

SEASONAL VARIATION OF POLYPHENOLS CONTENT AND THEIR BIOLOGICAL ACTIVITY IN TWO SPECIES OF RED MARINE MACRO-ALGAE (*CORALLINA* SP) COLLECTED FROM THE ALGERIAN WEST COAST

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Abstract. The seasonal variations of polyphenol contents and their antioxidant activities in *Corallina officinalis* and *Corallina elongata* were assessed. The highest total phenolic content was recorded during summer in *C. officinalis* and during autumn in *C. elongata*, however the highest total flavonoid contents were observed in *C. officinalis* in the same season but in spring for *C. elongata*. Antioxidant levels (EC50) were the highest in spring in both species, the same season showed highest total antioxidant capacity in *C. elongata* but *C. officinalis* presented the highest value in autumn, we found a positive correlation between total flavonoid content and in both tests for antioxidant activity, the HPLC analysis of the extracts which gave the best results (spring and summer extracts of *C. officinalis* and spring extract of *C. elongata*) showed that the 3 extracts contain catechin in large quantities, more coumarin which is found in spring extracts of *C. officinalis* and *C. elongata* and myrecitin in summer extract of *C. officinalis* in second quantity, and caffeine which is in spring extract of *C. elongata* in third quantity.

Keywords: *Corallina officinalis*, *Corallina elongata*, Phenolic compounds, flavonoids, antioxidant activity

Introduction

Algae are photosynthetic organisms with a wide variety of forms ranging from unicellular to multicellular macroalgae (Arica et al., 2017). Macroalgae (commonly referred to as seaweed) are commonly divided into three groups based on algal body or thallus pigmentation. There are generally three major pigmentation groups; Phaeophyta (brown algae), Chlorophyta (green algae), and Rhodophyta (red algae) (Manzelat et al., 2018).

These organisms are sessile, exposed to various environmental conditions, and thus have generated a number of important physiological adaptations that promote defense; one of these consisted of the synthesis of bioactive compounds (Duffy and Hay, 1990; Charzeddine and Fariñas, 2001).

Biotic factors, such as reproductive state (Robles-Centeno et al., 1996) and different thallus portions of algae (Vlachos et al., 1999), and abiotic factors such as seasonality and geographic location (Rao and Parekh, 1981; Moreau et al., 1984; Robles-Centeno et al., 1996) can influence the bioactivity of algal extracts.

Seaweed has an important potential to supply new bioactive substances (Roussis et al., 2000; El Gamal, 2010; Mohamed et al., 2012). Their capacity to produce a variety of secondary metabolites (Güven et al., 2010) that exhibit various biological activities such as antibacterial, anti-inflammatory, antiviral (Barbosa et al., 2004; Seenivasan et al., 2010); antifungal (de Felício et al., 2010), anticancer, antidiabetic, antihypertensive, antihyperlipidemic, and antioxidant activities (Ren et al., 1994; Santoso et al., 2004;

Devi et al., 2011; Kim et al., 2011; Samarakoon and Jeon, 2012; Xu et al., 2012) is increasingly recognized.

these substances are characterized by their solubility and polarity (El-Chaghaby et al., 2019; Ganesan et al., 2019).

These photosynthetic organisms are exposed to a combination of high oxygen concentrations and sunlight, which induce the formation of free radicals and other reactive oxygen species. The absence of structural damage in algae implies that these organisms are able to generate natural antioxidants including polyphenols, vitamins and polyunsaturated fatty acids (Vadalà and Palmieri, 2015).

Among these bioactive compounds, a distinctive place is reserved for phenolic compounds, as these Algae have been recognized as a rich source of biologically active phenolic compounds (Thomas and Kim, 2011) which are commonly found in seaweeds and have been reported to have a wide range of biological activities.

Polyphenols can be divided into several classes, such as phenolic acids (hydroxybenzoic acids, hydroxycinnamic acids), flavonoids (flavones, flavonols, flavanones, flavanonols, flavanols, anthocyanins), isoflavonoids (isoflavones, coumestans), stilbenes, lignans, and phenolic polymers (proanthocyanidins—condensed tannins and hydrolysable tannins) (Manach et al., 2004).

The Algerian Mediterranean coast is an exclusive habitat for a number of algae species and investigating these species may lead to the identification of novel therapeutic agents to treat human diseases such as cancer, inflammation, allergies and numerous bacterial and fungal infections (Tarhouni and Kharrat, 2011).

The objective of the present study is to follow the seasonal variation of the biochemical composition and the antioxidant activity of the methanolic extracts in two different Algerian red algae, to select the best season to harvest and extract these bioactive compounds.

Materials and methods

Collection and processing of marine algae

Corallina officinalis is collected from the intertidal region of SBIAAT beach (35°33'09"N; 1° 11'51"W) and *Corallina elongata* is collected from the intertidal region of MADDAGH 2 beach (35°37'53"N; 1° 04'01"W), in western coast of Algeria, each season of the year 2019-2020.

In the laboratory, samples were rinsed with sterile distilled water, shade dried, cut into small pieces and powdered in a mixer grinder. They were stored in polyethylene bags or airtight container at room temperature.

Polyphenol extraction from seaweeds

Ten grams of the powder were soaked in 100 ml of methanol; the mixture was stirred at room temperature for 24 h. The total extracts were filtered and the obtained filtrates (crude extracts) were concentrated in BUCHI Rotavapor R-114. The dried extract were dissolved in methanol and stored at 4°C before testing (Cho et al., 2007).

Estimation of total phenolic content

Phenolic contents of crude methanolic extracts were estimated by the method of Singleton and Rossi (1965).

A quantity of 200 ml of the extract is mixed with 1 ml of Folin-Ciocalteu reagent (1/10) freshly prepared and 0.8 ml of 7.5% sodium carbonate (Na₂CO₃). The whole is incubated at room temperature in the dark for 30 min. Absorbance of all the sample solutions was measured at 765 nm using JENWAY 7305 spectrophotometer.

A calibration curve is produced in parallel under the same operating conditions using gallic acid as a positive control. Phenolic content was expressed as gallic acid equivalent per gram (GAE/g) of extract.

Estimation of total flavonoid content

Total flavonoid content were estimated by the method of Jia et al. (1999).

400 µl of extract was added to 120 µl of NaNO₂ 5%. After 5 min, 120 µl of AlCl₃ 10% were added and well mixed using a vortex. After 6 min, a volume of 800 µl NaOH 1 M was added to the mixture. The absorbance is read immediately at 510 nm using spectrophotometer.

The standard curve was calibrated by methanolic solution of quercetin. The results were showed as milligram of quercetin equivalents per gram (QE/g) of extract.

Antioxidant activities

Free radical scavenging activity (DPPH - decolorization assay)

Radical scavenging/antioxidant activities of the different extracts were assessed using the DPPH (2,2-diphenyl-1-picrylhydrazyl) free-radical method (Sánchez-Moreno et al., 1998). A volume of 50 µl of different concentrations of each extract is added to 1950 µl of the methanolic solution of DPPH (0.025 g/l) freshly prepared. As for the negative control, 50 µl of methanol is mixed with the same methanolic solution of DPPH. The positive control is represented by a standard antioxidant (ascorbic acid).

After incubation in the dark for 30 min and at room temperature, the reading of the absorbance is carried out at 515 nm using a spectrophotometer against the white.

The calculation of the inhibition percentages is done by the following formula:

$$I \% = ((Ac - At) / Ac) \times 100$$

where Ac: absorbance of the negative control; At: extract absorbance.

Extract concentration providing 50% inhibition (EC₅₀) was calculated from the graph plotting inhibition percentage against extract concentration.

Total antioxidant activity

Total antioxidant activity of methanol extracts was determined according to the method of Prieto et al. (1999). Briefly, 0.3 mL of sample was mixed with 3.0 mL of reagent solution (0.6 M sulfuric acid, 28 mM sodium phosphate and 4 mM ammonium molybdate). Reaction mixture was incubated at 95° for 90 min in stove. Absorbance of all the sample mixtures was measured at 695 nm. Total antioxidant activity is expressed as the number of equivalents of ascorbic acid.

HPLC analysis

After obtaining the results, the seasons that gave the best results for each species were analyzed by HPLC, where the extracts were carried out with YL 9100 HPLC

System consist of manual-sampling with 20 µl fixed loop and an YL9120 UV-Visible detector. The separation was performed on a SGE Protocol PC18GP125 (250mm×4.6 mm, 5 µm) column at 25°C.

The mobile phase is made up in gradient mode of acidified water (1% formic acid) with acetonitrile (95:05 v/v) for 50 min and (05:95 v/v) for 60 min, the separations having was performed using the single run mode, elution performed at a flow rate of 1 ml/min. The samples were run for 60 min; detection was done at 254 nm by UV detector. All chromatographic data were recorded and processed using YL Clarity software.

Phenolic compounds were identified by comparing the retention time of sample chromatographic peaks with those of authentic standards using the same HPLC operating conditions.

Statistical analysis

All analyses were carried-out in triplicates and the experimental data were expressed as means ± standard deviation using Microsoft Office Excel 2007. Means differences were determined by two-way ANOVA (season-species) and were followed by Tukey's HSD comparison test, correlations between all of parameters were computed as Spearman Rank Correlations coefficient using STATISTICA Stat Soft (version 6.0).

Results and discussion

Biochemical variation of algal extracts

Phenolic compounds are considered among the most important natural products. They are considered as antioxidants due to their ability to inhibit enzymes involved in the generation of radicals and exhibit anticancer, antibacterial, antiallergic, antidiabetic, antiaging and anti-HIV activities (Fresco et al., 2006; Li et al., 2011).

The total phenolic and total flavonoid contents of methanolic extracts of *Corallina officinalis* and *Corallina elongata* of 4 seasons of the year were evaluated and the results are presented in *Tables 1* and *2*.

Table 1. Seasonal variation of total phenolic content (mg EAG/g DM) in methanolic extract of *Corallina officinalis* and *Corallina elongata*

	<i>C. officinalis</i>	<i>C. elongata</i>
Winter	20.55 ± 0.1b	13 ± 0.01e
Spiring	9.2 ± 0.08f	13.3 ± 0.02e
Summer	36.35 ± 0.01a	8.6 ± 0.02f
Autumn	15.95 ± 0.01c	14.6 ± 0.08d

Table 2. Seasonal variation of total flavonoid content (mg EQ/g DM) in methanolic extract of *Corallina officinalis* and *Corallina elongata*

	<i>C. officinalis</i>	<i>C. elongata</i>
Winter	157.625 ± 0.02 f	162.875 ± 0.01 e
Spiring	66.8125 ± 0.1 h	240 ± 0.02 c
Summer	315.75 ± 0.02 a	145.875 ± 0.02 g
Autumn	259 ± 0.01 b	175.125 ± 0.02 d

The total phenolic contents of *Corallina officinalis* were found to be higher in summer extract (36.35 ± 0.01 mg EAG/g DM) followed by (20.55 ± 0.10 and 15.95 ± 0.01 mg EAG/g DM) in winter and autumn extracts, respectively, the lowest value is that of spring extract (9.2 ± 0.08 mg EAG/g DM). Significant seasonal differences (two-way ANOVA, $p < 0.05$) were observed in the total phenolic contents of *Corallina officinalis*, this seaweed gave much higher content comparing with the work of Abou Gabal et al. (2021) who reported 6.0 ± 0.02 mg GA/g DM, and of Fayzi et al. (2022), 07 ± 0.40 mg EAG/g DM in the aqueous extract.

Autumn extract presented the highest values of total phenolic contents in *Corallina elongata* (14.6 ± 0.08 mg EAG/g DM) followed by (13.3 ± 0.02 and 13 ± 0.01 mg EAG/g DM) in spring and winter, respectively, the lowest value is that of summer extract (8.6 ± 0.02 mg EAG/g DM). The Tukey test revealed that all seasons had significant difference with the exception of spring and winter which have an insignificant difference ($p < 0.05$), in the same work of Abou Gabal et al. (2021) this seaweed gave slightly lower content 5.9 ± 0.02 mg GA/g DM, but in works of Aydin (2022) the content was very high 45.32 ± 9.03 mg EAG/g DM.

Between all the seaweed species and in all seasons, there was significant difference but insignificant differences between spring extract of *Corallina officinalis* and summer extract of *Corallina elongata* ($p < 0.05$).

Similar observations have been reported in Fellah et al. (2017) where their results demonstrate that the total phenolic content was higher in summer for *Zonariatourne fortii* and in autumn for two species *Sphaerococcus coronopifolius* and *Halopteris scoparia*.

The total flavonoid contents of *Corallina officinalis* presented the highest values in summer extract (315.75 ± 0.02 mg EQ/g DM) followed by (259 ± 0.01 and 157.625 ± 0.02 mg EQ/g DM) in autumn and winter extracts, respectively, the lowest value is that of spring extract (66.812 ± 0.1 mg EQ/g DM).

In *Corallina elongata*, spring extract presented the highest values of total flavonoid contents (240 ± 0.02 mg EQ/g DM), followed by (175.125 ± 0.02 and 162.875 ± 0.01 mg EQ/g DM) in autumn and winter extracts, respectively, the lowest value is that of summer extract (8.6 ± 0.02 mg EAG/g DM). This test showed a significant difference between the two species and for all seasons ($p < 0.05$).

These results are really very important compared to those of Abou Gabal et al. (2021) who reported 3.82 ± 0.09 mg EQ/g DM in *Corallina officinalis* and 3.17 ± 0.04 mg EQ/g DM in *Corallina elongata*, and even for Fayzi et al. (2022) with 2.21 ± 0.12 mg EQ/g DM in *Corallina officinalis*, and for Aydin (2022) with 1.82 ± 0.75 mg EQ/g DM in *Corallina elongata*.

Benmahdjoub et al. (2022) found results that are in agreement with those of *Corallina elongata* who showed that total flavonoid contents of *Cystoseira amentacea* var. *stricta* peak occurred in spring (April); Concerning *Corallina officinalis*, their results are similar with *Padina gymnospora* contained the highest concentration in summer (Ramah et al., 2014).

In the present results, there is a significant correlation (71%) between the seasonal variation of phenolic compounds contents and flavonoids contents in both species, where it was found that the summer gave the highest value of phenolic compounds and flavonoids in *Corallina officinalis* and spring gave the lowest value.

In *Corallina elongata*, autumn gave the best value in phenolic compounds followed by the spring season while for the flavonoid contents this alga gave the opposite, spring

is ranked the first and autumn the second, the summer season gave the lowest values for the two contents.

Differences in the seasonal pattern of total phenolic content and flavonoid contents, and in the period of maximum production were also observed between the two species, this difference perhaps could be depending on species (Stiger-Pouvreau et al., 2014), time of collection and geographic location (Farasat et al., 2013; Tanniou et al., 2014).

This change is due to seasonal variations in abiotic factors that influence metabolic responses (photosynthesis and growth rates) and levels of proximate constituents of seaweeds (Orduña-Rojas et al., 2002; Connan et al., 2004; Kamiya et al., 2010), especially the temperature which is the most important factor controlling survival, growth, reproduction and thus geographical distribution of seaweeds (Yarish et al., 1986), plus the change in biotic parameters that influence the production of phenolic compounds (Lalegerie et al., 2020).

Antioxidant activities

Marine algae are exposed to a combination of ultraviolet (UV) light and environmental stressors that readily leads to the formation of free radicals and ROS. Despite their exposure to harmful ROS, healthy algae lack oxidative damage in their structural components (i.e. fatty acids), indicating the presence of protective antioxidant defense systems in their cells (vitamins, pigments, and polyphenols) (Freile-Pelegrin and Robledo, 2013).

(1) DPPH radical scavenging activity

In this test high EC₅₀ values indicated low antioxidant activity (Trigui et al., 2013), where the highest antioxidant activity is that of the spring extract of *Corallina elongata* (extract concentration: 12.75 ± 0.02 mg/ml providing 50% inhibition) followed by (13.79 ± 0.01 mg/ml, 17.22 ± 0.1 mg/ml and 17.22 ± 0.1 mg/ml) in summer and winter and the lowest activity in autumn, respectively for the same species. These values showed Significant seasonal differences ($p < 0.05$), this seaweed gave much higher activity comparing with the work of Aydin (2022) where it presented an EC 50 of 0.52 ± 13.2 mg/ml.

Corallina officinalis presented highest activity in spring (22.99 ± 0.02 mg/ml) followed by (28.58 ± 0.1 mg/ml, 36.29 ± 0.01 mg/ml and 41.71 ± 0.02 mg/ml) in winter and autumn and the lowest value in summer, respectively. All seasons had significant difference with the exception of spring and summer which have an insignificant difference ($p < 0.05$), but in work of Fayzi et al. (2022) this seaweed gave much higher activity 0.72 ± 0.15 mg/ml (Table 3).

Between the two species and for all seasons there was significant difference, except that insignificant differences between spring extract of *Corallina officinalis* and autumn extract of *Corallina elongata* ($p < 0.05$)

The seasonal variation presented by radical scavenging activity test shows a significant correlation with the seasonal variation of phenolic compounds contents (73%) and insignificant correlation (38%) with the seasonal variation of flavonoids contents, but here it is the opposite because the antioxidant activity presented by this test is higher when the value of the concentration of the extract is low.

Spring gave the best radical scavenging activity in both species this was already mentioned by Celis-Plá et al. (2016) and this corresponds to the content of *C elongata*

in flavonoids, this positive correlation between flavonoids content and DPPH radical scavenging activity is already described by Farasat et al. (2013) in his study where he discovered that among the different species tested, *Chaetomorpha linum* has the highest flavonoids content and the highest radical scavenging potential.

Table 3. seasonal variation of EC 50 (mg/ml) DPPH radical scavenging activity in methanolic extract of *Corallina officinalis* and *Corallina elongata*

	<i>C. officinalis</i>	<i>C. elongata</i>
Winter	28.58 ± 0.1 c	17.22 ± 0.1 e
Spring	22.99 ± 0.02 d	12.75 ± 0.02 f
Summer	41.71 ± 0.02 a	13.79 ± 0.01 f
Autumn	36.29 ± 0.01 b	21.36 ± 0.1 d

(2) Total antioxidant capacity

Corallina officinalis showed highest total antioxidant capacity in autumn extract (3.94 ± 0.1 mg EAA/g DM) followed by (1.49 ± 0.02 and 0.62 ± 0.02 and 0.32 ± 0.01 mg EAA/g DM) in summer and winter and the last in spring, respectively, with significant difference (p < 0.05).

While *Corallina elongata* presented highest value in spring extract (1.13 ± 0.01 mg EAA/g DM), followed by (0.95 ± 0.08 and 0.59 ± 0.1 and 0.53 ± 0.1 mg EAA/g DM) in winter and autumn and the last in summer, respectively, with significant difference in all seasons except that insignificant differences between summer and autumn extract (p < 0.05) (Table 4).

Table 4. seasonal variation of total antioxidant capacity (mg EAA/g DM) in methanolic extract of *Corallina officinalis* and *Corallina elongata*

	<i>C. officinalis</i>	<i>C. elongata</i>
Winter	0.62 ± 0.02 e	0.95 ± 0.08 d
Spring	0.32 ± 0.01 f	1.13 ± 0.01 c
Summer	1.49 ± 0.02 b	0.53 ± 0.1e f
Autumn	3.94 ± 0.1 a	0.59 ± 0.1 e

Between the species there was significant difference except that insignificant differences between winter extract of *Corallina officinalis* with summer extract and autumn extract of *Corallina elongata*, and spring extract of *Corallina officinalis* with summer extract of *Corallina elongate* (p < 0.05).

This antioxidant activity test gave insignificant correlation (66%) with the seasonal variation of phenolic compounds contents and significant correlation with the seasonal variation of flavonoids contents (90%), and insignificant correlation (38%) with radical scavenging activity which is of course the opposite.

Autumn extract of *C officinalis* gave a very significant total antioxidant capacity, which is the same season with the highest value for aqueous extract of *Halopteris scoparia*, but this does not correlate well with its composition of phenolic compounds and flavonoids, indicating that phenolic compounds are not always responsible for antioxidant activity (Fellah et al., 2017), and this may be due to the presence of other

compounds which have antioxidant power which was already raised in the literature such as mycosporine-like amino acids (Heo et al., 2006), pigments (Kumar et al., 2021), sulfated polysaccharides (Costa et al., 2010), followed by the summer extract which contains the highest content of phenolic compounds and flavonoids.

In *Corallina elongata*, spring showed the same capacity in both tests of antioxidant activity, which is always in agreement with *C stricta* in the study of Benmahdjoub et al. (2022) and with red alga *Sphaerococcus coronopifolius* in the study of Fellah et al. (2017).

Both tests of antioxidant activity have a positive correlation with seasonal variation of flavonoids contents, and this is due to their ability to reduce the formation of free radicals and eliminate them (Carocho and Ferreira, 2013; Catarino et al., 2016).

HPLC analysis

After obtaining the results of the various parameters tested, it was observed that the seasons which gave the best results are:

- For *C officinalis*, summer with the highest content of phenolic compounds, flavonoids, and the second in total antioxidant capacity, and spring which gave the lowest EC 50 for the DPPH radical scavenging activity test.
- For *C elongata*, spring gave the highest concentration of flavonoid content and the second highest in phenolic compound content, plus the lowest EC 50 value of the DPPH radical scavenging activity test, and the best total antioxidant capacity.

HPLC analysis of these extracts showed the presence of several compounds which are presented in the following figures:

The chromatograms of the 3 extracts gave peaks in different retention times, and each peak presents a precise compound which corresponds to a reference compound which has already given the same retention time.

- The spring extract of *C elongata* gave 3 peaks in 15.503; 18.433; 29.673 min respectively which present the compounds: caffeine, coumarin, and catechin respectively, the latter presented the highest peak with a height of 335.192 followed by caffeine with a weight of 51.886 then coumarin with a height of 43.945 (*Fig. 1*).
- The spring extract of *C officinalis* gave 2 peaks in 19.017; (28.570 and 30.157) min respectively which present the compounds: coumarin and catechin (for peaks of 28 and 30) respectively, the highest peak is that of catechin with a height of 201.537 then coumarin with a height of 43.945 (*Fig. 2*).
- The summer extract of *C officinalis* gave 2 peaks in 16.930; 29.253 min respectively which present the compounds: myricetin and catechin respectively, the highest peak is that of catechin with a height of 110.704 then myricetin with a height of 29.607 (*Fig. 3*).

It is observed that the spring extract of *C elongata* contains 3 compounds caffeine, coumarin, and catechin compared to the other extracts which presented 2 compounds the acid and the catechin in the spring extract of *C officinalis*, and mycerin and catechin in the summer extract of the same species, and this confirms the best radical scavenging activity of spring extract of *C elongata*.

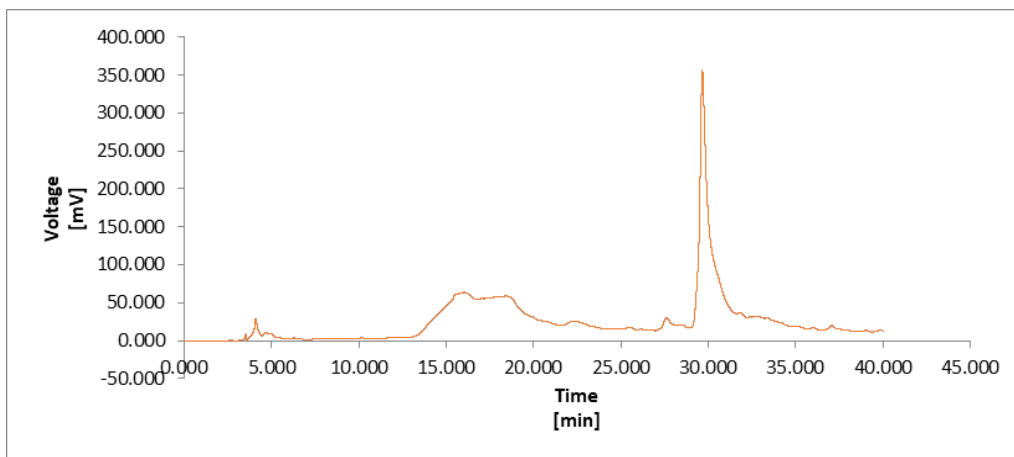


Figure 1. Chromatogram of *C. elongata* spring extract

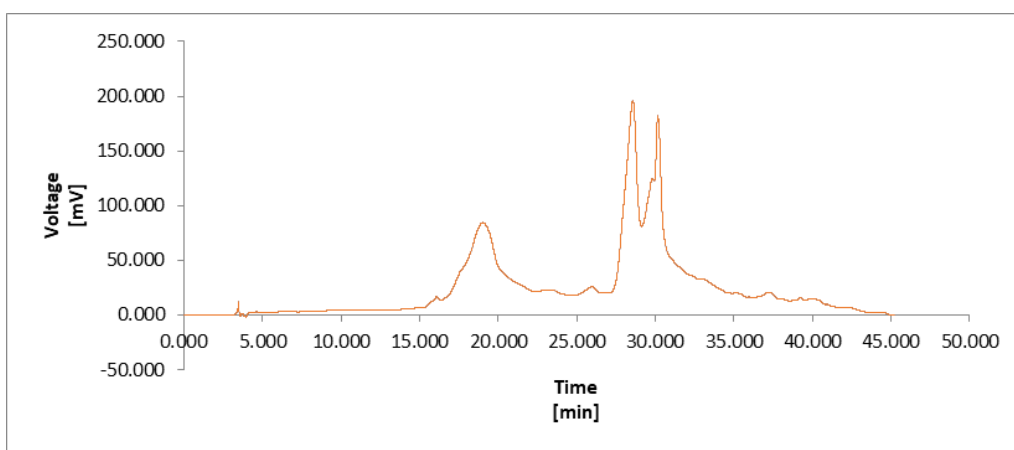


Figure 2. Chromatogram of *C. officinalis* spring extract

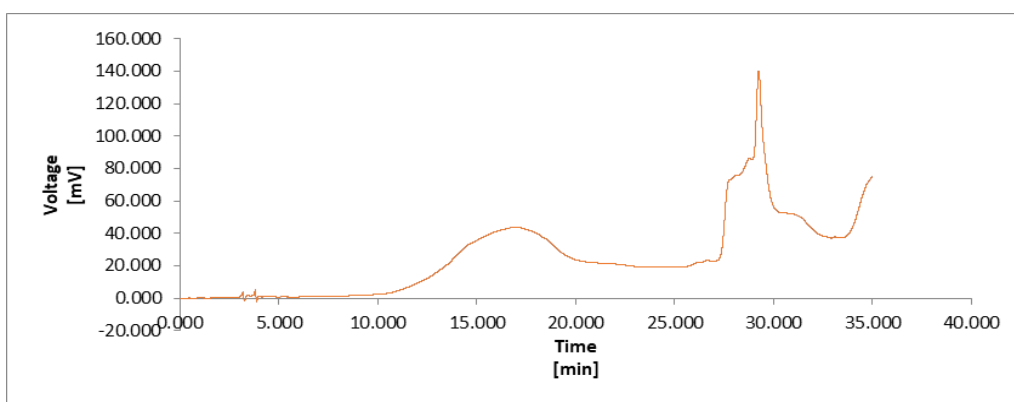


Figure 3. Chromatogram of *C. officinalis* summer extract

Coumarin is found in spring extract of *C. officinalis* with an area of 16766.949 mV.s; and in spring extract of *C. elongata* with 6400.964 mV.s which is non-flavonoid polyphenolic compounds (Andrés-Lacueva et al., 2010) (Figs. 1 and 2).

Spring extract of *C elongata* contain also Caffeic acid with an area of 3404.311 mV.s which is a Phenolic acid (non-flavonoid polyphenolic compounds) (Tsao, 2010) (Fig. 1).

Summer extract of *C officinalis* does not contain coumarin but it contain myricetin with 9310.137 mV.s; which is also a flavonoid (Ghedira, 2005) (Fig. 3).

Catechin is found in all three extracts but with different quantities, the highest quantity is that of spring extract of *C officinalis* with an area of 34225.389 mV.s, followed by spring extract of *C elongata* with 12696.252 mV.s, then summer extract of *C officinalis* with 10268.910 mV.s, this compound belongs to the flavonoids (Ghedira, 2005; Tsao, 2010), which explains the high flavonoids content of the extracts studied; (Santos et al., 2019) showed that seaweeds are a rich source of catechin (Figs. 1, 2, and 3).

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