria, syphilis, gastritis, dermatitis, and gastrointestinal and cardiovascular disorders ^[4,21,28]	Antimicrobial, antiprotozoal, antioxidant, and anti-diarrheal activities, and cardioprotective effect ^[28]
<i>Murraya exótica</i>	Pain, analgesic, sedative ^[6,29]	Antioxidant, ^[30] anticancer, ^[31] anti-inflammatory, ^[32] antiplasmodial, and antipyretic ^[33]
<i>Hippomane mancinella</i>	Toxic, causes stomatitis, lip lesions, pharyngeal edema, dermatitis, and eye lesions ^[34,35]	-
<i>Capparis odoratissima</i>	Dermatological conditions ^[6]	-

were isolated and tested against *Plasmodium berghei* in murine models.^[37]

Previous studies based on using trophozoite maturation delays to slow the invasive cycle of infection suggested that this response could be a consequence of inhibition of parasite proteases and phosphatases, according to the activity of maslinic acid and other related triterpenoid molecules, where a parasitostatic effect was suggested.^[15] On the other hand, the presence of alkaloids in all of the active extracts tested is also notable. In previous reports,^[38] guanidine-type alkaloids exhibited a broad bioactivity profile, especially as enzyme inhibitors.

We cannot finally discard that the compounds present in these active plant extracts may also act by blocking essential enzymatic pathways for the development of the erythrocyte cycle of the parasite, compromising survival. Consequently, the results of this screening suggest further pursuing fractionation and biological activity

tests to isolate the active compounds responsible for this promising inhibition of *P. falciparum* and to determine their mechanism of action.

CONCLUSIONS

This study on the *in vitro* antiplasmodial activity and cytotoxicity of the *B. simaruba* (bark), *G. ulmifolia* (whole plant), *M. exotica* (leaves), *H. mancinella* (seeds), and *C. odoratissima* (leaves) extracts showed their inhibitory effect on *P. falciparum* growth with nearly negligible cytotoxic effects and no hemolytic damage. Thus, those extracts should contain active molecules responsible for such biological effects on the malaria parasite, which supports future bioassay-guided fractionation to identify the specific compounds to test their activity and unravel their mechanisms of action against *P. falciparum* in the potential discovery of new compounds for the development of antimalarial drugs.

Ethical clearance

The ethical and scientific procedures of this study were certified by the Ethics Committee of the Faculty of Medicine, University of Cartagena, Colombia (study number 80/5-03-2015).

Highlights

- Extracts from five Colombian plants had promising antiplasmodial activity
- Active plant extracts did not show cytotoxic effects on human cells
- Pyknotic forms and alterations in trophozoites were observed in the active extracts
- The extract of *Bursera simaruba* stands out with the lowest 50% inhibitory concentration (IC₅₀) value
- Alkaloids and triterpenes could be responsible for the antiplasmodial activity.

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Conflicts of interest

There are no conflicts of interest.

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