Volume 05, Issue 01 (January-February 2022), PP 37-43 www.ijmsdr.org
ISSN: 2581-90

International Journal of Medical Science and Dental Research

Bioactivity and Phytochemical Compound Test on Black Betel Leaves (*Piper betle* var. *nigra*) A Literature Review

Khalish Arsy Al Khairy Siregar[1], Hasyrul Hamzah[1], Paula Mariana Kustiawan[1], Wirnawati[1], Chaerul Fadly Mochtar Luthfi M[1]

[1]*Faculty Of Pharmacy, Muhammadiyah University Of East Borneo, East Borneo, Samarinda Indonesia, 75124*

Abstract : Indonesia has abundant biodiversity throughout its land and seas. The use of plants as treatment has been carried out for a long time by people in Indonesia. Biodiversity Indonesia has abundant potential herbal plants. One of the potential herbal plants is the black betel leaf (Piper betel). The people of Indonesia have long used black betel. Black betel leaf contains phytochemical compounds, namely alkaloids, saponins, tannins, and flavonoids. Empirically, this plant has been used by the community for several uses and also has many bioactivities, namely as an antiseptic, analgesic, antioxidant, antibacterial, antidiarrheal, anti-inflammatory, and other activities that are good for the body where it is hoped that this plant can be developed into output in the form of products that are good for the body. The community can use it. The results of a journal search where we found many secondary compounds found in black betel leaf, which are in the flavonoid, terpenoid, alkaloid, and other groups, besides that we found several activities that were scientifically recorded, including antibacterial, antioxidant, antihyperglycemic, antifungal activity. and others. Black betel leaf has many activities, including antioxidant, antibacterial, anti-inflammatory, antihyperglycemic, and others supported by supporting secondary compounds.

Keywords - *Black Betel Leaf, Phytochemistry, bioactivity, Piper betel, potency*

I. INTRODUCTION

Indonesia has abundant biodiversity throughout its land and seas. The use of plants as treatment has been carried out for a long time by people in Indonesia [1]–[4]. Every plant contains various chemical substances called phytochemicals, where these materials have many activities that are good for the body and can function as compounds that can fight disease. Phytochemicals are chemical compounds that occur naturally in plants and have more specific functions [5]–[7] . Plant secondary metabolites have important roles in plant defense against pests and defense between other species. Humans use secondary metabolites as medicine, flavoring, and recreational drugs. Treatment using herbal plants is currently increasingly widespread using various types of plants [8]–[12]. There is no doubt about Indonesia's biological diversity, with an abundance of herbal plants. One of the Indonesian herbal plants that has efficacy is Black Betel leaves or Piper betle var. This plant is still very rarely discussed, and not much is known about its content and activities. Piper betle var. is a species of the betel tribe which is included in the Piperaceae family [13]. Empirically, traditional people use this plant as a treatment for stomach pain, ulcers, diabetes and others. This study aims to determine the phytochemical content and trace bioactivity in Piper betle var. Black Betel leaves , which is expected to be used in the future as a medicinal ingredient used to fight various types of diseases [14].

II. MATERIALS AND METHODS

This article research uses the literature review method, as used by collecting international and national articles and journals. Using the goggle platform and Pubmed using the keywords Black Betel Leaf, Phytochemistry, bioactivity, Piper betel, this research was conducted in November 2021.

III. RESULT

***Description of Black Betel* Leaves (*Piper betle* var. *nigra.*)**

Betel leaf is a plant that is vines and depends on other plants for its life. And also this black betel leaf is one of the betel betel tribe or Piperaceae, the position of black betel plants in plant taxonomy is as follows:

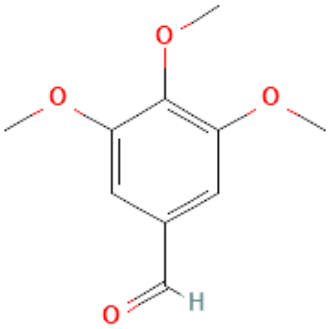
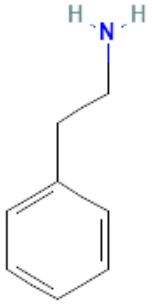
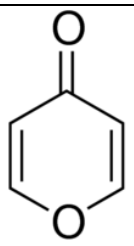
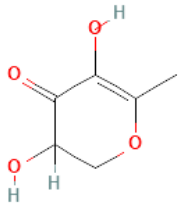
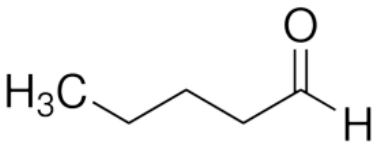
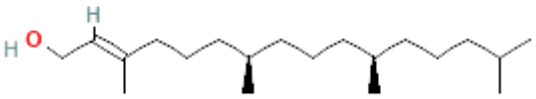
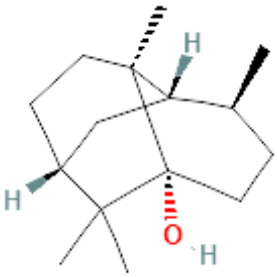
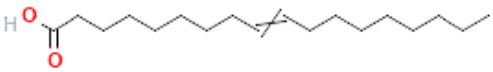
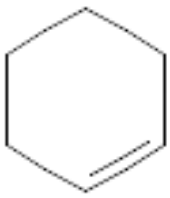
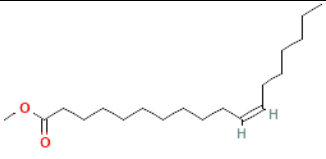
Kingdom	:	Plantae
Sub Kingdom	:	Tracheobionta
Super Divisi	:	Spermatophyta
Divisi	:	Magnoliophyta
Kelas	:	Magnoliopsida
Sub Kelas	:	Magnolidae
Ordo	:	Piperales
Familia	:	Piperaceae
Genus	:	Piper
Species	:	Piper Betle var nigra

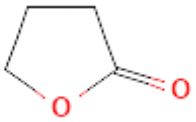
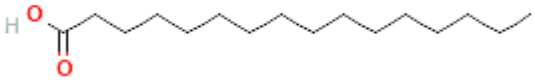
Black betel is one type of betel plant that has many uses as medicine. Black Betel leaves has a unique characteristic, namely the shape of the leaves resembles a heart, stems, the leaves are dark green blackish, and when held, the leaves feel thick and stiff [15]. The use of Black Betel leaves (*Piper betle* var. *nigra.*) The practical use of Black Betel leaves related to antioxidants is that Black Betel leaves is used in the treatment of diabetes mellitus, hepatitis, kidney stones, lowering cholesterol, preventing stroke, gout, hypertension, and others [16], [17].

Phytochemical Screening

From the journals that have been reviewed, several compounds have been found that play a role in Black Betel leaves (*Piper betle* var. *nigra.*), where Black Betel leaves contains volatile, volatile oils. The derivative of the essential oil is found in the compound Betel leaves containing volatile, volatile oil. Among the largest are chavicol and betlephenol. In addition, other compounds found were allylcocotechol, cinede, charryophyllene, menthone, eugenol, methyl ether, in addition to vitamin C compounds and arakene alkaloids [18]. Black Betel leaves contains secondary metabolites of alkaloids, carotenoids, phenolic compounds, flavonoids, polyphenols, saponins, tannins, steroids, and triterpenoids [8], [9], [13], [19]–[21]. Chemical compounds that are thought to function in this case are tannins, phenolic compounds, saponins, flavonoids, alkaloids, and steroids [15]. The secondary metabolites contained in Black Betel leaves include:

Tabel 1. Chemical Compoud in Black Betel (*Piper betle* var. *nigra.*)

Category	Chemical Compound	
Alkaloids [22]–[24]	 3,4,5-trimetoxy	 Phenethylamine
Flavonoid [25]–[28]	 4H-pyran-4-one	 2,3-dihydro 3,5-dihydroxy-6-methyl
	 Veleraldehyde	 Phytol
Terpenoid [29]–[33]	 Patchouli alcohol	 9-Octadecenoic acid
Etanol [34]–[37]		 11-octadecenoic acid

Cyclohexene	
	
Butyrolactone	Palmitic acid

Bioactivity in Black Betel Leaf (Piper betle var.)

Tabel 2. Bioactivity in Black Betel (*Piper betel* var. *nigra.*)

Activity	Description
Antioxidant	Black Betel leaves extract has antioxidant activity shown in methanol extract, ethyl acetate fraction extract and n-butanol fraction extract, Black Betel leaves extract which does not have antioxidant activity is shown in n-hexane fraction extract, and the best IC50 value is shown in methanol extract which is 158.53 ppm [15].
	The results of testing the cytotoxic potential of the Black Betel leaves extract *(Piper betle* var. *nigra)* obtained the LC50 value of each, namely the young Black Betel leaves extract was 69.18 ppm and the dark Black Betel leaves extract was 5.13 ppm [38].
	The results showed that the Rf values of compounds with antioxidant potential in n-hexane extract, ethyl acetate extract, and ethanol extract were 0.6625, respectively; 0.525 and 0.475. Antioxidant potential in the form of IC_{50} values possessed by n-hexane extract, ethyl acetate extract, and ethanol extract, respectively were 72.440; 25.009, and 8.123 g/ml [39].
Antihyperglycemia	Betel leaves decoction has an antihyperglycemic effect in male rats. It is expressed as a significance value < 0.05. Betel leaves boiled water does not affect reducing blood cholesterol levels in male rats. This is indicated by a significance value greater than 0.05. From the data above, it can be concluded that the boiled water of Betel leaves can be used as an herbal alternative to lower blood sugar [40].
	There is a significant effect between the treatment of Betel leaves decoction on reducing blood sugar levels in alloxan-induced white rats. There is a very significant correlation between the treatment and the decrease in blood glucose, where the correlation is directly proportional. The most effective dose of Betel leaves decoction in reducing blood sugar levels in white rats is 3 ml/150 grams BW/day [41].
	Giving 2% Betel leaves extract reduced blood glucose levels in experimental animals, namely male white rats (*Rattus Copernicus*) [17].
Antibacterial	The study results concluded that the ethanolic extract of Black Betel leaves (*Piper betle* L. var *Nigra*) has antibacterial activity on the growth of Propionibacterium acne bacteria. Moreover, storage time has an effect on the antibacterial activity of the ethanolic extract of Black Betel leaves, which on day 7 produces the largest bacterial inhibition zone compared to the bacterial inhibition zone on days 3 and 10 [42].
Antioxidant	Black Betel leaves extract has antioxidant activity shown in methanol extract, ethyl acetate fraction extract and n-butanol fraction extract, Black Betel leaves extract which does not have antioxidant activity is shown in n-hexane fraction extract, and the best IC50 value is

	shown in methanol extract which is 158.53 ppm [43].

IV. CONCLUSION

Search results from several articles found secondary compounds found in Black Betel leaves (*Piper betle* var. *nigra*.), including 4H-pyran-4-one, Veleraldehyde, Phytol, Patchouli alcohol, 9-Octadecenoic acid, Cyclohexene, 11-octadecenoic acid, Butyrolactone, Palmitic acid, 3,4,5-trimetoxy Phenethylamine 4H-pyran-4-one 2,3-dihydro 3,5-dihydroxy-6-methyl. In addition, several activities were found in Black Betel leaves, including antifungal, antioxidant, antihyperglycemic, and antioxidant activities.

Acknowledgements

We would like to thank the Directorate General of Higher Education, Research and Technology, Ministry of Education and Culture for funding this research through the 2021 Talent Innovation Program based on decree 4613/E4/AK.04/2021

REFERENCES

[1] Kementerian Kehutanan Republik Indonesia, "Lokakarya Nasional Tanaman Obat Indonesia," 2010. www.dephut.go.id (accessed Feb. 27, 2021).

[2] K. A. A. K. Siregar, N. M. Aisyiyah, and P. M. Kustiawan, "Tinjauan Artikel: Potensi Tanaman Lakum (Cayratia Trifolia) Sebagai Imunomodulator Review," *Farmagazine*, vol. VIII, no. 2, pp. 13–19, 2021, doi: 10.47653/farm.v8i2.549.

[3] W. Rahmah, E. Nandini, and K. A. A. khairy Siregar, "POTENSI TANAMAN MANGROVE SEBAGAI AGEN ANTIKANKER : LITERATURE REVIEW," *J. Penelit. Farm. Indones.*, vol. 10, no. 1, 2021.

[4] H. Hamzah, T. Hertiani, S. U. T. Pratiwi, T. Nuryastuti, and A. P. Gani, "Antibiofilm studies of zerumbone against polymicrobial biofilms of *staphylococcus aureus, escherichia coli, pseudomonas aeruginosa,* and *candida albicans*," *Int. J. Pharm. Res.*, vol. 12, no. September, pp. 1307–1314, 2020, doi: 10.31838/ijpr/2020.SP1.211.

[5] H. Hamzah, K. A. A. K. Siregar, A. Nurwijayanto, R. Wahyuningrum, and S. Sari, "Effectiveness of Oxalis corniculata L . Ethanol Extract against Mono- Species of Biofilm Staphylococcus aureus," *Borneo J. Pharm.*, vol. 4, no. 3, pp. 184–191, 2021, doi: 10.33084/bjop.v4i3.2418.

[6] E. Feriadi, W. Wahyuni, and M. I. Yusuf, "Antimitotic Activity of Cayratia trifolia Ethanol Extract on Zygote Cells of Tripneustes gratilla," *Pharmacol. Clin. Pharm. Res.*, vol. 1, no. 2, pp. 69–75, 2016, doi: 10.15416/pcpr.v1i2.15205.

[7] P. M. Kustiawan, K. A. A. K. Siregar, L. O. Saleh, M. A. Batistuta, and I. M. Setiawan, "A Review of Botanical Characteristics, Chemical Composition, Pharmacological Activity and Use of Scorodocarpus borneensis," *Biointerface Res. Appl. Chem.*, vol. 12, no. 6, pp. 8324–8334, Dec. 2021, doi: 10.33263/BRIAC126.83248334.

[8] J. Reveny, "Daya Antimikroba Ekstrak dan Fraksi Daun Sirih Merah (Piper betle Linn .) Antimicrobial Activity of the Extract and Fraction of Red Betel Leaf (Piper betle Linn .)," *J. Ilmu Dasar*, vol. 12, no. 1, pp. 6–12, 2011.

[9] R. Naufalin and T. Yanto, "Antioxidant activity of red betel (Piper crocatum) and green betel (Piper betle L.)," 2009.

[10] N. M. Aisyiyah, K. A. A. K. Siregar, and P. M. Kustiawan, "Review: Potensi Daun Sirih Merah (Piper Crocatum) Sebagai Antiinflamasi Pada Rheumatoid Arthritis," *J. Farm. Sains dan Prakt.*, vol. 7, no. 2, pp. 197–206, 2021, doi: 10.31603/pharmacy.v7i2.5283.

[11] H. Hamzah, T. Hertiani, S. U. T. Pratiwi, and T. Nuryastuti, "Efek Saponin Terhadap Penghambatan Planktonik Dan Mono-Spesies Biofilm *Candida albicans* ATCC 10231 Pada Fase Pertengahan , Pematangan Dan Degaradasi," *Maj. Farm.*, vol. 17, no. 2, pp. 198–205, 2021, doi:

10.22146/farmaseutik.v17i2.54444.

[12] H. Hamzah, N. Rasdianah, N. Nurwijayanto, and E. Nandini, "Aktivitas Ekstrak Etanol Daun Calincing Terhadap Biofilm *Candida Albicans*," *J. Farmasetis*, vol. 10, no. 1, pp. 21–28, 2021.

[13] A. Rukmini, D. H. Utomo, and A. N. Laily, "Family Piperaceae Phytochemical Screening," *J. Biol. dan Pembelajarannya*, vol. 7, no. 1, pp. 28–32, 2020, doi: 10.29407/jbp.v7i1.14805.

[14] F. Manoi, "Sirih merah sebagai tanaman obat multifungsi," 2007.

[15] N. Maulidha, A. Fridayanti, and M. A. Masruhim, "Uji Aktivitas Antioksidan Ekstrak Daun Sirih Hitam (Piper sp.) terhadap DPPH (1,1-diphenyl-2-picryl hydrazyl)," *J. Sains dan Kesehat.*, vol. 1, no. 1, pp. 16–20, Mar. 2015, doi: 10.25026/jsk.v1i1.10.

[16] R. Afsari, Kusmiyati, and I. W. Merta, "The Effect of Giving Red Betel Leaf Extract (Piper Crocatum) Against Reducing Blood Sugar Levels in Mice (Mus musculus)," *J. Biol. Trop.*, vol. 16, no. 1, pp. 49–55, 2016.

[17] Y. F. Dewi, M. S. Anthara, and A. A. G. O. Dharmanyudha, "The Effectiveness of Red Betel Leaf Extract (Piper Crocatum) Against Weight Gaining in Male White Rats (Rattus Novergicus) Diabetic Conditions Induced by Alloxan," *Bul. Vet. Udayana*, vol. 6, no. 1, pp. 73–79, 2014.

[18] R. Wilis and A. Andriani, "Efektifitas Berkumur Rebusan Daun Sirih Dibandingkan Rebusan Daun Saga terhadap Perubahan Derajat Keasaman Air Ludah," *AcTion Aceh Nutr. J.*, vol. 2, no. 1, p. 67, May 2017, doi: 10.30867/action.v2i1.39.

[19] M. Safithri and F. Fahma, "Potency of Piper crocatum Decoction as an Antihiperglycemia in Rat Strain Sprague dawley," *HAYATI J. Biosci.*, vol. 15, no. 1, pp. 45–48, 2008.

[20] A. Fitriyani, L. Winarti, S. Muslichah, and Nuri, "Uji Antiinflamasi Ekstrak Metanol Daun Sirih Merah (Piper crocatum Ruiz & Pav) pada Tikus Putih," *Majalah Obat Tradisional*, vol. 16, no. 1, pp. 34–42, 2011.

[21] R. I. Ardiyana, N. E. K. Putri, and F. Prasetya, "Formulasi Sediaan Patch Bukal Ekstrak Daun Sirih Hitam (Piper betle L. var Nigra," 2021.

[22] N. E. Udeh, A. Anaga, and I. U. Asuzu, "Effects of Gnetum africanum (Welw) methanol leaf extract on weight and haematological profile of wistar rats following chronic oral administration," *Sokoto J. Vet. Sci.*, vol. 16, no. 3, p. 49, Sep. 2018, doi: 10.4314/sokjvs.v16i3.7.

[23] L. R. Tembrock, C. D. Broeckling, A. L. Heuberger, M. P. Simmons, F. R. Stermitz, and J. M. Uvarov, "Employing Two-stage Derivatisation and GC-MS to Assay for Cathine and Related Stimulant Alkaloids across the Celastraceae," *Phytochem. Anal.*, vol. 28, no. 4, pp. 257–266, Jul. 2017, doi: 10.1002/pca.2671.

[24] R. Yendapally *et al.*, "A review of phenformin, metformin, and imeglimin," *Drug Dev. Res.*, vol. 81, no. 4, pp. 390–401, Jun. 2020, doi: 10.1002/ddr.21636.

[25] L. Čechovská, K. Cejpek, M. Konečný, and J. Velíšek, "On the role of 2,3-dihydro-3,5-dihydroxy-6-methyl-(4H)-pyran-4-one in antioxidant capacity of prunes," *Eur. Food Res. Technol.*, vol. 233, no. 3, pp. 367–376, Sep. 2011, doi: 10.1007/s00217-011-1527-4.

[26] M. N. Sarian *et al.*, "Antioxidant and Antidiabetic Effects of Flavonoids: A Structure-Activity Relationship Based Study," *Biomed Res. Int.*, vol. 2017, pp. 1–14, 2017, doi: 10.1155/2017/8386065.

[27] D. Tungmunnithum, A. Thongboonyou, A. Pholboon, and A. Yangsabai, "Flavonoids and Other Phenolic Compounds from Medicinal Plants for Pharmaceutical and Medical Aspects: An Overview," *Medicines*, vol. 5, no. 3, p. 93, Aug. 2018, doi: 10.3390/medicines5030093.

[28] S. Kasturi *et al.*, "Synthesis, molecular modeling and biological evaluation of aza-flavanones as α-glucosidase inhibitors," *Medchemcomm*, vol. 8, no. 8, pp. 1618–1630, 2017, doi:

10.1039/C7MD00162B.

[29] B. Salehi *et al.*, "Piper Species: A Comprehensive Review on Their Phytochemistry, Biological Activities and Applications," *Molecules*, vol. 24, no. 7, p. 1364, Apr. 2019, doi: 10.3390/molecules24071364.

[30] M. E. Bergman, B. Davis, and M. A. Phillips, "Medically Useful Plant Terpenoids: Biosynthesis, Occurrence, and Mechanism of Action," *Molecules*, vol. 24, no. 21, p. 3961, Nov. 2019, doi: 10.3390/molecules24213961.

[31] D. Cox-Georgian, N. Ramadoss, C. Dona, and C. Basu, "Therapeutic and Medicinal Uses of Terpenes," in *Medicinal Plants*, Cham: Springer International Publishing, 2019, pp. 333–359.

[32] M. T. Islam *et al.*, "Phytol: A review of biomedical activities," *Food Chem. Toxicol.*, vol. 121, pp. 82–94, Nov. 2018, doi: 10.1016/j.fct.2018.08.032.

[33] T. Goto, N. Takahashi, S. Hirai, and T. Kawada, "Various Terpenoids Derived from Herbal and Dietary Plants Function as PPAR Modulators and Regulate Carbohydrate and Lipid Metabolism," *PPAR Res.*, vol. 2010, pp. 1–9, 2010, doi: 10.1155/2010/483958.

[34] E. Fattore and R. Fanelli, "Palm oil and palmitic acid: a review on cardiovascular effects and carcinogenicity," *Int. J. Food Sci. Nutr.*, vol. 64, no. 5, pp. 648–659, Aug. 2013, doi: 10.3109/09637486.2013.768213.

[35] W. Wu *et al.*, "Butyrolactone- I, an efficient α- glucosidase inhibitor, improves type 2 diabetes with potent TNF- α–lowering properties through modulating gut microbiota in db/db mice," *FASEB J.*, vol. 33, no. 11, pp. 12616–12629, Nov. 2019, doi: 10.1096/fj.201901061R.

[36] K. Mazumder, A. Nabila, A. Aktar, and A. Farahnaky, "Bioactive Variability and In Vitro and In Vivo Antioxidant Activity of Unprocessed and Processed Flour of Nine Cultivars of Australian lupin Species: A Comprehensive Substantiation," *Antioxidants*, vol. 9, no. 4, p. 282, Mar. 2020, doi: 10.3390/antiox9040282.

[37] J. Lee and S.-H. Lee, "Patchouli Alcohol from Pogostemon Cablin Prevents Development of Obesity and Improves Glucose Tolerance in High Fat Diet-induced Obese Mice (P06-107-19)," *Curr. Dev. Nutr.*, vol. 3, no. Supplement_1, Jun. 2019, doi: 10.1093/cdn/nzz031.P06-107-19.

[38] N. R. K. Dewi, H. Kuncoro, and L. Rijai, "Potensi Sitotoksik Ekstrak Air Daun Sirih Hitam (Piper sp.)," *J. Sains dan Kesehat.*, vol. 1, no. 1, pp. 11–15, 2015, doi: 10.25026/jsk.v1i1.9.

[39] H. R. Rija'i, L. Syafnir, and E. Rismawati, "Uji Aktivitas Antioksidan Ekstrak Bertingkat Daun Sirih Hitam (Piper Acre Blume.) Dengan Peredaman Radikal Bebas DPPH (1,1-DIFENIL-2-PIKRIL HIDRAZIL)," *Prosiding Farmasi SPeSIA 2015*. pp. 58–64, 2015.

[40] D. Y. Shinta and S. Sudyanto, "Administration Of Red Belt Leaves (Piper Crocatum Ruiz & Pav) Water On Glucose And Blood Cholesterol Levels Of Male White Miice," *Sainstek J. Sains dan Teknol.*, vol. 8, no. 2, p. 180, 2017, doi: 10.31958/js.v8i2.480.

[41] K. Hati, M. Setiawan, and D. Yuliarta, "The Effect of Red Betel Leaf (Piper Crocatum) Decoction On Reducing Blood Sugar Level in White Rats (Alloxan-induced Rattus norvegicus)," *Saintika Med.*, vol. 9, no. 1, p. 59, 2017, doi: 10.22219/sm.v9i1.4127.

[42] F. E. Aprillia, M. Ardana, and H. Kuncoro, "Daya Antibakteri Ekstrak Jintan Hitam dan Daun Sirih terhadap Staphylococcus aureus pada Plat Gigi Tiruan," in *Proceeding of Mulawarman Pharmaceuticals Conferences*, 2021, pp. 74–79.

[43] Y. P. I. Ummah, "Uji daya antifungal ekstrak etanol daun sirih hitam (Piper betle L. Var Nigra) dan daun sirih hijau (Piper betle L.) terhadap penghambatan pertumbuhan Candida albicans secara invitro," Universitas Negeri Malang, 2014.