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The potential of five therapeutic medicinal herbs for dental treatment : A review

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Abstract. Indonesia, especially in Aceh Province, has a huge biodiversity of natural resources in herbal medicine. *Calotrophis gigantea* (L), *Acrostichum aureum* (L), *Pluchea indica* (L), *Cissus adnata* and *Abutilon indicum* (L) are considered to have secondary metabolite that are potential for dental therapeutic treatments because the compounds have anti-inflammatory, antibacterial, antifungal, antioxidant, antiseptic and wound healing ability. The utilization of medicinal herbs in dentistry is still limited, thus in this study we provide valuable information of each five medicinal herbs for dental therapeutic treatments. The results indicated that all the five medicinal herbs have different abilities and potentials in treating diseases / abnormalities in the oral cavity. The selection and the use of appropriate medicinal herbs can give an effective therapeutic treatment to improve the health of oral cavity. The qualities of the five herbs are directly proportional to their ability as an alternative therapeutics in dentistry. To produce a good herbal medicines in dentistry, a lot of supporting researches are needed.¹

1. Introduction

Herbs are plants that can be used to cure diseases. The use of herbs is greatly improved from year to year because the raw material has a high availability, inexpensive price and low side effects compared to commercial chemical drugs [1]. The raw materials for herbal medicine in Indonesia, especially in Aceh, is readily available thus can be used for alternative therapies. Some herbs are grown in the province include: *Calotrophis gigantea* (L), *Acrostichum aureum* (L), *Pluchea indica* (L), *Cissus adnata* and *Abutilon indicum* (L).

Those plants grow in the wild shrubs and in a tropical climate. The plants are commonly used by the public as antioxidants, painkillers, antiviral/bacterial, anti-inflammatory, antidiabetic, wound

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medications, cardioprotection, anti-cancer, and anti-ageing. In the field of dentistry, the use of the five is still very limited. Some researches suggests that the use of these herbs are still limited to as antimicrobial, anti-inflammatory and wound medications [1,2].

The antibacterial activity studies of these plants are still limited especially on the bacteria that cause caries. Sharma et al., (2015) and Fatimatuzzahra *et al.* (2016) reported that *Calotropis gigantea* could inhibit the growth of *Streptococcus mutant*, *Lactobacillus casei* *Enterococcus fecalis* and could heal wounds [3-5]. Sharma et al., (2015) also reported that the secondary metabolites from *Calotropis gigantea* can be widely used as an antiseptic, antibacterial, antimicrobial, antifungal, antioxidant, antiviral, anticancer, anti-tumour analgesic, antioxidant, antiviral, anticancer, anti-tumour and analgesic [3]. This is agreed by Agbor (2015), stated that this plant is potential to be used as a pain reliever (analgesic), gingivitis, periodontitis, ulcerative stomatitis corner, ulcers, and oral thrush in dental treatment, and also some other malignant diseases such as cancers and tumours [6].

The potential of these plants are correlated to their secondary metabolites such as phenolic, terpenoids, polysaccharides, and related phenolic compounds such as flavonoids, phenyl propanoid, rosmarinik acid, catechins, tannins, and polyketides. These secondary metabolites are believed to have antiinflammatory, estrogenic, inhibition of enzymes, antimicrobial activity, antiallergic activity, antioxidant, antitumor, and has a vascular activity. The terpenoids that have been isolated from these plants such as mono and sesquiterpenes, iridoids, and saponins are believed to have anticancer, antimalarial, anti-nflamatory, antibacterial, and antiviral activity. These plants are also known to contain alkaloids, glucosides, cardiac glycosides or esters [7-10]. Based on the reports above, in this short review, we would like to present the potential use of these five therapeutic medicinal herbs in dental treatments. It is expected that this review would provide valuable information pertaining the five therapeutic medicinal herbs such as *Calotropis gigantea* (L), *Acrostichum aureum* (L), *Pluchea indica* (L), *Cissus adnata* and *Abutilon indicum* (L) in the field of dentistry.

2. Review on Therapeutic Medicinal Herbs

Calotropis gigantea (L)

Calotropis gigantea (L), also known as Biduri, has a large availability in Indonesia, especially in Aceh Province. All parts of this plant can be used to treat diseases because of the secondary metabolites contents such as alkaloids, steroids, heart glycosides, and terpenoids [3,11]. Some researchers have identified that there are 21 compounds in the leaves and fruits parts of this plant, 43 compounds in the flowers, and some compounds are identified in latex [12]. The common compounds found in leaves, fruits, and flowers are 3-Hexene-1-ol, benzaldehyde, benzyl alcohol, \pm linalol, oct-3-en-2-ol, phenethyl alcohol, α -terpineol, 2,4-dimethyl -acetophenone, 4-vinyl guaiacol and *n*-tetradecane, while the latex contains lignanglycosides, pinosresinol 4-*O*-[6 "-*O*-vanilloyl]- β -D-glucopyranoside and other phenolic compounds such as 6'-*O*-vanilloyltachioside, 6'-*O* -vanilloylisotachioside, and cardenoline such as uskarin (Figure 1). Stems and seeds of this plant also have a potential use for medicinal treatment because of the containing halocellulose, cellulose, lignins and alkali-soluble substances [13,14].

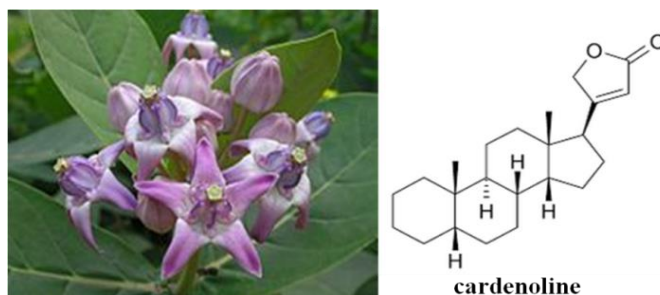


Figure 1. The cardenolide compound isolated from *Calotropis gigantea* (L) [14]

The pharmacological benefit of the secondary metabolites from this plant are usually used as an analgesic, antiasthma, sedative, antiinflammatory, antidiarrhea, hepatoprotective, and anticancer. Another study also mentioned that this plant is a potential antibacterial, antioxidant and reinforcing material composites [3,13-15]. The potential evaluation of this plant in dentistry is still limited, the recent reports mentioned that this plant is potentially used as an anticarcinogenic medicine that inhibits *Streptococcus mutants* and *Lactobacillus sp.*, where these bacteria are known to have a role in cavities formation [3].

***Acrostichum aureum* L**

Acrostichum aureum L or also known as sea fern, is normally grow in brackish water area (mangrove area) [16]. Sea fern is very easy to grow in tropical regions in countries like Brazil, Ecuador, Paraguay, India, Sri Lanka, Bangladesh and Indonesia. Ethnobotanically, this plant is often used traditionally as analgesic (pain killer), antifibrinolytic and antitumor [16-18] Hossaini et al (2011) reported that *Acrostichum aureum* contains glycosides, saponins, flavonoids, steroids, fatty acids and long-chain hydrocarbon compounds. [19]

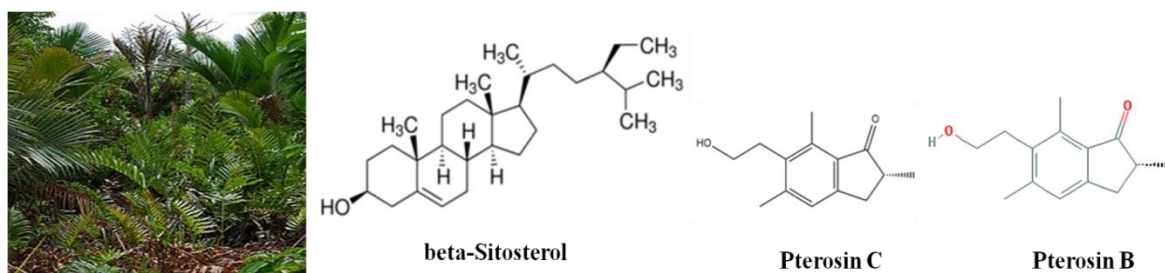


Figure 2. Sea fern (*Acrostichum aureum* L) and its compounds such as β -sitosterol, Pterosin C, and Pterosin.

Two new sesquiterpenes (Figure 2) compounds such as (2*R*, 3*S*)-dulfated pterosin C and (2*S*, 3*S*)-sulfated pterosin C, or also known as, (2*R*, 3*S*)-pterosin C and (2*R*)-pterosin B and β -sitosterol are reported to have been succesfully isolated from aerial parts of this plant. Pterosins C is reported to have citotoxicity effect on AGS, HT-29, MDA-MB-231, MCF-7, and NIH3T3 cell lines in mice with the MIC₅₀ value ranged from 23.9 to 68.8 pM [17]. The activity of this plant in dentistry treatment has been not yet reported, but ethnomedicine studies reported that this plant can be used as an alternative therapeutic in dentistry [16-18].

***Pluchea indica* (L)**

Pluchea indica (L) is widely available in Asia and Australia, in Indonesia this plant also known as Bluntas (Figure 3). *Pluchea indica* is often used as antipyretic, antiinflammatory, muscle relaxant, hepatoproteksi, astringent, wound medication and ulcers. Pharmacologically, this plant has a high antioxidant activity. Other references mentioned that this plant also has antibacterial, antimalarial, antifungal, antitumor activity and wound healing properties [4,20,21]. The activities of this plant is associated with the secondary metabolites it contained, such as tannins, flavonoids and essential oils. The leaves of *Pluchea indica* have been reported to contain flavonoids, saponins, phenolic hydroquinone, alkaloids, sterols, tannins, and reducing sugars [21-24].



Figure 3. A. *Pluchea indica* (L) and B. *Cissus adnata* (L).

In dentistry, this plant has been used as an antibacterial activity against *Streptococcus mutans*, *Enterococcus faecalis*, and *Lactobacillus* and *Fusobacterium nucleatum*. This plant also has been used as wound healing on gingival enlargement and as astrigen on mouthwash [4,5]. Also, this plant has been reported to act as anticarcinogenic and antibacterial root-canal in endodontic treatment failure[20].

Cissus adnata

Cissus adnata is well known as *Cissus pallida*, this plant is classified as vines herbs (Figure 3). The use of this plant is not as popular as other *Cissus* family such as *Cissus quadrangularis*. However, this plant is reported to contain alkaloids, carbohydrates, flavonoids, phenols, terpenoids, saponins, and tannins. This plant also contains antioxidant compounds such as polyphenols which are known for the antioxidant, antibacterial, and antihelmintic activities [24]. The mostly used parts of this plant for therapeutic treatments are leaves, stems, and roots. The leaves of this plant can be used as therapeutic in treating wounds, abdominal pain, peptic ulcer disease, syphilis, ulcers, broken bones, urolithiasis, arthritis pain, and reducing pain during menstruation. The stalks are also often used as therapy for jaundice and paralysis. The roots of this plant are very useful as an anti-diuretic, blood purifier and elephantiasis. Also, this plant is helpful to treat cancer, hemorrhoids, dysentery, epilepsy, fever, asthma, malaria, and food poisoning.[25-26]

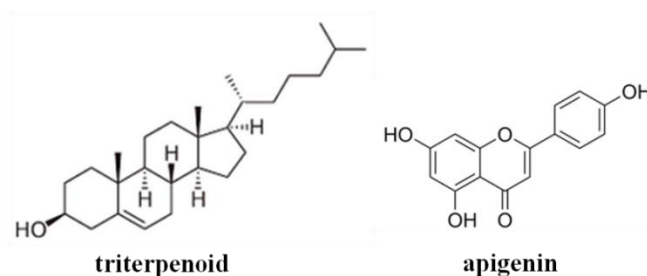


Figure 4. Structure triterpenoid and apigenin isolated in *Cissus adnata*

Phytochemical screening showed this plant contains α - and β -amyrins, β -sitosterol, ketosteroid, carotene, vitamin C, tannins, and phenols. While, the leaves contain triterpenoids, flavonoids, and apigenin (Figure 4). The pharmacological studies showed that this plant has an antioxidant activity and also can be used as therapeutic treatment in dentistry [24-26]. However, the literature of *Cissus* as therapeutic agents in dentistry is very limited and still required an effective research for the development of this plant as therapeutics in dentistry.

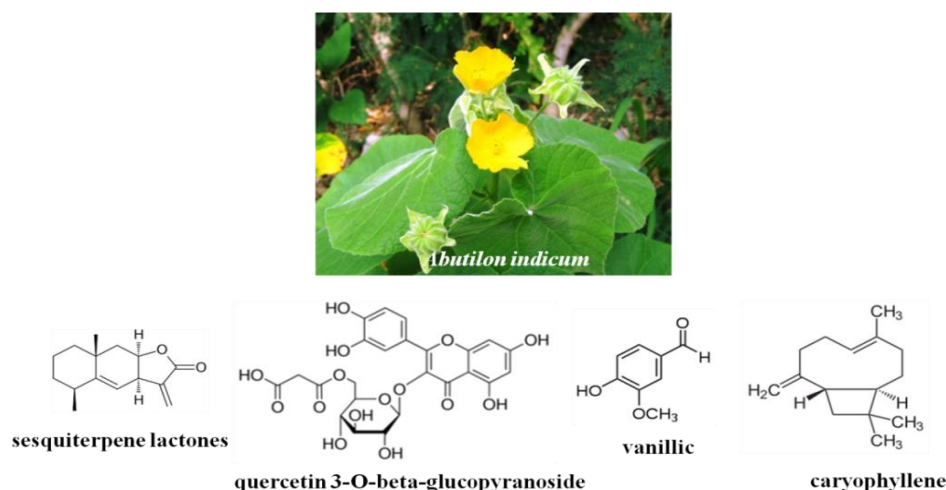


Figure 5. The compounds that isolated from *Abutilon indicum*: sesquiterpene lactones, quercetin 3-O-beta-glucopyranoside, vanillic, and caryophyllene.

Abutilon indicum (L)

Abutilon indicum (L) is classified as herbal plant from the family of *Malvaceae*. This plant widely grow in the Aceh Province. In Indonesia, this plant has several names, Jeukeupa (Aceh), Belalang Sumpah (South of Sumatera), Cemplok (Java) and Kembang Sore (Moluccas). All Parts of this plant such as leaves, seeds, flowers and roots are widely used as a medical therapeutics.

This plant has been reported to contain various secondary metabolites such as saponins, flavonoids, alkaloids, hexoses, *n*-alkane mixtures (C₂₂-C₃₄), alkanols, β -sitosterol, vanillic, fumaric acid, *p*-coumaric, caffeic acid, sesquiterpene lactones and amino acids. In addition, this plant also contains essential oils such as α -pinene, caryophyllene, caryophyllene oxide, endesmol, farnesol, borenol, geraniol, geranyl acetate, elements and 1:8-cineole. Seven flavonoids compounds have been isolated from the flowers of *Abutilon indicum*, the compounds are; luteolin, chrysoeriol, luteolin 7-O-beta-glucopyranoside, chrysoeriol 7-O-beta-glucopyranoside, apigenin 7-O-beta-glucopyranoside, quercetin 3-O-beta-glucopyranoside, quercetin 3-O-alpha-rhamnopyranosyl (1-6)-beta-glucopyranoside. Other compounds such as guanethidine, eugenol (4-allyl-2-methoxyphenyl), vitamin E also isolated from *Abutilon indicum*. [27-29]. The activities of those flavonoids compounds are presented in Table 1.

Table 1. The compound and its biological activity of plant *Abutilon indicum* [29]

Name of the compounds	Biological activity
Benzofuran, 2,3-Dihydro-4H-Pyrans-4-one 2,3-dihydro-3,5-dihydroxy-6- methyl-	Neuropathic pain, analgesic, anti-inflammatory
α -D-Glucopyranose, 4-OD-galactopyranosyl-	Antimicrobial, antioxidant, anti-inflammatory
Hexadecanoic acid, ethyl ester	Preservative Antioxidant, nematicide, pesticides, hypocholesterolemic, hemolytic, reductase inhibitors, anti-sandrogenic flavor
Phenol, 3-methyl-5- (1-methylethyl) -, Methylcarbamate	Antifungal, anti-cancer
9,12,15-Octadecatrienoic acid, 2,3-bis [(trimethyl) oxy] propyl ester	Anti-inflammatory and CNS depressant activity
Phytol	Antimicrobial, anticancer, anti-inflammatory, diuretic
vitamin E	Antiageing, analgesic, anti-diabetic anti-inflammatory, antioxidant, anti-dermatitic, anti-leukemic, anti-tumor, anti-cancer, hepatoprotective, hypocholesterolemic, anti-ulcerogenic, vasodilator, anti-spasmodic, anti-

Guanethidine	bronchitic, anticoronary
trans-isoeugenol	antihypertensive drug
Antioxidant	Anticancer, antioxidant
γ -Tocopherol	Antioxidant, anticancer
Stigmasterol	Anti-inflammatory anti-osteoarthritic
β -sitosterol	Anti-inflammatory, anti-pyretic, anti-arthritis, anti-ulcer,
Campesterol	Anti-inflammatory

Pharmacologically, this plant is widely used as an anti-inflammatory, antifibrinolytic, antioxidant, antibacterial, antiulcer, antifungal and wound medication. *Abutilon indicum* capability is already being developed in dentistry as antiinflammation analgesic, anti-bacterial are also caused by the content of eugenol from *A. indicum* [28-30].

3. Potential Herbal Medicines in Dental Treatment

The oral cavity is the gateway contamination in the human body. Due to high contamination, many bacteria can be detected in the oral cavity. Dewhurst et. al., (2010) indicates at least 619 of taxon are identified in the oral cavity [31]. Due to the frequent occurrence of the infections in the oral cavity, thus preventive treatment of the diseases is needed. One of the prevention can be done by exploiting these five herbal medicine as therapeutic in dental treatment.

Based on several studies mentioned above the five plants of *Calotrophic gigantea* (L), *Acrostichum aureum* (L), *Pluchea indica* (L), *Cissus adnata* and *Abutilon indicum* (L) are considered to have polyphenolic compounds such as flavonoids. Flavonoids are polyphenolic compounds play an important role for an antidote to catch free radicals (free radical scavenger) as antioxidant and antimicrobial. Shoibe and You (2012) reported that the flavonoids from *Calotrophic gigantea* (L) and *Cissus adnata* (L) play an important role in preventing cancer, cardiovascular, macular degeneration, cataracts and asthma diseases, and can improve immune function [13,24,32]. Another flavonoids compounds such as isoflavones, gallic acid, and quercetin are potentials to develop in dental therapeutic. *Calotrophic gigantea* reported contains gallic acid and flavonoids as much as 19.86 ± 0.02 mg/g and quercetin as much as 5.10 ± 0.60 mg/g, this causes *Calotropis gigantea* to have a capability to inhibit dental caries causing bacteria with the inhibition zone of 16 mm [33]. While, *Abutilon indicum* is reported to contain flavonoids of 64.6 ± 1.20 mg/g and quercetin of 85.3 ± 0.8 mg/g [30]. Meanwhile, *Pluchea indica* has been reported to contain flavonoids as much as 0.831 ± 0.129 mg/g [23].

Several studies have not been able to explain the mechanism of these flavonoids compounds against the bacterial. However, based on the literature, the mechanism of the flavonoids on the bacterial inhibition is by damage the extracellular membrane of the bacteria, the other mechanism is by forming a complex with soluble extracellular proteins of the bacteria, the other possible mechanism is by interacting with the cell wall of the bacteria. However, Singh (2006), reported that the flavonoids compounds from these plants are potential to be used for wound-healing treatment.[8] Rahman et al., (2014) also reported that flavonoids were able to stimulate red blood cells (erythrocytes) in proliferating and differentiation [5]. The cardenolide and terpenoids compounds from these plants are able to prevent of tumors and cancers cells, these compounds are reported to be able to induce the apoptosis in tumors cell and also able to regulate cancers cells through multiple signaling pathways [33]. The steroids from these plants are also reported to have inhibition capability against the development of tumors and cancers cells. The terpenoids compounds from these plants are reported to be capable of stimulating the signaling cells through the NF- κ B pathway through different mechanisms, particularly through the I κ B phosphorylation, DNA binding, translocation of p65, and others [34]. The eugenol has been used traditionally in Asian countries as antiseptic, analgesic and antibacterial, eugenol also used as refresher in cosmetics and food products. Meanwhile, in dentistry eugenols is used as cement restorations, painkillers and medicament intracanal [35].

4. Conclusion

These five plants could potentially be used for dental therapy in dentistry because of secondary metabolites, were very supportive. These compounds cause the five plants to have a function as antimicrobial, anti-inflammatory, anti-cariogenic, anti-cancer, anti-tumor and wound healing medicine.

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