Antibacterial activity of various medicinal plants in North Sumatra against common human pathogens

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Abstract
The necessity for new antibiotic compounds is becoming urgent, given the increasing number of bacteria that are resistant to one or several antibiotics. This study was aimed to assess the potential of 24 North Sumatra, Indonesia medicinal plants as a source of antibacterial compounds. Maceration with acetone solvents was used to extract the content from the medicinal plant samples. Then, antibacterial activity tests were conducted via in vitro on 6 pathogenic bacteria. The antibacterial screening was carried out using the M02-A11 Clinical and Laboratory Standard Institute (ClSI) diffusion method followed by the determination of Minimum Inhibitory Concentration (MIC) with Microdilution Methods M07-A9 (CSSI) and determination of Minimum Bactericide Concentration (MBC). Phytochemical tests were carried out on extracts which showed high activity.

The results confirmed that most of the samples showed antibacterial activity against 4 to 5 of test bacteria. Strong antimicrobial activity was shown by Phyllantus urinaria L extract against S. saprophyticus and Cassia angustifolia plant extracts against B. cereus and S. saprophyticus bacteria, each with a concentration of 312.5 ug/mL. The C. angustifolia is bacteriostatic, whereas P. urinaria L is bactericidal with an MBC value of 1250 ug/mL. Furthermore, P.urinaria contains alkaloids, flavanoids, terpenoids, saponins and tannins and so does C. Angustifolia.

Keywords: Screening, Medicinal plants, North Sumatra, Antibacterial activity, Pathogens.

Introduction

The development of bacterial strains that are resistant to one or several antibiotic has become a serious problem that must be addressed immediately[3,16,20]. Therefore, in the last decade, the demand for new antimicrobial substances has increased[19,25]. The existence of these phenomena is increasingly encouraging the importance and need for research to find new compounds that have the potential as effective drugs. One approach to obtain antimicrobial compounds is carried out through studies of compounds derived from plants[14,15]. Natural materials have been used since ancient times and have traditionally been used for the treatment of various diseases[5] as well as treatments that have been carried out in the Indian Olive Traditional Ayurveda and Unani treatment systems[18]. In Indonesia, especially in North Sumatra, the Batak ethnic groups have used plants as traditional medicine. However, this vast utilization has not been researched and analyzed optimally.

Therefore, this research is intended to examine the potential (exploring antibacterial plants) of North Sumatra medicinal plants as a source of candidate drug compounds, as well as a form of scientific support for traditional medicine.

Material and Methods

Plant material: Samples of various North Sumatra medicinal plants were obtained from traders of medicinal plants in the traditional market of Pancur Batu, North Sumatra, Indonesia. The selection was based on the number of plants used as traditional medicine. Furthermore, the sample was identified in Medan Herbarium, Indonesia.

Plants extract preparation: As much as 100 g of 24 dried sample samples were extracted by macerating process with 500 ml of 100% (v / v) acetone for 3 x 24 hours at room temperature. Then, it was filtered with filter paper. The filtrate was evaporated using a rotary at a temperature of 50°C to obtain a crude extract.

Antibacterial agents: The sample was dissolved in 10% dimethyl sulfoxide. The sample which was not soluble in 10% DMSO was dissolved in 100% DMSO to obtain a sample concentration of 10,000 µg/mL. Chloramphenicol concentration as a standard antibiotic is 500 µg/mL. 10% and 100% DMSO did not show antibacterial activity.

Antibacterial strains and inoculums preparation: The six pathogenic bacteria which were going to be tested consisted of 4 gram positive bacteria of *Bacillus cereus* ATCC 1178, *Salmonella enterica* ATCC 14028, *Staphylococcus saprophyticus* ATCC (49907), *Propionibacterium acne* ATCC (27853) and 2 gram negative bacteria of *Escherichia coli* ATCC 25922 and *Citrobacter freundii* ATCC 8090.

Bacterial suspension (inoculum) was prepared based on the growth method. Briefly, three to five bacterial colonies that grow well and have the same type of culture were chosen to use sterile needle loops and then suspended into 4-5 mL of 0.9% NaCl. The bacterial suspension was then incubated at 37°C for 24 hours. The incubation results were then synchronized with 0.5 McFarland standards equivalent to the number of colonies of 5 × 104 CFU / mL[22]. The inoculum was used within 15 minutes after preparation.

***In vitro* susceptibility tests:** Antibacterial screening of acetone extract from North Sumatra medicinal plant samples was carried out by M02-A11 paper disc diffusion method. As much as 100 µL of inoculums of the bacterial species were applied on Muller Hinton Agar (MHA, Oxoid) plates evenly using a sterile spreader. Furthermore, paper discs were placed on the surface of the inoculum layer on the MHA plate regularly. Then, as much as 15-20 µL of the test solution was dropped on each paper disc. The MHA plate was closed and then incubated aerobically at 37 ºC for 24 hours.

The MIC determination was based on the Micro-dilution Broth Method (M07-A9). MIC determination was carried out on extract using micro plate (96-well). The first well was used for negative controls containing only media while the second well was for positive controls containing media and inoculum.

Other wells were filled with a series of sample concentrations with the highest concentration in the twelfth well and the lowest concentration in well number three. The method was to enter 100 µL of MHB liquid media containing the inoculum into each micro plate well.

The concentration variation was carried out by entering 100 µL of the sample in the twelfth well, then 100 µL of the solution from the twelve wells was moved to eleven wells. The same thing was done from eleven wells to the third well, so the number of solutions in each well was 100 µL. The micro plates were then incubated at 37ºC for 24 hours.

Lastly, the MBC determination is a continuation of MIC determination where the MBC determination follows the procedure performed by Igbinosa et al[11]. Briefly, each 10 µL mixture in each well on the micro titer plate MIC test results was inoculated into the MHA plate. The number one well (negative growth control) and number two well (positive growth control) are included in the MBC test. MHA plates were incubated at 37ºC for 24 hours or until the growth was seen in positive controls.

Phytochemical screening: The identification of groups of secondary metabolites was conducted through flavonoids, terpenoids, saponins, tannins steroids test.[10,24]

Results and Discussion

In this study, as many as 24 samples of medicinal plants samples were commonly used in traditional medicine and traded in herbal medicine stores or in traditional markets. Antibacterial activity tests were carried out *in vitro*. The preliminary test of acetone extract of medicinal plants in North Sumatra was performed using the paper disc diffusion method. Then, the potential for antibacterial properties of the extract is determined from the clear zone around the filter paper. Finally, the screening results showed a minimum antibacterial activity of acetone extract against one bacterium tested. Data on bacterial growth inhibition are summarized in table 1.

Based on table 1, all medicinal plants in North Sumatra show antibacterial activity. Most of the samples showed activity on 4 and 5 bacteria with a percentage of 37.5% respectively. Samples that showed activity on 3 bacteria were 16.6%. Then, only 4.2% were recorded to be active against all bacteria, namely *Curcuma heyneana* extract. Based on these data, it is not surprising that the medicinal plant that has been used as a traditional medicine has shown real efficacy. The extract which showed activity was continued with the determination of MIC and MBC. MIC is used to determine the lowest concentration of antibacterial agents in inhibiting bacterial growth whereas MBC is defined as the lowest antibacterial concentration in which all microbes are killed. The results of the MIC determination are summarized in table 2.

An extract is categorized as active if the MIC value is less than 100 µg/mL, moderate if the MIC value ranges from 100 < MIC < 625 ug / mL and is not active if the MIC value is > 625 µg/mL respectively[6]. Most of the North Sumatra medicinal plants show activity with a MIC value of 625-5000 µg / mL. Therefore, in practical, traditional medicine is combining several plants to obtain a sufficient concentration of active compounds.

The lowest concentration of anti-bacterial agents was shown by *C. Angustifolia* plant extract which was able to inhibit strongly with a concentration of 312.5 ug/mL against *B. cereus* and *S. saprophyticus* bacteria. The results of this study are consistent with previous studies where the genus *cassia* showed antibacterial activity, as published by Akhtar et al[2] who reported that ethanol extract of *C. Didymobotyra* had activity against *S. aureus* ATTC 25923 with MIC of 6.25 mg/mL and against *E. coli* ATCC 25922, *S. Typhimurium* ATTC 13311, *P. Aerugenosa* ATCC 27853 with MIC of 12.50 mg/mL. Likewise, Neog et al[13] reported that *C. Javanica L.* extract showed activity against *S. aureus* ATTC 25923. Moreover, Ehiowemwenguan discovered that *S. Alata* shows activity against *Salmonella typhii* with MIC of 8.00 mg/mL.[7]

Similar result was shown by the extract of *P. urinaria L* which inhibits strongly (312.5 ug / mL) against *S. saprophyticus*. The results of this study are also in line with previous studies, namely the genus *Phyllanthus* which has antibacterial properties. The research included plant extracts of the genus *Phyllanthus, P. acidus* and *P. pulcher* which had antimicrobial activity against the *S. aureus* bacteria, *P. myrtifolius* against *P. stutzeri* [8], *P. emblica* against *S. aureus* and *Klebsiellae pneumoniae*[21].

MBC data shows that in general, the ability of samples to kill bacteria requires a higher concentration of 1-4 times the value of MIC. The ability to eliminate C. Angustifolia against *B. cereus* and *S. saprophyticus* bacteria is > 5000 ug

/ mL. Thus, *C. Angustifolia* is bacteriostatic with respect to these bacteria. Meanwhile, *P. urinaria* L against *S. saprophyticus* bacteria is bactericidal with a MIC value of 1250 ug/mL.

The medicinal efficacy of a plant is caused by the content of secondary metabolites. The results of phytochemical screening of most medicinal plants in North Sumatra contain 3-5 groups of secondary metabolites. The data on the results of phytochemical screening are summarized in table 4.

Acetone extract of *C. Angustifolia* which showed good anti-bacterial activity against cereus and *S. saprophyticus* bacteria showed various chemical compounds. Phytochemical test results of acetone extract of *C. Angustifolia* proved to contain alkaloids, flavonoids, steroids, saponins and tannins. This is in line with the report by France et al and the results of a review of 50 Cassia species including anthraquinone derivatives, flavonoids, chromones, proanthocyanidin, naphthopyrone and cantonoid[9,12].

Table 1
Zone data for sample inhibition of medicinal plants in North Sumatra

S.N.	Species Name	Family	Used part	Bacteria					
				Pa	Se	Bc	Ss	Cf	Ec
1	*Morinda elliptica*	*Rubiaceae*	Seeds	+	+	+	+	-	+
2	*Parkia P. roxburghii*	*Fabaceae*	Seeds	+	-	-	-	-	-
3	*Selaginella doederleinii*	*Selaginellaceae*	Whole part	-	+	-	+	+	+
4	*Cassia angustifolia*	*Fabaceae*	Leaves	+	+	+	+	+	-
5	*Helicteres isora L*	*Malvaceae*	Wood fruit	+	+	+	+	+	-
6	*Vitis gracilis Wall*	*Vitaceae*	Leaves	+	-	+	-	+	-
7	*Justicia gandarusa*	*Acantaceae*	Leaves	+	-	+	-	+	-
8	*Bidens chinensis (L.) Willd.*	*Asteraceae*	Leaves	+	-	+	+	+	-
9	*Leersia hexandra*	*poaceae*	Seeds	+	+	+	+	+	-
10	*Curcuma heyneana*	*Zingiberaceae*	Rhizome	+	+	+	+	+	+
11	*Amomum compactum*	*Zingiberaceae*	Seeds	+	-	+	+	+	+
12	*Saurauia bacteosa*	*Actinidiaceae*	Bark	+	+	+	+	+	-
13	*Curanga sp*	*Araceae*	Leaves	+	-	+	+	-	-
14	*Elatostema strigosum Hassk*	*Araceae*	Leaves	+	-	-	+	+	+
15	*Hemigraphis alternate (Blume) Hallier f*	*Achantaceae*	Whole part	+	-	+	+	+	+
16	*Litsea sp*	*Lauraceae*	Leaves	+	-	+	+	+	+
17	*Pisona umberelliifera J.R. Forst & G. Forst*	*Nygtaginaceae*	Leaves	+	-	+	+	+	-
18	*Phyllantus urinaria L*	*Phyllantaceae*	Whole part	+	-	+	+	-	+
19	*Molugo sp.*	*Molluginaceae*	Leaves	+	-	+	+	-	+
20	*Hoya revolute Wight ex Decne*	*Asclepi adaceae*	Leaves	+	-	+	+	+	-
21	*Blumea lacera (Burm.f.) DC*	*Asclepidiaceae*	Leaves	+	-	+	+	+	-
22	*Cayratia japonica (Thunb.) Gapneb*	*Vitaceae*	Leaves	+	-	+	+	-	+
23	Oldenlandia sp	*Rubiaceae*	Leaves	+	-	+	+	+	+
24	*Clerodendrum sp*	*Araceae*	Leaves	+	-	+	+	-	+

*Note: Pa = *P. acne* ATCC (27853); Se = *Salmonella enterica* ATCC 14028; Bc = *B. cereus* ATCC 1178; Ss = *S. saprophyticus* ATCC 49907; Cf = *C. freundii* ATCC 8090; Ec = *Escherichia coli* ATCC (25922), (+) the clear zone was present around paper discs and (-) the clear zone was not present around paper discs

Table 2
MIC value of acetone extract of medicinal plants in North Sumatera

S.N.	Species Name	Family	*P.acne*	*E.coli*	*S. enterica*	*B. cereus*	*S. saprophyticus*	*C. freundii*
1	*Chloramphenicol*	*Osphronemidae*	0,49	0,97	0,48	0,48	0,48	1,9
2	*Morinda elliptica*	*Rubiaceae*	1250	1250	625	>5000	625	ND
3	Parkia *P. roxburghii*	*Fabaceae/ Mimosaceae*	2500	ND	ND	ND	ND	ND
4	*Selaginella doederleinii*	*Selaginellaceae*	1250	>5000	625	>5000	1250	>5000
5	*Cassia Angustifolia*	*Fabaceae*	2500	ND	625	**312,5**	**312,5**	625
6	*Helicteres isora L*	*Malvaceae*	1250	ND	625	1250	625	625
7	*Vitis gracilis Wall*	*Vitaceae*	1250	ND	ND	1250	ND	1250
8	*Justicia gandarusa*	*Acantaceae*	1250	ND	ND	1250	ND	1250
9	*Bidens chinensis (L.) Willd.*	*Asteraceae*	1250	ND	ND	625	1250	1250
10	*Leersia hexandra*	*poaceae*	5000	ND	625	625	625	312,5
11	*Curcuma heyneana*	*Zingiberaceae*	1250	5000	625	625	1250	1250
12	*Amomum compactum*	*Zingiberaceae*	1250	>5000	ND	1250	1250	1250
13	*Saurauia bacteosa*	*Actinidiaceae*	1250	ND	1250	1250	1250	2500
14	*Curanga sp*	*Araceae*	2500	ND	ND	1250	1250	ND
15	*Elatostema strigosum Hassk*	*Araceae*	1250	2500	ND	ND	2500	ND
16	*Hemigraphis alternate (Blume) Hallier f*	*Achantaceae*	1250	2500	ND	625	1250	1250
17	*Litsea sp*	*Lauraceae*	1250	5000	ND	5000	1250	1250
18	*Pisona umberelliifera J.R. Forst & G. Forst*	*Nygtaginaceae*	1250	ND	ND	>5000	1250	1250
19	*Phyllantus urinaria L*	*Phyllantaceae*	1250	>5000	ND	1250	**312,5**	ND
20	*Molugo sp.*	*Molluginaceae*	>5000	2500	ND	>5000	>5000	ND
21	*Hoya revolute Wight ex Decne*	*Asclepi adaceae*	1250	ND	ND	1250	1250	1250
22	*Blumea lacera (Burm.f).DC*	*Asclepidiaceae*	1250	ND	ND	1250	625	1250
23	*Cayratia japonica (Thunb.) Gapneb*	*Vitaceae*	1250	2500	ND	1250	1250	ND
24	Oldenlandia sp	*Rubiaceae*	1250	2500	ND	1250	1250	1250
25	*Clerodendrum sp*	*Araceae*	1250	5000	ND	625	625	ND
Active count			**24**	**12**	**7**	**22**	**21**	**16**

*Note: Pa = *P. acne* ATCC (27853); Se = *Salmonella enterica* ATCC 14028; Bc = *B. cereus* ATCC 1178; Ss = *S. saprophyticus* ATCC 49907; Cf = *C. freundii* ATCC 8090; Ec = *Escherichia coli* ATCC (25922), ND = not determined

Table 3
MBC value of acetone extract of North Sumatera medicinal plants

S.N.	Species	Family	*P.acne*	*E.coli*	*S.enterica*	*B.cereus*	*S.saprophyticus*	*C. freundii*
1	*Chloramphenicol*	*Osphronemidae*	31,5	31,3	7,8	1,95	56,3	62,5
2	*Morinda elliptica*	*Rubiaceae*	>5000	2500	1250	>5000	1250	ND
3	Parkia *P. roxburghii*	*Fabaceae/ Mimosaceae*	>5000	ND	ND	ND	ND	ND
4	*Selaginella doederleinii*	*Selaginellaceae*	>5000	ND	2500	>5000	1250	>5000
5	*Cassia Angustifolia*	*Fabaceae*	>5000	ND	1250	>5000	>5000	>5000
6	*Helicteres isora L*	*Malvaceae*	>5000	ND	1250	>5000	1250	>5000
7	*Vitis gracilis Wall*	*Vitaceae*	>5000	ND	ND	>5000	ND	>5000
8	*Justicia gandarusa*	*Acantaceae*	>5000	ND	ND	>5000	ND	>5000
9	*Bidens chinensis (L.) Willd.*	*Asteraceae*	>5000	ND	ND	>5000	1250	>5000
10	*Leersia hexandra*	*poaceae*	>5000	ND	625	625	1250	>5000
11	*Curcuma heyneana*	*Zingiberaceae*	>5000	5000	625	>5000	1250	>5000
12	*Amomum compactum*	*Zingiberaceae*	>5000	ND	ND	5000	1250	>5000
13	*Saurauia bacteosa*	*Actinidiaceae*	>5000	ND	5000	2500	1250	>5000
14	*Curanga sp*	*Araceae*	>5000	ND	ND	>5000	1250	ND
15	*Elatostema strigosum Hassk*	*Araceae*	>5000	2500	ND	ND	2500	ND
16	*Hemigraphis alternate (Blume) Hallier f*	*Achantaceae*	>5000	2500	ND	>5000	1250	>5000
17	*Litsea sp*	*Lauraceae*	>5000	>5000	ND	>5000	1250	>5000
18	*Pisona umberelliifera J.R. Forst & G. Forst*	*Nygtaginaceae*	>5000	ND	ND	>5000	1250	>5000
19	*Phyllantus urinaria L*	*Phyllantaceae*	>5000	ND	ND	>5000	1250	ND
20	*Molugo sp.*	*Molluginaceae*	>5000	2500	ND	ND	ND	ND
21	*Hoya revolute Wight ex Decne*	*Asclepi adaceae*	>5000	ND	ND	>5000	>5000	>5000
22	*Blumea lacera (Burm.f).DC*	*Asclepidiaceae*	>5000	ND	ND	1250	2500	ND
23	*Cayratia japonica (Thunb.) Gapneb*	*Vitaceae*	>5000	2500	ND	1250	1250	ND
24	Oldenlandia sp	*Rubiaceae*	>5000	2500	ND	1250	1250	>5000
25	*Clerodendrum sp*	*Araceae*	>5000	5000	ND	625	1250	ND

*Note: Pa = *P. acne* ATCC (27853); Se = *Salmonella enterica* ATCC 14028; Bc = *B. cereus* ATCC 1178; Ss = *S. saprophyticus* ATCC 49907; Cf = *C. freundii* ATCC 8090; Ec = *Escherichia coli* ATCC (25922), ND = not determined

Table 4
The phytochemical screening result of acetone extract of North Sumatera medicinal plants

S.N.	Nama Latin	Family	Alkaloid	Flavanoid	Terpenoid	Steroid	Saponin	Tannin
1	*Morinda elliptica*	*Rubiaceae*	V	V	-	V	-	-
3	*ParkiaP. roxburghii*	*Fabaceae/ Mimosaceae*	-	-	-	V	-	-
4	*Selaginella doederleinii*	*Selaginellaceae*	-	V	-	-	V	V
5	*Cassia Angustifolia*	*Fabaceae*	V	V	V	-	V	V
7	*Helicteres isora L*	*Malvaceae*	V	V	-	V	V	V
8	*Vitis gracilis Wall*	*Vitaceae*	V	V	-	-	V	V
9	*Justicia gandarusa*	*Acantaceae*	V	V	-	-	V	V
10	*Bidens chinensis (L.) Willd.*	*Asteraceae*	V	V	V	-	-	V
11	*Leersia hexandra*	*Poaceae*	V	V	V	-	-	V
12	*Curcuma heyneana*	*Zingiberaceae*	V	V	-	V	-	-
13	*Amomum compactum*	*Zingiberaceae*	V	V	-	V	-	V
14	*Saurauia bacteosa*	*Actinidiaceae*	V	V	-	V	V	V
15	*Curanga sp*	*Araceae*	V	V	-	V	-	V
16	*Elatostema strigosum Hassk*	*Araceae*	V	-	-	-	V	V
17	*Hemigraphis alternate (Blume) Hallier f*	*Achantaceae*	V	V	-	-	V	V
18	*Litsea sp*	*Lauraceae*	V	V	-	V	-	V
19	*Pisona umberelliifera J.R. Forst & G. Forst*	*Nygtaginaceae*	V	-	-	-	V	-
20	*Phyllantus urinaria L*	*Phyllantaceae*	V	V	V	-	V	V
21	*Molugo sp.*	*Molluginaceae*	V	V	V	-	V	V
22	*Hoya revolute Wight ex Decne*	*Asclepi adaceae*	V	V	-	V	-	-
23	*Blumea lacera (Burm.f.) DC*	*Asclepidiaceae*	V	V	V	-	V	V
24	*Cayratia japonica (Thunb.) Gapneb*	*Vitaceae*	V	-	-	-	V	V
25	*Oldenlandia sp*	*Rubiaceae*	V	V	-	-	V	V
26	*Clerodendrum sp*	*Araceae*	V	-	-	-	V	V

*Note: (V) = Positive Result; (-) = Negative Result

In addition, *P.urinaria* which has good activity against *S. saprophyticus* contains various chemical compounds which contain alkaloids, flavonoids, terpenoids, saponins and tannins. The results of this study are in accordance with those reported by Padua et al.[17] Calixto et al[4] stated that the genus Phyllanthus is a producer of compounds in the class of lignans, alkaloids, flavonoids, terpenoids, steroids and phenolic acids[17].

Conclusion

North Sumatra medicinal plants contain secondary metabolites and various activities. Therefore, it can be concluded that they are potential sources of new antibiotic compounds to fight certain bacteria.

Acknowledgement

Authors would like to acknowledge Ministry of Research, Technology and Higher Education of Indonesia for funding the research via contract number of 027/UN33.8/2018. Furthermore, gratitude is addressed to Dr. Nursahara Pasaribu, from Herbarium Medan for being able to identify sample plants.

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(Received 23rd July 2019, accepted 28th September 2019)