

Evaluation of anti-staphylococcal activity and acute toxicity of hexane extracts of *Macaranga occidentalis* (Mull. Arg.) Mull. Arg (Euphobiaceae)

Prosper E. K. Lele¹, Soreille R. Y. Sofeu¹, Aimé G. Fankam^{1*}, Jason B. T. Kuete¹, Remi R. Nsatar¹, Victor Kuete¹

Abstract

Background: *Macaranga occidentalis* is well known in traditional medicine for the treatment of various ailments like bruises, boils, cuts, sores, and diarrhea. This study aimed to investigate *in vitro* and *in vivo* the anti-staphylococcal activity of *Macaranga occidentalis* extracts on selected *Staphylococcus aureus*, including multidrug resistance (MDR) isolates. Moreover, the acute toxicity of the active extract was assessed.

Methods: Extracts were prepared by maceration of *M. occidentalis* in hexane. The *in vitro* activity of the extracts was determined using the broth microdilution method. The *in vivo* anti-staphylococcal activity and acute toxicity of the hexane extract were assessed in *Wistar* rats.

Results: The hexane leaves and bark extracts of *M. occidentalis* demonstrated antibacterial activity, with minimum inhibitory concentrations (MIC) ranging from 64 to 2048 µg/mL. *In vivo*, the hexane leaf extract (the most active) significantly reduced the bacterial load in *S. aureus* D021-infected *Wistar* rats after the tenth day of the experiment. It showed no toxic effect on blood cells and even enhanced hemoglobin production. Furthermore, at a dose of 5000 mg/kg body weight, this extract showed no signs of toxicity in rats, indicating that the median lethal dose (LD50) is greater than 5000 mg/kg body weight.

Conclusion: *Macaranga occidentalis* extracts, especially its leaf hexane extract, constitute promising alternative therapeutic sources for infections caused by MDR *Staphylococcus aureus*. Therefore, further studies including its subacute and chronic toxicity, as well as the identification of its active ingredients, should be envisaged.

Keywords: acute toxicity; Anti-staphylococcal activity; *Macaranga occidentalis*; multidrug resistance; *Staphylococcus aureus*.

*Correspondence: Tel.: +237 693 00 31 87; E-mail address: aqfankam@yahoo.fr; ORCID: <https://orcid.org/0000-0001-7008-7453> (Aimé Gabriel Fankam)

¹Department of Biochemistry, Faculty of Science, University of Dschang, Dschang, Cameroon.

Other authors

E-mail: lelekamgaelvisprosper@gmail.com (Prosper E. K. Lele); E-mail: sorellesoffo@gmail.com (Sorelle R. Y. Sofeu); E-mail: kuetejason7@gmail.com; ORCID: <https://orcid.org/0009-0001-0242-9092> (Jason B. T. Kuete); E-mail: remiridha6@gmail.com (Remi R. Nsatar); E-mail: kuetevictor@yahoo.fr; ORCID: <http://orcid.org/0000-0002-1070-1236> (Victor Kuete)

Citation on this article: Lele, PEK, Sofeu SRY, Fankam AG, Kuete JBT, Nsatar RR, Kuete V. Evaluation of anti-staphylococcal activity and acute toxicity of hexane extracts of *Macaranga occidentalis* (Mull. Arg.) Mull. Arg (Euphobiaceae). *Investigational Medicinal Chemistry and Pharmacology* (2026) 9(1):133; Doi: <https://dx.doi.org/10.31183/imcp.2026.00133>



Background

Infectious diseases remain a leading cause of mortality worldwide, second only to ischemic heart disease [1]. The advent of antibiotics has revolutionized the management of infectious diseases in both human medicine and agriculture; however, misuse and natural evolution of bacterial pathogens have rendered many bacteria resistant to most conventional antibiotics [2]. Multidrug resistance (MDR) is responsible for approximately 1.27 million deaths in 2019 and 4.95 million deaths in 2023 [3]. *Staphylococcus aureus* is the predominant pathogen responsible for a wide range of nosocomial infections, including endocarditis, septicemia, and skin infections. It poses a significant challenge in community-acquired and healthcare-associated settings owing to its diverse virulence factors and increasing antibiotic resistance [4]. *S. aureus* displays a remarkable capacity for resistance to many conventional antibiotics, including fluoroquinolones and β -lactamines [5]. This is achieved through multiple means, including overexpression of efflux pumps, production of β -lactamases, reduction of porin expression, and mutation of quinolone targets [6]. Faced with an alarming and rapid increase in antibiotic ineffectiveness, researchers are revisiting natural resources, such as plants. Medicinal plants synthesize diverse secondary metabolites, such as terpenoids, alkaloids, and phenolic compounds, which may circumvent known resistance mechanisms [7].

Macaranga occidentalis (Mull. Arg.) Mull. Arg., a plant belonging to the family Euphorbiaceae, is traditionally used to treat various diseases, including swellings, cuts, sores, diarrhea, cough, stomachache, hypertension, boils, furuncles, and bruises [8-10]. Natural compounds isolated from the genus *Macaranga* have demonstrated a range of biological activities, including antioxidant [11], antimicrobial [10, 12, 13], anti-inflammatory [14], antiplasmodial, and antitumor [15] activities. Previous phytochemical studies have shown that *M. occidentalis* contains steroids, triterpenes, flavonoids, stilbenoids, and ellagic acid derivatives, with schweinfurthin B being the most potent compound [10]. In the continuous quest for novel and efficient antibacterial substances from plants, this study aimed to investigate the *in vitro* and *in vivo* anti-staphylococcal activity of *M. occidentalis* against MDR *Staphylococcus aureus*. Additionally, the acute toxicity of the leaf hexane extract of this plant was evaluated.

Methods

Plant material

The leaves and stem bark of *Macaranga occidentalis* were collected in November 2024 in Bangangte, West Cameroon. The plant was identified at the National Herbarium of Cameroon, Yaoundé, in comparison with reference samples kept under the identification code 43778/HNC.

Preparation of extracts

The leaves and bark of *M. occidentalis* were cleaned and dried away from sunlight, then ground into powder using a blender. Thereafter, 100 g of each powder was soaked in 300 mL of hexane for 48 h. The mixture was then filtered using Whatman filter paper grade 1, and the extractive solvent was removed using a rotary evaporator (BÜCHI R-200) under reduced pressure to obtain the extracts. The extract was collected, dried in an oven at 40°C, and stored at 4°C until use.

Microorganisms and culture conditions

The microorganisms used in the present study included one strain (ATCC 29213) and 11 MDR isolates (D018SA, D020SA, D021SA, D047SA, D049SA, D050SA, D051SA, and D052SA) of *S. aureus*. Their antibiotic resistance features can be found in the Supporting Information (Table S1, Supplementary material). Mueller–Hinton agar (MHA) and Mueller–Hinton broth (MHB) (Accumix, India) were used for microbial culture and antibacterial assays, respectively.

Evaluation of the *in vitro* anti-staphylococcal activity of extracts

The minimal inhibitory concentration (MIC) of the extracts was determined by broth microdilution using p-iodonitrotetrazolium chloride (INT) colorimetric assay [16, 17]. Briefly, the extract solutions were serially diluted two-fold in 96-well microplates. Subsequently, 100 μ L of inoculum (2×10^6 CFU/mL) prepared in MHB was added to each well. The plates were covered with a sterile plate sealer, agitated to homogenize the content of the wells, and then incubated at 37°C for 18 h. The MIC, which is defined as the lowest concentration of the sample that prevents bacterial growth (absence of pink color), was then determined after the addition of 40 μ L INT (0.2 mg/mL) in each well of the plate and incubation at 37°C for 30 min. The MICs of the extracts were classified according to the Cut-off values established by Wamba et al. (2023) as follows: outstanding activity if MIC < 8 μ g/mL, excellent activity if $8 < \text{MIC} \leq 40$ μ g/mL, very good activity if $40 < \text{MIC} \leq 128$ μ g/mL, good activity if $128 < \text{MIC} \leq 320$ μ g/mL, average activity if $320 < \text{MIC} \leq 625$ μ g/mL, weak activity if $625 < \text{MIC} \leq 1024$ μ g/mL, and not active if MIC > 1024 μ g/mL [18]. The minimum bactericidal concentration (MBC), which is defined as the lowest concentration of a sample that kills bacteria, was determined after 50 μ L aliquots of each sample that did not show bacterial growth during MIC determination was added to 150 μ L of MHB and incubated for 48 h at 37°C. After the addition of INT as described above, the MBC was determined [17]. An extract was considered bactericidal if MBC/MIC ≤ 4 and bacteriostatic if MBC/MIC > 4 [19].

Evaluation of the *in vivo* anti-staphylococcal activity

Animal and maintenance conditions

Experiments followed institutional guidelines for animal care and use. Thirty-six *Wistar* rats (male/female, 6–8 weeks old, 100–150 g) were obtained from the Department of Biochemistry, University of Dschang. Rats were housed in plastic cages under standardized conditions: with access to food and water, at 20–30°C, and under a 10/14-h light/dark cycle. Blood samples from the tails were inoculated on mannitol salt agar; rats showing colony growth after 24 h (indicating *S. aureus* infection) were excluded. The study was conducted in accordance with the guidelines of the European Union Institutional Ethics Committee on Animal Care (Council EEC 86/609). All sections of this report are in accordance with the ARRIVE guidelines for reporting research.

Experimental design

- Groups 1 (n = 6): Infected rats received extract at 50 mg/kg of body weight.
- Groups 2 (n = 6): Infected rats received extract at 100 mg/kg of body weight.
- Group 3 (n=6): Infected rats received vancomycin at 25 mg/kg body weight.
- Group 4 (infected control, n = 6): Infected rats received 2% Tween 80.

- Group 5 (neutral, n = 6): Uninfected rats received normal saline.

Treatments were administered orally 24 h post-infection and continued for 10 days 48 h interval [20].

Determination of bacterial load

Two drops of blood samples were collected from the tails 72 h post-treatment, diluted in 100 μ L distilled water, plated on mannitol salt agar, and incubated at 37°C for 48 h. After incubation, the colonies were counted. This process was repeated every 48 h for five cycles [20].

Blood collection and serum preparation

At the end of the study period, the animals were sacrificed after the administration of a ketamine and diazepam combination (0.2/0.1 mL per 100 of body weight), and blood was collected by cardiac puncture. Approximately 1 mL of the collected blood was stored in anticoagulant blood tubes for biochemical analysis, and the remaining blood was kept in a dry tube for centrifugation. Serum was obtained and used for antioxidant assays.

Determination of hematological parameters

Blood samples collected in tubes containing EDTA were analyzed to evaluate hematological parameters using an automated hematology analyzer (QBC Autoread Plus, London, ©). Cell counting is based on an impedance system in which blood cells are detected and counted according to their size, shape, and internal complexity using fluorescent markers. When cells pass through a laser beam, it provokes an elevation of electrical resistance, generating a pulse with an amplitude proportional to the cellular volume. The collected signals are then analyzed by a computer to establish the leukocyte formula. The parameters included: red blood cells (RBC), platelets (PLT), lymphocytes (LYM), granulocytes (GRA), white blood cells (WBC), hemoglobin (HGB), hematocrit (HCT), and mean corpuscular volume (MCV).

The hematocrit level was calculated using the following formula: Hematocrit (%) = (red blood cell count \times mean corpuscular volume) / 10.

Hemoglobin was quantified after hemolysis of red blood cells using a spectrophotometer at wavelengths ranging from 525 to 550 nm.

Acute toxicity

The acute toxicity of the hexane extract from *M. occidentalis* leaves was evaluated in rats according to OECD Guideline 425 (2022), specifically the limit test (paragraph 26) [21]. Nine female rats were divided into three groups, each consisting of three animals: a control group and two treatment groups. After a seven-day acclimatization period, a single dose of *M. occidentalis* extract was administered by endogastric gavage to the treated groups at doses of 2000 mg/kg and 5000 mg/kg body weight, respectively, while the control group received Tween 80 at 2% v/v. All animals were closely monitored for two hours after administration to detect any signs of toxicity (drowsiness, hypomotility, salivation, etc.), and then periodically for 48 h after exposure. The animals were then monitored for an additional 14 days before being euthanized for examination of target organs (liver, kidneys, lungs, heart, and spleen).

Statistical analysis

Data were expressed as Mean \pm standard deviation and analyzed using the Statistical Package for Social Sciences (SPSS) version 22. Analysis of Variance (ANOVA) was used to compare treatment to the control using the Waller-Duncan test. The difference between means was set at a 95% confidence level ($P < 0.05$).

Results

In vitro anti-staphylococcal activity of extracts

The MIC and MBC values of *M. occidentalis* extracts were determined against MDR *S. aureus* isolates (Table 1). The extracts displayed a wide range of activities, with MICs ranging from 64 to 2048 μ g/mL. Among them, the hexane leaf extract demonstrated the highest antibacterial activity, with a MIC of 64 μ g/mL against *S. aureus* D021, D051, and D052. Chloramphenicol (reference antibacterial) displayed high activity against most strains compared to the extracts, with MICs ranging from 2 to 128 μ g/mL. Globally, both extracts showed bactericidal effect (MBC/MIC \leq 4). MBC/MIC $>$ 4 was observed with chloramphenicol on all the isolates, indicating its known bacteriostatic effect.

In-vivo anti-staphylococcal activity

Effect of the extract on bacterial load in infected rats

Figure 1 shows the variation in bacterial load over time in the different test groups. A gradual decrease in bacterial load was observed in all groups; however, the treated groups showed a higher rate of decrease. The groups treated with *M. occidentalis* hexane leaf extract had a greater reduction in bacterial load than the group treated with vancomycin. It is also evident that the activity of the extract is dose- and sex-dependent. The group treated with a dose of 100 mg/kg body weight showed a greater rate of recovery than the group treated at 50 mg/kg. Additionally, male rats demonstrated faster recovery than females.

Hematological profiles of rats

The hematological profiles of rats exposed to different doses of *M. occidentalis* hexane leaf extract are presented in Tables 2 and 3. No significant variation ($p > 0.05$) was observed in total white blood cell counts (WBC), lymphocytes (LYM), and granulocytes (GRN), compared with the control groups, in both female (Table 2) and male (Table 3) rats. The red blood cells, hemoglobin, hematocrit, mean corpuscular volume (MCV), did not differ significantly ($p > 0.05$) between treated groups and controls. Moreover, no significant variation ($p > 0.05$) in platelet counts, in both treated male and female rats, compared with controls, was observed.

Acute toxicity

Clinical observations

No subject died throughout the experiment, signifying that the lethal 50 dose (LD₅₀) of the hexane leaf extract of *M. occidentalis* is above 5000 mg/kg (Table 4).

Variation in rats' body weight

Table 5 presents the results of the mass variation in *Wistar* rats over 14 days during an acute toxicity study. There is a general increase in animals' masses throughout the experiment, which increase is generally not significant ($p > 0.05$) compared to that of the control group. This suggests that the hexane leaf extract of *M. occidentalis*, even at 5000 mg/kg of body weight, has no adverse impact on the animals' growth.

Variation in organs weight

Figure 2 shows the variations in the organs' weight throughout our acute toxicity test. Results show that there was significant variation in relative organ weights (heart, spleen, kidneys, liver, and lungs) across the groups, except that the lungs of both test groups were significantly inflamed compared to the control group. This indicates that, apart from pulmonary inflammation, the extract had no toxic impact on these vital organs based on mass variation.

Discussion

The global spread of multidrug-resistant (MDR) pathogens is leading to a reduction in the arsenal of antibiotics, and therefore, the need for the development of new drugs. This work was designed to investigate *in vitro* and *in vivo* the anti-staphylococcal activity of *M. occidentalis* extracts on MDR isolates. Moreover, the acute toxicity of the active extract was assessed.

According to the MIC Cut-off values established by Wamba et al. (2023), the hexane extracts of *M. occidentalis* displayed weak to very good to moderate anti-staphylococcal activity [21]. The hexane leaf extract exhibited the strongest activity, with MIC values of 64 $\mu\text{g/mL}$. Chloramphenicol, used as a control, was generally more effective but less active against some resistant strains (MIC up to 128 $\mu\text{g/mL}$), highlighting the challenge posed by MDR bacteria [3]. These results are consistent with prior studies on *M. occidentalis* and related *Macaranga* species. In a previous study, the dichloromethane/methane/methanol extract of *M. occidentalis* displayed MIC values of 250 to 1000 $\mu\text{g/mL}$ against bacteria, including *S. aureus*. These antimicrobial activities were associated with bioactive secondary metabolites, such as flavonoids and

prenylated phenolic compounds. For example, Schweinfurthin B, a C-prenylated phenolic isolated from *M. occidentalis*, showed moderate activity against *S. aureus* with an MIC of 62.5 $\mu\text{g/mL}$ [10]. The variation in activity across extracts and isolates reflects differences in phytochemical composition, supporting the idea that multiple synergistic compounds contribute to the antibacterial effects [22]. Our findings are also in agreement with those in the literature which demonstrated the antimicrobial activity of the methanol extract of other *Macaranga* species [12]. To the best of our knowledge, this is the first study to evaluate the anti-staphylococcal activity of the hexane extract of *M. occidentalis*. Proven *in vitro* antibacterial activity does not always guarantee *in vivo* antibacterial activity, making *in vivo* studies indispensable [23-25]. In MDR *S. aureus* infected *Wistar* rats, the hexane extract, at both 50 mg/kg and 100 mg/kg, led to a significant reduction in bacterial loads over time, particularly in females. Vancomycin treatment yielded the most effective bacterial clearance, and untreated controls maintained high infection levels, confirming the extract's antibacterial potential. Quantification of hematological parameters also suggested that this extract enhanced white and red blood cell counts and hemoglobin levels, particularly in males, indicating improved immune response and oxygen transport. Similar immunomodulatory and hematological effects have been reported with other medicinal plant extracts used against bacterial infections [26].

The results from the acute toxicity test revealed that the hexane leaf extract of *M. occidentalis* has a good safety profile as far as acute toxicity is concerned. The studies revealed that the LD₅₀ is above 5000 mg/kg of body weight. There was also little or no significant variation in relative body organs among the groups, except that of the spleen, whose mass was significantly low in the group receiving the plant extract at a concentration of 5000 mg/kg. There was equally no clinical sign of toxicity except the erection of fur on day two of the experiment. These results corroborate those of Kamsu et al. (2021), which showed that plant extracts can demonstrate good security profiles with LD₅₀ greater than 5000 mg/kg of body weight [27]. This finding agrees with the study of N'cho et al. (2025) who demonstrated that *M. heterophyllais* is safe in acute toxicity, with a LD₅₀ estimated to be higher than 6400 mg/kg [28]. The current study confirms that Africa's flora is a valuable and safe source of drugs to address various human ailments [29-33].

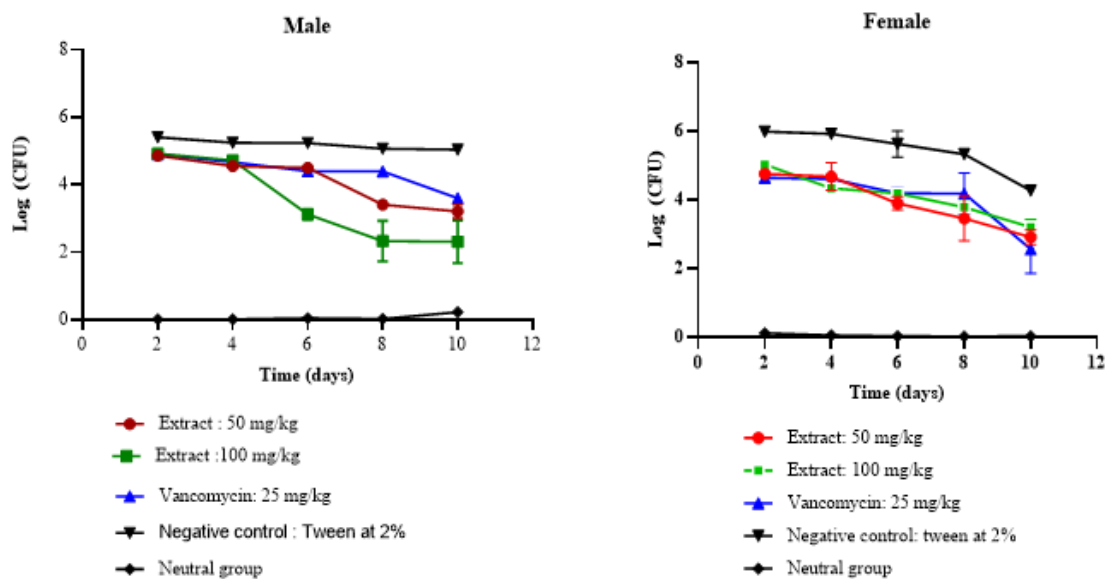


Figure 1. Effect of the extract on bacterial load in treated rats.

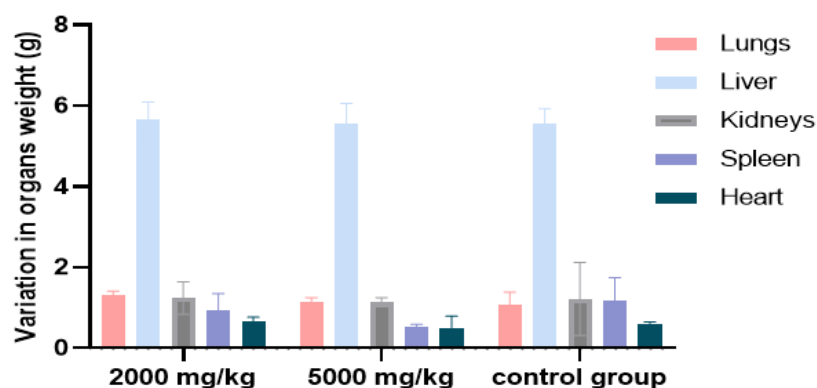


Figure 2. Effect of extract on the relative weight of the organs. The values in the table are presented as mean ± standard deviation of 3 replicates.

Table 1. In vitro anti-staphylococcal activity of *M. occidentalis* extracts

<i>S. aureus</i> strains	Samples, MIC and MBC (µg/mL)								
	MOL			MOB			Chloramphenicol		
	MIC	MBC	MBC/MIC	MIC	MBC	MBC/MIC	MIC	MBC	MBC/MIC
ATCC 29213	1024	1024	1	>2028	nd		2	32	>16
D009	2048	>2028	nd	512	2048	4	128	>256	>16
D018	>2028	>2028	nd	128	1024	8	32	128	4
D020	>2028	>2028	nd	>2028	>2028	nd	>256	>256	nd
D021	64	64	1	64	256	4	>256	>256	nd
D047	>2028	>2028	nd	>2028	>2028	nd	>256	>256	nd
D049	256	512	2	512	1024	2	16	32	2
D050	2048	>2028		2048	>2028	>1	128	>256	>16
D051	64	512	8	64	512	8	16	128	8
D052	64	128	2	128	256	2	64	128	2
D057	256	512	2	128	256	2	8	128	16
D060	1024	>2028	>2	1024	>2028	>2	4	128	32

MIC: Minimum inhibitory concentration; MBC: Minimum bactericidal concentration; MOL: *Macaranga occidentalis* leaf extract; MOB: *Macaranga occidentalis* bark extract; nd: not determined.

Table 2. Variation in hematological parameters in female rats

Groups	WBC	RBC	HGB	HCT	PLT	LYM	MCV	GRA
Extract (50 mg/Kg)	3.8±0.49 ^a	6±1.27 ^a	14.76±0.38 ^{ab}	43.7±18.1 ^{ab}	54.95±2.19 ^a	11.02±1.44 ^a	62.45±3.61 ^a	8.02±1.4 ^a
Extract (100 mg/Kg)	6±1.41 ^b	6.9±0.14 ^{ab}	11.7±0.42 ^a	27.65±2.33 ^a	63.5±4.95 ^a	81.44±1.44 ^a	61.25±5.3 ^a	9.42±1.84 ^a
VAN (25 mg/Kg)	5.4±0.21 ^{ab}	8.58±0.2 ^b	19.15±1.48 ^c	60.3±1.56 ^b	67±48.79 ^a	83±16.83 ^a	59.70.42 ^a	13.1±3.39 ^{ab}
Tween 2%	5.05±0.35 ^{ab}	6.95±0.47 ^{ab}	17.25±0.07 ^{bc}	46±1.41 ^{ab}	61.9±0.14 ^a	86.1±9.33 ^a	59.45±0.7 ^a	5.05±0.14 ^a
Neutral	4.8±0.92 ^{ab}	6.47±1.6 ^{ab}	14.25±3.04 ^{ab}	40.2±6.08 ^{ab}	62.9±6.08 ^a	77±4.24 ^a	59.55±2.51 ^a	14.9±5.27 ^b

WBC: White Blood Cell, RBC: Red Blood Cell, HGB: hemoglobin, HCT: hematocrit, MCV: Mean Corpuscular Volume, PLT: Platelets, LYM: Lymphocytes, GRA: granulocytes. The values in the table are presented as mean ± standard deviation of 3 replicates; within the same column, values assigned different letters are significantly different at the 5% probability level (p<0.05) according to the Waller-Duncan test and are compared to the negative and neutral controls.

Table 3. Variation in hematological parameters in male rats

Groups	WBC	RBC	HGB	HCT	PLT	LYM	MCV	GRA
Extract (50 mg/Kg)	6.5±0.71 ^b	7.92±0.11 ^a	16.25±1.77 ^b	43.5±4.94 ^b	62.45±3.61 ^a	205±7.07 ^b	65.35±7.57 ^a	19.7±1.84 ^a
Extract (100 mg/Kg)	3.5±0.1 ^a	5.38±0.87 ^a	11.25±1.06 ^a	27.7±0.35 ^a	61.25±5.3 ^a	20.50±1.12 ^a	71.02±1.13 ^a	17.5±1.84 ^a
VAN (25 mg/Kg)	4.25±0.7 ^{ab}	8.39±0.08 ^a	18.05±0.7 ^b	48.08±1.65 ^b	59.7±0.42 ^a	203.5±11.12 ^b	81.25±7.28 ^a	3.55±3.88 ^a
Tween 2%	6.25±0.49 ^{ab}	7.71±0.42 ^a	16.65±0.78 ^b	44.8±1.13 ^b	59.45±0.07 ^a	248±43.84 ^b	73.95±7.84 ^a	15.35±6.72 ^a
Neutral	4.7±0.14 ^{ab}	7.31±1.15 ^a	15.75±0.92 ^b	43.45±1.48 ^b	59.55±1.34 ^a	177±125.86 ^{ab}	59±21.21 ^a	21.45±10.81 ^a

WBC: White Blood Cell, RBC: Red Blood Cell, HGB: hemoglobin, HCT: hematocrit, MCV: Mean Corpuscular Volume, PLT: Platelets, LYM: Lymphocytes, GRA: granulocytes. The values in the table are presented as mean ± standard deviation of 3 replicates; within the same column, values assigned different letters are significantly different at the 5% probability level (p<0.05) according to the Waller-Duncan test and are compared to the negative and neutral controls.

Table 4. Clinical observations

Groups	Number of deaths	Sign of toxicity/ behavior changes
Control	0/3	No toxic effect
2000 mg/kg	0/3	Calm for approximately the first two hours after administration. No dryness of the eyes or abnormal mucus production by the nostrils or mouth. No paralysis, sign of dizziness or agitation
5000 mg/kg	0/3	Calm for approximately the first two hours after administration. No dryness of the eyes or abnormal mucus production by the nostrils or mouth. No paralysis, sign of dizziness, or agitation.

Table 5. Body weight variation in *Wistar* rats

Groups	Average body weight after every two days (g)							
	0	Day 2	Day 4	Day 6	Day 8	Day 10	Day 12	Day 14
2000 mg/kg	114.67±17.67 ^a	118.67±10.97 ^a	135±1.81 ^a	146±7 ^b	152±9.5 ^a	160±11.79 ^b	162±10.81 ^b	162±10.82 ^b
5000 mg/kg	100±00 ^a	99.33±0.58 ^a	100±2.84 ^a	106±4.7 ^a	115.67±3.05 ^b	125±2.65 ^a	134±1.73 ^a	134±1.73 ^a
Control	100±00 ^a	133.67±32.33 ^a	134.67±0.57 ^a	137±3.54 ^b	135±18.08 ^b	144±7.07 ^b	148±4.24 ^b	148±4.2 ^{ab}

The values in the table are presented as mean ± standard deviation of 3 replicates. Within the same column, values assigned different letters are significantly different (p < 0.05) according to the Waller-Duncan test and are compared to the control group.

Conclusion

This study has provided valuable information on the antibacterial activity of *M. occidentalis* extracts. It showed that the hexane leaf extract of *M. occidentalis* has both *in vitro* and *in vivo* antibacterial activity against MDR isolate of *S. aureus* with a good security profile, hence placing this extract as a potential weapon against infections caused by MDR *S. aureus*. Therefore, further studies including its subacute and chronic toxicity, as well as the identification of its active ingredients, should be envisaged.

Additional file

Table S1. Bacteria used and their resistance features: available at <https://www.investchempharma.com/wp-content/uploads/2018/01/www.investchempharma.com-supporting-information.pdf>

Abbreviations

GRA: granulocytes
 HCT: hematocrit
 HGB: hemoglobin
 HNC: Cameroon national herbarium
 INT: p-Iodonitrotetrazolium chloride
 LYM: Lymphocytes
 MBC: Minimum bactericidal concentration
 MCV: Mean corpuscular volume
 MDR: Multidrug-resistant
 MHA: Mueller Hinton Agar
 MHB: Mueller Hinton Broth
 MIC: Minimum inhibitory concentration
 MOB: *Macaranga occidentalis* bark extract
 MOL: *Macaranga occidentalis* leaf extract
 PLT: Platelets
 RBC: Red blood cells
 WBC: White blood cells
 WHO: World Health Organization

Authors' Contribution

PEKL, SRYS, RRN, and JBTK carried out experiments. AGF supervised the study. PEKL, RRN, and AGF analyzed data and wrote the original draft. VK reviewed and edited the original draft. All authors have read and approved of the final version of the manuscript.

Acknowledgments

The authors thank the National Herbarium of Cameroon, Yaoundé, Cameroon for the identification of the studied plant.

Conflict of interest

The authors declare no conflict of interest

Article history:

Received: 22 February 2026

Received in revised form: 27 April 2026

Accepted: 03 May 2026

Available online: 03 May 2026

References

- Ikuta K, Swetschinski L, Robles Aguilar G et al. 2022. Global mortality associated with 33 bacterial pathogens in 2019: A systematic analysis for the Global Burden of Disease Study 2019. *The Lancet*. 400(10369): 2221–2248.
- Yalew ST. 2020. Review on Antibiotic Resistance: Resistance Mechanisms, Methods of Detection and Its Controlling Strategies. *Biomed J Sci Tech Res*. 24(5).
- World Health Organization. 2023. World health statistics 2023: monitoring health for the SDGs, Sustainable Development Goals. Geneva: World Health Organization; Licence: CC BY-NC-SA 3.0 IGO.
- Ondusko DS, Nolt D. 2018. *Staphylococcus aureus*. *Pediatr Rev*. 39(6):287-298.
- Alabbosh K. F, Zmantar T, Bazaid AS, Snoussi M, Noumi E. 2023. Antibiotic Resistance and Adhesive Properties of Clinical *Staphylococcus aureus* Isolated from Wound Infections. *Microorganisms*, 11(5):1353.
- Martinez JL. 2019. Mechanisms of antibiotic resistance: Old and new. *Front Microbiol*. 10: 1297.
- Kuete V. 2023. African Flora to Fight Bacterial Resistance, Part II: The Best Source of Herbal Drugs and Pharmaceuticals. 660 p.
- Magadula JJ. 2014. Phytochemistry and pharmacology of the genus *Macaranga*: A review. *J Med Plant Res*. 8(12):489-503.
- Segun PA, Ogbale OO, Ismail FM, Nahar L, Evans AR, Ajaiyeoba EO, Sarker SD. 2019. Bioassay-guided isolation and structure elucidation of cytotoxic stilbenes and flavonols from the leaves of *Macaranga barteri*. *Fitoterapia*. 134:151–157.
- Kamsu VFK, Simo Fotso CC, Kanko Mbekou IM, Toussie BT, Ndjakou Lenta B, Boyom FF, Sewald N, Frese M, Ngadjui BT, Wabo Fotso G. 2022. Chemical Constituents of *Macaranga occidentalis*, Antimicrobial and Chemopreventive Studies. *Molecules*. 27(24):8820.
- Matsunami K, Takamori I, Shinzato T, Aramoto M, Kondo K, Otsuka H, Takeda Y. 2006. Radical-scavenging activities of new megastigmane glucosides from *Macaranga tanarius*. *Chem Pharm Bull*. 54:1403-1407.
- Lim TY, Lim YY, Yule CM (2009). Evaluation of antioxidant, antibacterial and anti-tyrosinase activities of four *Macaranga* species. *Food Chem*. 114:594-598.
- Hashim I, Onyari JM, Omosa LK, Maru SM, Nchiozem-Ngitedem VA, Karpoomath R. 2022. Conglomeratin: a new antibacterial flavonol derivative from *Macaranga conglomerata* Brenan (Euphorbiaceae). *Nat Prod Res*. 36(23):6012–6020.
- Jang DS, Cuendet M, Hawthorne ME, Kardono LBS, Kawanishi K, Fong HHS, Mehta RG, Pezzuto JM, Kinghorn AD. 2002. Prenylated flavonoids of the leaves of *Macaranga confiera* with inhibitory activity against cyclooxygenase-2. *Phytochemistry*. 61:867-872.
- Zakaria I, Ahmat N, Jaafar FM, Widyawaruyanti A. 2012. Flavonoids with Antiplasmodial and Cytotoxic Activities of *Macaranga triloba*. *Fitoterapia*. 83(5):968-72.
- Eloff JN. 1998. A sensitive and quick microplate method to determine the minimal inhibitory concentration of plant extracts for bacteria. *Planta Med*. 64(8):711-13.
- Kuete V, Ngameni B, Simo CC, Tankeu RK, Ngadjui BT, Meyer JJ, et al. 2008. Antimicrobial activity of the crude extracts and compounds from *Ficus chlamydocarpa* and *Ficus cordata* (Moraceae). *J Ethnopharmacol*. 120(1):17-24.
- Wamba BE, Mbaveng AT, Kuete V. 2023. Fighting Gram-positive bacteria with African medicinal plants: Cut-off values for the classification of the activity of natural products. In *Advances in Botanical Research*, Academic Press, Vol. 106, pp. 413-522.
- Levison ME. 2004. Pharmacodynamics of antimicrobial drugs. *Infect Dis Clin N Am*. 18(3):451–465.
- Yunana, B. T., Bukar, B. B., & Aguiyi, J. C. (2018). In vitro and in vivo evaluation of antibacterial activity of *Bridelia ferruginea* extracts on some clinical isolates. *Phytopharmacology*. 7(4):239-248.
- Organisation for Economic Co-operation and Development (OECD). (2022). Test No. 425: Acute Oral Toxicity: Up-and-Down Procedure. OECD Guidelines for the Testing of Chemicals, Section 4. OECD Publishing.
- Cowan MM. 1999. Plant products as antimicrobial agent. *Clin Microbiol Rev*. 4(12):564-582.
- Zak O, Tosch W, Sande MA. 1985. Correlation of antibacterial activities of antibiotics in vitro and in animal models of infection. *J Antimicrob Chemother*. 15(suppl A):273-2822.
- Terblanche SE, Kotze MJ. 2012. Antioxidant properties in vitro and in vivo: Realistic assessments of botanical extracts. *Proc S Afr Soc Anim Prod*. 42(3):15–22.
- Nambiar S, Laessig K, Toerner J, Farley J, Cox E. 2014. Antibacterial Drug Development: Challenges, Recent Developments, and Future Considerations. *Clin Pharmacol Ther*. 96(2):147-149.
- Ojo AA, Adeoye T.O, Afolayan AJ. 2021. Immunological and hematological effects of plant extracts: A review. *Phytother Res*. 35(4):1901-1915.
- Kamsu GT, Djamen Chuisseau DP., Fodouop Chegaing SP, Laure Feudjio HB, Ndel Famen L.-C, Kodjo N, Gatsing, D. 2021. Toxicological profile of the aqueous extract of *Tectona grandis* L. F. leaves: A medicinal plant used in the treatment of typhoid fever in traditional Cameroonian medicine. *J Toxicol*. 2021: 6646771.
- N'cho Guy-R A, N'guessan BB, Adjei S, Seidu MA, Mamyrbekova-Békro JA, Békro YA. 2025. Acute and sub-chronic toxicity studies of an aqueous extract of the leaves of *Macaranga heterophylla* Müll. Arg. (Euphorbiaceae) in Sprague-Dawley rats. *J Ethnopharmacol*. 349:119941.
- Dzoyem JP, Tohuenguem RT, Kuate JR, Teke GN, Kechia FA, Kuete V. 2014. *In vitro* and *in vivo* antifungal activities of selected Cameroonian dietary spices. *BMC Complement Altern Med*. Feb 17;14:58.
- Fankam AG, Kuate JR, Kuete V. 2017. Antibacterial and antibiotic resistance modulatory activities of leaves and bark extracts of *Recinodindron heudelotii* (Euphorbiaceae) against multidrug-resistant Gram-negative bacteria. *BMC Complement Altern Med*. Mar 24;17:168.
- Kuete V, Mbaveng AT, Zeino M, Fozing CD, Ngameni B, Kapche GD, Ngadjui BT, Efferth T. 2015. Cytotoxicity of three naturally occurring flavonoid derived compounds (artocarpesin, cycloartocarpesin and isobavachalcone) towards multi-factorial drug-resistant cancer cells. *Phytomedicine*. Nov 15;22:1096-1102.
- Mbaveng AT, Hamm R, Kuete V. 2014. 19 - Harmful and protective effects of terpenoids from african medicinal plants. In: *Toxicological Survey of African Medicinal Plants*. Elsevier. p. 557-576.
- Nayim P, Mbaveng AT, Wamba BEN, Fankam AG, Dzotam JK, Kuete V. 2018. Antibacterial and antibiotic-potentiating activities of thirteen Cameroonian edible plants against gram-negative resistant phenotypes. *ScientificWorldJournal*.2018:4020294.