J Med Sci
Volume 46, No. 4, December 2014: 161-166

Antimicrobial activity of bioactive compounds isolated from *Swietenia mahagoni* (L) Jacq. against *Staphylococcus aureus* and *Pseudomonas aeruginosa*

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ABSTRACT

Widespread bacterial resistance has led to more difficult to treat infectious diseases with available antibiotics. Therefore, new antibiotics are needed face of the growing antibiotic resistance. *Swietenia mahagoni* (L.) Jacq. is one of potential medicinal plants as a source new antibiotics. Five compounds have been isolated from an ethanolic extract of *S. mahagoni* (L.) Jacq., however its antimicrobial activity has not been investigated, yet. This study was conducted to evaluate the antimicrobial activity of these compounds. Minimal Inhibitory Concentration (MIC) and Minimal Bactericidal Concentration (MBC) were determined against *Staphylococcus aureus* and *Pseudomonas aeruginosa* strains. Among five compounds tested, compound 3 (3,4,5,6,7-pentaethyl-1-methoxy-1H-indazole) and compound 4 (5-ethyl-6-methoxymethyl-2-methyl-1,2-dihydropyridine) were found to be active against the bactrial strains tested with the MICs and MBCs values ranged from 50 to 100 µg/mL. In conclusion, among five compounds isolated from *S. mahagoni* (L.) Jacq., compound 3 and 4 showed moderate antimicrobial activity against *S. aureus* and *P. aeruginosa* strains.

ABSTRAK

Penyebaran secara luas resistensi bakteri menyebabkan pengobatan penyakit infeksi menjadi lebih sulit dengan antibiotik yang tersedia. Adanya antibiotik baru dengan demikian diperlukan menghadapi penyebaran resistensi antibiotik tersebut. *Swietenia mahagoni* (L.) Jacq adalah salah satu tanaman obat yang potensial sebagai penghasil antibiotik baru. Lima senyawa telah diisolasi dari ekstrak etanol biji *S. mahagoni* (L) Jacq. namun demikian aktivitas antimikrobanya belum dikaji. Penelitian ini bertujuan untuk mengkaji aktivitas antimikroba ke lima senyawa hasil isolasi tersebut. Kadar Hambat Minimal (KHM) dan Kadar Bunuh Minimal (KBM) ditetapkan terhadap strain *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Diantaran lima senyawa yang diuji, senyawa 3 (3,4,5,6,7-pentaetil-1-metoksi-1H-indazol) dan 4 (5-etil-6-metoksimetil-2-metil-1,2-dihidropiridin) aktif terhadap strain bakteri yang diuji dengan nilai KHM dan KBM antara 50 sampai 100 µg/mL. Dapat disimpulkan, diantaran lima senyawa yang diisolasi dari *S. mahagoni* (L.) Jacq. senyawa 3 dan 4 mempunyai aktivitas antimikroba moderat terhadap strain *S. aureus* and *P. aeruginosa*.

Keywords: *Swietenia mahogany* – active compounds – antimicrobial activity - *Staphylococcus aureus* - *Pseudomonas aeruginosa*

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INTRODUCTION

Infectious diseases still become a major health problem in developing and developed countries. They are leading cause of illness and death throughout the world. According to the Special Programme for Research and Training in Tropical Diseases, World Health Organization (TDR-WHO), infectious diseases kill 3.5 million people annually, mostly the poor and young children who live in low and middle income in countries.[1] Antibiotics are commonly used to treat of the infectious diseases. However, irrational use of antibiotics in the treatment of the diseases has led to the development of widespread bacterial resistance to antibiotics which becoming increasingly more difficult to treat the infectious diseases with currently available antibiotics.[2] Face of growing antibiotics resistance, a strategy is needed to discover and develop new antibiotics.[3]

In the past few decades, the searh for new antimicrobial agents has occupied many research groups in the field of ethnopharmacology. Many medicinal plants from different part of the world have been studied.[4] *Swietenia mahagoni* (L.) Jacq., locally known as the *mahoni*, belonging to the family Meliaceae, is one of potential medicinal plants as a source new antimicrobial agents that extensively investigated. The flower, leaf and bark extract of *S. mahagoni* (L.) Jacq. showed activity against Gram positive and Gram negative bacteria.[5,6] Moreover, the seed extract *S. mahagoni* (L.) Jacq. was active against *Bacillus subtillis, Sarcina lutea, Xanthomonas campestris, Klebsiella pneumoniae,* and *Escherichia coli.*[7]

In order to find out new antimicrobial agents, five compounds have been isolated from an ethanolic extract of *S. mahagoni* (L.) Jacq. (FIGURE 1) included 7-hydroxy-2-(4-hydroxy-3-methoxyphenyl)-chromen-4-one (**compound 1**), 3,6,7-trimethoxy-4-methyl-1,2,3,4-tetrahydro-isoquinoline (**compound 2**), 3,4,5,6,7-pentaethyl-1-methoxy-1H-indazole (**compound 3**), 5-ethyl-6-methoxymethyl-2-methyl-1,2-dihydropyridine (**compound 4**) and 1,4-bis (3,4,5-trimethoxy-phenyl)-tetrahydrofuro(3,4-c)furan (**compound 5**). In this study we reported the antimicrobial activity of these compounds against *Staphylococcus aureus* and *Pseudomonas aeruginosa* strains.

MATERIALS AND METHODS

Bacterial strains

The test bacteria employed in this study i.e. methicillin resistant *S. aureus* (MRSA), *S. aureus* (ATCC 25923), *P. aeruginosa* clinical isolate, and *P. aeruginosa* (ATCC 27853) were obtained from the Department of Microbiology, Faculty of Medicine, Universitas Gadjah Mada, Yogyakarta. These bacterial strains were maintained in viable state via inoculation on Brain Heart Infusion Double Strength (BDHI DS) media and overnight incubation at 37°C.

Tested compounds

The tested compounds were isolated from an ethanolic extract of *S. mahagoni* (L.) Jacq. seed by Dra. Mursiti, MSi. from the Department of Chemistry, Universitas Negeri Semarang. The structure of these tested compounds are presented in FIGURE 1.

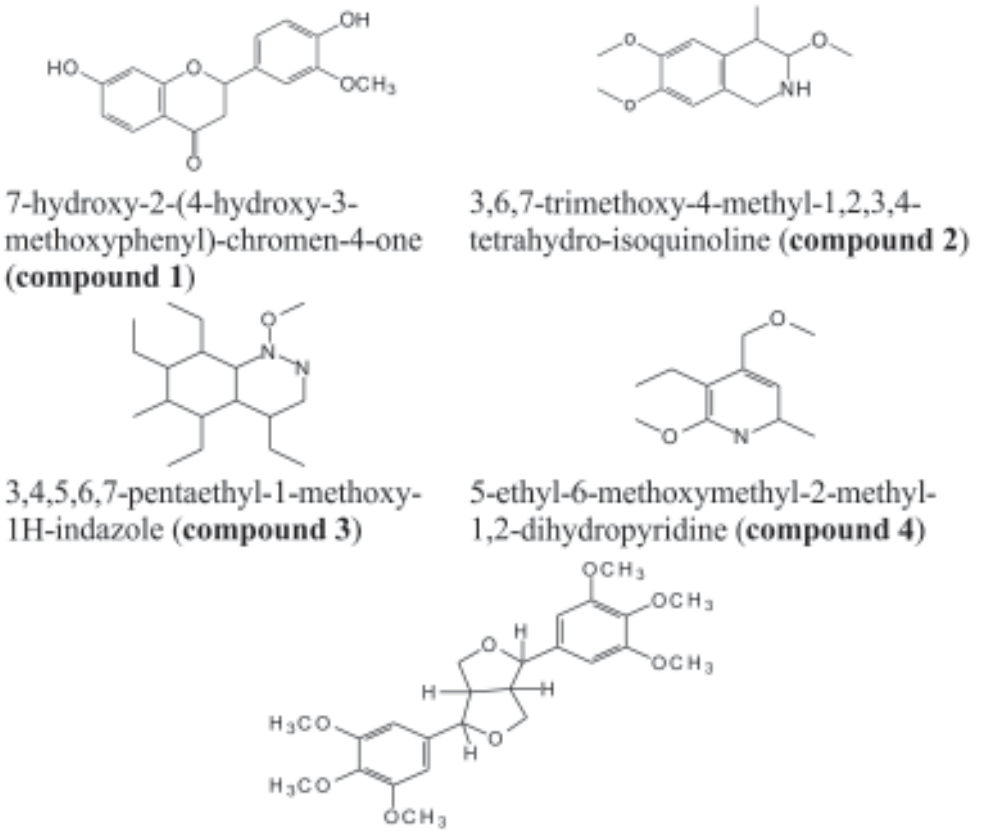

FIGURE 1. Tested compounds isolated from from an ethanolic extract of *S. mahagoni* (L.) Jacq. seed

Antimicrobial activity determination

Minimal Inhibitory Concentration (MIC) determination. The MIC of tested compounds was determined using the tube dilution method. Bacterial colonies were picked from freshly culture plates and diluted with Brain Heart Infusion Double Strength (BDHI DS) media to final concentration of 10^6 CFU/mL. Serial dilution of the tested compounds ranged from 1.56 to 800.00 µg/mL were prepared by diluting the stock solution with BHI DS media. One mL of the diluted bacterial suspension was added to tube containing one mL of serial the tested compounds dilution to yield the appropriate density 5 x 10^5 CFU/mL. The tubes were then incubated for 24 h at 37 °C. As negative control was a tube containing the diluted bacterial suspensions without the tested compounds, whereas as positive control was a tube containing the diluted bacterial suspensions with levofloxacin. The MICs were defined as the lowest concentration of the tested compounds that completely inhibits the growth of the organism as detected by the unaided eye. All MIC determination were conducted three times on independent experiments.

Minimal Bactericidal Concentration (MBC) determination. The bactericidal activities of the tested compounds were determined on the methicillin resistant *S. aureus* and *P. aeruginosa* clinical isolates. The suspentions of all the macroscopically clear tubes were inoculated onto plates of blood agar and were then incubated for

24 h at 37 °C. As control was a tube containing sterile distilled water and no the tested compounds were included. At the end of the incubation, the number of bacteria was counted in each of the tubes and was compared with the number of bacteria of the control tube. The MBCs were defined as the lowest concentration giving 0.1% bacterial survival.[8]

RESULTS

Antimicrobial activity of the tested compounds was investigated *in vitro* against Gram positive bacteria [MRSA and *S. aureus* (ATCC 25923)] and Gram negative bacteria [*P. aeruginosa* clinical isolate and *P. aeruginosa* (ATCC 27853)]. The antimicrobial activity was expressed by MICs and MBCs. The MICs values of the tested compounds are presented in TABLE 1. Among the five tested compounds, two compounds i.e. **compound 3** and **4** showed antimicrobial activity against the bacterial strains tested. The **compound 3** showed highest activity against *P. aeruginosa* (ATCC 27853) strain with the MIC value of 50 µg/mL, whereas the **compound 4** showed highest activity against both *S. aureus* (ATCC 25923) and *P. aeruginosa* (ATCC 27853) strains with the MICs values of 50 µg/mL. However, the MICs of the **compound 3** and **4** were lower than the MIC of levofloxacin (1 – 4 µg/mL) as positive control.

TABLE 1. The MICs values (µìg/mL) of tested compounds against the bacterial tested

Compound	Bacterial strain			
	MRSA	*S. aureus* ATCC	*P. aeruginosa* isolate	*P. aeruginosa* ATCC
Compound 1	NA	NA	NA	NA
Compound 2	NA	NA	NA	NA
Compound 3	200	100	100	50
Compound 4	100	50	100	50
Compound 5	NA	NA	NA	NA
Levofloxacin	1	1	4	4

NA: non activity against bacterial tested

The MBCs values of the tested compounds are presented in TABLE 2. The MBCs values of the **compound 3** and **4** were similar with its MICs values. The MBCs of these two compounds were also lower than the MBCs of the levofloxacin ((1 – 4 µg/mL).

TABLE 2. The MBCs values (ìg/mL) of tested compounds against the bacterial tested

Compound	Bacterial strain			
	MRSA	*S. aureus* ATCC	*P. aeruginosa* isolate	*P. aeruginosa* ATCC
Compound 1	NA	NA	NA	NA
Compound 2	NA	NA	NA	NA
Compound 3	200	100	100	50
Compound 4	100	50	100	50
Compound 5	NA	NA	NA	NA
Levofloxacin	1	1	4	4

ND: no activity against bacterial tested

DISCUSSION

Various parts of *Swietenia mahagoni* (L.) Jacq. have been used traditionally for the treatment of hypertension, diabetes, malaria, amoebiasis, coughs, tuberculosis, antiseptic, astringent, diarrhea, and tonic.[9-11] *Swietenia mahagoni* (L.) Jacq. seeds are also reported to have medicinal value for the treatment of hypertension, diabetes, malaria,[12] cancer, amoebiasis, coughs and intertinal parasitism.[13] Furthermore, the seed extract *S. mahagoni* (L.) Jacq. have been accounted to possess antimicrobial activity.[7]

In these study we have tested the antimicrobial activity of five compounds isolated from *S. mahagoni* (L.) Jacq. Among the five compounds tested, two compounds i.e. **compound 3** and **4** showed antimicrobial activity against *S. aureus* and *P. aeruginosa* strains tested with the MICs and MBCs values ranged from 50 to 100 µg/mL. The MICs and MBCs values of these **compound 3** and **4** were lower than the MICs and MBCs values of levofloxacin (1-4 µg/mL) as positive control indicating the antimicrobial activity of these compounds were moderate.

Some bioactive compounds have been isolated from *S. mahagoni* (L) Jacq. and their antimicrobial activity has been investigated. Kader *et al*.[7] isolated two limonoids, swietenine and 3-*O*-tigloylswietenolide from the chloroform soluble fraction of an ethanolic extract of *S. mahagony* (L) Jacq. seeds and evaluated its antimicrobial activity against a series of Gram positive and Gram negative bacteria. The most potent antimicrobial activity of these compounds were against *B. megatorium* and *E. coli*. Ghosh *et al*.[14] isolated other limonoids i.e. swietenolide and 2-hydroxy-3-*O*-tigloylswietenolide and also evaluated its antimicrobial activity against eight multiple-drug-resistant bacterial strains including Gram positive and Gram negative bacteria. 2-Hydroxy-3-*O*-tigloylswietenolide had, overall, more potent activity than swietenolide. The most potent antibacterial activity of swietenolide was against *Haemophilus influenzae*, *Salmonella typhi*, and *Salmonella paratyphi*, and 2-hydroxy-3-*O*-tigloylswietenolide was most active against *Streptococcus pneumoniae*, *Salmonella typhi*, and *Salmonella paratyphi*. Both the compounds were least effective against *Klebsiella pneumoniae*.

Both of the **compound 3** (3,4,5,6,7-pentaethyl-1-methoxy-1H-indazole) and **compound 4** (5-ethyl-6-methoxymethyl-2-methyl-1,2-dihydropyridine) are a class of alkaloids which are well known for their wide range of pharmacological activities including antimicrobial activity.[15,16] Although the antimicrobial activity of the **compound 3** and **compound 4** were found to be moderate, however the antimicrobial activity of these compounds have not been reported, yet. Therefore, these compounds could be used as starting points for new antimicrobial discovery.

CONCLUSION

In conclusion, among five compounds isolated from *S. mahagoni* (L.) Jacq., **compound 3** (3,4,5,6,7-pentaethyl-1-methoxy-1H-indazole) and **compound 4** (5-ethyl-6-methoxymethyl-2-methyl-1,2-dihydropyridine) showed moderate antimicrobial activity against *S. aureus* and *P. aeruginosa*.

ACKNOWLEDGEMENTS

The authors would like to thank all technicians from Department of Microbiology, Faculty of Medicine, Universitas Gadjah Mada for all valuable assisstances during the study.

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