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Potential Use of Indonesian Medicinal Plants for Cosmetic and Oral Health: A Review

Irmanida Batubara[1,2*], Muhammad Eka Prastya[3]

[1]Department of Chemistry, Faculty of Mathematics and Natural Sciences, IPB University, IPB Dramaga Campus, Bogor, West Java 16680, Indonesia
[2]Tropical Biopharmaca Research Center, IPB University, Taman Kencana Street No 3, Bogor 16128, Indonesia
[3]Department of Biology, Faculty of Mathematics and Natural Sciences, IPB University, IPB Dramaga Campus, Bogor, West Java 16680, Indonesia

**Corresponding author: ime@apps.ipb.ac.id*

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Abstract

Medicinal plants have gained much importance in cosmetic development due to their abundant bioactive compounds and relatively fewer side effects. Indonesia comprises a diverse range of medicinal plants, along with multiple ethnicities and cultures. For decades, Indonesian traditional medicinal plants, known as jamu, had been utilized for skin care, skin whitening, and oral health. In the present review, several Indonesian medicinal plants have been discussed in relation to their potency for cosmetic and oral health. Recent scientific evidences showed that medicinal plants reviewed in this paper have the appropriate bioactivities with the major requirements for cosmetic and oral health including antioxidant, antiglycation, skin whitening via tyrosinase inhibitor and melanogenesis inhibition, antiacne activities (against *Propionibacterium acnes* and *Staphylococcus epidermidis*) and biofilm degradation against *Streptococcus mutans*, *Staphylococcus aureus* and *Candida albicans*. One of plant, namely *Zingiber officinale* reported having all of those requirements indicating the most potential for cosmetic and oral health agents. In summary, further research on Indonesian medicinal plants should be conducted to provide holistic knowledge for the development of cosmetic and oral health products.

Keywords: cosmetic, oral health, antioxidant, skin whitening, biofilm.

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1. INTRODUCTION

During aging, skin tissue becomes fragile, thinner, and loses its natural ability to maintain hydration, and with the new society paradigms pertaining beauty and youth have emerged new concerns about appearance. Today, the use of cosmetics and their ingredients is part of the daily routine of millions of consumers. A cosmetic product could be defined as any substance or mixture intended to be contacted with the external parts of the human body including epidermis, lip, nails, hair system and external genital organs, or with the teeth and the mucous membranes of the oral cavity with mainly to cleaning, changing their appearance, protecting, and keeping in good condition or correcting body odors (Pimentel *et al.*, 2017).

On the other hand, oral health is one of the cosmetic concerns. Oral health is defined as a state of being free from facial and mouth pain, throat, oral cancer, tooth loss, oral infection, periodontal diseases, and tooth decay as well as the other diseases that could diminish an individual ability in chewing, biting, speaking, and psychological wellness (Razak *et al.*, 2014). Healthy primary teeth play an important role in the maintenance of health since it is associated with supporting essential human body functions such as eating, speaking, smiling, and socializing. Thus, the maintenance of oral health is an essential part of human life.

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Recently, plant active compounds are gaining increased popularity as cosmetic ingredients since they can protect and cure skin and oral health. Compared with synthetic cosmetic products, plant compounds are mild, biodegradable, lack of side effects, and have diverse biological and therapeutic activities (Abdullah and Nasreen, 2012). Of note, Indonesia is the second richest country in terms of plant biodiversity. There is about 40,000 medicinal plant that has been identified. Thus, it is no coincidence that Indonesia could be developed as one of the most extensive sources of natural cosmetic compounds (Wathoni *et al.*, 2018).

More importantly, medicinal plants have been used as traditional remedies in various human diseases for centuries around the globe. There are numerous success stories of traditional medicine in the maintenance of general health, cosmetic and oral health by some entities, such as Ayurveda, Chinese and Korea traditional medicine, etc. (Karygianni *et al.*, 2016). In Indonesia, traditional herbal medicine, known as *Jamu* has been utilized for centuries in various Indonesian ethnic groups. *Jamu* is a traditional herbal comprising one or mixtures from some medicinal plants in the form of capsules or powders. These substances have a beneficial effect on maintaining good health, treat numerous diseases, and use for cosmetic materials (Wathoni *et al.*, 2018).

The following sections will provide an overview of 15 medicinal plant species belong to 11 families in relation to 5 ethnic groups in Indonesia. Interestingly, each of those plants was traditionally reported for the treatment or curing various disorders in a wide range from cough, diarrhea, skincare, whitening agent, etc. Indeed, even though it comes from a different ethnic group, a part of some plants, including *Curcuma aeruginosa*, *Curcuma domestica*, *Curcuma xanthorriza*, *Oryza sativa*, *Helminthostachys zeylanica*, *Xylocarpus granatum* and *Zingiber officinale* have the similar function as for traditional skincare (Table 1). Through this review, we successfully summarized the recent scientific evidence that reported the bioactivity of all 15 plants as for cosmetic and oral health properties.

2. THE POTENCY OF INDONESIAN MEDICINAL PLANTS FOR COSMETIC

Numerous main factors, including climate conditions, UV radiation, and environmental pollutants, can reduce the protective capability of skin and promote its premature aging. Generally, this condition continuous exposure leads to oxidative stress due to the imbalance between free radicals (oxidants) and antioxidants, which contributes to skin health (Pimentel *et al.*, 2017). In cosmetic formulations, the main functions of natural ingredients may be antioxidant, anti-wrinkles, or even collagen-boosting (Thomas and Kim, 2013). The foremost criteria of natural ingredients include those intended for cosmetic, including protection against free radicals (antioxidant) and glycation product (antiglycation), anti-photoaging, prevention of skin flaccidity and wrinkles, photo-protection against UV radiation, moisturizing, antiacne activity and skin whitening (Anunciato and Filho, 2012). In this review, we elaborate some bioactivities attributed to cosmetic characters, including antioxidant, antiglycation, skin whitening and antiacne activities derived from 15 Indonesian medicinal plants.

Use of Indonesian Medicinal Plants for Antioxidant

The skin has multiple endogenous antioxidant systems, including enzymatic and non-enzymatic, to maintain a balance between free radical and antioxidant. However, the presence of excess free radicals leads to loss of cellular integrity, due to modification of DNA, abnormal expression of cellular genes, and thus inducing to increase in matrix metalloproteinases, which is responsible for the extracellular matrix protein degradation, resulting in wrinkle formation and metastases (Saewan and Jimtaisong, 2015). Antioxidant substances are required to slow down skin aging while endogenous antioxidants become depleted and are insufficient.

Interestingly, we identify that all of 15 medicinal plants reviewed in this paper have antioxidant activity at least in one method of 2, 2'-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging activity, which particular fraction from *C. domestica* rhizome extract have the strongest activity with the

IC_{50} of 8.01 µg/mL (Table 2). On the other hand, one of plant namely *Acalypha indica* was reported as having antioxidant activity through more methods than other, including DPPH, Ferric Reducing Antioxidant Power (FRAP), H_2O_2 scavenging, hydroxyl radical degradation, lipid peroxidation, along with in vivo antioxidant in diabetic rats through increasing in catalase and glutathione peroxidase.

Antiglycation Activity of Indonesian Medicinal Plants

Glycation is defined as a non-enzymatic reaction between amino groups of proteins and the carbonyl group of reduced sugars or other carbonyl compounds to create the particular product namely advanced glycation end products (AGEs) (Poulsen *et al.*, 2013).

The abundance level of AGEs molecules in the cells will interact with the tissue and organs in the body and, subsequently, will generate in the dysfunctionality of those organs. As for the skin aging process, AGEs molecule can interact with collagen and develop helix bonds then promoting skin aging symptoms, such as skin dullness, wrinkles, and loss of skin elasticity and integrity (Ichihashi *et al.* 2011). Therefore, substantial compounds with the ability to inhibit the AGEs production (antiglycation activity) become a prospective material to be cosmetic ingredients. Of note, only 7 plants had been reported as having antiglycation activity including *A. lavenia*, C. *aeruginosa*, *C. domestica*, *C. xanthorriza*, *X. granatum*, *Z. officinale*, and *Z. purpureum* (Table 2). A fraction from the stem extract of *X. granatum* shows the highest antiglycation activity with IC_{50} of 71.55 µg/mL (Noviarni *et al.*, 2020).

Table 1. List of Indonesian medicinal plants reviewed in this article.

No	Scientific Name	Local Name	Traditional use in Indonesia	References
1	*Acalypha indica* (Euphorbiaceae)	Anting-anting (Jawa)	Treating diarrhea, malnutrition, and malaria	Arisandi and Andriani, 2008
2	*Adenostemma lavenia* (Asteraceae)	Legetan warak (Jawa)	Treating fever, cough, sore throat, and thrush illness	Kusumawati *et al.*, 2003
3	*Curcuma aeruginosa* (Zingibereceae)	Temu ireng (Jawa)	Skin softener, and appetite enhancer	Marni and Ambarwati, 2015
4	*Curcuma domestica* (Zingibereceae)	Kunyit/kunyir (Jawa, Sunda)	Body slimming, and skin softener	Hartati, 2013
5	*Curcuma xanthorriza* (Zingibereceae)	Temulawak (Jawa, Sunda)	Skin care, treating fever, and liver disorder	Sangat *et al*., 2000
6	*Daemonorops draco* (Aracaceae)	Jernang rattan (Jambi)	Treating fever, headache, and wound healing	Purwanto *et al.*, 2005
7	*Helminthostachys zeylanica* (Ophioglossaceae)	Akar telunjuk langit (Kutai)	Antidiabetic, and face powder	Sangat *et al*., 2000
8	*Intsia palembanica* (Fabaceae)	Merbau (Maluk)	Treating impotency	Sangat *et al*., 2000
9	*Oryza sativa* (Poaceae)	Beras putih (Jawa)	Skin care, whitening, softener, and face mask	Kusumanti *et al.*, 2017
10	*Pinus oocarpa* (Pinaceae)	Pinus (Jawa)	Skin care and whitening mixture	Darmastuti *et al.*, 2016
11	*Stelechocarpus burahol* (Annonaceae)	Kepel (Jawa)	For fragrance, deodorant, and reduce the smell sweat	Heyne, 1987
12	*Syzygium polyanthum* (Myrtaceae)	Salam (Jawa)	Culinary additive, treating diarrhea, and diabetes	Sumono and Wulan, 2008
13	*Xylocarpus granatum* (Meliaceae)	Boli (Dayak ngaju)	Skin care	Sangat *et al*., 2000
14	*Zingiber officinale* (Zingibereceae)	Jahe (Jawa)	Skin care, antiacnes, deodorant, wound healing	Susila *et al.*, 2014
15	*Zingiber purpureum* (Zingibereceae)	Bangle hantu (Jawa)	Treating fever, gout, constipation, and colds	Astarina *et al.*, 2013

Utilization of Indonesian Medicinal Plants for Skin Whitening

Melanin, which is the major determinant of skin color, absorbs UV radiation along with prevents free radical generation and thus protecting skin from sun damage and aging. However, the excessive production of melanin can induce dermatological disorders and a serious cosmetic issue such as hyperpigmentation, malaise, freckles, solar lentigo, and thus it should be controlled. Tyrosinase catalyzes melanin synthesis in two different pathways.

It is including the hydroxylation of L-tyrosine to 3, 4-dihydroxy-l-phenylalanine (L-dopa), and the oxidation of L-dopa to dopaquinone, followed by subsequent conversion to melanin. Therefore, it is possible to control the melanin biosynthesis by inhibiting L-dopa and tyrosinase action, which ultimately can inhibit the melanogenesis as well as consequently preventing skin hyperpigmentation (Robert *et al.*, 2009).

Among of all 15 plants, 11 of them have the activity to inhibit the melanogenesis process via tyrosinase inhibitor (through L-tyrosine and L-dopa substrates) or reduce melanogenesis in cell line. Those 11 plants are *A. lavenia*, C. *aeruginosa*, *C. domestica, C. xanthorriza, H. zeylanica, I. palembanica, O. sativa, S. polyanthum, X. granatum, Z. officinale,* and *Z. purpureum* (Table 2). The highest activity for inhibiting L-tyrosine substrate (monophenolase reaction) is *S. polyanthum*, as for L-dopa substrate (diphenolase reaction) is *C. domestica* with the IC_{50} of 35.45 and 31.40 µg/mL, respectively. On the other hand, another plant namely *A. lavenia* (9 µg/mL) leaves extract have the particular activity to inhibit 100% melanogenesis process in B16F10 melanoma cell line and also can suppress hair pigmentation in mice, therefore potentially to develop for skin whitening agent.

Indonesian Medicinal Plants as Antiacne Agent

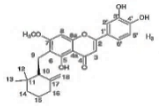
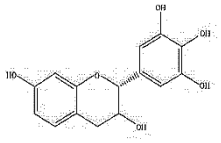
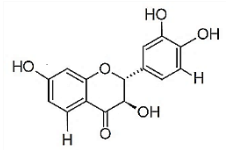
Acne is known as an inflammatory disorder of pilosebaceous units and is common in adolescent skin. Lesions of acne occur primarily on the face, neck, chest, and upper back. Particular characteristic its lesions are closed (white) and open (black) comedones, pustules, inflammatory papules, cyst, and nodules, which may lead to skin pigmentary changes. Of note, the pathogenesis of acne is multifactorial, including increased production of sebum secondary to hyperandrogenism, abnormal follicular keratinization, cell inflammation, and colonization of pathogenic bacteria such as *Propionibacterium acnes* and *Staphylococcus epidermidis* (Kraft and Freiman, 2011).

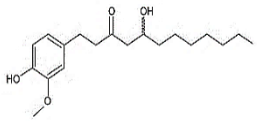
In this review, we identify that 5 plants, including *A. indica, C. domestica, C. xanthorriza, H. zeylanica*, and *I. palembanica* have the activity to inhibit the growth of *P. acnes*. Two other plants, namely *S. burahol* and *Z. purpureum* can inhibit the growth of *S. epidermidis* (Table 2). Interestingly, *Z. officinale* has been reported to have antibacterial activity against both *P. acnes* and *S. epidermidis.* Indeed, essential oil isolated from its rhizome has been applied as one of the ingredients to make antiacne lotion and effectively to inhibit the growth of those pathogenic bacteria (Indriati *et al.*, 2018). The effectiveness of a total of 8 plants to inhibit *P. acnes* and/or *S. epidermidis* growth indicated that those plants have the potency as antiacne.

Table 2. Bioactivities of Indonesian medicinal plants in correlation with cosmetic properties

Code	Extract/Compound	Bioactivities	References
1.	MeOH stem extract	In vivo antioxidant in diabetic rats (SOD: 6.04 U/mg proteins; catalase: 12.16 µMoles of H_2O_2 consumed/mg protein; GPx: 14.70 GSH utilized/min per mg protein) from 300 mg/kg b.wt.	Priya and Rao, 2016
	Water leaves extract	Antioxidant (FRAP assay: 33 µg AAE/mg; DPPH: inhibition of 92% from 6.25 mg/mL extract)	Teklani and Perera, 2016
	MeOH leaves extract	Antibacterial against *P.acnes* (MIC: 0.740 mg/mL), additional ingredients for antiacne	Ansila *et al.*, 2017

		cream (0.75%), inhibition zone of cream against *P. acnes* of 1.3 cm	
	MeOH leaves extract	Antioxidant (DPPH: IC_{50} of 28.33 µg/mL; H_2O_2 scavenging: IC_{50} of 84.41 µg/mL; Hydroxyl radical degradation: IC_{50} of 35.93 µg/mL; Lipid peroxidation: IC_{50} of 84.77 µg/mL),	Ravi *et al.*, 2017
2.	Water plant extract	Antioxidant (DPPH: IC_{50} of 121.82 µg/mL; ABTS: 3.38 mg TE/g extract), Antiglycation (Inhibition of 87.87% from 1000 µg/mL extract)	Budiarti *et al.*, 2019
	Water leaves extract	Antimelanogenic against B16F10 melanoma cells (9 µg/mL with inhibition of 100%), and suppress hair pigmentation in mouse (0.3 mg/mL)	Hamamoto *et al.*, 2020
3.	Essential oil isolated from leaves	Antioxidant (ABTS: 5.10 g AEAC/ 100 g essential oil), and antiglycation (IC_{50} of 243.57 µg/mL)	Batubara *et al.*, 2016a
	EtOAc leaves extract	Tyrosinase inhibition (% inhibition for monophenolase of 41.41% and diphenolase of 16.34%) from 250 mg/L extract	Batubara *et al.*, 2016b
	EtOH rhizome extract (accession: Cirebon)	Antioxidant (DPPH: IC_{50} of 131.40 µg/mL)	Safitri *et al.*, 2017
	Essential oil isolated from rhizome	Axillary hair growth suppressant and axillary skin brightness enhancer (in vivo treatment in women, 1 and 5% w/w essential oil)	Srivilai *et al.*, 2017
4.	MeOH rhizome extract	Antioxidant (DPPH: IC_{50} of 16.92 µg/mL)	Batubara *et al.*, 2009
	EtOAc fraction from MeOH rhizome extract	Antioxidant (DPPH: IC_{50} of 8.01 µg/mL), tyrosinase inhibitory against L-dopa (IC_{50} value of 31.40 µg/mL), antimelanogenic against B16F10 melanoma cells (inhibition OD_{490} of 0.07 from 10 µg/mL extract	Park *et al.*, 2010
	EtOH rhizome extract	Antiacnes (one of the ingredients, 15%w/w, on gel-HPMC against *P.acnes*, *S. epidermidis* and *M. furfur* with the absorbance OD_{600} of 0.1)	Rasheed *et al.*, 2011
	MeOH rhizome extract	Reducing the human skin sebum secretion (one of the ingredients, 5%, on cream decreases of 24.76% in week 12)	Zaman and Akhtar, 2013
	Essential oil isolated from leaves	Antioxidant (ABTS: 4.19 g AEAC/ 100 g essential oil), and antiglycation (IC_{50} of 221.26 µg/mL)	Batubara *et al.*, 2016b
5.	MeOH flower bract extract	Antibacterial *P. acnes* (MIC: 2 mg/mL; MBC: >2 mg/mL), (DPPH: IC_{50} of 6.60 µg/mL).	Batubara *et al.*, 2015
	EtOH flower bract extract	Lipase inhibition *P. acnes* (80.50%), tyrosinase inhibition (IC_{50} monophenolase 1.97 mg/mL;diphenolase of 1.57 mg/mL)	
	Essential oil isolated from leaves	(ABTS: 0.57 g AEAC/ 100 g essential oil), antiglycation (IC_{50} of 221.60 µg/mL)	Batubara *et al.*, 2016a
	EtOAc leaves extract	Tyrosinase inhibition (monophenolase of 37.72%; diphenolase22.24%) from 250 mg/L	Batubara *et al.*, 2016b
	MeOH leaves extract	(DPPH: IC_{50} of 282.35 mg/L), antiglycation (IC_{50} of 274.14 mg/L)	Zahra *et al.*, 2016
	EtOH rhizome extract	Antibacterial *S. epidermidis* (inhibition zone of 9.2 mm from 100% extract)	Warmasari *et al.*, 2020
6.	Fraction (F.4) from EtOAc resin extract	Antioxidant (DPPH: IC_{50} of 14.19 µg/mL)	Purwanti *et al.*, 2019
	EtOH resin extract	One of ingredient from skin wound healing formulation (Reducing skin irritation and treatment for skin injured, 10% extract)	Yusnelti and Muhaimin, 2019
7.	MeOH leaves extract	Antibacterial against *P. acnes* (MIC: 1.0 mg/mL; MBC: 2.0 mg/mL)	Batubara *et al.*, 2009
	EtOH root extrac	Antioxidant (DPPH: IC_{50} of 51.26 µg/mL)	
	Compounds isolated	Melanogenesis activity in B16-F0 melanoma	Yamauchi *et al.*,

	from 50% EtOH root extract Ugonin K 	cells of 8% from 25 µM compound, tyrosinase activity (IC_{50} both L-tyrosine and L-dopa of > 100 µg/mL)	2015
8.	MeOH stem extract	Antioxidant (DPPH: IC_{50} of 3.87 µg/mL), lipase (*P. acnes*) inhibition (IC_{50} of 4.1 µg/mL)	Batubara *et al.*, 2009
	• Compound isolated from MeOH wood extract  (-)robidanol	Tyrosinase inhibition (IC_{50} for monophenolase of 8.7 µM and diphenolase of 26.6 µM), melanin inhibition of 20% from 1.6 µM compound	Batubara *et al.*, 2011
	• A compound isolated from plant extract  Fustin	Lipase (*P. acnes*) inhibition (IC_{50} of 3.95 µg/mL)	Batubara *et al.*, 2014
	EtOAc heartwood extract	Antioxidant (DPPH: EC_{50} of 7.9 µg/mL; Fe^{2+} chelation: EC_{50} of 19.95 mg/mL; inhibition of *tert*-butylhydroperoxide: IC_{50} of 1.26 µg/mL)	Hasan *et al.*, 2019
9.	EtOH grain extract	• Antioxidant (ABTS: IC_{50} of 145.67 µg/mL; FRAP: 21.26 µM Fe(III)/µg extract) Collagenase inhibitory (IC_{50} of 816.78 µg/mL), elastase inhibitory (IC_{50} of 107.51 µg/mL),	Widowati *et al.*, 2016
	MeOH rice extract	Antioxidant (DPPH: IC_{50} of 1.29 mg/mL), tyrosinase inhibition (IC_{50} for monophenolase and diphenolase of 3.22 and 3.77 mg/mL, respectively)	Batubara *et al.*, 2017
10.	*n*-hexane resin extract	Antioxidant (DPPH: IC_{50} of 154.50 mg/mL)	Tillah *et al.*, 2017
11.	Water leaves extract	Antioxidant (DPPH: IC_{50} of 2.57 mg/mL from kepel cream (7.5 g in 100 g formula)	Suwandi *et al.*, 2012
	Fraction (F V) from MeOH leaves extract	Antibacterial against *S. epidermidis* (MIC: 0.06 mg/mL; MBC: 0.50 mg/mL)	Indariani *et al.*, 2017
	EtOAc fraction from fruit pulp extract	Antioxidant (DPPH: IC_{50} of 1.30 µg/mL; ABTS: IC_{50} of 0.35 µg/mL	Herlina *et al.*, 2018
12.	EtOAc leaves extract	Antioxidant (DPPH: IC_{50} of 56.7 µg/mL; ABTS: IC_{50} of 40.17 µg/mL)	Hidayati *et al.*, 2017
	• MeOH leaves extract	Tyrosinase inhibition (IC_{50} for L-tyrosine and L-dopa substrates of 35.45 and 93.61 µg/mL, respectively), extracellular melanogenesis activity of 20% from 100 µM extract	Setyawati *et al.*, 2018
	EtOH leaves extract	Antioxidant (DPPH: IC_{50} of 437.89 µg/mL; FRAP value of 684 µg/mL)	Hartanti *et al.*, 2019
13.	MeOH stem extract	Antioxidant (DPPH: IC_{50} of 23.75 µg/mL)	Batubara *et al.*, 2009
	Fraction (F3) from MeOH stem extract	Tyrosinase inhibition (IC_{50} for monophenolase and diphenolase of 18.02 and 21.15 µg/mL, respectively)	Darusman *et al.*, 2011
	MeOH waste fruit peel extract	Tyrosinase inhibition (IC_{50} for monophenolase and diphenolase of 784.87 and 1176.66 µg/mL, respectively)	Gazali *et al.*, 2014
	MeOH seed kernel	Antioxidant (DPPH: IC_{50} of 10.61 µg/mL),	Zamani et al., 2015

	extract	tyrosinase inhibition (IC_{50} for monophenolase and diphenolase of 323.11 and 1926.03 µg/mL, respectively)	
	EtOH (40%) stem extract, ratio of sample:solvent (1:6)/(g/mL)	Antioxidant (DPPH: % inhibition of 70.92%; ABTS: % inhibition of 0.38 (TEAC)), antiglycation (% inhibition of 84.94%), all from 100 µg/mL extract	Sapitri *et al.*, 2019
	• EtOH fruit flesh extract	• Tyrosinase inhibition (IC_{50} for monophenolase and diphenolase of 393.8 and 448 mg/L, respectively)	Batubara *et al.*, 2020
	EtOH stem bark extract	Antioxidant (DPPH: IC_{50} of 8.9 mg/L) Antiglycation (IC_{50} of 118.1 mg/L)	
	• MeOH fraction from MeOH stem extract	• Antioxidant (DPPH: IC_{50} of 8.52 µg/mL), antiglycation (IC_{50} of 71.55 µg/mL)	Noviarni *et al.*, 2020
	Sub-fraction (F1) from MeOH stem fraction	Antiglycation (IC_{50} of 67.25 µg/mL), antioxidant (DPPH: IC_{50} of 7.58 µg/mL)	
14.	• Essential oil isolated from leaves	Antiglycation (IC_{50} of 207.95 µg/mL), antioxidant (ABTS: 0.66 g AEAC/ 100 g essential oil)	Batubara *et al.*, 2016a
	EtOAc leaves extract	Tyrosinase inhibition (% inhibition for monophenolase of 15.71% and diphenolase of 12.14%) from 250 mg/L extract	Batubara *et al.*, 2016b
	MeOH leaves extract	Antioxidant (DPPH: IC_{50} of 516.21 mg/L; antiglycation (IC_{50} of 203.85 mg/L)	Zahra *et al.*, 2016
	Essential oil isolated from rhizome	One of ingredient in antiacne lotion (7.5% oil in lotion, zone of 29 and 12.3 mm against *P. acnes* and *S. epidermidis* ,respectively)	Indriati *et al.*, 2018
	• Compound isolated from MeOH rhizome extract (*var. rubrum*)  8-Gingerol	Intra and extra melanogenesis activity (B16 melanoma cells) of 92% and 37%, respectively from 50 µM compound with cell viability of 80%.	Yamauchi *et al.*, 2019
15.	• EtOAc leaves extract	Tyrosinase inhibition (% inhibition for monophenolase of 82.86% and diphenolase of 41.78%) from 250 mg/L extract	Batubara *et al.*, 2016b
	MeOH leaves extract	Antioxidant (DPPH: IC_{50} of 622.69 mg/L; ABTS: TEAC of 7.48 mg/g extract), antiglycation (IC_{50} of 305.79 mg/L)	Zahra *et al.*, 2016

Note: IC_{50}: Inhibition concentration of 50%, EC_{50}: Effective concentration of 50%, ABTS: 2, 2'-azino-bis (3-ethylbenzothiazoline-6-sulphonic acid), FRAP: Ferric Reducing Antioxidant Power, TE: Trolox Equivalent, TEAC: Trolox Equivalent Antioxidant Capacity, AEAC: Ascorbic Acid Equivalent Antioxidant Capacity, MIC: Minimal Inhibitory Concentration, MBC: Minimum Bactericidal Concentration, SOD: Superoxide Dismutase, GPx: Glutathione Peroxidase.

3. THE POTENCY OF INDONESIAN MEDICINAL PLANTS FOR ORAL HEALTH

Human mouths are filled with a high amount of microorganisms, including bacteria, fungi, etc. Pathogenic bacteria in the oral cavity generate the acids derived from converting the sugar from food. Subsequently, the acids attack the tooth by creating tooth decay and thus leading to a cavity. Those bacteria, along with mucus and some other particles also produce a sticky and colorless film on teeth known as plaque (Gupta *et al.*, 2013). Bacterial plaque plays a major role in the development of dental biofilm, colorless, and sticky film that creates teeth prosthesis. The existence of this biofilm in teeth is a serious issue pertaining to several oral

disorders such as osteomyelitis, peri-implantitis, candidiasis, and dental caries (Jeon *et al.*, 2011).

Of note, dental caries pathogenesis is modulated by some virulence factors, including the formation of extracellular polysaccharide (EPS)-rich biofilm matrix, the acidification of the milieu, and the maintenance of a low-pH environment at the interface of tooth-biofilm (Koo *et al.*, 2013). Biofilms consist of pathogenic bacteria namely *Streptococcus mutans* as the primary producers of the EPS-rich matrix, even though it is also flooded with other pathogenic microorganisms such as *Staphylococcus aureus*, *Enterococcus faecalis*, *Streptococcus sobrinus*, *Porphyromonas gingivalis*, *Fusobacterium nucleaum*, *Candida albicans*, and *Candida krusei* (Kim *et al.*, 2018). This mechanism of pathogenesis involves on three processes, including the effective utilization of dietary sucrose for the rapid synthesis of EPS by the activity of fructosyl transferase and glucosyl transferase (Gtfs), followed by the adhesion to glucan-coated surfaces, and finally the acidogenic along with the acid-tolerant nature. Through this process, *S. mutans* and other pathogenic bacteria or fungi expose out from the complex oral microbiome as cariogenic biofilms (Koo *et al.*, 2013).

The activity of medicinal plants to counteract the oral disease is in many dimensions, such as influencing the bacterial adhesion to surfaces, alleviating the symptoms of oral diseases, or reducing dental biofilm development. Interestingly, among 15 plants discussed in this review, 14 plants have been reported to inhibit the growth of some pathogenic bacteria or fungi as the main cause of dental biofilm production. In detail, 5 plants including *A. indica*, C. *aeruginosa*, *C. domestica*, *C. xanthorriza*, and *Z. officinale* have antibacterial activities against both *S. mutans* and *S. aureus* along with antifungi against *C. albicans*. As for the other nine plants have antibacterial or antifungi activities against only one or two of those pathogenic bacteria or fungi (Table 3). The highest activity against *S. mutans* is showed by *Z. officinale* with the same value for MIC and MBC of 15.6 µg/mL along with the biofilm degradation activity with the IC_{50} value of 20.96 µg/mL (Batubara *et al.*, 2019). As for the best activity against *S. aureus* is in *P. oocarpa* with the MIC and MBC values of 125 and 250 µg/mL, respectively (Sari *et al.*, 2018). In addition, *C. xanthorriza* shows the highest activity against pathogenic fungi *C. albicans* with the MIC value of 25 µg/mL (Diastuti *et al.*, 2019). This information suggested that almost all of these plants potentially develop as oral health agents, at least in part via the particular mechanism through inhibiting the growth of microorganism as the main factor of dental biofilm development.

Table 3. Bioactivities of Indonesian medicinal plants in relation to oral health properties

Code	Extract/Compound	Bioactivities	References
1.	Alkaloid compound in fraction (F3) from *n*-hexane leaves extract	Antibacterial against *S. mutans* (MIC: 250 µg/mL; MBC: 2000 µg/mL), biofilm degradation (IC_{50} of 56.8 µg/mL)	Batubara *et al.*, 2016c
	MeOH leaves extract	Antifungi against *C. albicans* (inhibition zone of 20 mm from 50 µg/mL extract)	Tariq *et al.*, 2016 Teklani and Perera, 2016
	Water leaves extract	Antibacterial against *S. aureus* (190 mg/mL with inhibition zone of 7.0 mm)	
3.	EtOH rhizome extract (accession: Cirebon)	Antibacterial against *S. aureus* (MIC: 250 µg/mL; MBC: 500 µg/mL)	Safitri *et al.*, 2017
	n-hexane leaves extract	Antibacterial against *S. mutans* (MIC: 15.6 µg/mL; MBC: 15.6 µg/mL), biofilm degradation (IC_{50} of 26.06 µg/mL)	Batubara *et al.*, 2019
4.	Essential oil isolated from	Antibacterial *S. mutans* (MIC: 2000	Batubara *et al.*,

	leaves	µg/mL), biofilm degradation (IC_{50} of 354.8 µg/mL)	2016d
	Essential oil isolated from rhizome	Antimicrobial against *S. aureus* and *C. albicans* (MIC: 486.53 and 301.47 µg/mL, respectively)	Zhang *et al.*, 2017
	EtOAc leaves extract	Antibacterial against *S. mutans* (MIC and MBC: >2000µg/mL), biofilm degradation (IC_{50} of 198.32 µg/mL)	Batubara *et al.*, 2019
5.	*n*-hexane fraction from acetone rhizome extract	Antibacterial against *S. aureus* (MIC and MBC of 62.5 µg/mL)	Diastuti *et al.*, 2014
	Essential oil isolated from leaves	Biofilm degradation against *S. mutans* (IC_{50} of 289.1 µg/mL)	Batubara *et al.*, 2016d
	Chloroform fraction from rhizome extract	Antifungi against *C. albicans* (MIC: 25 µg/mL)	Diastuti *et al.*, 2019
6.	MeOH resin extract	Antibacterial against *S. aureus* (MIC: 0.5 mg/mL, MBC: 1.0 mg/mL) Inhibition (*S. aureus* biofilm attachment of 100% from 0.5 mg/mL extract)	Wahyuni *et al.*, 2018
	n-hexane resin extract	Antifungi against *C. albicans* (inhibition zone of 13 mm)	Waluyo and Pasaribu, 2015
7.	Leaves extract	Antibacterial against *S. aureus* (Inhibition zone of 10 mm from 1 mg extract)	Wiart *et al.*, 2004
	MeOH flower extract	Antibacterial against *S. sobrinus* (IC_{50} of 257.82 µg/mL)	Kuspradini *et al.*, 2010
8.	MeOH wood extract	Antibacterial against *S. sobrinus* (IC_{50} of 28.12 µg/mL)	Kuspradini *et al.*, 2010
9.	MeOH rice extract	Antibacterial against *S. aureus* (Inhibition zone from 2 mg/mL 3.3 mm; MIC: 200 µg/mL)	Godakumbura *et al.*, 2017
10.	*n*-hexane resin extract	Antibacterial against *S. aureus* (inhibition zone of 8.20 mm from 500 µg/mL)	Tillah *et al.*, 2017
	Fraction (F.1.1.2) from *n*-hexane resin extract	Antibacterial against *S. aureus* (MIC: 125 µg/mL; MBC: 250 µg/mL)	Sari *et al.*, 2018
11.	EtOH leaves extract	Antifungi against *C. albicans* (Inhibition zone of 2 cm from 45% extract)	Anggara *et al.*, 2014
	EtOAc fraction from EtOH fruit extract	Antibacterial against *P. gingivalis* and *F. nucleaum* (inhibition zone from 60 mg/mL of 13.33 and 13.53 mm, respectively; MIC of both pathogenic bacteria of 0.1 mg/mL)	Amin *et al.*, 2018
12.	EtOH leaves extract	Antifungi against *C. albicans* (inhibition zone of 9.32 mm from 10 mg/mL; MIC: 5mg/mL; MFC: 10 mg/mL)	Fitriani *et al.*, 2012
	EtOH leaves extract	Biofilm degradation (*E. faecalis*) of 100% from 13% extract	Aini *et al.*, 2016
	MeOH leaves extract	Antibacterial against *S. aureus* (IC_{50}: 23.16 µg/mL)	Ramadhania *et al.*, 2018

13.	EtOH bark extract	Antibacterial *S. aureus* (both inhibition zone of 20 mm from 50 µg/mL extract) Antifungal *C. albicans* (inhibition zone of 15 mm from 50 µg/mL extract)	Saheb *et al.*, 2017
14.	EtOH rhizome extract	Antifungal against *C. albicans* and *C. krusei* (MIC: 10 and 5 mg/mL, respectively), inhibition of biofilm formation against *C. albicans* and *C. krusei* from the same concentration of 5 mg/mL	Aghazadeh *et al.*, 2016
	EtOH rhizome extract	Antibacterial against *E. faecalis* (Inhibition zone of 13.87 mm from 15.62 mg/mL extract; MBC: 15.625 mg/mL)	Azhar *et al.*, 2018
	MeOH leaves extract	Antibacterial against *S. mutans* (MIC: 15.6 µg/mL; MBC: 15.6 µg/mL), biofilm degradation (IC_{50} of 20.96 µg/mL)	Batubara *et al.*, 2019
15.	Essential oil isolated from leaves	Antibacterial against *S. mutans* (MIC: 2000 µg/mL), biofilm degradation (IC_{50} of 314.8 µg/mL)	Batubara *et al.*, 2016d
	Essential oil isolated from rhizome	One of ingredient on antibacterial liquid soap (against pathogenic *E. coli* and *S. aureus*, inhibition zone of 8.67 and 9.5 mm from soap liquid with 2.5 mL oil	Wulandari *et al.*, 2018
	EtOH rhizome extract	Antibacterial against *S. aureus* (Inhibition zone of 17.75 mm from 75% extract)	Citradewi *et al.*, 2019

4. CONCLUSION

The effectiveness of 15 Indonesian medicinal plants for cosmetic and oral health has been explored thoroughly in this review. Specifically, on *Z. officinale* plant reported having the most substantial requirements to be cosmetic and oral health agents. However, it is also crucial to assess other cosmetic and oral health requirements, the safety and efficacy of the plant extracts, purified phytochemicals, and essential oils in the ongoing clinical trials for the development of cosmetic and oral health product. In addition, an effort to investigate the bioactivities of other medicinal plants are also needed to provide a comprehensive insight from those plants in association with health issues.

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