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Research Article

Composition of Flatbreads Prepared from Blue, Red, Yellow, and White Corn Flours Supplemented with Edible *Ecklonia cava* Algae: Relationship to Health Benefits

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Abstract

The objective of the present study was to determine the composition of flatbreads prepared from corn and wheat flours supplemented with edible *Ecklonia cava*, which is a health-promoting medicinal food used as a dietary supplement. The Corn flours used were Whole Blue, Purcell Whole Blue, Purcell Whole Red, Purcell Whole Yellow, Purcell Whole White and Giant White and King Arthur Whole Wheat. Because the colored corn flours are reported to contain health-promoting anthocyanins and the *Ecklonia* alga contains multiple biologically active polyphenolic and other health-promoting compounds reported to show anti-asthma, anti-cancer, anti-diabetes, antimicrobial, anti-neurotoxicity, anti-obesity, and cardioprotective effects, the resulting flatbreads have the potential for multiple health benefits in humans after consumption. To facilitate the development of the newly created flatbreads for consumption, we determined, using standard methods, the effect of added *E. cava* on the proximate composition of protein, fat, carbohydrate, dry matter, ash (mineral), and water content of the flatbreads. The unexpected results, for which we have no explanation, show that the measured protein, mineral, and water content of the *E. cava*-supplemented flatbreads increased, whereas the fat, carbohydrate, and dry matter contents of the *E. cava*-supplemented flatbreads decreased compared to un-supplemented ones, suggesting that consumers will be able to select flatbreads with a high-protein and low-fat content.

Keywords: Flatbreads; Blue Corn; Red Corn; Yellow Corn; White Corn; Hard Red Whole Wheat; *Ecklonia Cava* Algae; Proximate Analysis; Health Benefits; Research Needs

Introduction

As part of efforts to create new functional foods that have the potential to ameliorate and treat human diseases, we reported that edible algae (*Ecklonia cava*) bioprocessed (fermented) in culture with shiitake mushroom mycelia was effective in neutralizing multiple biomarkers associated with allergic asthma in mice [1]. We also published a series of studies on the preparation of experimental, mostly gluten-free, flatbreads with other health benefits, as well as with a low content of the heat-induced toxin acrylamide formed during the baking process [2-5]. Because edible *E. cava* algae contain multiple antioxidative polyphenolic compounds that are reported to be safe to consume (discussed below) and to have multiple health benefits *in vitro* and *in vivo* (highlighted below), and colored (pigmented) corn flours also contain different health-promoting phenolic compounds and anthocyanins (highlighted below), expectations are that the combination of biologically active compounds present in colored corn flour and the alga might act additively or synergistically against human diseases. These considerations motivated us to prepare another set of flatbreads from colored corn flour and *E. cava* that might act additively or synergistically in ameliorating the adverse effects of human diseases. The objective of the present study was therefore to prepare and determine the composition of flatbreads from blue, yellow, red, and white corn flours (colored corn flours containing anthocyanins and phenolic compounds) and hard red whole wheat flour supplemented with health-promoting purified commercial *E. cava*.

Materials and Methods

Ecklonia cava BioPure 300 mg capsules manufactured for BHP Holdings, Inc., Woodinville, WA (info@biopures.com) were purchased online from Amazon. The following corn seeds were purchased online from Purcell Mountain Farms, Moyie Springs, ID, USA (https://purcellmountainfarms.com, accessed on 17 October 2021): Corn, Blue Purcell Corn, Red Corn, White Corn, White Giant Corn, and Yellow Corn. The corn seeds were milled in our laboratory into flour using the Blendtec Kitchen Mill Model 91 at medium setting (Blendtec Inc., Orem, UT 84058, USA). King Arthur hard red whole wheat flour was purchased from the local grocery store.

Preparation of Flatbreads

The composition of flatbreads prepared (170 mL water and 178.65 g ingredients) is given in **Table 1**. Flatbread dough was prepared by adding 49 ml water to 51 g of ingredients, as shown in **Table 2**. Water was added slowly in small volumes to flatbread ingredients until the dough began forming a ball. The dough was kneaded until it became smooth and elastic, which determined the exact amount of water needed for each batch of flatbreads. The dough was placed in a Pyrex bowl, covered with a polyvinyl film, and held at room temperature for 30 min. Dough (45 g) was placed on parchment paper (nonstick, oven safe up to 216 ˚C) and pressed into a thickness of 1–1.5 mm and to a circle of about 17 cm diameter in a 20-cm Alpine Cuisine flatbread Press (Aramco Imports, Inc., Commerce, CA, USA). Flatbreads were cooked between the upper and lower hot irons of the flatbread maker for 2 min (1 min each side) at 165–195 ^{O}C on parchment paper in a 1000 Watt CucinaPro Flatbread Maker (SCS Direct, Inc., Trumbull, CT, USA). The cooking temperature was measured by Fluke 61 Infrared Thermometer (www.fluke.com, accessed on 4 April 2022). For crispier or chewier flatbreads, cooking time can be adjusted as desired. The pliable flatbreads could be filled and rolled to make wraps. The resulting flatbreads weighed ~3l g before drying and ~19 g after drying.

Flatbread Proximate Composition analysis

For proximate analysis, cooked flatbreads were chopped for 30 sec in a Cuisinart coffee grinder Model DCG-20N (Cuisinart East Windsor, NJ, USA). Chopped flatbreads were then dried at 130 ˚C for l hr. Complete dryness was confirmed with an additional 30 min of drying. Dried flatbreads were ground to fine powders using a coffee grinder (Cuisinart Model DCG-20N E Windsor NJ, USA). Ground flatbreads were analyzed for Kjeldahl nitrogen using AOAC method 951.03; for crude fat by Soxhlet extraction with petroleum ether using method 963.15; ash, using method 923.03; and moisture, using method 925.10.

Results

Table 1 shows the composition of the dough recipe (flour, guar gum, *Ecklonia cava*, olive oil, salt, and water) used to bake the flatbreads in terms of grams of each ingredient, Table 2, the corresponding values on a percent basis, and Table 3 nutrient composition on a dry matter basis. The data show that values for protein content on a gram basis for the six corn and one wheat flour ranged from 5.19 (Purcell Whole Giant White) to 8.65 (Purcell Whole Red), and 15.14 (King Arthur Whole Wheat). Table 3 also shows that, for fat content, the values for the six corns varied by 3.62%, ranging from 10.39 (Purcell Whole White) to 14.01 (Whole Blue), whereas the value for King Arthur Whole wheat of 4.43 was about one-third that of the corns. The carbohydrate (67.43–71.75), dry matter (88.37–91.15), and water (9.85–11.61) values of all samples were within close range. This seems to be the first report on the proximate composition of an *E. cava* sample, which shows the following values: protein, 2.17; fat, l.27; minerals, 1.09; carbohydrates, 91.17; dry matter, 95.70; and water 4.31. Table 4 shows the composition of the *E. cava*-supplemented flatbreads on percent dry matter basis. The protein content for the six corns ranged from 6.01 (Purcell Whole Giant White) to 9.78 (Purcell Whole Red) and 5.35 for King Arthur Whole Wheat. The corresponding values for the fat content are 4.69 (Whole Blue) to 6.67 (Purcell Whole Red) and 3.81 (King Arthur Whole Wheat). The values for carbohydrate dry matter, and water are in close range. The following results demonstrate the large changes in the composition of the analyzed flatbreads that resulted from adding the *E. cava* to the dough recipe. The last column in Table 5 shows that the protein content on a dry matter basis of the eight flatbreads increased, ranging from a 46.59% increase (King Arthur Wheat) to a 76.41% increase (Giant White Corn). Table 6 shows that the protein content on a wet weight basis increased from 20.41% (Purcell Whole Giant White) to 45.34% (Purcell Whole Red). Table 7 shows that the fat content decreased, ranging from -32.99% (King Arthur Whole Wheat) to -60.35% (Whole Blue Corn). Table 8 shows that increases in mineral content ranged from 2.57% (King Arthur Whole Wheat) to 14.02% (Purcell Whole Blue Corn). Table 9 shows that the carbohydrate content decreased, ranging from -5.84% (Whole Blue Com) to -17.72% (King Arthur Whole Wheat). Table 10 shows that dry matter also decreases from -4.74% (Purcell Whole Red Corn) to -18.13% (Purcell Whole Giant White Corn). Finally, Table 11 shows that the increase in water content ranged from 13.48% (Purcell Whole Red Corn) to 23.84% (Purcell Whole Giant White Corn). We have no explanation for the described positive and negative changes in the composition of the flatbreads apparently caused by added *E. cava*.

Flatbread	Flour	Guar Gum	*Ecklonia cava*	Olive oil	Salt	Water mL
Whole Blue Corn	150	6	15	6	1.65	170
Purell Whole Blue Corn	150	6	15	6	1.65	170
Purell Whole Red Corn	150	6	15	6	1.65	170
Purell Whole Yellow Corn	150	6	15	6	1.65	170
Purell Whole White Corn	150	6	15	6	1.65	170
Purell Whole Gian White Corn	150	6	15	6	1.65	170
King Arthur Whole Wheat	150	6	15	6	1.65	170

Table 1: Composition of whole colored corn and whole wheat *E. cava* flatbreads (g).

Flatbread	Flour	Guar Gum	*Ecklonia cava*	Olive oil	Salt	Water
Whole Blue Corn	43.02	1.72	4.30	1.72	0.47	48.7
Purell Whole Blue Corn	43.02	1.72	4.30	1.72	0.47	48.7
Purell Whole Red Corn	43.02	1.72	4.30	1.72	0.47	48.7
Purell Whole Yellow Corn	43.02	1.72	4.30	1.72	0.47	48.7
Purell Whole White Corn	43.02	1.72	4.30	1.72	0.47	48.7
Purell Whole Giant White Corn	43.02	1.72	4.30	1.72	0.47	48.7
King Arthur Wholewheat	43.02	1.72	4.30	1.72	0.47	48.7

Table 2: Composition of whole colored corn and whole wheat *E. cava* flatbreads (%).

Ingredients	Protein	Fat	Minerals	Carbohydrates	Dry matter	Water
Whole Blue Corn	6.43±0.02^{d}	14.01±0.12^{a}	1.18±0.01^{e}	68.29±0.12^{f}	89.91±0.09^{c}	10.09±0.09^{f}
Purell Whole Blue Corn	6.49±0.01^{d}	12.43±0.17^{b}	1.31±0.01^{c}	69.57±0.30^{e}	89.80±0.07^{d}	10.20±0.07^{e}
Purell Whole Red Corn	8.65±0.06^{b}	11.03±0.42^{e}	1.26±0.04^{d}	67.81±0.36^{g}	88.75±0.05^{g}	11.25±0.05^{b}
Purell Whole Yellow Corn	5.81±0.04^{e}	11.46±0.29^{d}	1.16±0.01^{e}	69.96±0.34^{d}	88.39±0.02^{h}	11.61±0.02^{a}
Purell Whole White Corn	6.82±0.06^{c}	10.39±0.02^{f}	1.19±0.03^{e}	71.75±0.07^{b}	91.15±0.02^{b}	9.85±0.02^{g}
Purell Whole Giant White Corn	5.19±0.05^{f}	12.16±0.26^{c}	1.51±0.04^{b}	70.06±0.07^{c}	88.92±0.10^{f}	11.08±0.10^{c}
King Arthur Whole Wheat	15.14±0.34^{a}	4.43±0010^{g}	2.37±0.06^{a}	67.43±0.35^{h}	89.37±0.10^{e}	10.63±0.10^{d}
Ecklonia cava	2.17±0.02^{g}	1.27±0.13^{h}	1.09±0.09^{f}	91.17±0.16^{a}	95.70±0.03^{a}	4.31±0.03^{g}
Values with different superscript letters differ significantly ($p \leq 0.05$), n=3. Colored corn data from [5].						

Table 3: Proximate composition of colored corn, wheat and *E. cava* ingredients, on a dry matter basis, mean ± SD.(%).

Ingredients	Protein	Fat	Minerals	Carbohydrate	Dry Matter	Water
Whole Blue Corn	7.32±0.02[d]	4.69±0.10[d]	1.82±0.02[d]	47.29±0.81[a]	61.11±0.72[b]	38.89±0.72[c]
Purell Whole Blue Corn	7.36±0.11[d]	4.92±0.76[d]	2.04±0.04[c]	47.02±0.84[a]	61.34±0.72[b]	38.66±0.72[c]
Purell Whole Red Corn	9.78±0.05[b]	6.67±0.12[a]	1.87±0.13[d]	44.95±1.66[c]	62.87±1.61[a]	37.13±1.61[d]
Purell Whole Yellow Corn	6.43±0.32[e]	5.46±0.11[c]	1.80±0.28[d]	46.34±0.59[ab]	60.02±0.40[c]	39.98±0.40[b]
Purell Whole White Corn	7.65±0.06[c]	5.73±0.08[b]	1.78±0.04[d]	46.21±0.14[b]	61.37±0.13[b]	38.63±0.13[c]
Purell Whole Giant White Corn	6.01±0.02[f]	6.32±0.15[a]	2.20±0.08[b]	43.85±0.16[d]	58.37±0.08[d]	41.63±0.08[a]
King Arthur Whole Wheat	5.35±0.12[g]	3.81±0.12[e]	2.37±0.06[a]	40.23±0.93[e]	61.77±0.73[b]	38.23±0.73[c]
Values with different superscript letters differ significantly ($p \leq 0.05$), n=3.						

Table 4: Composition of colored corn *E. Cava* flatbreads on a dry matter basis (%), mean ± SD.

Flatbreads	Corn	Ecklonia	Corn Protein	Corn-Ecklonia Protein	Protein Change	Change %
Blue Corn-EC	38.68	4.3	7.15	11.98	4.83	67.49
Purcell Blue Corn-EC	38.18	4.3	7.23	12.00	4.77	66.02
Purcell Red Corn-EC	38.18	4.3	9.75	15.56	5.81	59.61
Purcell Yellow Corn-EC	38.03	4.3	6.57	10.71	4.14	62.98
Purcell White Corn-EC	38.78	4.3	7.57	12.47	4.90	64.77
Giant White Corn-EC	38.25	4.3	5.84	10.30	4.46	76.41
King Arthur Wheat-EC	38.45	4.3	16.95	24.85	7.90	46.59
Corn protein from ingredients in Table 3, Kjeldahl determination for protein = (N x 6.25), n=3.						

Table 5. Change in protein content in flatbreads with the addition *E. cava* (EC) on a dry matter basis (g).

Ingredients	Corn	Guar Gum	Ecklonia	Total	Corn-Ecklonia	FB change	Change %
Whole Blue Corn	2.487	0.839	0.089	3.415	4.473	1.058	30.986
Purcell Whole Blue Corn	2.507	0.839	0.089	3.435	4.515	1.079	31.423
Purcell Whole Red Corn	3.303	0.839	0.089	4.231	6.149	1.918	45.340
Purcell Whole Yellow Corn	2.209	0.839	0.089	3.137	3.859	0.722	23.015
Purcell Whole White Corn	2.645	0.839	0.089	3.753	4.695	1.122	31.399
Purcell Whole Giant White Corn	1.985	0.839	0.089	2.913	3.508	0.595	20.414
King Arthur Whole Wheat	5.821	0.839	0.089	6.749	9.482	2.733	40.4994
Data calculated from Tables 2, 3 and 4 except Guar Gum. Guar Gum data from [6].							

Table 6: Protein content of flatbread ingredients and corn-Ecklonia flatbread (g).

Ingredients	**Corn**	**Guar Gum**	**Ecklonia**	**Olive Oil**	**Total**	**Corn-Ecklonia**	**FB change**	**Change (%)**
Whole Blue Corn	5.419	0.037	0.052	1.72	7.728	2.866	-4.362	-60.347
Purcell Whole Blue Corn	4.802	0.037	0.052	1.72	6.611	3.018	-3.593	-54.349
Purcell Whole Red Corn	4.211	0.037	0.052	1.72	6.020	3.942	-2.078	-34.521
Purcell Whole Yellow Corn	4.358	0.037	0.052	1.72	6.167	3.277	-2.890	-46.858
Purcell Whole White Corn	4.030	0.037	0.052	1.72	5.838	3.517	-2.322	-39.770
Purcell Whole Giant White Corn	4.652	0.037	0.052	1.72	6.461	3.689	-2.772	-42.900
King Arthur whole wheat	1.703	0.037	0.052	1.72	3.512	2.353	-1.159	-32.991
Data calculated from Tables 2, 3 and 4 except Guar Gum. Guar Gum data from [6].								

Table 7: Fat content of flatbread ingredients and Corn-Ecklonia flatbread (g).

Ingredients	**Corn**	**Guar Gum**	**Ecklonia**	**Salt**	**Total**	**Corn-Ecklonia**	**FB change**	**Change (%)**
Whole Blue Corn	0.456	0.077	0.045	0.47	1.048	1.112	0.064	6.146
Purcell Whole Blue Corn	0.506	0.077	0.045	0.47	1.097	1.251	0.154	14.020
Purcell Whole Red Corn	0.481	0.077	0.045	0.47	1.072	1.176	0.103	9.624
Purcell Whole Yellow Corn	0.441	0.077	0.045	0.47	1.032	1.080	0.048	4.637
Purcell Whole White Corn	0.462	0.077	0.045	0.47	1.053	1.092	0.039	3.750
Purcell Whole Giant White Corn	0.578	0.077	0.045	0.47	1.169	1.284	0.115	9.848
King Arthur Whole Wheat	0.912	0.077	0.045	0.47	1.503	1.464	0.039	2.571
Data calculated from Tables 2, 3 and 4 except Guar Gum. Guar Gum data from [6].								

Table 8. Mineral content of flatbread Ingredients and corn-Ecklonia flatbread (g).

Ingredients	Corn	Guar Gum	Ecklonia	Total	Corn-Ecklonia	FB change	Change (%)
Whole Blue Corn	26.414	0.526	3.752	30.672	28.899	-1.793	-5.842
Purcell Whole Blue Corn	26.876	0.526	3.752	31.154	28.842	-2.312	-7.421
Purcell Whole Red Corn	25.890	0.526	3.752	30.168	28.260	-1.908	-6.324
Purcell Whole Yellow Corn	26.603	0.526	3.752	30.880	27.813	-3.067	-9.332
Purcell Whole White Corn	27.826	0.526	3.752	32.104	28.359	-3.745	-11.666

Purcell Whole Giant White Corn	26.800	0.526	3.752	31.078	25.595	-5.483	-17.643
King Arthur Whole Wheat	25.925	0.526	3.752	30.203	24.850	-5.353	-17.722
Data calculated from Tables 2, 3 and 4 except Guar Gum. Guar Gum data from [6].							

Table 9. Carbohydrate content of flatbread ingredients and corn-Ecklonia flatbread (g).

Ingredients	Corn	Guar Gum	Ecklonia	Olive oil	Salt	Total	Corn-Ecklonia	FB change	Change (%)
Whole Blue Corn	34.777	1.478	3.938	1.72	0.47	42.383	37.350	-5.032	-11.873
Purcell Whole Blue Corn	34.692	1.478	3.938	1.72	0.47	42.298	37.626	-4.672	-11.045
Purcell Whole Red Corn	33.885	1.478	3.938	1.72	0.47	41.491	39.526	-1.965	-4.735
Purcell Whole Yellow Corn	33.611	1.478	3.938	1.72	0.47	41.217	36.030	-5.186	-12.584
Purcell Whole White Corn	34.962	1.478	3.938	1.72	0.47	42.569	37.663	-4.906	-11.525
Purcell Whole Giant White Corn	34.015	1.478	3.938	1.72	0.47	41.621	34.076	-7.545	-18.127
King Arthur Whole Wheat	34.360	1.478	3.938	1.72	0.47	41.966	38.149	-3.817	-9.096
Data calculated from Tables 2, 3 and 4 except Guar Gum. Guar Gum data from [6].									

Table 10. Dry matter content of flatbread ingredients and corn-Ecklonia flatbread (g).

Ingredients	Corn	Guar Gum	Ecklonia	Water	Total	Corn-Ecklonia	FB change	Change (%)
Whole Blue Corn	3.903	0.116	0.177	48.7	52.896	62.650	9.753	18.438
Purcell Whole Blue Corn	3.940	0.116	0.177	48.7	52.934	62.374	9.440	17.833
Purcell Whole Red Corn	4.295	0.116	0.177	48.7	53.289	60.474	7.185	13.482
Purcell Whole Yellow Corn	4.415	0.116	0.177	48.7	53.409	63.970	10.561	19.775
Purcell Whole White Corn	3.820	0.116	0.177	48.7	52.814	62.337	9.523	18.032
Purcell Whole Giant White Corn	4.238	0.116	0.177	48.7	53.232	65.924	12.691	23.842
King Arthur Whole Wheat	4.087	0.116	0.177	48.3	53.081	61.581	8.770	16.522
Data calculated from Tables 2, 3 and 4 except Guar Gum. Guar Gum data from [6].								

Table 11. Water content of flatbread ingredients and corn-Ecklonia flatbread (g).

Discussion

Safety Aspects

Highlights from the literature seem to show that *E. cava* and bioactive compounds have a high order of safety in humans and rodents. An oral toxicity study by the European EFSA Panel on Dietetic Products, Nutrition, and Allergies (NDA) reported that phlorotannins from *E. cava* are safe for use in food supplements at a maximum intake level of 163 mg/day for adolescents 12 to 14 years of age, 230 mg/day for adolescents above 14 years of age, and 263 mg/day for adults [7]. Based on subchronic oral toxicity and genotoxicity studies in rats and dogs, Yun *et al*. [8] reported that the no-observed-adverse-effect level of *E. cava* was 3000 mg/kg/day for male and female rats; and that it was not mutagenic or clastogenic (chromosome-damaging). A review by Javed *et al.* [9] on the pharmacology of phlorotannins concluded that their curative functions could be attributed to their antioxidant properties.

Health Benefits of Colored Corn and *Ecklonia cava*

Colored corns and *E. cava* alga and their bioactive components have been shown to have multiple health benefits in cells and rodents, including anti-Alzheimer disease, antibiotic, anti-viral, anti-anxiety, anti-cancer, anti-cognitive decline, anti-diabetes, anti-obesity, anti-constipation, anti-hearing loss, anti-hypertension, anti-insomnia, anti-neurodegeneration, anti-ovarian dysfunction, anti-periodontitis, and anti-photo-ageing of the skin effects. To facilitate much needed human studies on one or more of these benefits of the new flatbreads that contain both these flours and the alga, we will highlight selected research to stimulate further studies on the potential benefits of these flatbreads.

Colored Corn Flours

Here, we briefly summarize the reported contents of bioactive antioxidative phenolic compounds in colored flours that are expected to contribute to the health benefits of the flatbreads. Ranilla *et al*. [10] reported on the content of bioactive compounds in white, orange, and red Peruvian corn harvested at different stages of maturity. All maize types contained free hydroxybenzoic and hydroxycinnamic acids and bounds ferulic acid, ferulic acid derivatives, and p-coumaric acid. Luteolin and anthocyanin flavonoids were present only in the orange and red samples. Xanthophylls (lutein, zeaxanthin, neoxanthin, and lutein isomer) were present in all maize types. In related studies, Chatham and Juvik [11] and Paulsmeyer *et al*. [12] evaluated anthocyanin diversity in purple corns, and Zhu *et al*. [13] related anthocyanin levels in maize, rice, wheat, barley, sorghum, millet, and rye to reported health effects that include anti-oxidation, anti-cancer, glycemic and body weight regulation, neuroprotection, retinal protection, hypolipidemia, hepatoprotection, and anti-ageing effects. A review by Ngamsamer *et al*. [14] suggests that that the consumption of anthocyanin-rich foods can protect against obesity-induced inflammation. Finally, Aguirre Lopez *et al*. [15] found that consuming an anthocyanin extract or anthocyanin-containing tortillas made with blue corn decreased anxiety-like behavior and improved learning and memory in a chronic rat stress model, suggesting the value of the blue tortillas as a potential functional food. Will flatbreads prepared from blue corn show similar health benefits?

Choi *et al*. [16] showed that the combination of the compound eckol isolated from *E. cava* and the medicinal drug ampicillin acted synergistically against the foodborne pathogens *Staphylococcus aureus* and *Salmonella* spp., suggesting the compound has potential for inhibiting the growth of these bacteria on contaminated food and in infected animals and humans. Kwon *et al*. [17] reported that phlorotannins isolated from *E. cava* inhibited porcine epidemic diarrhea coronavirus *in vitro*, a virus that causes a high mortality rate in piglets. Karadeniz *et al*. [18] reported that a phlorotannin derivative inhibited HIV-1 activty and Cho *et al*. [19] used mass spectrometry to determine antiviral activities of phlorotannins from *E. cava*.

Lee *et al*. [1] obtained a new functional food by bioprocessing (fermenting) *E. cava* with shiitake mushroom mycelia that protected mice against ovalbumin-induced allergic asthma. The new functional food also reversed the thickening of the airway wall and infiltration of bronchial and blood vessels and inflammatory cells. In addition to ameliorating adverse effects of asthma, the novel food product might have other therapeutic uses in humans including prevention of peanut protein and other food allergies.

Fucoidan, extracted from *E. cava*, was shown by Zhang *et al*. [20] to induce anti-metastatic lung cancer immunity when administered intranasally in mice. Additional data suggest that the fucoidan extract functioned as a mucosal adjuvant that enhanced the immunotherapeutic effect of immune checkpoint inhibitors against lung cancer. A review by Jin *et al*. [21] collates information on molecular and cellular aspects and anti-cancer effects fucoidan, a natural marine anticancer agent.

Dieckol from *E. cava* has also been shown to have therapeutic effects. For example, Lu *et al*. [22] reported that dieckol isolated from *E. cava* promoted blood flow velocity and vasodilation of blood vessels in zebra fish by enlarging the dorsal aorta diameter, suggesting its potential clinical use as a vasodilator. In related studies, Oh *et al*. [23] found that dieckol reduces muscle atrophy in hypertensive rats and Byun *et al*. [24] discovered that *E. cava* extracts decreased hypertension-related vascular calcification.

Cho *et al*. [25] found that dieckol isolated from *E. cava* inhibited advanced glycation end products associated with the pathogenesis of diabetic nephropathy in mouse glomerular mesangial cells, suggesting dieckol might have the potential to treat diabetic nephropathy in humans. A related study by Hwang *et al*. [26] reported that phloroglucinol and dieckol suppressed angiogenesis in diabetic vascular complications. Almutairi *et al*. [27] reported that administering 600 mg of polyphenolic-rich *E. cava* extract to 20 Saudi Arabian prediabetic patients for up to 120 min reduced the postprandial blood glucose level with no associated side effects.

Park *et al*. [28] discovered, using a behavioral test, that a water extract of *E. cava* effectively prevented learning and memory declines in mice caused by pollution-induced neurotoxicity. The extract also improved oxidative damage of the lungs and brain and regulated cognition-related proteins. It decreased amyloid precursor protein (APP) and p-Tau and increased Brain-Derived

Neurotrophic Factor (BDNF) associated with induced cognitive dysfunction. The bioactive compound in the extract consisted of a polysaccharide and phenolic compounds. Jo *et al*. [29] reported that an *E. cava* extract decreased the activity of biomarkers association with inflammation as well as with neurodegenerative disease in the cerebellum and hippocampus of mice, suggesting the extract might protect against neuroinflammation and neurodegenerative diseases. Yang *et al*. [30,31] found that phloroglucinol, a component of *E. cava*, inhibited the generation of cell-damaging Reactive Oxygen Species (ROS) in astrocytes, the most abundant cell types of the Central Nervous System (CNS). The compound also ameliorated the expression of glial fibrillary acidic protein, a marker of reactive astrocytes, suggesting its potential value against Alzheimer's disease and Kwon *et al*. [32] used ophlorotannins to treat neurodegenerative disorders.

There are many other reported wide-ranging health benefits for *E. cava* extracts or fractions. For example, a review by Kim *et al*. (2023) states that the Korean Ministry of Food and Drug Safety approved the use of an *E. cava* supplement containing phlorotannin as a health-functional product that helps improve sleep quality. The paper covers the sedative-hypnotic mechanisms in animal models as well as human clinical trials.

In addition, fucoidan fractions isolated from *E. cava* remarkably reduced lipid accumulation in 3T3-Ll adipocyte cells and significantly reduced body weight gain, serum and liver lipid contents, and white adipose tissue mass in mice on a high-fat diet, suggesting that the anti-obesity extracts could be used in food [33]. Abbas *et al*. [34] observed similar results with a 70% *E. cava* extract orally administered to rats, suggesting the extract also represents a potential candidate for the prevention of obesity. A mass spectrometry-based metabolomics analysis of urine samples of individuals after consumption of seapolynol isolated from *E. cava* shows that decreased body fat is related to an increase in the antioxidant effect of riboflavin, which was associated with the Body Mass Index (BMI), body weight, fat mass, and percent body fat [35].

In another application, He *et al*. [36] reported that 6,6'-bieckol from *E. cava* reduced UVB radiation-induced oxidative stress damage in human immortalized keratinocyte cells, suggesting its potential value as a functional food and skin care ingredient that might prevent photo-ageing damage of human skin caused by UVB-radiation from the sun. In oral health, Jung *et al*. [37] showed that applying an *E. cava* extract to Lipopolysaccharide (LPS)-stimulated Human Gingival Fibroblasts (HGF-I) in mice mitigated gingival tissue destruction and bone resorption associated with chronic oral disease. Reproductive effects have also been observed. Yang *et al*. [38] found that *E. cava* extracts restored ovarian dysfunction and anti-inflammatory responses in rats with PCOS-like symptoms, suggesting its potential value to treat ovarian failure. Li *et al*. [39] found that administering the *E. cava* component dieckol to the inner ear of rats prevented ototoxic hearing loss, suggesting that the procedure may be a safe and effective method to prevent drug-induced hearing loss. Park *et al*. [40] reported that a water extract of *E. cava* acts as a potential therapeutic agent against fine dust induced health damage in mice by regulating gut function of the microbiota and Kim *et al*. [41] provides evidence for the use of phlorotannin against constipation in rats.

The cited observations on the actual and potential health benefits of' the colored corn flours, the *Ecklonia cava* alga, and the new flatbreads containing both ingredients suggest the need for clinicians to translate the described health benefits in animal models to human therapies.

Conclusions

The *Ecklonia cava* alga widely consumed in Asian countries as a medicinal food is now available from commercial sources in the United States. To demonstrate therapeutic applications, the described potential health benefits of *Ecklonia cava*-containing flatbreads need to be confirmed by studies with human patients to determine their value to ameliorate, prevent, and treat human diseases. Moreover, the newly colored-corn-based flatbreads can contribute additional benefits in the diet that can result in additive or synergistic effects after consumption. These include: (a) preparation from whole grains reported to have cardioprotective effects compared to refined grains; (b) the use of olive oil in the recipe that contains unsaturated fats reported to reduce the incidence of cardiovascular disease [42]; and (c) the lack of gluten that can benefit consumers that are allergic to its adverse effects. These highlights reinforce the need for commercial and home production of the flatbreads that requires only a 2-min baking step. Finally, because the amino acid tryptophan is nutritionally limiting in corn [43,44] and is transformed to serotonin that benefits cognitive function, we are also challenged to prepare flatbreads using high-tryptophan, as well as high-lysine, corn that will be expected to show improved nutrition and health benefits.

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