

## Research Article

# Macroalgae as Alkalizing Marine Drugs with a Low Potential Renal Acid Load

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A growing interest in more sustainable and alternative food sources has brought seaweed and macroalgae to the spotlight for the general worldwide cuisine. Algae are often praised for their high nutritional value and are rich in potassium, calcium, and magnesium. Abundant in base precursors, algae are particularly interesting from an acid-base perspective. Their unique biochemical composition suggests a low potential renal acid load (PRAL), which is a commonly used estimate for the amount of acid or base a certain food produces in humans. Here, we analyzed the PRAL value of  $n = 106$  macroalgae. Results suggested a strong alkalizing potential, with a mean PRAL value of  $-86.76$  mEq/100 g. The lowest PRAL values were found for *Laminaria ochroleuca* ( $-286.78$  mEq/100 g), *Gelidium micropterum* ( $-268.46$  mEq/100 g), and *Palmaria palmata* ( $-259.16$  mEq/100 g). We observed a strong inverse relationship of PRAL with algae's potassium content (Spearman's  $\rho = -0.79$ ,  $p < 0.001$ ) and a moderate relationship with algae's calcium content (Spearman's  $\rho = -0.34$ ,  $p < 0.001$ ). Our data point at a potential role for several macroalgae as potent alkalizing marine drugs and suggest that a 10 g edible portion of some algae alone could contribute to a substantial PRAL reduction of up to  $-28.68$  mEq. This might be of particular importance for individuals who benefit from a more alkaline diet and warrants further investigation in future studies.

## 1. Introduction

A growing interest and awareness for more sustainable and alternative food sources and gradual changes toward more plant-based dietary patterns have brought seaweed and macroalgae to the spotlight for the general worldwide cuisine [1]. Traditionally popular in Asia [2], macroalgae are often praised for their high nutritional value [3–5]. Macroalgae are considered good sources of fiber, omega-3 and omega-6 fatty acids, selenium, iodine, and vitamin B<sub>12</sub> [1, 6–9]. They are also abundant in calcium, magnesium, and potassium [10–13].

The combination of these nutritional features and the biochemical composition of algae is particularly interesting from an acid-base perspective on foods. Foods rich in alkali precursors (particularly potassium salts and magnesium salts) and low in phosphorus and phosphate additives are

usually characterized by a low PRAL (potential renal acid load) value [14–16].

The PRAL value is the most commonly used estimate for the amount of acid or base a certain food produces in the human body [17, 18]. Low PRAL values indicate that a specific food is abundant in base precursors, whereas high values indicate that a food is rich in acid precursors [19, 20]. Typical examples of acidifying high-PRAL foods include fish, cheese, and meats [21, 22]. Alkalizing low-PRAL foods, on the other hand, are largely of plant-based origin, including tomatoes, kale, spinach, raisins, carrots, and celery [23, 24].

The PRAL value of different algae has rarely been subject to a dedicated and systematic PRAL quantification in the scientific literature. We deemed this to be important, however, because the popularity of seaweeds and macroalgae is rapidly increasing in Western societies [25–27].

Macroalgae also have a varying nutritional profile, depending on their origin and the surrounding environmental conditions in which they grow [28, 29]. Further to that, harvesting and processing techniques are also supposed to affect algae's nutrient content. As such, a "one-size-fits-all" PRAL estimation for algae in general might be too imprecise, and family or genus-specific approaches are warranted.

Here, we argue that macroalgae could be used as potent marine drugs with strong alkalizing properties due to their very specific nutritional profiles, which could help in offsetting the health repercussions from a high dietary acid load. We hypothesized that algae would be largely characterized by alkalizing properties due to their high calcium and potassium content. We also hypothesized that significant differences in PRAL between the different algae phyla/classes (*Chlorophyta*, *Rhodophyta*, and *Phaeophyceae*) exist. Finally, we sought to identify those macroalgae candidates with the strongest alkalizing properties, examining their potential use to reduce the overall acid load burden from diet.

## 2. Materials and Methods

**2.1. Data Extraction.** We extracted the nutrient content of the examined macroalgae from previous publications in the field of phycology. For this, we identified original articles and scientific reviews using three different search engines: PubMed, Web of Science, and Google Scholar. The following search terms were used in various combinations during the search process: macroalgae, seaweed, nutrients, calcium, magnesium, potassium, phosphorus, composition, and minerals. The search was restricted to publications from the last 15 years. Only articles in English language were considered. Reference lists and cross-references as well as Google Scholar's "cited by" function were used to capture additional articles of interest. Only macroalgae with a complete nutrient composition profile (including protein and the following minerals: calcium, magnesium, potassium, and phosphorus) in g or mg/100 g were considered. No data were imputed and incomplete profiles for PRAL-relevant nutrients were not considered. The literature research was performed in July 2023.

**2.2. Potential Renal Acid Load Estimation.** PRAL (in mEq/100 g) was estimated using the commonly used and validated formula by Remer and Manz [16]:

$$\text{PRAL (mEq/100 g)} = (0.49 * \text{total protein intake (in g/100 g)}) + (0.037 * \text{phosphorus intake (in mg/100 g)}) - (0.021 * \text{potassium intake (in mg/100 g)}) - (0.026 * \text{magnesium intake (in mg/100 g)}) - (0.013 * \text{calcium intake (in mg/100 g)})$$

This formula considers the average intestinal absorption rates of anions and cations present in foods and has been tested against urinary pH in the past [30]. PRAL values were estimated for 100 g portion sizes (which reflects the standard procedure [31]) and 10 g portion sizes, which might be practically relevant for a potential future application of macroalgae as alkalizing marine drugs.

**2.3. Statistical Analysis.** Data were analyzed with STATA 14 statistical software (StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP). Histograms and Stata's Shapiro–Wilk test were used to check whether the examined data were normally distributed or not. Normally distributed data were described with the mean and standard deviation, whereas non-normally distributed data were described with the median and interquartile range in parenthesis. We also used the rank-based nonparametric Kruskal–Wallis H test to check for statistically significant differences in selected nutrients between the examined algae phyla. A  $p$  value  $<0.05$  was considered statistically significant. Further to that, we ran Spearman's rank-order correlations to assess the relationship between the content of selected nutrients and PRAL for the examined algae items. Scatterplots and separated scatter plots were created to visualize the results.

## 3. Results

**3.1. Sample Description.** We identified  $n = 106$  macroalgae items with a complete nutrient profile to estimate the PRAL [32–47]. Of these,  $n = 28$  belonged to the Chlorophyta phylum,  $n = 52$  belonged to the Rhodophyta phylum, and  $n = 26$  belonged to the Phaeophyceae class. The majority of the analyzed macroalgae originated from India ( $n = 35$ ), followed by Sweden ( $n = 22$ ) and Russia ( $n = 14$ ).

Table 1 shows the macro- and micronutrient content, as well as the PRAL value of these items in great detail. The mean PRAL value of the entire sample ( $n = 106$  items) was  $-86.76 \pm 87.47$  mEq/100 g. Based on dry weight data only, the mean PRAL value of the sample ( $n = 101$  items) was  $-90.69 \pm 87.75$  mEq/100 g. The lowest PRAL value was found for *Laminaria ochroleuca* (Phaeophyceae) with  $-286.78$  mEq/100 g, followed by *Gelidium micropterum* (Rhodophyta) and *Palmaria palmata* (Rhodophyta) with PRAL values of  $-268.46$  and  $-259.16$  mEq/100 g, respectively. Approximately 11% of the sample ( $n = 11$  algae items) were characterized by acidifying properties (as suggested by a PRAL value  $>0$  mEq), whereas the remaining items had alkalizing properties (PRAL values  $<0$  mEq).

We generally observed a large heterogeneity with regard to the calcium, potassium, magnesium, and phosphorus content of the examined  $n = 106$  algae items. The median potassium content was 2900 (3521.7) mg/100 g and ranged from 22.32 mg/100 g in *Ulva flexuosa* (formerly *Enteromorpha flexuosa*) (Chlorophyta) to 12480 mg/100 g in *Palmaria palmata*. The median calcium content was 1035 (1351) mg/100 g and also varied considerably, ranging from 151.4 mg/100 g in *Pyropia tenera* (formerly *Porphyra tenera*) (Rhodophyta) to 8220 mg/100 g in *Delesseria sanguinea* (Rhodophyta). Median magnesium and phosphorus content (in mg/100 g) were as follows: 765 (1018.48) and 214 (253). The median protein content was 15.4 (9.76) g/100 g and also varied widely across the examined food items. *Gracilaria corticata* (Rhodophyta) had the lowest protein content with 3.3 g/100 g, whereas *Porphyra* sp. had the highest with 53.9 g/100 g.

TABLE 1: Macro- and micronutrient content as well as PRAL values of  $n = 106$  macroalgae.

| Name   | Protein<br>(g/100 g) | Ca (mg/100 g) | K (mg/100 g) | Mg (mg/100 g) | P (mg/100 g) | PRAL<br>(mEq/100 g) | Origin                  | Type* |
|--|----------------------|---------------|--------------|---------------|--------------|---------------------|-------------------------|-------|
| <i>Acanthophora spicifera</i> [40]   | 20.2                 | 430           | 52.08        | 480           | 210          | -1.50               | India                   | Rho   |
| <i>Ahnfeltia plicata</i> [44]  | 5.57                 | 654           | 347          | 205           | 141          | -13.17              | Russia, White Sea       | Rho   |
| <i>Ahnfeltia plicata</i> [42]  | 20.1                 | 4000          | 2300         | 680           | 182          | -101.40             | Sweden, West Coast      | Rho   |
| <i>Amphiroa anceps</i> [45]  | 6.9                  | 1630          | 10900        | 420           | 470          | -240.24             | India, Saurashtra coast | Rho   |
| <i>Amphiroa fragilissima</i> [33]  | 29                   | 1596          | 5139         | 1478          | 1757         | -87.88              | Egypt, Alexandria       | Rho   |
| <i>Ascophyllum nodosum</i> [42]  | 5.9                  | 1240          | 2600         | 870           | 67           | -87.97              | Sweden, West Coast      | Pha   |
| <i>Bifurcaria bifurcata</i> [46]   | 8.92                 | 996.42        | 9316.28      | 528.04        | 169.54       | -211.68             | Spain, Galician coast   | Pha   |
| <i>Vertebrata byssoides</i> (formerly <i>Brongniartella byssoides</i> ) [42] | 15.8                 | 4940          | 6300         | 770           | 202          | -201.32             | Sweden, West Coast      | Rho   |
| <i>Caulerpa racemosa</i> [32]  | 24.57                | 2660          | 2070         | 1260          | 140          | -93.59              | India, North-West Coast | Chl   |
| <i>Caulerpa racemosa</i> [45]  | 8.68                 | 5970          | 3920         | 1130          | 190          | -178.03             | India, Saurashtra coast | Chl   |
| <i>Caulerpa scalpelliformis</i> [45]   | 12.24                | 3820          | 4300         | 1390          | 280          | -159.74             | India, Saurashtra coast | Chl   |
| <i>Caulerpa veravalensis</i> [45]  | 9.19                 | 2320          | 3220         | 860           | 250          | -106.39             | India, Saurashtra coast | Chl   |
| <i>Ceramium</i> sp. [42]   | 15.8                 | 550           | 6700         | 1510          | 242          | -170.41             | Sweden, West Coast      | Rho   |
| <i>Ceramium virgatum</i> [44]  | 32.25                | 578           | 1018         | 647           | 252          | -20.59              | Russia, White Sea       | Rho   |
| <i>Chondrus crispus</i> [42]   | 10.3                 | 1250          | 3000         | 800           | 103          | -91.19              | Sweden, West Coast      | Rho   |
| <i>Chondrus crispus</i> [35]   | 12.4                 | 2230          | 3410         | 750           | 160          | -107.36             | Spain, Galicia          | Rho   |
| <i>Chondrus crispus</i> [41]   | 15.7                 | 420           | 4100         | 650           | 110          | -96.70              | Portugal                | Rho   |
| <i>Chorda filum</i> [42]   | 6.3                  | 1490          | 8400         | 780           | 105          | -209.08             | Sweden, West Coast      | Pha   |
| <i>Cladophora glomerata</i> [33]   | 27.5                 | 931           | 505          | 1693          | 5757         | 159.76              | Egypt, Alexandria       | Chl   |
| <i>Lychaete pellucida</i> (formerly <i>Cladophora pellucida</i> ) [33]       | 25                   | 746           | 445          | 1256          | 3700         | 97.45               | Egypt, Alexandria       | Chl   |
| <i>Cladophora rupestris</i> [42]   | 18.4                 | 760           | 4200         | 440           | 142          | -95.25              | Sweden, West Coast      | Chl   |
| <i>Cladophora</i> sp. [42]   | 13.9                 | 540           | 8500         | 760           | 171          | -192.14             | Sweden, West Coast      | Chl   |
| <i>Coccotylus brodiei</i> [44]   | 15.87                | 450           | 705          | 313           | 138          | -15.91              | Russia, White Sea       | Rho   |
| <i>Corallina officinalis</i> [33]  | 19                   | 1304          | 101          | 1530          | 1834         | 18.32               | Egypt, Alexandria       | Rho   |
| <i>Cystoclonium purpureum</i> [44]   | 27.1                 | 395           | 1499         | 461           | 228          | -26.89              | Russia, White Sea       | Rho   |
| <i>Cystoclonium purpureum</i> [42]   | 17.2                 | 580           | 6500         | 910           | 226          | -150.91             | Sweden, West Coast      | Rho   |
| <i>Polycladia indica</i> (formerly <i>Cystoseira indica</i> ) [45]           | 12.95                | 1810          | 9070         | 700           | 500          | -207.35             | India, Saurashtra coast | Pha   |
| <i>Delesseria sanguinea</i> [42]   | 18.3                 | 8220          | 2200         | 950           | 227          | -160.39             | Sweden, West Coast      | Rho   |
| <i>Desmarestia aculeata</i> [42]   | 11.5                 | 4790          | 2500         | 880           | 216          | -124.02             | Sweden, West Coast      | Pha   |
| <i>Dilsea carnosa</i> [42]   | 15.2                 | 320           | 3500         | 510           | 230          | -74.96              | Sweden, West Coast      | Rho   |
| <i>Ulva compressa</i> (formerly <i>Enteromorpha compressa</i> ) [32]         | 29.54                | 770           | 3420         | 2230          | 350          | -112.39             | India, North-West Coast | Chl   |
| <i>Ulva compressa</i> (formerly <i>Enteromorpha compressa</i> ) [38]         | 17.48                | 4760          | 1380         | 890           | 1640         | -44.75              | India, North-West Coast | Chl   |
| <i>Ulva flexuosa</i> (formerly <i>Enteromorpha flexuosa</i> ) [40]           | 17.29                | 712           | 22.32        | 436           | 270          | -2.60               | India                   | Chl   |
| <i>Ulva linza</i> (formerly <i>Enteromorpha linza</i> ) [38]                 | 12.5                 | 5120          | 230          | 1180          | 410          | -80.78              | India, North-West Coast | Chl   |
| <i>Enteromorpha prolifera</i> [33]   | 22                   | 1323          | 2737         | 1799          | 3813         | 30.41               | Egypt, Alexandria       | Chl   |
| <i>Ulva flexuosa</i> (as <i>Enteromorpha tubulosa</i> ) [38]                 | 19.09                | 5070          | 270          | 1560          | 390          | -88.36              | India, North-West Coast | Chl   |
| <i>Euthora cristata</i> [44]   | 13.06                | 673           | 185          | 483           | 237          | -10.02              | Russia, White Sea       | Rho   |
| <i>Fucus serratus</i> [42]   | 7.1                  | 1040          | 2900         | 730           | 123          | -85.37              | Sweden, West Coast      | Pha   |
| <i>Fucus vesiculosus</i> [36]  | 12.4                 | 779           | 3696         | 813           | 117          | -98.48              | Portugal, West Coast    | Pha   |
| <i>Fucus vesiculosus</i> [46]  | 12.99                | 1160.27       | 3745.05      | 732.37        | 193.57       | -99.24              | Spain, Galician coast   | Pha   |
| <i>Fucus vesiculosus</i> [42]  | 7.1                  | 1140          | 3800         | 890           | 102          | -110.51             | Sweden, West Coast      | Pha   |
| <i>Furcellaria lumbricalis</i> [44]  | 15.98                | 218           | 609          | 555           | 129          | -17.45              | Russia, White Sea       | Rho   |
| <i>Furcellaria lumbricalis</i> [42]  | 17.1                 | 2560          | 4600         | 1100          | 131          | -145.25             | Sweden, West Coast      | Rho   |

TABLE 1: Continued.

| Name  | Protein<br>(g/100 g) | Ca (mg/100 g) | K (mg/100 g) | Mg (mg/100 g) | P (mg/100 g) | PRAL<br>(mEq/100 g) | Origin                    | Type* |
|---|----------------------|---------------|--------------|---------------|--------------|---------------------|---------------------------|-------|
| <i>Gelidium micropterum</i> [45]  | 12.66                | 6140          | 8740         | 890           | 320          | -268.46             | India, Saurashtra coast   | Rho   |
| <i>Chondracanthus teedei</i> (formerly <i>Gigartina teedei</i> ) [33]   | 21                   | 1072          | 4359         | 1551          | 5212         | 57.33               | Egypt, Alexandria         | Rho   |
| <i>Gracilaria corticata</i> [45]  | 17.14                | 1300          | 10860        | 630           | 240          | -244.06             | India, Saurashtra coast   | Rho   |
| <i>Gracilaria dura</i> [32]   | 14.29                | 210           | 5560         | 290           | 190          | -113.00             | India, North-West Coast   | Rho   |
| <i>Gracilaria edulis</i> [40]   | 18.04                | 410           | 52.12        | 580           | 124          | -8.08               | India                     | Rho   |
| <i>Gracilaria gracilis</i> [36]   | 28.8                 | 624           | 8920         | 402           | 415          | -176.42             | Portugal, West Coast      | Rho   |
| <i>Gracilaria salicornia</i> [45]                                       | 10.34                | 1340          | 9680         | 510           | 340          | -216.31             | India, Saurashtra coast   | Rho   |
| <i>Gracilaria corticata</i> [39]  | 3.3                  | 4337          | 2819         | 3568          | 5500         | -3.23               | India, Central West Coast | Rho   |
| <i>Halidrys siliquosa</i> [42]  | 7.9                  | 990           | 3600         | 660           | 71           | -99.13              | Sweden, West Coast        | Pha   |
| <i>Himanthalia elongata</i> [35]  | 6.4                  | 1030          | 7110         | 750           | 120          | -174.62             | Spain, Galicia            | Pha   |
| <i>Jania rubens</i> [33]  | 26                   | 1656          | 105          | 1638          | 2076         | 23.23               | Egypt, Alexandria         | Rho   |
| <i>Kappaphycus alvarezii</i> [32]                                       | 7.94                 | 450           | 5590         | 340           | 270          | -118.20             | India, North-West Coast   | Rho   |
| <i>Kappaphycus alvarezii</i> Doty [43]                                  | 19.25                | 840           | 4100         | 740           | 120          | -102.39             | India, North-West Coast   | Rho   |
| <i>Laminaria digitata</i> [42]  | 6.6                  | 1240          | 2900         | 650           | 179          | -84.06              | Sweden, West Coast        | Pha   |
| <i>Laminaria ochroleuca</i> [35]  | 8.1                  | 1060          | 8430         | 4100          | 180          | -286.78             | Spain, Galicia            | Pha   |
| <i>Palisada cruciata</i> (formerly <i>Laurencia cruciata</i> ) [45]     | 16.11                | 1200          | 6040         | 640           | 290          | -140.46             | India, Saurashtra coast   | Rho   |
| <i>Lobophora variegata</i> [47]   | 34.2                 | 1020.6        | 1078.3       | 1712.6        | 1477.3       | -9.02               | India, South-East Coast   | Pha   |
| <i>Odonthalia dentata</i> [44]  | 14.78                | 407           | 1070         | 286           | 125          | -23.33              | Russia, White Sea         | Rho   |
| <i>Padina gymnospora</i> [40]   | 12.07                | 820           | 30.02        | 780           | 164          | -19.59              | India                     | Pha   |
| <i>Padina pavonica</i> [33]   | 11                   | 708           | 257          | 1765          | 1787         | 11.02               | Egypt, Alexandria         | Rho   |
| <i>Padina tetrastrumatica</i> [45]                                      | 22.11                | 6650          | 2490         | 1140          | 190          | -150.52             | India, Saurashtra coast   | Pha   |
| <i>Palmaria palmata</i> [35]  | 10.7                 | 430           | 7620         | 230           | 180          | -159.69             | France, Bretagne          | Rho   |
| <i>Palmaria palmata</i> [36]  | 41.8                 | 1591          | 3452         | 222           | 110          | -74.40              | Portugal, West Coast      | Rho   |
| <i>Palmaria palmata</i> [41]  | 14.4                 | 160           | 12480        | 250           | 120          | -259.16             | Portugal                  | Rho   |
| <i>Palmaria palmata</i> [44]  | 19.94                | 161           | 1999         | 92            | 212          | -28.85              | Russia, White Sea         | Rho   |
| <i>Petalonia fascia</i> [33]  | 10                   | 1307          | 4165         | 1533          | 5104         | 49.43               | Egypt, Alexandria         | Pha   |
| <i>Phycodrys rubens</i> [44]  | 13.21                | 666           | 142          | 855           | 268          | -17.48              | Russia, White Sea         | Rho   |
| <i>Polyides rotunda</i> [44]  | 9.23                 | 369           | 486          | 315           | 99           | -15.01              | Russia, White Sea         | Rho   |
| <i>Polysiphonia stricta</i> [44]  | 18.58                | 449           | 1033         | 350           | 122          | -23.01              | Russia, White Sea         | Rho   |
| <i>Pyropia columbina</i> (formerly <i>Porphyra columbina</i> ) [34]     | 24.61                | 443.7         | 1444.17      | 491.52        | 379.9        | -22.76              | Argentina, San Jorge Gulf | Rho   |
| <i>Porphyra dioica</i> [36]   | 35.7                 | 225           | 2863         | 617           | 393          | -47.06              | Portugal, West Coast      | Rho   |
| <i>Pyropia haitanensis</i> (formerly <i>Porphyra haitanensis</i> ) [37] | 32.16                | 460.6         | 2734         | 612           | 885.4        | -30.80              | Japan/Korea               | Rho   |
| <i>Porphyra</i> sp. [41]  | 23.7                 | 160           | 1920         | 370           | 210          | -32.64              | Portugal                  | Pha   |
| <i>Porphyra</i> sp. [32]  | 36.19                | 420           | 4400         | 650           | 330          | -84.82              | South Korea, Wando Island | Rho   |
| <i>Porphyra</i> sp. [35]  | 53.9                 | 640           | 3190         | 440           | 320          | -48.50              | Spain, Galicia            | Rho   |
| <i>Pyropia tenera</i> (formerly <i>Prophyra tenera</i> ) [37]           | 36.88                | 151.4         | 2802         | 420.3         | 820.1        | -23.32              | Japan/Korea               | Rho   |
| <i>Ptilota gunneri</i> [44]   | 8.92                 | 663           | 872          | 334           | 242          | -22.29              | Russia, White Sea         | Rho   |
| <i>Rhodomela confervoides</i> [44]                                      | 24.26                | 544           | 1432         | 503           | 245          | -29.27              | Russia, White Sea         | Rho   |
| <i>Rhodomela confervoides</i> [42]                                      | 14.8                 | 2480          | 5800         | 560           | 158          | -155.50             | Sweden, West Coast        | Rho   |
| <i>Saccharina latissima</i> [42]  | 6.9                  | 950           | 1500         | 460           | 144          | -47.10              | Sweden, West Coast        | Pha   |
| <i>Sarcomena filiforme</i> [45]   | 10.57                | 1580          | 9080         | 480           | 480          | -200.76             | India, Saurashtra coast   | Rho   |
| <i>Sargassum ilicifolium</i> [39]                                       | 3.86                 | 4320          | 4640         | 3348          | 3500         | -109.26             | India, Central West Coast | Pha   |
| <i>Sargassum swartzii</i> [45]  | 11.21                | 1860          | 7710         | 700           | 430          | -182.89             | India, Saurashtra coast   | Pha   |

TABLE 1: Continued.

| Name  | Protein<br>(g/100 g) | Ca (mg/100 g) | K (mg/100 g) | Mg (mg/100 g) | P (mg/100 g) | PRAL<br>(mEq/100 g) | Origin                    | Type* |
|---|----------------------|---------------|--------------|---------------|--------------|---------------------|---------------------------|-------|
| <i>Sargassum tenerimum</i> [45]                     | 10.75                | 2510          | 8360         | 820           | 380          | -210.18             | India, Saurashtra coast   | Pha   |
| <i>Sargassum vulgare</i> [33]                       | 16                   | 708           | 198          | 898           | 5260         | 174.57              | Egypt, Alexandria         | Pha   |
| <i>Savoiea arctica</i> [44]                         | 24.95                | 419           | 856          | 257           | 112          | -13.74              | Russia, White Sea         | Rho   |
| <i>Spatoglossum asperum</i> [45]                    | 9.89                 | 2740          | 2940         | 1200          | 140          | -118.53             | India, Saurashtra coast   | Pha   |
| <i>Sphacelaria cirrosa</i> [42]                     | 12                   | 2560          | 3300         | 860           | 212          | -111.22             | Sweden, West Coast        | Pha   |
| <i>Ulva lactuca</i> (as <i>Ulva fasciata</i> ) [40] | 22.7                 | 740           | 27.2         | 420           | 142          | -4.73               | India                     | Chl   |
| <i>Ulva lactuca</i> (as <i>Ulva fasciata</i> ) [39] | 3.45                 | 3940          | 3125         | 3478          | 3125         | -89.96              | India, Central West Coast | Chl   |
| <i>Ulva lactuca</i> (as <i>Ulva fasciata</i> ) [33] | 27                   | 1091          | 2320         | 1781          | 4183         | 58.79               | Egypt, Alexandria         | Chl   |
| <i>Ulva lactuca</i> (as <i>Ulva fasciata</i> ) [45] | 14.3                 | 3300          | 4340         | 2180          | 130          | -178.90             | India, Saurashtra coast   | Chl   |
| <i>Ulva intestinalis</i> [42]                       | 9                    | 840           | 1700         | 2620          | 100          | -106.63             | Sweden, West Coast        | Chl   |
| <i>Ulva lactuca</i> [32]                            | 14.48                | 2040          | 2590         | 2680          | 150          | -137.94             | India, North-West Coast   | Chl   |
| <i>Ulva lactuca</i> [33]                            | 16                   | 1253          | 2444         | 1874          | 3637         | 26.07               | Egypt, Alexandria         | Chl   |
| <i>Ulva lactuca</i> [42]                            | 9.3                  | 1040          | 3000         | 2660          | 97           | -137.53             | Sweden, West Coast        | Chl   |
| <i>Ulva linza</i> [33]                              | 13                   | 1901          | 422          | 1855          | 200          | -68.04              | Egypt, Alexandria         | Chl   |
| <i>Ulva reticulata</i> [45]                         | 16.72                | 4700          | 3690         | 2330          | 220          | -182.84             | India, Saurashtra coast   | Chl   |
| <i>Ulva rigida</i> [45]                             | 18.57                | 2640          | 4710         | 1770          | 160          | -164.23             | India, Saurashtra coast   | Chl   |
| <i>Ulva rigida</i> [36]                             | 19.5                 | 354           | 1364         | 1860          | 127          | -23.83              | Portugal, West Coast      | Chl   |
| <i>Ulva</i> sp. [41]                                | 15.6                 | 550           | 2180         | 5580          | 180          | -183.71             | Portugal                  | Chl   |
| <i>Ulva</i> sp. [35]                                | 7                    | 910           | 1950         | 3300          | 110          | -131.08             | Spain, Galicia            | Chl   |
| <i>Undaria pinnatifida</i> [35]                     | 18.6                 | 1120          | 370          | 760           | 540          | -13.00              | Spain, Galicia            | Pha   |

Table 1 is based on data from References [32–47]. Ca = Calcium. Mg = Magnesium. K = Potassium. P = Phosphorus. \*Chl. = Chlorophyta; Rho. = Rhodophyta; Pha. = Phaeophyceae. The nutrient content is based on 100 g dry weight, except for the following five items: *Acanthophora spicifera*, *Ulva flexuosa* (formerly *Enteromorpha flexuosa*), *Gracilaria edulis*, *Padina gymnospora*, and *Ulva fasciata*, which were obtained from Reference [40].

**3.2. Analyses by Phylum.** We additionally compared the PRAL-relevant nutrient content of the examined algae items by phylum (Chlorophyta vs. Rhodophyta vs. Phaeophyceae). For this analysis, only algae with nutrient content data based on dry weight were considered ( $n=101$ ). Significant differences between the three examined phyla were detected for protein, calcium, and magnesium. The highest median calcium and magnesium content were observed for the Chlorophyta phylum (Table 2). The PRAL values for the different phyla were as follows:  $-100.82$  ( $-159.74$  -  $(-67.35)$ ),  $-74.68$  ( $-150.91$  -  $(-20.59)$ ), and  $-105.90 \pm 94.66$  mEq/100 g. The PRAL differences were not statistically different ( $p = 0.367$ ).

**3.3. Correlation Analyses.** We ran multiple Spearman's correlations to assess the relationship between PRAL and the micronutrient content of the examined algae items. To visualize the interrelationship, we used portion sizes of 10 g of edible algae. As expected, a moderate and significant positive correlation was found for PRAL and protein (Figure 1), with a Spearman's rho of 0.35 ( $p < 0.001$ ). In a similar style, Figure 2 shows the relationship between PRAL and the potassium content of the examined algae. Hereby, a strong and significant inverse relationship (Spearman's rho =  $-0.79$ ,  $p < 0.001$ ) was observed.

Figures 3 and 4 display the calcium and phosphorus content of the examined macroalgae and their relationship with PRAL. Calcium content was inversely associated with PRAL (Spearman's rho:  $-0.34$ ,  $p < 0.001$ ), whereas phosphorus was positively associated with PRAL (Spearman's rho: 0.31,  $p = 0.001$ ). No significant relationship was observed between PRAL and magnesium content (not shown).

Figures 5–8 display phylum-separated scatterplots visualizing the PRAL value and the content of potassium, calcium, magnesium, and protein of each group. Apart from magnesium, no clear clustering was observed for the examined nutrients and PRAL values, indicating that not the phylum but the family and genus are important when it comes to the identification of alkalizing macroalgae.

## 4. Discussion

The present analysis explored the PRAL of  $n=106$  macroalgae. Results largely confirmed our hypothesis that algae have a strong alkalizing potential, with a mean PRAL value of  $-86.76 \pm 87.47$  mEq/100 g in the entire sample. We also found a strong inverse relationship of PRAL with algae's potassium content (Spearman's rho =  $-0.79$ ,  $p < 0.001$ ) and a moderate relationship with algae's calcium content (Spearman's rho:  $-0.34$ ,  $p < 0.001$ ). Both are important base precursors and can be readily found in algae. The median potassium content of the examined algae (2900 (3521.7) mg/100 g) is particularly noteworthy and substantially contributed to their low PRAL values in the examined sample. A reservation must be made, though, that our results could not confirm our second hypothesis: we found no

significant PRAL differences between the examined algae phyla/classes. In fact, the obtained separated scatterplots suggested that the family and genus are potentially more important when it comes to the PRAL value of algae.

Macroalgae and seaweed nowadays enjoy growing popularity in Western societies [1]. Their potential benefits in terms of dietary acid load and their alkalizing properties, however, have been rarely discussed. We raised the hypothesis that algae could be used as alkalizing agents due to their high content of base precursors. The very low (and to our best knowledge unmatched) PRAL value of many algae supports this idea. A typical contemporary Western diet produces between 60 and 100 mEq of acid per day [48, 49]. The human kidneys, in contrast, can only excrete 40–70 mEq of acid within 24 h [50]. Once that limit is reached, acid is retained in the human body, with potentially harmful effects for human health [51–56]. As summarized in a previous review, dietary acid load has been linked to several cardiovascular disease risk factors, unfavorable metabolic alterations, diabetes, and chronic kidney disease [20]. Algae could play an important role here, as our results suggest that the daily intake of only 10 g of algae may decrease the total PRAL score by up to  $-28.68$  mEq, depending on the consumed algae type. This might be of particular importance in patients with kidney disease, who benefit from the key features of an alkaline diet [57, 58]. A reservation must be made, however, that the alkalizing effect of algae is likely variable and depended on various other factors, including harvesting and processing.

Macroalgae are also considered good sources of other important and frequently under-consumed nutrients in the human diet, including fiber, omega-3 and omega-6 fatty acids, selenium, iodine, and vitamin B<sub>12</sub> [1, 6–9]. Including them in menus on a more frequent basis could thus serve many concomitant purposes beyond a simple PRAL reduction. Algae supplements of particularly alkalizing species (*Laminaria ochroleuca*, *Gelidium micropterum*, and *Palmaria palmata*) are also a possible idea but have not yet been tested to the best of our knowledge.

While seaweeds have been suggested as important functional ingredients for a healthy diet [2], their high biosorption and accumulation capacities must also be kept in mind [1]. Some macroalgae have been reported to include high amounts of potentially harmful elements, including (but not limited to) lead, cadmium, mercury, and inorganic arsenic [59–61]. While a detailed discussion of this topic is beyond the scope of this PRAL analysis, one must keep in mind that an excessive algae consumption could be harmful, as well. Finally, algae also stand out for their high iodine content [62, 63]. While not contributing to the PRAL of algae, a regular and excessive intake of iodine could be problematic in certain individuals and patient groups, potentially inducing autoimmune thyroiditis and other adverse medical conditions [64]. Whether suitable under such circumstances remains an individual decision and warrants thorough context-specific considerations.

While our analysis fills a gap in the field of PRAL and dietetics, it has several limitations that must be considered.

TABLE 2: Macro- and micronutrient content of  $n = 101$  macroalgae based on 100 g dry weight.

| Nutrient          | Chlorophyta ( $n = 26$ ) | Rhodophyta ( $n = 50$ ) | Phaeophyceae ( $n = 25$ ) | $p$ value |
|-------------------|--------------------------|-------------------------|---------------------------|-----------|
| Protein (g/100 g) | 16.31 $\pm$ 6.75         | 16.05 (11.95)           | 10 (5.85)                 | 0.001     |
| Ca (mg/100 g)     | 1612 (2980)              | 647 (1160)              | 1160.27 (839.4)           | <0.001    |
| K (mg/100 g)      | 2517 (2310)              | 3095 (4767)             | 3600 (4610)               | 0.170     |
| Mg (mg/100 g)     | 1790 (1074)              | 557.5 (450)             | 813 (198)                 | <0.001    |
| P (mg/100 g)      | 210 (1498)               | 238.5 (239)             | 190 (307)                 | 0.581     |

Ca = Calcium. Mg = Magnesium. K = Potassium. P = Phosphorus.

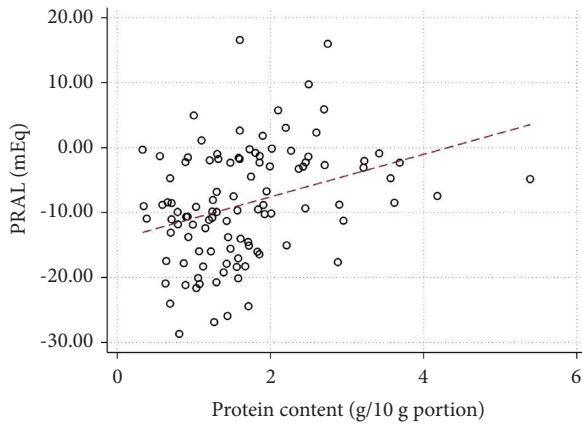


FIGURE 1: Scatterplot visualizing the relationship between PRAL (in mEq) and the protein content (in g in a 10 g edible macroalgae portion).  $n = 101$  algae were considered for this analysis.

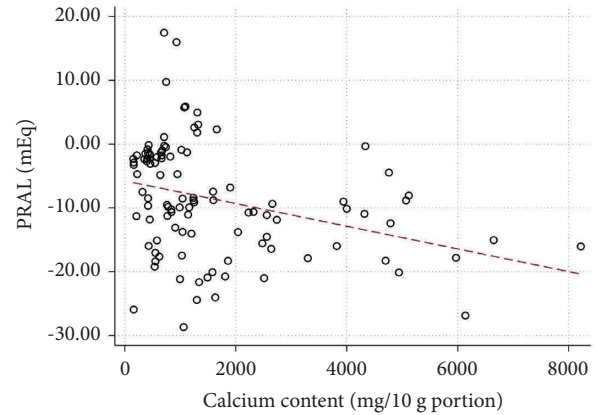


FIGURE 3: Scatterplot visualizing the relationship between PRAL (in mEq) and the calcium content (in mg) in a 10 g edible macroalgae portion.  $n = 101$  algae were considered for this analysis.

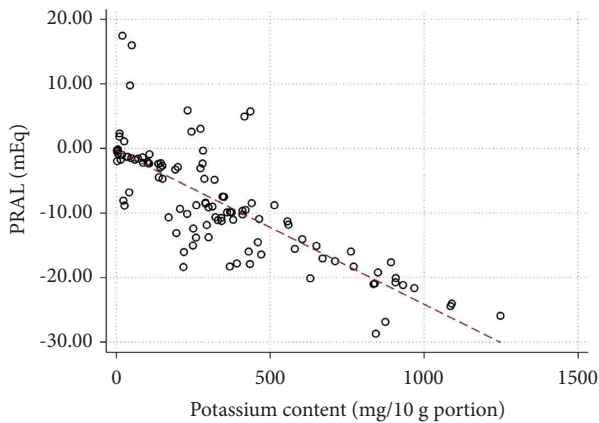


FIGURE 2: Scatterplot visualizing the relationship between PRAL (in mEq) and the potassium content (in mg) in a 10 g edible macroalgae portion.  $n = 101$  algae were considered for this analysis.

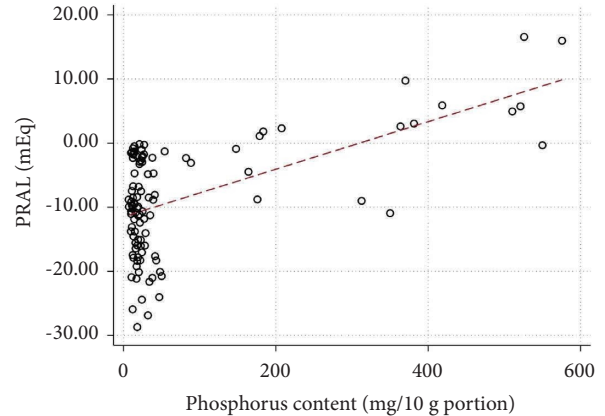


FIGURE 4: Scatterplot visualizing the relationship between PRAL (in mEq) and the phosphorus content (in mg) in a 10 g edible macroalgae portion.  $n = 101$  algae were considered for this analysis.

The cross-sectional analysis does only allow for preliminary statements, and randomized-controlled trials will be necessary to test the alkalinizing potential of algae in a clinical setting. We also observed a large heterogeneity in the PRAL value of the examined macroalgae. While origin was registered, other factors were not considered in the present analysis. These include harvesting techniques, harvesting season, and processing methods to name a few. As for the origin, we mainly investigated mainly algae

found in India ( $n = 35$ ), Sweden ( $n = 22$ ), and Russia ( $n = 14$ ). Additional items came from Argentina ( $n = 1$ ), Egypt ( $n = 13$ ), France ( $n = 1$ ), Japan and Korea ( $n = 3$ ), Portugal ( $n = 9$ ), and Spain ( $n = 8$ ). It is known that macroalgae have a varying nutritional profile, depending on their origin and the surrounding environmental conditions in which they grow [28, 29]. The diverse origin of the examined algae items must thus be kept in mind when discussing our results.

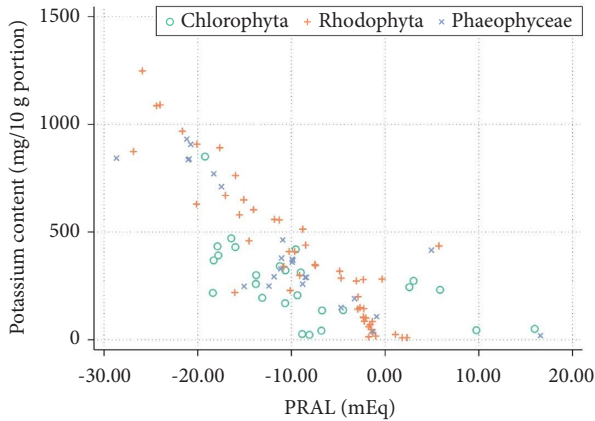


FIGURE 5: Scatterplot visualizing the PRAL value (in mEq) and the potassium content (in mg) in a 10 g edible macroalgae portion by phylum/class.  $n = 101$  algae were considered for this analysis.

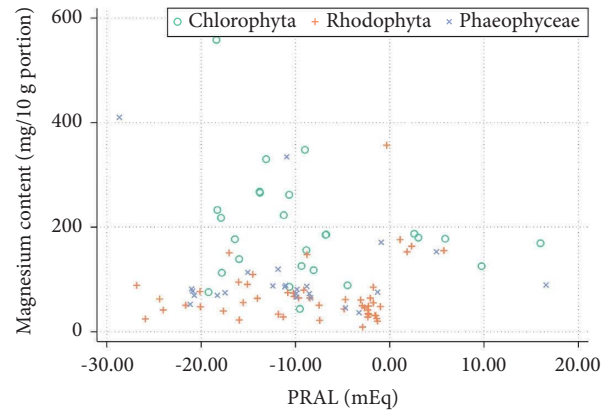


FIGURE 8: Scatterplot visualizing the PRAL value (in mEq) and the magnesium content (in mg) in a 10 g edible macroalgae portion by phylum/class.  $n = 101$  algae were considered for this analysis.

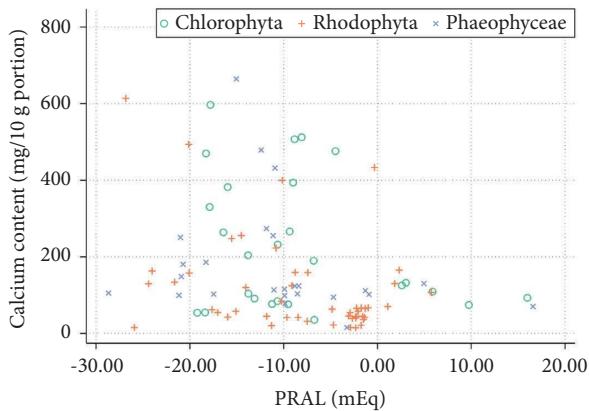


FIGURE 6: Scatterplot visualizing the PRAL value (in mEq) and the calcium content (in mg) in a 10 g edible macroalgae portion by phylum/class.  $n = 101$  algae were considered for this analysis.

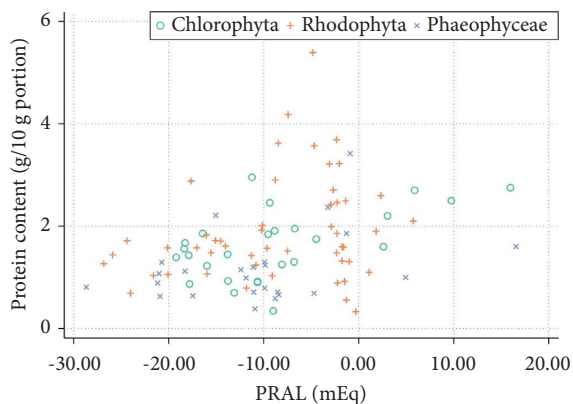


FIGURE 7: Scatterplot visualizing the PRAL value (in mEq) and the protein content (in g in a 10 g edible macroalgae portion by phylum/class.  $n = 101$  algae were considered for this analysis).

Further to that, it must be emphasized that the laboratory methods to determine the nutrient content of the examined algae items varied from study to study. Supplementary Table 1 gives a brief overview about the employed

analytical methods (Supplementary Table 1). The varying analytical techniques must also be kept in mind when glancing at our results and could pose a potential confounder.

Future studies will be necessary to explore these factors in greater detail. Despite these limitations, this analysis also builds upon a number of strengths, including its innovative character, the rigorous search strategy, and the modest sample size. Nevertheless, additional studies will be necessary to understand the role of macroalgae in PRAL management.

## 5. Conclusion

Many macroalgae apparently exert a strong alkalinizing potential. This suggests a potential role for algae as alkalinizing marine drugs for individuals who benefit from a more alkaline diet.

## Data Availability

The datasets used and analyzed to support the findings of this study are available from the corresponding author upon reasonable request.

## Additional Points

*Institutional Review Board Statement.* This study is a secondary data analysis that does not involve human participants or animals.

## Disclosure

This study is a secondary data analysis that does not involve human participants or animals.

## Conflicts of Interest

The author declares that they have no conflicts of interest.



## Authors' Contributions

Maximilian Andreas Storz is the sole author of this article.

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## Supplementary Materials

Supplementary Table 1 gives a brief overview about the employed analytical methods that were used in the original studies to determine algae's nutrient content (Supplementary Table 1). (*Supplementary Materials*)

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