

BIBLIOGRAPHIC RECORDS

STUDIES AND RESEARCH

Ecklonia Bicyclis

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SUMMARY

1. - Botanical Information:
2. - Introduction:
3. - Traditional use:
4. - Properties:
5. - Antioxidant and anti-inflammatory effect:
6. - Orac test:
7. - Comparing antioxidant activity of *Ecklonia bicyclis* to other algae:
8. - Antioxidant activity between *Ecklonia bicyclis*, *Ecklonia cava* and
9. *Ecklonia stolonifera*:
10. - Anti-inflammatory effect:
11. - Radio-protective effect against irradiations:
12. - Neuroprotective effect and role on Alzheimer disease:
13. - *Ecklonia bicyclis* role in Parkinson disease:
14. - Other effects:
15. - Safety data:

1 ECKLONIA BICYCLIS KJELLMAN

1.1 Botanical Information

Commune name: Brown Algae (Arame)

Botanical Name: Ecklonia Bicyclis Kjellman or Eisenia Bicyclis Kjellman Setchell

Family: Lessoniaceae

English name: Ecklonia Bicyclis or Eisenia Bicyclis

Parts used: Thallus

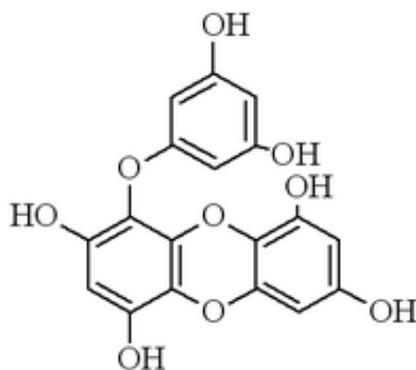
Country of origin: China

1.2 Introduction

Ecklonia Bicyclis is a type of brown algae which is manufactured with a water based extraction process to a 13% polyphenols, 25:1 ratio extract. The parts used in the process is the thallus and particularly the fronds. Its powerful antioxidant properties are used in food supplemental products.

Over the course of several years, we have isolated polyphenols from Eckloniam'/m Bicyclis, which we have called phlorotannins. These phlorotannins are specialized types of polyphenols which consist of very powerful antioxidants. They are beneficial on many levels including medical.

Most phloritannins are oligomers of phloroglucinol (1,3,5-trihydroxybenzene) that can be broken down in 6 catagories: fucols, phlorethols, fucophlorethols, fuhalols, isofuhalols and eckol. This last category, Eckol, is most common in the Ecklonia specie.



Eckol phlorotannin molecular structure in Ecklonia Bicyclis

1.3 Traditional use:

Ecklonia Bicyclis is mostly found in the coastal areas of Korea and Japan, but is particularly abundant on the island of Ulleung-do in South Korea known under the name of Dagelet for Europeans. Ecklonia bicyclis has been and is still a part of Asian culinary cuisine culture as is Ecklonia Cava and Ecklonia Stolonifera.

1.4 Properties:

1.4.1 Antioxidant and anti-inflammatory effect:

The powerful antioxidant effects of Ecklonia Bicyclis have been the subject of many studies and research.

Free radicals are produced in our bodies by many endogenous factors such as respiration, digestion, external factors that are metabolized, smoking and ultraviolet rays. Oxygen is highly reactive to free radicals and generates a type of reactive oxygen (ROS) and types of reactive nitrogen (RNS). These ROS and RNS can cause oxidative stress to many cells and provoke inflammation or lesions to many organs. Oxidative stress is also associated with a number of different degenerative diseases including cancer, rapid aging, arteriosclerosis, rheumatoid arthritis and allergies.

Many studies have shown the powerful antioxidant and anti-inflammatory effects of phlorotannins found in Ecklonia Bicyclis. One of the main reasons phlorotannins work so well as antioxidant and anti-inflammatory agents, is because of their unique molecular rings. (Ahn and al., 2007)

In 2011, an in-vitro study was done to understand the antioxidant activities from alcohol (methanol) extracted Ecklonia bicyclis with different concentrations of phlorotannins. This study demonstrated that the antioxidant activities of phlorotannins is primarily due to their redox playing an important role as such with hydrogen, in the absorption and neutralization of free radicals and as such of the deactivation of oxygen (Na Young Yoon et al, 2011)

Orac test:

Recently the H-Orac test has captured the attention of many scientific experts. Today, this test is considered as the best method for in-vitro measurements of

antioxidant activities for algae, vegetables, fruits, agricultural and photochemical products.

In this study, researchers had isolated the phloroglucinol and eckols of the *Ecklonia bicyclis* algae. They evaluated their antioxidant properties by using the H-Orac method. By comparison with well known antioxidants, phlorotannins were equally tested. The results from this study are as follow:

Table 1. H-ORAC values of phloroglucinol and phlorotannins isolated from the brown alga *E. bicyclis*.

Samples	ORAC ($\mu\text{mol TE}/\mu\text{mol}$)
Phloroglucinol	2.57 ± 0.14
Phlorotannins	
Eckol	4.97 ± 0.36
Fucofuroeckol A	9.82 ± 0.70
Phlorofucofuroeckol A	8.97 ± 0.89
Dieckol	10.22 ± 0.85
8,8'-Bieckol	8.62 ± 0.92
Positive controls	
L-Ascorbic acid	0.76 ± 0.24
Epigallocatechin gallate	4.65 ± 0.80
Resveratrol	7.18 ± 0.24

The data is expressed as the mean \pm standard deviation from three independent measurements.

These results demonstrate that the phlorotannins group “Eckol” shows antioxidant activities significantly more efficient in trapping free radicals than ascorbic acid, Epigallocatechin gallate (EGCG), and even Resveratrol. (Yohei Fujii et al, 2013)

Comparing antioxidant activity of *Ecklonia bicyclis* to other algae:

Another study was done in 2015 with the objective of comparing the antioxidant activity of *Ecklonia bicyclis* with other commercial available algae. Hence, the total phenolic content was evaluated by the Folin-Ciocalteu method, the content of nine phenolic structures by HPLC. We determined the antioxidant capacity of water soluble structures by a Photoluminescence method of the following marine

algae: ***Laminaria Japonica*, *Eisenia Bicyclis*, *Hizikia Fusiformis*, *Undaria Pinnatifida*. Red algae such as *Porphyra Tenera*, *Palmaria Palmata*. Green algae such as *Chlorella Pyrenoidosa* and *Cyanobacterias (Spirulina Platensis)***

HPLC analysis has shown that the most abundant phenolic structure was epicatechin. According to spectrophotometry, it was evident that the brown algae, *Ecklonia bicyclis*, had the highest level of phenolic and highest antioxidant activity: 193 mg/g gallic acid equivalent (GAE), 7,53 μmol of ascorbic acid (AA)/g, respectively. There is a linear existence between antioxidant activity and phenolic content.

Eisenia bicyclis (*Ecklonia Bicyclis*) seems to be the most promising algae as an antioxidant due to its high level of polyphenols. (Machu et al, 2015)

Algae	(1)	(2)	(3)	(4)	(5)
<i>Eisenia bicyclis</i>	192.6 \pm 3.3 ^a	192.8 \pm 0.8 ^a	143.2 \pm 9.5 ^b	84.1 \pm 0.3 ^c	9.5 \pm 0.5 ^d
<i>Hizikia fusiformis</i>	34.5 \pm 5.8 ^a	26.9 \pm 0.1 ^b	9.5 \pm 0.1 ^c	13.1 \pm 0.1 ^c	6.0 \pm 0.1 ^c
<i>Laminaria japonica</i>	8.7 \pm 0.3 ^a	8.5 \pm 0.3 ^a	14.9 \pm 0.1 ^b	8.8 \pm 0.1 ^a	0.7 \pm 0.1 ^c
<i>Undaria pinnatifida</i> (W)	8.6 \pm 0.4 ^a	3.7 \pm 0.1 ^b	5.9 \pm 0.1 ^c	5.7 \pm 0.1 ^c	1.3 \pm 0.1 ^d
<i>Undaria pinnatifida</i> (Wi)	8.0 \pm 0.5 ^a	5.0 \pm 0.1 ^b	6.5 \pm 0.1 ^c	4.6 \pm 0.1 ^b	8.4 \pm 0.2 ^a
<i>Palmaria palmata</i>	31.8 \pm 1.0 ^a	22.1 \pm 0.7 ^b	26.5 \pm 0.4 ^c	25.0 \pm 0.1 ^d	10.7 \pm 0.3 ^e
<i>Porphyra tenera</i>	18.2 \pm 0.6 ^a	16.2 \pm 0.4 ^b	15.1 \pm 0.1 ^b	11.1 \pm 0.1 ^c	4.7 \pm 0.6 ^d
<i>Chlorella pyrenoidosa</i>	18.0 \pm 0.2 ^a	13.2 \pm 0.2 ^b	16.8 \pm 0.1 ^{a,c}	15.5 \pm 0.1 ^c	25.8 \pm 1.7 ^d
<i>Spirulina platensis</i>	43.2 \pm 1.0 ^a	17.0 \pm 0.5 ^b	23.9 \pm 0.1 ^c	18.4 \pm 0.1 ^d	24.4 \pm 0.2 ^c

^{a-e} values in the same line sharing a common letter are not significantly different at $p < 0.05$.

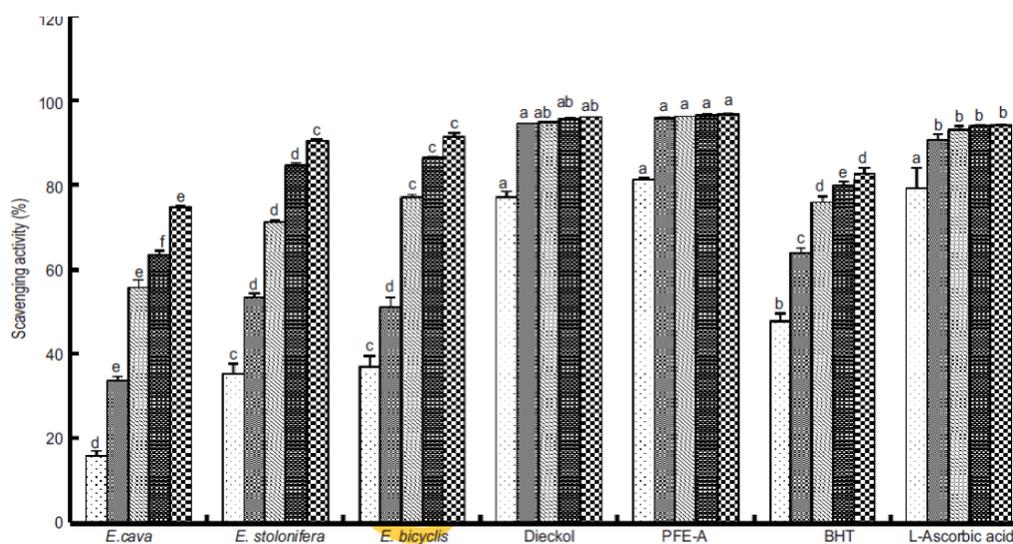
Table 1. Amounts ($\text{mg}\cdot\text{g}^{-1}$ GAE) of total phenolic content of edible algal products after various extraction processes: (1)—extraction by distilled water (80 °C for 10 min in water bath with constant shaking); (2)—extraction by methanol-water-acetic acid (30:69:1, v/v/v) (70 °C for 50 min in water bath with constant shaking); (3)—extraction by 80% methanol (70 °C for 1 h in water bath with constant shaking); (4)—extraction by 70% acetone (30 °C for 30 min in water bath with constant shaking); (5)—extraction by 100% methanol (lab temperature \approx 23 °C for 24 h, constant shaking). Results are shown as mean \pm SD ($n = 4$).

Antioxidant activity between Ecklonia bicyclis, Ecklonia cava and Ecklonia stolonifera:

Even though their molecular structure is similar in terms of natural constituents, there are notable differences between these 3 species of brown algae, (*Ecklonia cava*, *Ecklonia bicyclis* and *Ecklonia stolonifera*) particularly in their phlorotannins content. All 3 species have Eckol, Bieckol, Dieckol and Phlorofucofuroeckol as natural constituents, however, the *Ecklonia bicyclis* species also has phloroglucinol, phloroglucinol tetramere and other bioactive constituents not yet identified. It has a greater variety of polyphenols, thus, is considered as more effective antioxidant.

A comparison of 2 major phlorotannins constituents, dieckol and Phlorofucofuroeckol-A (PFE-A) were studied from the 3 brown algae, *Ecklonia cava*, *Ecklonia bicyclis* and *Ecklonia stolonifera*, by HPLC method in inverse phase for rapid and regular quantization.

Comparatively, the recovery efficiency of dieckol from the water extracted *E. cava*, *E. stolonifera* and *E. bicyclis* were respectively 86%, 93% and 98%. The recovery efficiency of PFE-A were respectively 74%, 86% and 62%. Antioxidant activity were detected for each species, *E. bicyclis* (91%) followed by *E. Stolonifera* (90%) and *E. cava* (74%). Dieckol and PFE-A had an antioxidant activity almost 9 to 7 times stronger than standard butylhydroxytoluene and 6 to 4 times stronger than ascorbic acid in molar concentration respectively.



We can, therefore, conclude that the antioxidant activity in water extracted *Ecklonia bicyclis* is much higher than in *Ecklonia cava* or *Ecklonia stolonifera*.

1.4.2 Anti-inflammatory effect:

Many studies have shown that *Ecklonia bicyclis* has inflammatory properties. Henceforth, it has been established that individual phlorotannins in eatable brown algae has a strong anti-inflammatory effect. In-vitro studies have confirmed that the anti-inflammatory effect of *Ecklonia bicyclis* have significantly reduced concentration of IL4 and IL5 by more than 60%, and those of TNF α by more than 70%. (Jung et al, 2009)

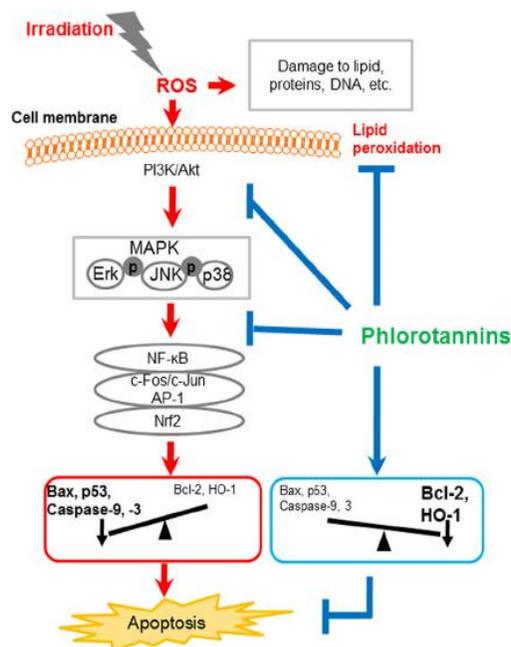
One study in 2013 evidenced that *E. bicyclis* and its constituents had an anti-inflammatory effect that could be attributed to the inhibition of generating nitric oxide and ROS as well as the suppression NF-kB pathway. (Jung et al, 2013)

Another study confirmed the effect of isolated Phloroglucinol from *Eisenia bicyclis* in suppressing production of pro-inflammatory cytokines. (Jung et al, 2013)

In humans, the facts are still fragmented and we have to wait for the results from many clinical studies to have an a more comprehensive idea on its effectiveness. But it is certain that in the future, *Ecklonia bicyclis* could be considered as an therapeutic approach and preventative tool against inflammatory and antioxidants diseases linked to stress.

1.4.3 Radio-protective effect against irradiations:

In 2014, a study evidenced the radio-protective role of phlorotannins from the brown algae *Ecklonia bicyclis*. Below, is a possible mechanism for radio-protective phlorotannins against gamma irradiation via anti-apoptotides signal activation and the cytoprotectors factors. (Taekyun Shina et al, 2014)



1.4.4 Neuroprotective effect and role on Alzheimer disease:

The usage of a neuroprotector with antioxidant activity could be effective in the treatment of Alzheimer. In a 2012 study, the neuroprotective effects from methanol extracted *Eisenia bicyclis* and its isolated phlorotannins, were evaluated. The results suggested that *E. bicyclis* and its active constituents mitigated the oxidative stress and reduced neuronal cell mortality, which suggests that it could be used as a supplemental neuroprotective agent for Alzheimer disease. (Ahn et al, 2012)

Moreover, a study done in 2015, evidenced that the *Ecklonia bicyclis* algae had promising inhibitory properties against Acetylcholinesterase, butyrylcholinesterase and types of reactive forms of oxygen responsible in part for Alzheimer disease. (Choi JS et al, 2015)

These results are indicative for the potential treatment with *E. bicyclis* and its phlorotannins in the development of therapeutic agents or preventive measures for Alzheimer disease marked by the inhibition of cholinesterase and the increase capacity of antioxydants and neuroprotectors.

1.4.5 E. Bicyclis role in Parkinson disease:

The inhibition of monoamine oxidase (MAO) plays an important role in the premature support for Parkinson disease. The goal of this recent study was to determine the efficacy of isolated eckol and dieckol stemming from methanol extracted *E. bicyclis* against Parkinson disease by the inhibition of MAO-A and human MAO-B (hMAO-A and hMAO-B). We used a sensitive enzymatic chemiluminescent trial and kinetic methods to study the enzymatic inhibition and the mode of inhibition. The results suggests that methanol extract of *Ecklonia bicyclis* and its isolated phlorotannins, eckol and dieckol, have powerful inhibitory effect against jMAO-A and hMAO-B, These results suggests that eckol and dieckol could be used as hMAO inhibitors in the management of Parkinson disease. (Jung et al, 2017)

1.4.6 Other effects:

There are other attributes that can be given to *Ecklonia Bicyclis* due to its antioxidant activities. It was observed that *E. bicyclis* (80/mg), *Serenoa repens* (320/mg), *Tribulus terrestris* (100/mg) and Glucosamine (100/mg) significantly improves erectile function in men after 2 months use. In another study, the formulation of *Ecklonia bicyclis* (150/mg), *Tribulus terrestris* (396/mg), Glucosamine and N-Glucosamine (144/mg) significantly elevates the libido in older men without prostatic dysfunction (Iacono et al,2012)

Researchers believe that the antioxidant and anti-inflammatory effects of *Ecklonia bicyclis* plays a major role in the prevention and treatment for cancer. Preliminary studies are under way to evaluate the effect *Ecklonia bicyclis* has on cancer and as a cardio-protective agent.

Thanks to the inhibition of cancerous cell proliferation by acting in various stages in their development, *Ecklonia bicyclis* could favor the fabrication of enzymes that would help the body rid itself of cancerous cells.

Researchers are therefore suggesting that *E. bicyclis* is potentially a strong candidate for functional food types, food supplement or drug for the prevention or treatment of various diseases. However, the constituents responsible for the antioxidant activity in *Ecklonia bicyclis* and its components, have not all been clearly identified. More detailed studies are necessary to isolate and identify all the active components in *Ecklonia bicyclis*.

1.5 Safety data:

All studies indicate that there is no toxicity at any level. Numerous clinical tests have been done and no adverse effects have been found at any human dosage level of 1-10mg/kg. Researchers have confirmed that no toxicity were reported in mice studies from isolated phlorotannins.