
Review Article

Biological and therapeutic potential of the edible brown marine seaweed *Padina australis* and their pharmacological mechanisms

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Abstract

Seaweeds have an important place in the ancient systems of medicine. In addition, they also find significant mention in farming and in nutritional diet due to their benefits such as, availability, cheaper price, renewable potential and the advantage of being easily accessible. There are over 10,000 species of seaweeds that reflect their immense diversity. They are further used for both, their flavour and nutritional properties. Edible seaweeds are rich sources of bioactive compounds. In the last three decades, the discovery of metabolites with biological activities from macroalgae has increased significantly. *Padina australis* has been reported to possess several therapeutic activities including, antioxidant, anti-inflammatory, antibacterial and larvicidal effects. In addition, studies have also reported on the antidiabetic and antihypertensive potential of *Padina australis*. Till date, there are limited or no scientific reviews that have been published on the pharmacological and therapeutical activities of *Padina australis* in specific. Thus, there is a need for such a review to appreciate the various biological actions of this potent seaweed.

Received 17 December 2019

Reviewed 05 June 2020

Accepted 07 July 2020

Published 15 October 2020

This review, in this direction, attempts to explore the various therapeutic activities of the brown marine seaweed *Padina australis*, from the current published literature along with their pharmacological and molecular mechanisms, underlying its therapeutic activities. The main limitation of this review is that ancient texts, leisure magazines and traditional manuscripts were not searched.

Keywords: *Padina australis*, seaweed, antibacterial, antioxidant, anti-inflammatory, larvicidal, anti-diabetic

Introduction

The inefficiency to contain deadly diseases has stimulated the urgent need for the identification and discovery of effective newer substances from nature and plant sources. From the current natural resources, the marine landscape has a great potential for medicinal drug discovery and investigation (Chandini et al., 2010). Seaweeds occupy a major proportion of the edible substances and they are employed very often in South East Asian diet. They are also used as therapeutic agents for various ailments. Marine seaweeds and their organic extracts are known to contain a variety of bioactive substances with diverse health benefits. There are large libraries of chemical compounds that have been isolated and characterised from marine herbs and seaweeds. There is a huge variation among the amount and quality of the chemical substances present in a specific species of seaweed owing to their habitat and location of existence. These also depend on geographical origin or area of cultivation. The other factors that affect the chemical and nutritional constituents are harvest season, environmental variations, physiological variations and water temperature (Ortiz et al., 2006). There is a renewed and increasing interest towards herbs and weeds from the sea in the past few decades. This is primarily due to the vast array of biomolecules that are present within them. Plenty of studies have been carried out on several seaweeds, which have proven to possess potential therapeutic activities ranging from free-radical scavenging to regulating inflammation in body tissues. Recent studies in the field of medical and pharmaceutical research have revealed promising compounds, isolated from marine seaweeds. A recently published study highlights the importance of seaweeds from oceans namely, from the genus *Padina*, which could be employed as an additional source in the manufacture of silver Nano substances, which can be eventually employed therapeutically for various bacterial infections (Bhuyar et al., 2020a). Although, some of the seaweeds are toxic in nature, there exist a large number of seaweeds that have exhibited enormous potential as therapeutic or medicinal substances. A range of bioactive group of compounds are found in these seaweeds, which

range from flavonoids, sugars, fats, and amino acids. These substances have been proven to demonstrate several activities in the biological system. Moreover, these are also used in the development of new pharmaceutical agents. Thus marine seaweeds occupy an important place as a source of rich bioactive compounds (Manilal et al., 2010). A recent study reported the free-radical scavenging and antibacterial potential of the red seaweed, *Kappaphycus alvarezii* when evaluated against several strains of harmful bacteria (Bhuyar et al., 2020b). The Malaysian marine ecosystem is unique and understudied compared to other marine ecosystems. Brown macroalgae species are constantly reported as potential sources of bioactive compounds with various therapeutic effects. For example, *Padina australis* which is a member of the Phaeophytes has shown potential antibacterial effects due to the presence of its bioactive compounds.

Marine brown algae along the coast of Malaysia have remained largely unexploited. Therefore, it is worthwhile to review the various therapeutic effects of the marine seaweed *Padina australis*. This review strives to provide a detailed account of all the current knowledge on the therapeutic effects of *Padina australis* which is found abundantly in Malaysian coastal waters.

Seaweeds have been widely used in pharmaceutical and food industries for decades due to its renewable properties. There are around 10,000 species of seaweeds found worldwide and they are all classified into three major classes which are red algae (Rhodophytes), brown algae (Phaeophytes) and green algae (Chlorophytes) (Mohsin et al., 2013). Seaweeds can be easily found all around the world, especially in Asian countries such as Japan, Philippines, Korea, Malaysia and Indonesia (Wang et al., 2013). Among the three major classes of seaweed, brown algae appear to be a popular food in Japan, Korea and China because seaweed is part of their main diet and they take it daily in most of their meals (Yan et al., 2007). Besides playing a significant role in the Asian diet and food substances, the brown algae also functions as an antioxidant that helps in preventing degenerative diseases such as cancer or cardiovascular disease by neutralizing the free radical mechanism (Yan et al., 2007; El Gamal, 2010). Furthermore, the brown algae has also been studied for its antibacterial effect which is shown through the inhibition of the growth and activity of the bacteria (bacteriostatic) or by destroying the bacteria (bactericidal). For example, *Padina australis* which is a member of the Phaeophytes had shown potential antibacterial effects due to the presence of several bioactive compounds. Moreover, the bioactive compounds of Phaeophytes have shown to have larvicidal effects (Canoy & Bitacura, 2018).

The aims of this study were to look out the functions of components extracted from *Padina australis*.

Morphology of the plant

Padina australis (Figure 1.) belongs to the Dictyotaceae family which is edible brown algae (Yan et al., 2007) *Padina australis* is a broadly flabellate plant with a stupose holdfast. *Padina* is the only genus of brown algae which is calcified. Both surfaces of the thallus are lightly calcified, especially at the stipe (Wang et al., 2013).



Figure 1. External morphology of *Padina australis* Hauck. (Dictyotaceae)

The erect thalli are flabelliform with a diameter up to 15cm. Its thalli are yellowish green to yellowish brown in colour. Besides, the thalli can also be divided into many segments. The thalli of *Padina australis* have bilayer thickness of an approximate of 11 μm to 120 μm thick at the base and 95 μm to 100 μm at other parts. The stipe is moderately long with a length of 2cm and width of 3mm (Szlachetko et al., 2014). Phaeophyceyan hairs are found alternatively on both sides of the thallus along the stipe in concentric rows, with the outer cortical origin of growth. *Padina australis* is found to grow in

the deeper sublittoral region, attached on rocks, corals or sands and sometimes seen epiphytic on the other microalgae. This species grows mainly in tropical and subtropical waters instead of temperate waters (Tronholm, Leliart & Sanson, 2012). *Padina australis* has two types of sori which are the non-indusiate antheridial sori that form patches mixing between the oogonial sori and the indusiate oogonial sori which form discontinuous lines. Both of the sori lined up continuously far adjacent to the hairlines on the inferior surface. The reproductive sori are located at the middle of the narrow glabrous zone, normally on the lower blade surface (Szlachetko et al., 2014). The locality of this plant is in Cape York, Queensland, Australia. The presence of *Padina australis* is distributed worldwide which it can be found in most Asia countries like Indonesia, Philippines, Thailand, Japan, Taiwan and others. Besides Asian countries, it can also be found in Ivory Coast, Cameroon, Gabon and Angola of West Africa, Hawaiian Islands of the Pacific Islands and also Queensland of Australia (Wang et al., 2013).

Taxonomical classification

Table 1. Taxonomical classification of *Padina australis*

Kingdom	Chromista
Phylum	Ochrophyta
Class	Phaeophyceae
Order	Dictyotales
Family	Dictyotaceae
Genus	<i>Padina</i>
Species	<i>Padina australis</i>

Therapeutic activities of Padina australis

Antibacterial

Antibiotics have been widely used to treat or cure bacterial disease in aquaculture. However, the use of antibiotics may cause the development of antibiotic-resistant bacteria and toxicity to the environment due to the misuse or overuse of antibiotics (Lee, 1995). Therefore, the use of seaweeds in preventing and treating bacterial disease had gradually increased because seaweeds are cheap and renewable sources that we can obtain easily from nature. Thus, seaweeds can be used as an antibacterial agent with greater effectiveness, minimal adverse effect, better bioavailability and are less toxic. The production of secondary metabolites in seaweeds are varied according to environment changes such as geographical location, light, temperature,

species, maturity and seasons (Perez, Falque & Dominguez, 2016). The secondary metabolite found in *Padina australis* which possess antibacterial activity includes phenol and its derivative. Flavanoid is a derivative of phenol which can act against gram-positive bacteria (*Bacillus cereus* and *Staphylococcus aureus*) and gram-negative bacteria (*Escherichia Coli* and *Pseudomonas aeruginosa*) (Chkhikvishvili & Ramazanov, 2000). The phenolic extracts of *Padina australis* inhibit the growth of bacteria by damaging the cytoplasmic membrane and thus leads to the leakage of cell contents. The hydrogen ion of phenol and flavonoids attack the phosphate group and this leads to the breakdown of phospholipid molecules of the bacteria's cell wall into carboxylic acid, glycerol and phosphoric acid. As a result, the growth of bacteria is retarded and eventually dies (Chkhikvishvili & Ramazanov, 2000).

There are many methods to evaluate the antibacterial activity of the metabolites of seaweeds. Normally, the studies on the antibacterial activity of seaweeds are either only *in vivo* or only *in vitro*, but sometimes *in vitro* screening will be conducted first and then followed by an *in vivo* study (Chkhikvishvili & Ramazanov, 2000). The *in vivo* assays are rarely used to screen the antibacterial activity of the seaweeds as there are many restrictions in *in vivo* studies. While for *in vitro* studies, agar disc diffusion test, growth inhibition assay, minimum inhibitory concentration (MIC) determination and minimum bactericidal concentration (MBC) are included (Perez, Falque & Dominguez, 2016). The disc diffusion test can only give the qualitative result as the size of the inhibition zone can be affected by molecular size, molecular mass and polarity of the extracts. In comparison, MIC and MBC assay are more important to give quantitative result on the antibacterial activity of the extracts (Perez, Falque & Dominguez, 2016). MIC is used to investigate the bacteriostatic concentration of the seaweed extracts while MBC assays are used to determine the bactericidal concentration of the seaweed extracts against the respective pathogenic bacterial strains. Hence, the lower the MIC and MBC values, the higher the antibacterial potential of the seaweed extracts (Vinayak, Sabu & Chatterji, 2011).

Padina australis has shown its inhibition against beta-lactamase negative *E. coli* ATCC 25922, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Bacillus cereus*. The percentage of the inhibition of *Padina australis* extracts against *Escherichia coli* ATCC 35218 is 77.78% and this result is obtained through the disc diffusion susceptibility testing. The lowest MIC value for *Padina australis* extracts against *Escherichia coli* ATCC 25922, *E. coli* ATCC 35218, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Bacillus cereus* were

0.833, 1.677, 0.261, 0.417 and 0.130 mg/ml respectively. Besides, the methanolic extracts of *Padina australis* have shown the lowest MBC value (0.182 mg/ml) when compared to the dichloromethane and n-hexane extracts against *Bacillus cereus*. The results showed that the MBC values are greater than the corresponding MIC values which indicates the bactericidal effect of the *Padina australis* extracts can only be exhibited when a higher amount of extracts is used. Since *Padina australis* only exhibited its bactericidal potential on *Bacillus cereus*, so this implies that *Padina australis* has narrow-spectrum antibacterial activity (Chkhikvishvili & Ramazanov, 2000).

Padina australis is proven to possess bacteriostatic and bactericidal activity towards the gram-positive and gram-negative bacteria by damaging the cytoplasmic membrane of the bacteria. However, *Padina australis* is an antibacterial agent with narrow spectrum bactericidal activity which only acts against one specific type of bacteria (Chkhikvishvili & Ramazanov, 2000).

Antioxidant

Reactive oxygen species (ROS) molecules or ions formed by the incomplete one-electron reduction of oxygen and ROS plays a significant role in regulating the signal transduction, microbial activity of phagocytes and gene expression. However, excessive production of ROS by endogenous or exogenous factor may lead to the formation of oxidative stress, loss of cell function and ultimately apoptosis and necrosis. Therefore, it is important to maintain the balance between the free radical productions and the antioxidant defences in the human body as this balance is vital for the cell function, regulation and adaptation to diverse growth conditions and health condition (Vinayak, Sabu & Chatterji, 2011).

In humans, there are two types of defence against free radical damage, the first line defence is formed by the enzymes such as superoxide dismutases (SOD), catalases (CAT), glutathione peroxidases (GPX) and small molecules antioxidants like ascorbic acid, tocopherol and uric acid, while the presence of the antioxidants will be responsible for the second line defence (Vinayak, Sabu & Chatterji, 2011).

Over the years, seaweed and its extract have generated a huge interest in the pharmaceutical industry as a fresh source of bioactive compound with immense medicinal potential. Seaweeds are rich in antioxidant compounds such as carotenoids, polyphenols, pigments, enzymes and diverse functional polysaccharides. Among all the antioxidants found in seaweeds, polyphenols

are found abundantly, especially in brown seaweeds (Phaeophyte) (Mandal et al., 2011). The seaweed polyphenols are also known as polytannins. They are a heterogeneous group of molecules that display a broad range of biological activities. These polyphenols are a class of powerful chain-breaking antioxidant which have the ability to scavenge ROS, inhibit lipid peroxidation and chelate the metal ions (Rice-Evans et al., 1995; Kahkonen et al., 1999; Duthie & Crozier, 2000; Vinayak, Sabu & Chatterji, 2011). The concentration of the phenolic compound is also shown as having a linear correlation with the antioxidant activity according to Stankovic *et al* (Chkhikvishvili & Ramazanov, 2000) Thus, high antioxidant activity can be shown in seaweeds such as *Padina australis* that has high phenolic content (Li et al., 2017).

ROS scavenging activity, metal ion chelation, ability to inhibit lipid peroxidation and maintenance of endogenous defence systems of poly phenols accounts for the high antioxidant activity of *Padina australis* (Figure 2).

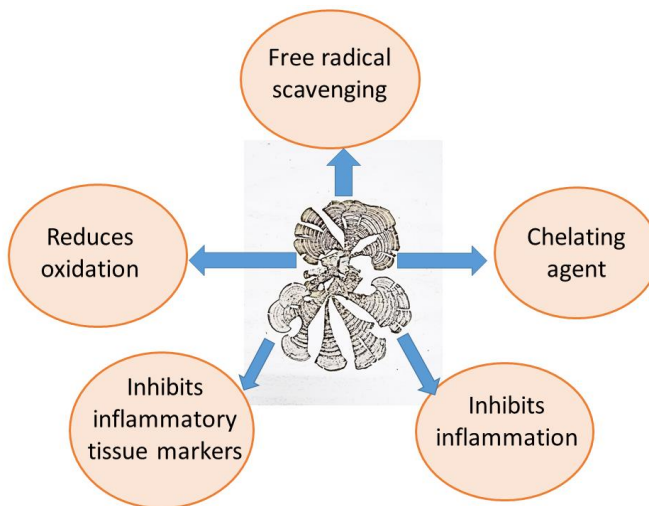
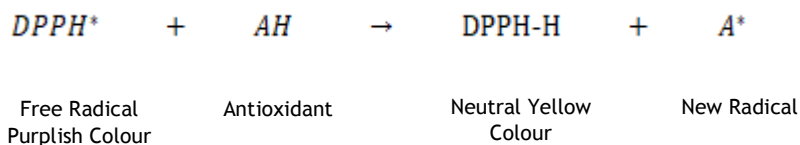


Figure 2. Different antioxidant mechanisms of *Padina australis*

To test the antioxidant activity in seaweeds, 1,1-diphenyl-2-picrylhydrazyl radical (DPPH) assay is used in which the antioxidant activities can be measured quantitatively based on the intensity of the purplish colour of the DPPH compound (Li et al., 2017). The effects of the antioxidant compound on

the DPPH radical scavenging is due to the hydrogen donating ability and this is shown when DPPH solution is mixed with a substrate as a hydrogen atom donor and a stable non-radical form of DPPH will be obtained with a simultaneous change of the DPPH solution from purple to yellow colour (Kedare & Singh, 2011; Araújo, 2017). The equation below shows the correlation between the decreasing intensity of the purplish colour of the DPPH and the antioxidant activity (Li et al., 2017):



A study used the DPPH method to test the antioxidant activities among 20 types of seaweed extracts that included 7 Chlorophyta (green algae), 9 Phaeophyte (brown algae) and 4 Rhodophyta (red algae). The results showed that *Padina australis* (Phaeophyta) as having the highest antioxidant activity of 53.3% among the other 19 seaweed extracts (El Gamal, 2010). Besides that, there is presence of antioxidant activity in *Padina australis* as there is reaction shown by its antioxidant compounds in scavenging the free radicals of the DPPH solution (Kedare & Singh, 2011).

Padina australis is shown to have potent antioxidant activities playing a role in delaying or preventing the oxidations of cellular oxidizable substrates and selectively inhibiting the ROS cascade events (Kedare & Singh, 2011). Apart from that, it can also help prevent degenerative diseases such as cancer and tumour or aging (Farasat et al., 2013).

Anti-inflammatory

Inflammation response can be triggered by infection, tissue damage or disruption of immune response and this process is usually followed by the release of inflammatory mediators (Guzmán-Álvarez et al., 2012; Thomas & Kim, 2013). Prostaglandin and leukotriene are potent mediators of inflammation that cause pain, oedema and vasodilation and all these conditions are derived from the arachidonic acid metabolism by cyclooxygenases (COXs) and lipoxidases (LOXs) respectively. Both COXs and LOXs play a significant role in modulating the inflammatory and allergic immune response by catalysing the oxygenation of n-6 polyunsaturated fatty

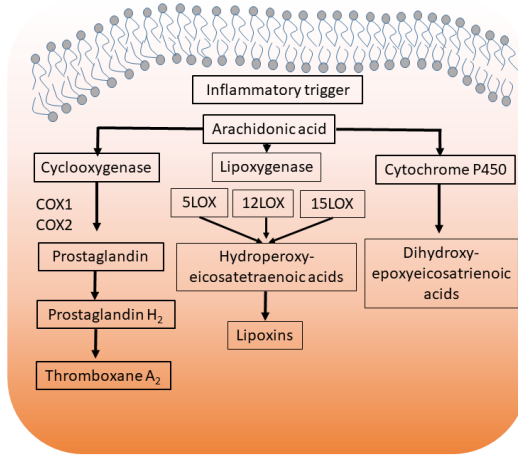


Figure 3. Inflammatory pathways in biological tissues

acid to form the biologically active prostaglandin and leukotriene metabolites (Tilley, Coffman & Koller, 2001). In order to relieve the swelling and pain caused by the inflammation, non-steroidal anti-inflammatory drugs (NSAIDs) are used nowadays. However, NSAIDs have been reported to cause some side effects such as the formation of stomach ulcer if NSAIDs is used frequently. Thus, it is imperative to target naturally renewable sources to relieve the inflammation or inflammation-induced oxidative stress so that it can reduce NSAIDs usage and hence decrease the adverse effects caused by the usage of NSAIDs (Mhadhebi, Mhadhebi & Robert, 2014).

Arachidonic acid (AA) exists in the cell membrane in the form of phospholipids. When the cell membrane is subjected to stimuli, especially the inflammatory reaction, the phospholipids are released from the cell membrane (Figure 3). Through the hydrolysis of phospholipids by Phospholipase A₂(PLA₂) and Phospholipase C(PLC) AA is released and then transformed into a bioactive metabolite with the help of different enzymes, thus promoting inflammatory cascades. Abundant resources of bioactive substances such as polyunsaturated fatty acids and fucoxanthin in *Padina australis* act as a competitive inhibitor of COXs or LOXs in the inflammatory reaction and lead to a decrease in the production of prostaglandins and leukotriene.

Among the natural renewable resources, seaweed extracts are reported as a potent inhibitor of COXs and LOXs in which a decreased effect in the

production of inflammatory prostaglandins and leukotrienes are shown (Mhadhebi, Mhadhebi & Robert, 2014). There are also several studies showing that brown seaweeds have anti-inflammatory effects in the presence of sulfate polysaccharides, polyunsaturated fatty acids (PUFA) and fucoxanthin (Barbosa, Valentão & Andrade, 2014). These compounds found in the seaweed extracts may act as a competitive inhibitor of COXs or LOXs in an inflammatory reaction and later lead to a decrease in the production of prostaglandins and leukotrienes (James, Gibson, & Cleland, 2000; Kang, Khan & Park, 2008).

A study reported the testing of the anti-inflammatory effect of *Padina* species and *Sargassum* species through the increase in volume of the mice feet after the injection of brown algae extracts and inflammation inducer (Thomas & Kim, 2013). The results showed a significant increase in the percentage of inflammation from the 1st to 4th hour after the injection of inflammation inducer and both the test groups, *Padina* species and *Sargassum* species. Among the two species of brown algae, *Padina* sp. shows a higher anti-inflammatory effect as compared to the *Sargassum* species because the inflammatory inhibition effect of the *Padina* sp. lasted for three hours while the *Sargassum* species only lasted for two hours. This indicates that the *Padina* species is a better anti-inflammatory agent with a longer half-life than *Sargassum* species (Thomas & Kim, 2013). There is also a high negative correlation shown between total phenolic content and COX_μ and LOX_γ inhibition value and this means that all compounds except the phenolic-like polysaccharides present in *Padina* species are considered as a good inflammatory agent (Mhadhebi, Mhadhebi & Robert, 2014).

Padina species has the potential to be used as a remedy in treating the inflammation-related symptoms and is a green natural alternative that is free from the adverse effect of NSAIDs (Kang, Khan & Park, 2008; Mhadhebi, Mhadhebi & Robert, 2014).

Larvicidal

Mosquito plays a vital role in the transmission of pathogen and parasites such as dengue, yellow fever, malaria, filariasis and other diseases which can be fatal to humans (Ali, Ravikumar & Beula, 2013). According to WHO, the cases of mosquito-borne diseases have gradually increased from year to year with statistics showing there were more than 1 million people who had died from mosquito-borne diseases (Yu, Wong & Ahmad, 2015). Dengue is one of the widespread mosquito-borne viral infection in the tropical and subtropical

regions all around the world (Roni et al., 2015). In Malaysia, the numbers of dengue deaths had increased up to 56% in 2015 as compared to 2014 (Yu, Wong & Ahmad, 2015). There are four types of serotype in dengue, and these are DENV-1, DENV-2, DENV-3 and DENV-4, but there is still no vaccine developed for the prevention of dengue (Yung, Lee & Thein, 2015).

Aedes aegypti and *Aedes albopictus* mosquitoes are the main vectors in spreading viral diseases such as dengue fever, yellow fever and chikungunya. Humans get infected after getting bitten by an infected female *Aedes* mosquito (Yu, Wong & Ahmad, 2015; Yung, Lee & Thein, 2015). It is essential to control the breeding of mosquitoes using organochlorine, organophosphate and carbamate larvicide or insecticides to kill mosquito (Salvador-Neto, Gomes & Soares, 2016). However, the excessive use of synthetic insecticides can cause toxicity to the environment, humans and other living organisms. The mosquitoes will also become resistant to the insecticides due to repeated use (Murray, Quam & Wilder-Smith, 2013). Many researchers found that marine halophytes such as seagrass, seaweed and mangrove are a group of plants that can adopt high saline conditions and they have been used in many therapeutic applications (Ali, Ravikumar & Beula, 2013; Ishwarya et al., 2018). According to Yu et al., 42 extracts and 13 bioactive compounds of the seaweeds have been found to act as an effective larvicide which can be used to replace chemical insecticides (Yu et al., 2015).

A separate study showed that the methanol extract of *Padina australis* possesses larvicidal activity with LC_{50} values between 200 to 500 $\mu\text{g/ml}$ on the swimming behaviour of *Aedes aegypti* and *Aedes albopictus*. The mosquito larvae will undergo three phases after treated with *Padina australis* extracts. The larvae showed abnormal restlessness, wiggle flying movement, sudden sinking and floating movement in phase 1. In phase 2, the larvae turn into inactive mode with random tremor movement at the bottom of the container and followed by the paralysis and death of the larvae in phase 3 (Yu et al., 2015)

Padina australis also showed to have adulticidal effect against mosquitoes. It showed a lethal effect with LC_{50} values 30.80 and 36.21 mg/cm^2 against female adults of *Aedes aegypti* and *Aedes albopictus* respectively. Two phases of intoxication can be observed for the female adults after treating by the seaweed extracts. The female adults showed sluggish movement and were incapable to stand still on the surface of holding the tube in phase 1. While at phase 2, the female adults were paralyzed and fell at the bottom of holding

the tube and died (Ghosh, Chowdhury & Chandra, 2012). This indicates that *Padina australis* has weak adulticidal activity. It is also reported that a combination of seaweed extracts together with other commercial insecticides which is known as binary insecticide mixtures will be more effective against adult mosquitoes (Ghosh, Chowdhury & Chandra, 2012; Vaikundamoorthy et al., 2018).

Therefore, *Padina australis* has proved its larvicidal activity against *Aedes aegypti* and *Aedes albopictus*.

Anti-hypertensive

In Malaysia, a wide variation of brown seaweeds can be found distributed along the Malaysian shores. Some of the brown seaweeds such as *Padina australis*, *Turbinaria ornata*, *Sargassum* species and *Padina tetrastromatica* are edible. In the past, brown seaweeds had already been used as a traditional Chinese medicine for cases of hypertension as it was believed that the brown seaweeds had the ability to lower down blood pressure (Lyu et al., 2017).

Hypertension is a disease of having abnormally high blood pressure within the arteries and the blood pressure reading will be based on both systolic blood pressure (SBP) and diastolic blood pressure (DBP) (Guyton, 1991). Based on the World Health Organisation (WHO) Guidelines, Joint National Committee on Prevention, Detection, Evaluation and Treatment on High Blood Pressure recommends, one will be hypertensive if their blood pressure reading exceeds 140/90 mmHg (Chobanian et al., 2003).

It is believed that seaweeds have the ability to absorb the ionic elements of the seawater which include potassium and sodium ions due to their growing environment in the sea (Sithranga Boopathy & Kathiresan, 2010). Van Leer et al., (1995) and Chobanian et al., (2003) both reported that diets that are rich in sodium and potassium can cause reduction of blood pressure in adults because the potassium ions may counteract with the effects of the sodium ions in the human body and reduce blood pressure (Van Leer, Seidell & Kromhout, 1995; Sithranga Boopathy & Kathiresan, 2010; Gotama, Husni & Ustadi, 2018; Gómez-Guzmán et al., 2018).

A study was conducted to test the antihypertensive effect of the edible brown seaweeds found in Malaysia using spontaneously hypertensive (SHR) rats and normotensive Wistar-Kyoto (WKY) rats and treated with different types of seaweeds such as *Turbinaria ornata*, *Sargassum* species, *Padina australis* and

Padina tetrastromatica. The results show a significant blood pressure reduction ($P < 0.05$) for all the three seaweeds in the spontaneously hypertensive (SHR) rats and normotensive Wistar-Kyoto (WKY) rats. The *Sargassum* sp. shows the effect of blood pressure reduction in SHR and WKY rats while the *Turbinaria ornata* and *Padina tetrastromatica* only shows the blood reduction effect in the SHR. In contrast to the effect on blood pressure, the brown seaweeds tested did not affect the heart rate with equal degrees of potency and only *Turbinaria ornata* was able to produce bradycardia effect in SHR. From this study, it suggests that only *Turbinaria ornate* contains negative chronotropic effect substance while *Sargassum* sp., *Padina australis* and *Padina tetrastromatica* will directly act on the blood vessels and it may cause vasorelaxation, and then followed by the reduction in TPR and blood pressure (Gotama, Husni & Ustadi, 2018).

Thus, further studies on the antihypertensive effect of *Padina australis* should be conducted, so that it can be used as a folk medicine in managing hypertension (Gotama, Husni & Ustadi, 2018).

Antidiabetic

Diabetes is a hyperglycemia condition caused by the decreasing of insulin secretion and action of insulin (Akbarzadeh et al., 2018). There are more than 20 million people worldwide suffering from type-1 diabetes mellitus and this was associated with an increase of 2% to 5% each year (Groop & Pociot, 2014; Lauritano & Ianora, 2016). There are insulin injections and oral anti-diabetic agents such as thiazolidinedione, biguanide and sulfonylurea available in the market that are used to control the blood sugar level in diabetic patients (Akbarzadeh et al., 2018). However, patients are found to suffer from unwanted side effects such as toxicity, gastrointestinal symptoms and cardiovascular disease for the prolonged consumption of antidiabetic drugs. Diabetes is divided into two types, which are type 1 diabetes mellitus and type 2 diabetes mellitus. 90 to 95% of diabetes patients are suffering from type 2 diabetes (Rekha & Sharma, 2013).

Enzyme α -glucosidase and α -amylase play a vital role in the intestinal absorption and breakdown of starch respectively. The inhibition of these enzymes can reduce the postprandial increase of blood glucose level which is important for the management of hyperglycaemia (Lordan et al., 2013). Enzyme α -glucosidase which located in the brush border surface membrane of the intestinal cell is important for the breakdown of maltose into glucose. The inhibition of α -glucosidase can prevent further hyperglycaemic level in blood.

Thus, the α -amylase is important for the breakdown of starch and glycogen (Lordan et al., 2013). The antidiabetic drugs used for type 2 diabetes normally inhibit the enzyme α -glucosidase by inhibiting the digestion of carbohydrates such as starch and sugar (Akbarzadeh et al., 2018).

According to another study, the inhibitory activity of brown seaweed *Padina*, *Sargassum* and *Tubinaria* against α -glucosidase enzyme are highest in laminaran and fucoidan fraction. It can be concluded that the laminaran and fucoidan fraction are able to lower the blood sugar level in blood and can be used for type 2 diabetes. Other than that, the IC_{50} value of laminaran fraction of *Sargassum duplicatum* showed the highest inhibiting activity against α -glucosidase, which is 36.13 ppm. It is then followed by the laminaran of *Turbinaria decurens* (44.48 ppm), fucoidan of *Tubinaria decurens* (63.39 ppm), fucoidan of *Sargassum duplicatum* (75.10 ppm) and alginate of *Sargassum* (115.50 ppm) and *Turbinaria* (166.45 ppm). The lower the IC_{50} value, the greater the inhibitory activity of the α -glucosidase enzyme (Akbarzadeh et al., 2018).

Moreover, the ethanol extracts of other brown algae such as *Fucus vesiculosus*, *Padina australis* and *Palvetia canaliculata* have shown their efficacy in inhibiting the enzymes α -amylase and α -glucosidase (Lordan et al., 2013). According to Kang et al., (2010) another brown algae *Ecklonia cava* has been proved to have antidiabetic potential by using streptozotocin-induced type 1 diabetes mellitus rats and C2C122 myoblasts. The methanolic extracts from *Ecklonia cava* can decrease the plasma glucose level significantly and increase the insulin concentration in type 1 diabetes mellitus (Kang et al., 2010). The polyphenolic compound of *Ecklonia cava* has shown its antidiabetic effect by having an insulin-like action through AMP-activated protein kinase (Lauritano & lanora, 2016).

However, the antidiabetic uses of *Padina australis* are still to be explored in detail and there is an urgent need to find a more natural product with potential therapeutic application which can be used in the treatment of various diseases or used as adjuvant therapy.

Conclusion

Marine seaweeds have become an alternative which can be used in the medical field in many ways. *Padina australis*, which is an example of edible brown seaweed has been used in the treatment of various medical conditions.

Padina australis may be used as an antibiotic in inhibiting the growth of bacteria or killing bacteria. Studies showed that its efficacy as an antibacterial agent against *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Bacillus cereus* while it only exhibits a narrow spectrum of antibacterial activity towards *Bacillus cereus*. Besides, the bioactive compound and extracts from *Padina australis* also exhibit an antioxidant effect by selectively inhibiting the ROS cascade events. In this case, DPPH assay is used to test the antioxidant activity of *Padina australis* extract which a colour change of the DPPH solution from purple to pale yellow colour observed. The usage of NSAIDs in treating inflammation has been gradually replaced by the usage of *Padina* species due to its greater anti-inflammatory effect when compared to *Sargassum* species. Moreover, *Padina australis* has been proved to possess larvicidal effect against *Aedes aegypti* and *Aedes albopictus* by effectively killing the female adults and larvae of these mosquitoes. Although some studies conducted have shown *Padina australis* have the ability to lower down blood pressure and blood glucose level, however, the results are still counteracted due to limited research data. We hope that more research can be done on *Padina australis* to find out more of its functions and offer new medical knowledge in treating different diseases in the future. This, in turn, can replenish the shortage of some medicines in the treatment of diseases by replacing these with renewable seaweeds.

Data Availability and Ethical Statement

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Acknowledgement

This work was financially supported by a student research fund of the International Medical University (Project Ref. no: BP I-01/2018(45)).

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List of abbreviations

1. DPPH: 1,1-diphenyl-2-picrylhydrazyl radical
2. CAT: Catalase
3. COXs: Cyclooxygenases
4. GPX: Glutathione peroxidase
5. LOXs: Lipoxidases
6. MBC: Minimum bactericidal concentration
7. MIC: Minimum inhibitory concentration
8. NSAIDs: Non-steroidal anti-inflammatory drugs
9. ROS: Reactive Oxygen Species
10. SOD: Superoxide dismutase