POTENCY OF *ENHALUS ACOROIDES* FROM INDONESIA REGION FOR HALAL PHARMACEUTICAL INDUSTRY: A REVIEW

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ABSTRAK

Saat ini penerapan sistem jaminan halal di Indonesia telah bersifat wajib. Selain makanan, farmasi, kosmetik, dan obat-obatan semuanya harus bersertifikat halal. Produk alami, khususnya produk berbahan dasar laut, menjadi alternatif pilihan bahan baku industri kosmetik dan farmasi. *Enhalus acoroides* banyak terdapat di sepanjang pantai Indonesia dan berpotensi untuk digunakan sebagai bahan baku kosmetik halal dan produk farmasi. Tujuan dari makalah ini adalah untuk mengkaji potensi *E. acoroides* yang dikumpulkan dari berbagai lokasi di Indonesia dalam kaitannya dengan senyawa bioaktif dan aplikasinya. Metabolit sekunder yaitu alkaloid, flavonoid, polifenol, steroid, triterpen, dan tanin telah dilaporkan dijumpai dalam ekstrak *E. acoroides* dari Indonesia, dan berpotensi untuk digunakan sebagai anti bakteri, anti penuaan, antivirus, antitumor, dan antioksidan dalam bidang farmasi dan industri kosmetik di Indonesia
Kata kunci: *senyawa bioaktif, Enhalus acoroides, industri farmasi, lamun*.

ABSTRACT

Currently, the implementation of the Halal assurance system in Indonesia is mandatory. A side from food, pharmaceuticals, cosmetics, and medicines must all be halal certified. Natural products, particularly marine-based products, are an alternative choice for the cosmetics and pharmaceutical industry's raw materials. *Enhalus acoroides* are common along Indonesia's coasts and have the potential to be used as raw materials in halal cosmetics and pharmaceutical products. The purpose of this paper is to examine the potential of *E. acoroides* samples collected from various locations in Indonesia in terms of bioactive compounds and their applications. Secondary metabolites namely alkaloids, flavonoids, polyphenols, steroids, triterpenes, and tannins have been reported in *E. acoroides* extract from Indonesia, and they have the potential to be used as antibacterial, antiaging, antiviral, antitumor, and antioxidants in the pharmaceutical and cosmetic industries in Indonesian.
Keywords: *bioactive compounds, Enhalus acoroides, pharmaceutical industry, seagrass*.

INTRODUCTION

All individuals around the world are always fighting to protect their health and find nutritious nourishment. Even though pesticides and synthetic chemicals are useful for achieving a certain goal, it is impossible to ignore the dangers they pose to living things. The natural toxins or biotoxins present in living organisms are considered a solution to this problem (Shanta et al., 2013). Muslim patients have special medical demands that set them apart from non-Muslim patients. Although Indonesian legislation guarantees consumer protection for the availability of halal products, it has not yet been fully applied. In Indonesia, the halal status of cosmetics and pharmaceutical preparations is still in doubt. The indicator is that 90% of the pharmaceutical industry's raw materials are imported, and there is no halal guarantee system in place for these products (Syahrir et al., 2019).

Pharmaceutical products that may contain active substances and other types of excipients are included in the phrase "halal pharmaceutical." Sources of each product's active components and excipients were evaluated for their halal status and categorization into halal, *mushbooh* or haram (Aziz et al., 2014; Sadeeqa et al., 2013). Halal food is free of any ingredient that Muslims are forbidden from eating. According to Al Quran, all good and clean foods are halal. Similarly to halal food, halal pharmaceuticals are supposed to come from halal, clean and healthy source because they are something which are eaten or consumed (Ab Halim et al., 2015). Surah Al Baqarah verse 172 of the Quran states that all pure and clean foods and pharmaceuticals are permissible for Moslem consumption, except those specifically prohibited.

The majority of cosmetics and pharmaceutical sources are obtained through synthetic processes because the products obtained through this technique have less impurity or contamination (Aziz et al., 2014). However, up until recently, plants served as a valuable resource for the discovery of new pharmacologically active chemicals, and many well-known medications today have some connection to plants, either directly or indirectly (Raskin et al., 2002). Plants provide a number of benefits, such as large biomass output at cheap cultivation costs, quick 'gene to protein' times, inexpensive start-up and ongoing costs, great scalability, and eucaryotic post-translational modifications. (i.e. glycosylation, folding and multimeric assembly), low risk of human pathogens and endotoxins and a relatively high protein yield (Raskin et al., 2002). According to Balunas and Kinghorn (2005), drugs made from medicinal plants can be used as both brand-new medications and drug leads for pharmaceutical and synthetic chemists to refine.

Terrestrial and aquatic plants have experienced various abiotic and biotic selective pressures ever since they evolved the structures and mechanisms that allowed them to live on land. Marine plants have acquired several unique chemical structures not seen in terrestrial plants because, unlike terrestrial plants, they have evolved and adapted to existence in a relatively stable yet saline environment (Gray, 2012). The marine environment is a rich source of chemical and biological diversity. The seagrass ecosystem is one of the ecosystems in the sea that has an important role in the life of marine biota and the most productive marine ecosystems, widely used as food ingredients (Nurafni and Nur, 2018; Simamora, 2019). They are also being potential for industrial development with the aquaculture, cosmetic, and pharmaceutical industries as priorities (Kannan et al., 2010a; Shanta, 2013; Shanta et al., 2013), since there has been an increasing interest in the marine resource for the discovery of novel bioactive compounds. The numerous types of seagrasses found in Indonesian coastal waters are not being utilized. In fact, there is no economic use of seagrass by the local community (Nurafni and Nur, 2018). The purpose of this paper was to highlight the potential of bioactive compounds derived from seagrass, specifically *Enhallus acoroides* found in Indonesia coastal areas for use in halal cosmetics and pharmaceuticals industries.

METHOD

The method or approach in this paper is the literature studies. The data was gathered from journal articles, and proceedings related to the topic of study. Data searches are conducted through online instruments using Science Direct, Garuda, and Google Scholar. Searches are conducted using the keywords "Enhalus", "bioactive compounds", "seagrass", and "Indonesia". Further searches are done manually on bibliographies that support relevant writing.

RESULT AND DISCUSSION

Distribution and ecological status of seagrass meadows in Indonesia

Seagrasses are submerged marine angiosperms growing abundantly in the intertidal and subtidal areas of the sea except in Polar Regions (Kannan et al., 2010a; Short et al., 2007). There are probably 57 species of seagrass worldwide (Ahmed et al., 2022), but species can have ranges the extend for thousands of kilometres of coastline. Seagrasses are crucial components of marine ecosystems because they reduce wave energy, maintain sand stability, and offer a huge amount of refuge to a variety of marine organisms (Supaphon et al., 2014). In addition, seagrass preserve genetic diversity and may be useful for metabolic processes (Short et al., 2007).

Based on a report by Hernawan et al (2021), Indonesia's seagrass meadows are the largest in Southeast Asia, has the potential to become the largest in the world. *E. acoroides* is widespread along the Indian Ocean coast and parts tropical of the western Pacific region (Sarinawati, 2020). Until 2018, 7 types of seagrass were known namely *Halodule, Cymodocea, Syringodium, Thalassodendron, Enhalus, Thalassia*, and *Halophila* (Sofiana et al., 2020), and 16 species of seagrass had been identified in the Indonesian Coral Triangle Centre (Hernawan et al., 2021). *Thalassia hemprichii* and *E. acoroides* were the most common species in Indonesia (Fahruddin, M. et al., 2022; Hernawan et al., 2021; Lessy and Ramili, 2018; Nurafni and Nur, 2018).

The distribution and ecological status of seagrass in Indonesia have been reported by Hernawan et al. (2021) and are listed in Table 1. In the study, nine seagrass species were observed across the monitoring locations in Indonesia. *Thalassia hemprichii* and *E. acoroides* were dominant at 12 locations each, with *E. acoroides* dominating in six locations. Seagrass cover ranges from 19 to 65%. The East Indonesia area had the highest seagrass cover (±45%), while the West Area had about 31%. The highest seagrass cover obtained in Biak and Sikka, while the lowest was found in Batam.

Table 1. Distribution and the Status Ecological Quality Index of Two Predominant Seagrass Found in Indonesian Coastal

West area	Level of seagrass dominance		SEQI*	East area	Level of seagrass dominance		SEQI
	E.acoroides	*T. hemprichii*			*E.acoroides*	*T. hemprichii*	
Nias	Low	Moderate	Good	Makassar	Low	High	Good
Tapanuli Tengah	High	Low	Moderate	Selayar	Moderate	High	Good
Mentawai	Low	Moderate	Moderate	Kendari	High	High	Moderate
Batam	High	Moderate	Moderate	Buton	Low	High	Good
Bintan	High	High	Good	Wakatobi	Low	High	Good
Lingga	High	Moderate	Moderate	Sikka	Low	High	Good
Lampung	High	Moderate	Moderate	Sawu	Low	High	Good
Karimun Jawa	Moderate	High	Moderate	Ternate	Moderate	High	Moderate
				Raja Ampat	Moderate	High	Moderate
				Biak	Low	High	Good

*SEQI : Status Ecological Quality Index
Source: Hernawan et al. (2021)

Secondary metabolites of seagrass and their function

Seagrass leaves have a reduced cuticle and an epidermis that lacks stomata and functions as the primary photosynthetic tissue. Papenbrock (2012), classifies seagrass based on its growth form, which ranges from small plants with thin leaves (e.g., *Halophila, Halodule*) to large plants with thick leaves (e.g., *Enhalus, Posidonia*, and *Thalassia*). Natural product compounds discovered in medicinal plants (and their analogs) have yielded a plethora of clinically useful drugs. The chemical compounds synthesized by secondary metabolic pathways usually have roles in adaptation processes under stress conditions. Alkaloids, flavonoids, steroid, triterpenes, phenolic compounds, saponins, and tannins are among the many compounds found in plant tissue (Hudaifah et al., 2020; Supaphon et al., 2014). The most abundant and biologically active phytonutrients are flavonoids (Soto et al., 2015). Flavonoids and their functional derivatives are thought to protect against marine microorganisms. Flavonoid compounds exhibit important activities such as feeding deterrence, antibacterial activity, and antilarval activity (Subhashini et al., 2013). Flavonoids, according to Soto et al. (2015), have antiaging, antimicrobial, proapoptotic and anti-angiogenic and antiviral properties, and can reduce inflammation, inhibit tumor growth, among other things, control the immune system, enhance capillary resistance, prevent the cardiovascular and neurological systems, reduce weight gain, and encourage healing of wounds, among other things.

Plants were rich in phenolic compounds (Kannan et al., 2010b) which were produced in response to various stresses such as infections, wounding, ultraviolet (UV) irradiation, ozone, pollutants, and so on. Phenolic compounds are important in protecting seagrasses from competitors, predators, and pathogens. Soluble phenolic acid has been found to be abundant in a variety of seagrasses, and seagrass extracts contain a high concentration of soluble phenol, which has been shown to inhibit the growth of bacteria, fungi, and algae (Subhashini et al., 2013). Simple phenol derivatives, phenylmethane derivatives, phenylethane derivatives, phenylpropane derivatives including esters and dimers, chalcones, flavonoids including catechins, phenylheptanoids, monoterpene derivatives, sesquiterpenes, diterpenoids, steroids were identified (Zidorn, 2016). Tannin is a type of phenolic metabolite compound which has free radical scavenging activity and can inhibit lipoxygenase and lipid peroxidase. According to Hasan et al. (2022), tannins are also able to provide a protective effect by acting as free radical scavengers and activating antioxidant enzymes.

Characteristics and nutritional value of *E. acoroides*

Enhalus sp is a group of seagrasses which are flowering aquatic plants (antophyta) as well as the ability to live and grow in a marine environment. It performs an important ecological function in the sea by acting as a large primary producer, and it is commonly used as an indicator of heavy metal contamination in waters (Ismarti et al., 2017). The species of *E. acoroides* can be distinguished by their distinct morphologies. The specific characteristics of *E. acoroides* as reported by Haryati and Kurniawan (2021) and Lessy and Ramili (2018) includes: large leaf size can reach 1 meter, a leaf-shaped ribbon with a length of 30-150 cm and a width of 1.25-1.75 cm; hairs on the rhizome of *E. acoroides* that has no stem, leaves that grow straight from the rhizome; and strong and thick roots that are white and not branched. The sample of *E. acoroides* is shown in Figure 1.

Several studies have revealed that *E. acoroides* can be used as an alternative to healthy food ingredients. The parts that can be used are the leaves, flowers and fruit (Marsel et al., 2021).

Figure 1. *E. acoroides* from Batam Coastal Water

The nutritional content of *E. acoroides* seagrass parts has also been reported by (A. Ibrahim et al., 2020; Kaya, 2017; Kole et al., 2020). The results of the proximate analysis of leaves, rhyzomes and seagrass seeds are as shown in Table 2. Moreover, the raw flour prepared from dried seeds of *E. acoroides* contained calcium (933 mg/kg), phosphorus (2392 mg/kg) and iron (2813 mg/kg) as mentioned by Kim et al. (2021). In Indonesia, very limited paper was reported about the utilization of *E. acoroides*. Some of the utilization of *E. acoroides*, include for herbal tea (Marsel, et al., 2021), tempeh (Kole et al., 2020), milk (Latuihamallo et al., 2019), and nuggets (A. Ibrahim et al., 2020).

Table 2. Proximate Analysis of the part of *E. acoroides*

Parametres	Carbohydrate	Protein	Lipid	Ash	Water	Reference
Rhyzoma	4.16	0.75	0.52	0.79	89.99	Kaya (2017)
Seed	72.40	8.10	0.20	6.40	9.80	Kole et al. (2020)
Fruit	59.26	5.65	0.76	-	-	A. Ibrahim et al. (2020)

Bioactive compounds of *E. acoroides* from Indonesian coastal area and their potential for application

Study on bioactive compounds of *E. acoroides* sampling from some areas in Indonesia showed that *E. acoroides* contains alkaloid, flavonoid (Ahmed et al., 2022; Dewi et al., 2012; Hasan et al., 2022; Menajang et al., 2020; Permana et al., 2020; Pradana et al., 2018), phenolic compounds (Ahmed et al., 2022; Menajang et al., 2020), triterpenoid (Pradana et al., 2018), tannin (Hasan et al., 2022; Permana et al., 2020), and steroid (Dewi et al., 2012; Hasan et al., 2022; Permana et al., 2020). These components have the potential to be a natural chemical antibacterial, antifungal, and other pharmaceutical raw materials. The studies about bioactive compounds of *E. acoroides* from different regions in Indonesia are listed in Table 3.

E. acoroides has been shown to have antimicrobial, antimalarial, vasoprotective, insecticidal, antiinflammatory, antioxidant and antialgal activity (Kim et al., 2021). In traditional medicine, *E. acoroides* has been used to treat a variety of ailments, including fever and skin diseases, muscle aches, wounds, stomach problems, drugs for stings from various types of rays, and as sedatives for babies (Menajang et al., 2020; Supaphon et al., 2014). *E. acoroides* produces antimicrobial compounds that can inhibit or control microbial growth, and numerous studies have reported antibacterial, antidiabetic, antifungal, anti-inflammatory, antioxidant, and antiviral activity (Menajang et al., 2020; Permana et al., 2020; Pradana et al., 2018). Also, after 24 hours, *E. acoroides* hexane extract (500 ppm) demonstrated 62% larvicidal activity against Aedes aegypti, whereas its ethanol extracts (500 ppm) demonstrated 50% larvicidal activity against *C. quinquefasciatus* (Monisha et al., 2020). Moreover, seagrass-associated bacteria were reported to have antimycobacterial activity against multi drug resistant tuberculosis bacteria (Sulistiyani et al., 2015).

Moreover, *E. acoroides* leaf extracts are rich sources of antioxidant compounds. Nowadays, the discovery of natural antioxidants is compelled by two factors: (1) epidemiological and clinical evidence indicating that eating vegetables and fruits reduces the risk of developing chronic diseases such as cancer; and (2) phytochemicals are generally safer than synthetic chemicals (Patra et al., 2008).

Table 3. Study on Bioactive Compounds of *E. acoroides* from Indonesia in the Recent Decade (2012-2022).

Sampling location	Finding	Functional use	Reference
Pramuka Island, DKI Jakarta	*E.acoroides* extracts contain flavonoids, alkaloids, and steroids. *E. accoroides* methanol extract is extremely toxic, with an LC50 value of 5.74 ppm.	Antitumor, antilarval	Dewi et al., 2012
Jepara, Central Java	Alkaloids, flavonoids, and triterpenoids were found in *E. acoroides extract. E. acoroides* extract at 25% (w/v) has been shown to increase the shelf life of tilapia fillets based on Total volatile-based Nitrogen, Total Plate Count, and pH values.	Antibacterial	Pradana et al., 2018
Karang Tirta Beach, Padang City, West Sumatera	The antibacterial activity of *E. accoroides* extract against Stapilococcus aureus is 15.62 g/mL of n-hexane solvent.	Antibacterial	Anthonius A & Meirina, 2018
Galala, Rutong and Waai, Central Moluccas	The flavonoid levels of *E.accoroides* extract from Galala, Rutong and Waai coastal waters were 0.0192%, 0.1475%, and 3.5697% respectively,	Antiaging, antimicrobial, antiviral	Tuapattinaya & Rumahlatu, 2019
Lae Lae island, Makassar, South Sulawesi	The ABTS radical (2,2'-azino-bis(3- thylbenzothiazoline-6-sulfonic acid) activity test of E. accoroides ethanol extract was 38.008 µg/ml.	Antioxidant	Sami et al., 2020
Biawak Island, Indramayu, West Java	Samples of *E.accoroides* leaves contain alkaloids, steroids and tannins. Methanol extract of E. *accoroides* leaf showed moderate antioxidant activity with an IC50 value of 148.67 ppm.	Antioxidant	Permana et al., 2020
North Sulawesi	*E. accoroides* extracts contain phenols, flavonoids, steroids, and superoxide dismutase. Ethyl acetate extracts of *E. accoroides* had an IC50 of 7 ppm.	Antioxidant	Menajang et al., 2020
Banggai Kepulauan, Sulawesi Tengah	At 50 mg/kg BW an extract of *E. acoroides* inhibits the -glukosidase enzyme.	antidiabetes	(Hasan et al., 2022)
East Lombok	*E. acoroides* methanol extract contains bioactive components such as phenolics, flavonoids, and terpenes.	antioxidant	(Windyaswari et al., 2019)

Polyphenolics are used as natural additives in a variety of industries, including food and cosmetics (nutritional additives , natural antioxidants, natural coloring agents, and conservative agents) (Soto et al., 2015). The ability of *E. acoroides* leaves to reduce Fe3+ was greater than that of the root and rhizome Total antioxidant activity in ethanol extracts of *E. acoroides* in the range 11.532-11.770 mg ascorbic acid. According to Kannan et al. (2010b), there is a correlation between antioxidant capacity and phenolic content of *E. acoroides* extract with a correlation coefficient (R^2) of 0.923. Similarly, a significant correlation between proanthocyanidin and total antioxidant activity was 0.977. As a result, it can be concluded that phenolic compounds were the primary contributors to *E. acoroides'* antioxidant capacities.

Higher plants have steroid hormones and fatty acids. In an ethanol extract of *E. acoroides* from the South China Sea, Qi et al., (2008) discovered a number of steroids and fatty acids. Five steroids were stigmasta-4,22-diene-6b-ol-3-one, stigmasta-4,22-diene-3,6-dione, stigmast-22-en-3-one, stigmasta-5,22-dien-3-O-b-D-glucopyranoside, and daucosterol. According to Hiola, et al. (2010), phytosterol (stigmasterol dan b-sitosterol) in the root, rhizome, and leaves of *E. acoroides* has a high potential for use as an antifertility agent. According to Kim et al. (2021), the seeds of the tropical seagrass *E. acoroides* were traditionally eaten in the Philippines and were considered to have aphrodisiac and contraceptive properties. Fatty acids derived from marine resources play important roles and have biological properties because they inhibit the growth of several dangerous pathogenic bacteria and fungi, as well as having potent antiviral efficacy (Bajpai, 2016).

CONCLUSION

Secondary metabolism in *E. acoroides* contains valuable compounds not found in other taxonomic groups. Some of the compounds could be useful in the cosmetics and pharmaceuticals industries. As a result, *E. acoroides* has potential as the source of compounds for antibacterial, anticancer, anti-HIV and immunostimulant, antitumor, and antioxidant research. Secondary metabolite information for *Enhalus* species from Indonesia is still limited. It has become necessary to investigate the bioactive and nutritional value so that these values can be recommended for biological and pharmaceutical applications in support of halal cosmetics and pharmaceuticals in Indonesia.

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