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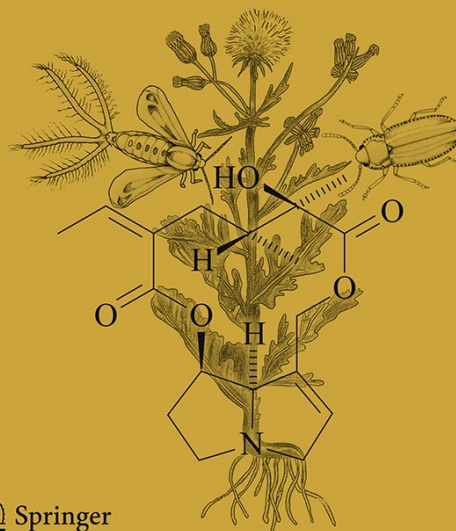
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Preliminary evidence that the feeding rates of generalist marine herbivores are limited by detoxification rates

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Abstract Herbivores tend to increase feeding rate and fitness when consuming a mixed diet relative to a single diet. According to the detoxification limitation hypothesis (DLH), feeding choices and rates when confronted with chemically rich plants are determined by herbivore physiology, and specifically by the metabolic pathways that herbivores use to manipulate secondary metabolites. We tested two predictions of the DLH using two generalist herbivores, the urchin *Arbacia punctulata* and amphipod *Ampithoe longimana*. These herbivores have geographic ranges which overlap with brown seaweeds that produce diterpenes (*Dictyota menstrualis*, *D. ciliolata*) and a green seaweed that produces sesquiterpenes and diterpenes (*Caulerpa sertularioides*). As predicted by the DLH, herbivore consumption rates in no-choice feeding assays were limited by extract intake rates. This suggests an upper limit in the herbivores' abilities to physiologically manipulate seaweed metabolites. Contrary to a second prediction of the DLH, urchins consumed equal amounts of foods coated with limiting concentrations of two seaweed extracts offered singly, as a mixture, or as a pairwise choice. This result suggests that secondary metabolites of these seaweeds are manipulated by a linked set of detoxification pathways. Improving our understanding of the mechanisms that underlie diet mixing depends on greater attention to the physiology of herbivore resistance to secondary metabolites.

Keywords Marine seaweed–herbivore interactions · Plant secondary metabolites · Generalist diets · Foraging

Introduction

Generalist herbivores play central roles in regulating and structuring ecosystems, determining spatial patterns of biodiversity, and the cycling of nutrients and materials through ecosystems (Stachowicz et al. 2007; Stephens et al. 2007). Many terrestrial (Novotny et al. 2002) and most marine herbivores (Poore et al. 2008) are generalists, and several studies demonstrate that generalist herbivores actively seek a mixed diet (e.g., Horn 1983; Kitting 1980; Lyons and Scheibling 2007; Pennings et al. 1993). Consumption of a mixed diet tends to increase overall feeding rates and can increase overall herbivore performance (growth, survival or fecundity) relative to single-species diets, although performance on the best single-species diet can match performance on mixed diets (see review by Stachowicz et al. 2007; Cruz-Rivera and Hay 2000; Hemmi and Jormalainen 2004; Lobel and Ogden 1981; Pennings et al. 1993; Scheibling and Anthony 2001; Steinberg and van Altena 1992).

Marine and terrestrial plants produce secondary metabolites (Sotka et al. 2009) and physiological limitations on herbivores' ability to manipulate plant secondary metabolites (or PSMs) can help explain why generalist herbivores tend to seek out a mixed diet (Freeland and Janzen 1974; Marsh et al. 2006a). Specifically, the detoxification limitation hypothesis (DLH) predicts that consumers maximize intake, and subsequently fitness, by actively selecting a mixed diet with non-overlapping detoxification pathways. An excellent example is the *brush-tail possum*, *Trichosurus vulpecula*, which consumed greater quantities of two PSMs

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when offered in paired-choice assays than when either were offered as a single diet, if and only if, those two compounds were metabolized via different biochemical pathways within the herbivore (e.g., Phase I hydrolysis versus Phase II conjugation; (Marsh et al. 2006b)). For marine consumers, it is unknown whether generalists' feeding strategies relate to limitations in detoxification or other factors promoting a mixed diet (e.g., nutrient complementarity (Raubenheimer et al. 2005) or sensory-specific satiety (Provenza 1996), as to our knowledge, there are no direct tests of these mechanisms. Thus, while the literature is replete with examples of the benefits of a mixed diet for feeding rates and fitness, the mechanisms that underlie these examples are rarely tested (Marsh et al. 2006a, b).

Here, we use two generalist herbivores and three seaweeds common to southeastern estuaries of the United States to test predictions of the DLH. The sea urchin *Arbacia punctulata* and amphipod *Ampithoe longimana* occur across a broad geographic range from subtropical Florida to New England. In North Carolina, both herbivores are known to consume a variety of seaweeds (Hay et al. 1986; McCarty and Sotka 2012). One seaweed genus that these herbivores encounter within North Carolina estuaries is the chemically rich genus *Dictyota* (*D. menstrualis* and *ciliolata*; Duffy and Hay 1994). The principal secondary metabolites of North Carolina *Dictyota* are diterpene alcohols: both *D. menstrualis* and *D. ciliolata* produce pachydictyol A and dictyodial, *D. menstrualis* produces dictyol E and *D. ciliolata* produces dictyol B acetate (Cronin and Hay 1996a, b). *Ampithoe longimana* is a generalist herbivore, but North Carolina populations have greater feeding tolerance for *Dictyota* species than do populations from New England or Florida (McCarty and Sotka 2012; Sotka and Hay 2002). We also collected and extracted Florida populations of the green seaweed *Caulerpa sertularioides*. This chemically rich green seaweed does have congeneric populations in North Carolina where *Arbacia* and *Ampithoe* reside (Alphin et al. 1997) and its geographic range overlaps with *Arbacia* and *Ampithoe* in subtropical Florida. We added this seaweed because the principal metabolites that deter herbivores are diterpenes and sesquiterpenes, and the latter are potentially detoxified by a separate enzymatic pathway than those used to detoxify diterpenes (Baumgartner et al. 2009; Meyer and Paul 1992). The fact that North Carolina herbivores encounter *Caulerpa* locally, but not *C. sertularioides* in particular admittedly may limit the ecological realism of our results. However, it is likely that NC herbivores are familiar with sesquiterpenes found in the *C. sertularioides*, as congeneric species consistently produce similar blends of broad classes of metabolites (Blunt and Munro 2008).

We are testing two predictions of the DLH. First, we test whether an herbivore will lower its feeding rate with increasing concentrations of PSM in a dose-dependent manner. Such dose dependency is indicative of limitations in the ability of the herbivore to absorb, distribute, metabolize (or detoxify), and excrete (or ADME; Sorensen et al. 2006). Terrestrial studies commonly use no-choice dose-dependent assays where herbivores are isolated with a single food choice, but to our knowledge, nearly all marine studies of anti-herbivory effects of seaweed metabolites utilize feeding-choice assays or no-choice assays at a single-metabolite dosage (e.g., Cruz-Rivera and Hay 2003). Choice assays are a more indirect proxy of ADME processes than no-choice assays.

Second, we test the notion that a mixture of seaweeds with distinct suites of secondary metabolites (especially *Dictyota* vs. *Caulerpa*) will increase total feeding rates relative to feeding rates on seaweeds that are offered singly. Although we have a reason to suspect that *Dictyota* and *Caulerpa* differ profoundly in their chemical constituents, we did not measure the levels or types of compounds ourselves, and more importantly do not know whether their metabolites are detoxified by distinct pathways. Thus, we tested whether an herbivore consumes more of foods with a mixture of metabolites from two seaweeds, relative to metabolites from a single food. In this way, our assays more directly mimic ecologically realistic choices than single-metabolite assays.

Materials and methods

Organisms

Amphipods were collected from a mixture of seaweeds at <1 m depth from Jamestown, R.I. (41.49°N 71.38°W) and Bogue Sound, NC (34.72°N 76.70°W) and returned to the Grice Marine Laboratory in Charleston, SC (32.78°N 79.93°W). Approximately 50 females were used to populate laboratory cultures for several months before assays began. We maintained cultures with a diversity of seaweeds available in Charleston Harbor [*Ulva* (formerly *Enteromorpha*) spp.; 32.75°N 79.90°W] and Bogue Sound, NC (*Sargassum filipendula*, *Hypnea musciformis*). Sixty sea urchins (*A. punctulata*) were collected from floating docks in Bogue Sound, NC and transported within aerated coolers to the Grice Marine Laboratory. Urchins were held within plastic cages punched with holes, and cages were floated within a large aerated tank with self-circulating seawater at room temperature and a salinity of 32 ‰. Urchins were allowed to feed on a diet of *Gracilaria vermiculophylla* seaweed collected in Charleston Harbor

(Byers et al. 2012). All urchin assays were performed within 3 weeks of collection.

Seaweeds used in the feeding assays were collected from Bogue Sound, NC (*H. musciformis*, *D. ciliolata* and *D. menstrualis*), Charleston Harbor [*G. vermiculophylla*, *Ulva lactuca*, and *Ulva* (formerly *Enteromorpha*) spp.], and Indian River Lagoon, FL (*C. sertularioides*; 27.45°N 80.32°W). Seaweeds used in feeding assays were immediately frozen on dry ice and returned to Grice Marine Laboratory for storage at −20 °C.

Extraction

The chemically rich seaweeds (*Dictyota* and *Caulerpa*) were lyophilized and ground into a fine powder with a Wiley mill, and then extracted thrice with a 1:1 solution of ethyl acetate and methanol (using a ratio of 40:1 total solvent to seaweed drymass). Solvents were removed by rotary evaporation and a gentle flow of N₂ gas. The natural concentrations of seaweed extracts were established by dividing extract drymass by total seaweed drymass.

Dose-dependent feeding assays

We offered herbivore populations foods coated with a range of extract concentrations (0–300 % of natural concentration) in no-choice feeding assays. For all assays, our basal food was a mixture of several species (29 % *Ulva* (formerly *Enteromorpha* spp.), 39 % *Gracilaria* spp., 4 % *U. lactuca*, and 27 % *H. musciformis*). The extracts were dissolved in 30 mL of ethyl acetate and mixed with the basal food (the drymass of extract and food summed to 6 g). Solvent was then removed using rotary evaporation. The food was mixed with 21 mL of H₂O and combined with 1.5 g of agar boiled in 56 mL of H₂O. The mixture was cooled slightly, and poured onto (1 mm mesh) window screening and allowed to harden. Window screen was cut into 1,000 square portions and offered singly to each urchin. Urchins were allowed to feed overnight (approximately 16–18 h) and in darkness and at room temperature, at which point the assay ceased and the number of food squares eaten was counted. Assay replicate size was $n = 8–10$, with the exception of the lower concentrations of *Dictyota ciliolata* and *D. menstrualis* in which we repeated assays to generate accurate estimates of limiting concentration ($n = 15–26$). Assays were generally similar for amphipods [see McCarty and Sotka 2012 for details], except that sample size was between $n = 4–10$. We recognize that these low sample sizes in amphipod assays may have limited our inferential power.

The dose-dependent feeding rates were then analyzed using permutation ANOVAs, in which a null distribution was generated by resampling the dataset 1,000 times and

Table 1 Limiting concentrations (extract concentrations at which feeding was reduced by 50 % relative to the control). Natural concentrations of extracts are 7.55 % (*Dictyota menstrualis*), 13.47 % (*D. ciliolata*), and 9.74 % (*Caulerpa sertularioides*)

Animal	<i>Dictyota menstrualis</i> (%)	<i>Dictyota ciliolata</i> (%)	<i>Caulerpa sertularioides</i> (%)
<i>Arbacia</i>	1.35	3.65	7.50
N.C. <i>Amphithoe</i>	5.57	10.09	N/A
R.I. <i>Amphithoe</i>	4.07	7.84	6.92

calculating F values (1,000 permutation replicates). Pairwise post hoc tests were analyzed using a series of permutation ANOVA ($\alpha = 0.05$). To provide an estimate of extract consumption, the total consumption rate was multiplied by extract concentration (e.g., 5 % \times 10 total squares = 0.5 squares of extract consumed). The limiting dose is the concentration at which each extract reduced the feeding rate by 50 % [sensu (Marsh et al. 2006b); Table 1]. These estimates were calculated by applying a linear regression (analyses not shown) across the lower extract concentrations (i.e., less than or equal to natural concentrations) where dose-dependent relationship is nearly linear.

Single- vs. multiple extract assays

In a second type of trials, we compared the feeding rates of individual *Arbacia* urchins offered one of five treatments: control foods (0 % extract), extracts from seaweed A, extracts from seaweed B, a pairwise choice of extracts from seaweed A vs. B, or a mix of the two extracts. Extracts were added at half the limiting dose in the mixed food, and at limiting dose for the other treatments. The assay was conducted and analyzed similarly as that for the dose-dependent feeding assay. Because Marsh et al. (2006b) indicates that the most robust test of DLH requires that the mixed food uses the limiting dose; we repeated the comparison of *D. ciliolata* and *C. sertularioides* using this higher dose. Assay replicate size was $n = 9–12$.

Results

Dose-dependent feeding assays

Herbivores were generally deterred by *Dictyota* and *Caulerpa* extracts in a dose-dependent manner (Fig. 1). At natural extract concentrations, herbivores had significantly lower feeding rates relative to control foods. The exception to these patterns were when North Carolina amphipods were offered extracts of *D. ciliolata*, which did not significantly lower feeding rates with dosage.

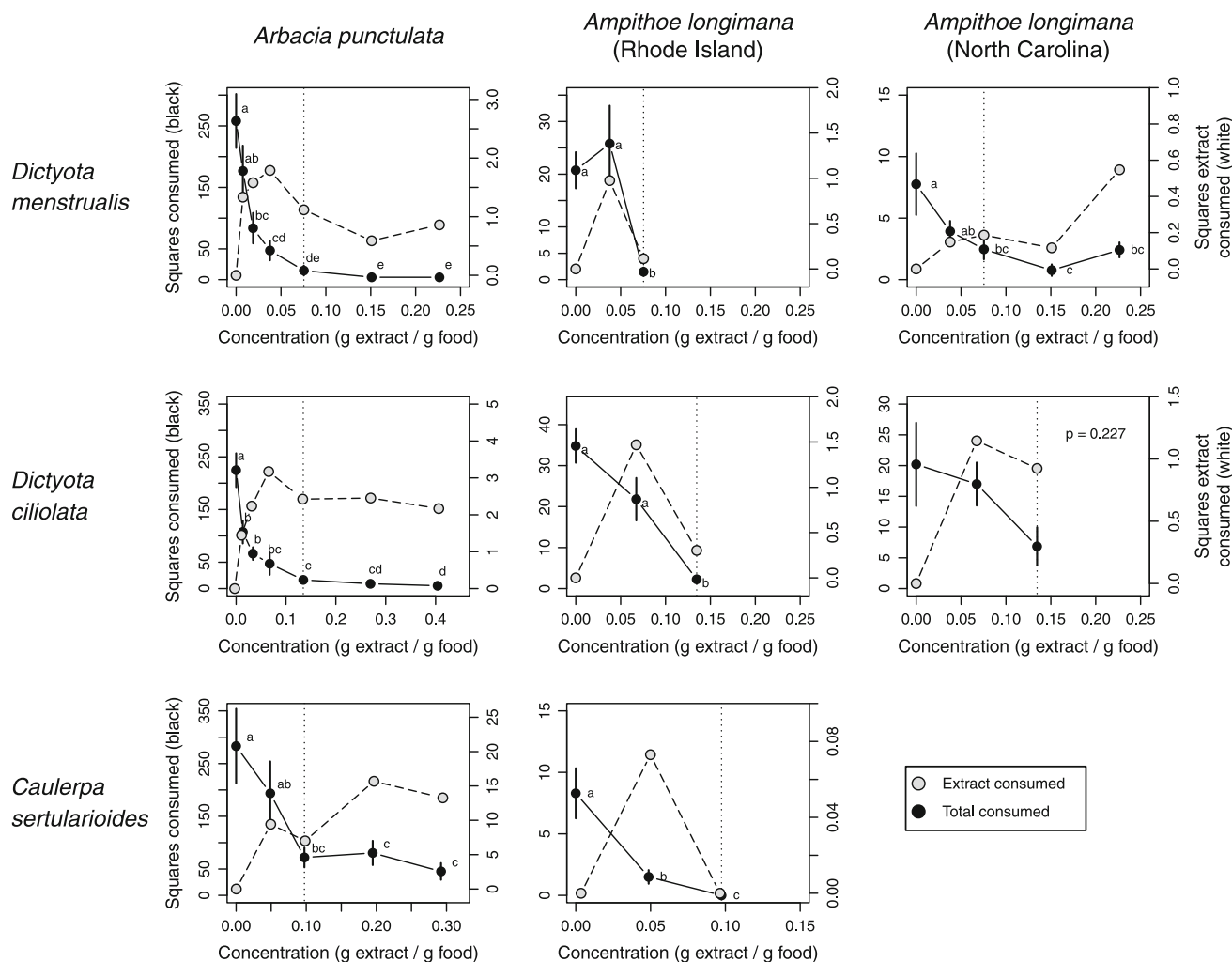


Fig. 1 Dose-response curves for the sea urchin *Arbacia punctulata*, and two populations of the amphipod *Ampithoe longimana* (Rhode Island and North Carolina) when offered foods coated with lipophilic

extract from the seaweeds *Dictyota menstrualis*, *D. ciliolata*, and *Caulerpa sertularioides*. The dashed line indicates the naturally occurring concentration of an extract

Herbivores generally increased their extract intake rate with increasing dosage until an upper limit was reached (note the extract-consumption rates indicated by the gray points in Fig. 1). In some cases, this upper limit was clear (e.g., *D. ciliolata* extracts consumed by *Arbacia*), while in others the limit was less clear (*D. menstrualis* extracts consumed by NC *Ampithoe*).

These no-choice assays clearly differentiated feeding tolerance for secondary metabolites across herbivore species and populations (Fig. 2). When offered *Dictyota* species at half-natural concentrations, *Ampithoe* amphipods consumed 300–2,100 % more extract-coated foods than did *Arbacia* urchins. Interestingly, the pattern reversed when offered *C. sertularioides*, where *Arbacia* urchins significantly extract more than did R.I. *Ampithoe*. Within *A. longimana*, North Carolina populations consumed 400 % more *D. menstrualis* extracts and 500 % more *D. ciliolata* extracts at natural concentrations than did Rhode

Island populations. In fact, the collapse in feeding resistance when offered natural concentrations of *Dictyota* extracts among Rhode Island *Ampithoe* was so complete that urchins and Rhode Island *Ampithoe* were statistically indistinguishable at natural concentrations of *Dictyota* extracts.

Single- vs. multiple extract assays

The feeding rates of *Arbacia* were statistically indistinguishable when offered foods coated with a single extract versus two artificial foods coated with separate extracts in a pairwise choice (Fig. 3). This was true in all paired comparisons. When herbivores were offered a mixture of extracts from *D. menstrualis* and *D. ciliolata* or *D. menstrualis* and *Caulerpa* (each at half-limiting concentrations), mixed and single diets were consumed at statistically equivalent rates (Fig. 3a, c). When *Caulerpa* and *D. ciliolata* were

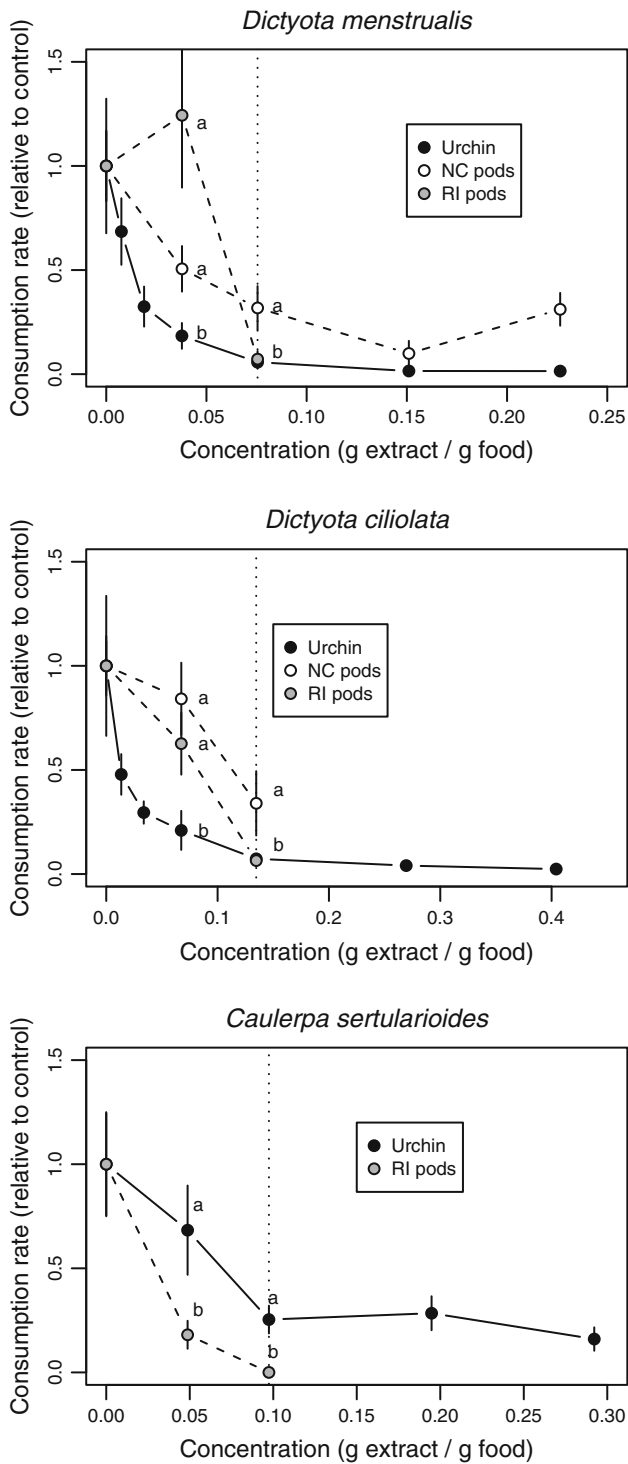


Fig. 2 Dose-response curves for *Arbacia* and two *Amphitoe longimana* populations on extracts from three seaweeds. All consumption rates were standardized by the average consumption rate on control foods. Means that share the same letter are statistically indistinguishable using pairwise permutation tests. The dashed line indicates the naturally occurring concentration of an extract

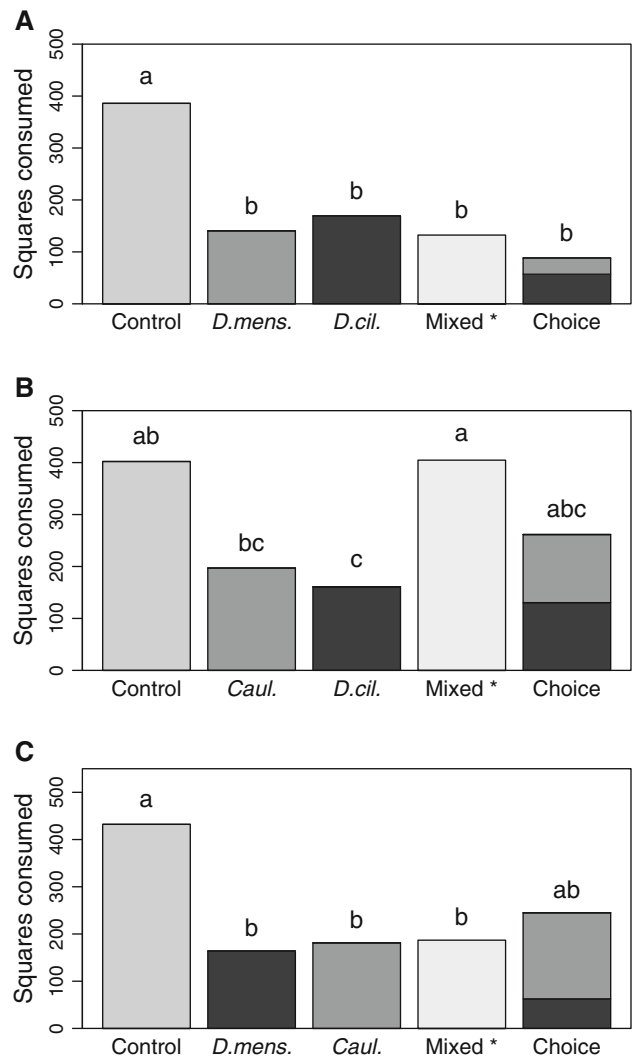


Fig. 3 Feeding rates by the sea urchin *Arbacia punctulata* on foods coated with or without lipophilic extracts. For each pairwise comparison (a *Dictyota menstrualis* vs. *D. ciliolata*, b *Caulerpa* vs. *D. ciliolata*, c *D. menstrualis* vs. *Caulerpa*), urchins were offered either control foods, a food coated with one extract, a food coated with both extracts ('Mixed'), or a choice between two extract-coated foods ('Choice'). The separate colors within 'Choice' indicate the proportion consumed of each seaweed extract. Extracts were applied at limiting concentrations (Table 1) in single extract and 'Choice' diets and at half-limiting-concentration within 'Mixed' diets. Letters indicate treatments that were consumed at statistically indistinguishable rates, as determined by permutation tests

offered at half-limiting concentrations in a mixture, this diet was more readily consumed than either of the single diets (Fig. 3b). When we repeated this assay using a mixture of extracts at limiting concentrations, the mixed diet and single diets were consumed at statistically equivalent rates (Fig. 4).

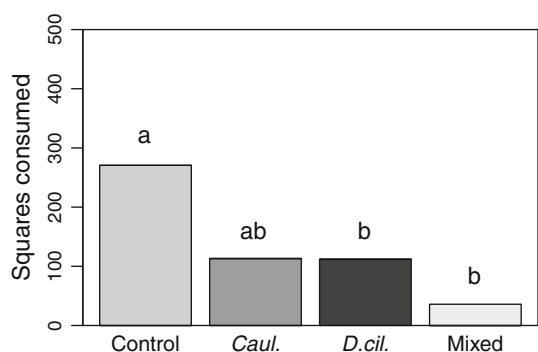


Fig. 4 No-choice feeding rates by the sea urchin *Arbacia punctulata* on lipophilic extracts from *Caulerpa* and *Dictyota ciliolata*. This assay partially replicates the assay presented in Fig. 3b, except that the 'Mixed' foods were coated with limiting concentrations of both extracts. Letters indicate treatments that were consumed at statistically indistinguishable rates, as determined by permutation tests

Discussion

We found support for one of two predictions of the DLH in this set of herbivores and seaweeds. First, feeding rates of herbivores forced to consume chemically defended foods were limited by extract intake rates, as predicted by the DLH. While this relatively straightforward result is not novel for terrestrial herbivores (Marsh et al. 2006a), we know of no analogous study of dose-dependent feeding rate in a marine herbivore. Previous marine studies tend to increase the dosage of metabolites across a series of pairwise choice assays (e.g., Baumgartner et al. 2009; Cronin and Hay 1996b; Cronin et al. 1997; Erickson et al. 2006). Such choice assays measure feeding preferences, and at best, are an indirect proxy for feeding rates and the extract concentrations that limit these feeding rates. Whether extract intake rates limit feeding rates of herbivores in the field will depend in part on nutritional considerations (Forbey et al. 2013; Raubenheimer and Simpson 2009). As an example, when herbivores are forced to consume chemically defended plants with low nutritional quality, herbivores may compensate by feeding at a higher rate and as a consequence, will consume higher levels of secondary metabolites than they can detoxify (Slansky and Wheeler 1992).

The results of no-choice feeding assays confirm patterns of feeding preferences between-species and between-populations that were previously documented. *Arbacia punctulata* avoids *Dictyota* species (Hay et al. 1986), is readily deterred by its whole extract (Bolser and Hay 1996) and natural concentrations of its diterpene alcohols. In contrast, North Carolina *A. longimana* uses *Dictyota* species as habitat and food, readily consumes *Dictyota* tissue, and is rarely deterred by whole tissue extracts (Duffy and Hay 1991; Sotka and Reynolds 2011) or its diterpene

alcohols at natural concentrations (Cronin and Hay 1996a, b). Populations of the *A. longimana* from Rhode Island do not co-occur with *Dictyota* and have evolved a lower feeding preference for and juvenile fitness on *Dictyota* relative to North Carolina amphipods, and a geographic difference in feeding resistance for *Dictyota* extracts is likely responsible (McCarty and Sotka 2012; Sotka and Hay 2002; Sotka et al. 2003). Consistent with these previous choice assays, North Carolina *Ampithoe* consumed significantly more *Dictyota* extracts than did either Rhode Island *Ampithoe* or *Arbacia*.

The second prediction of the DLH is that herbivores will have greater total consumption rates when two diets are offered as a mixture or choice, relative to consumption rates on single diets. We did not confirm this prediction, as there were no significant differences in consumption rates among choice and single food replicates. One type of mixed diet (*Caulerpa* and *D. ciliolata*) was consumed at a rate greater than either separately; however, this initial assay used half-limiting concentrations. When repeated at limiting concentrations (following conventions of Marsh et al. 2006b), mixed and single diets were consumed at statistically equivalent rates. Thus, we infer that *Arbacia* detoxifies *Caulerpa* extracts (containing both diterpenoids and sesquiterpenoids) and *Dictyota* extracts (containing only sesquiterpenoids) in a similar manner. This has to be considered a preliminary interpretation, because understanding the mechanism of detoxification is central to a proper test of DLH (Marsh et al. 2006a, b) and we have no a priori information on detoxification pathways.

It is unlikely that neither nutritional complementarity nor sensory-specific satiety play a role in this set of herbivores and seaweeds. Our solvents (ethyl acetate and methanol) extract include all lipophilic and slightly polar compounds and may include chemical constituents that are required by urchins. However, the strongly negative correlation between feeding rate and extract concentration does not suggest feeding rates are motivated by nutritional concerns. Moreover, we found no difference in feeding rates when offered mixed versus choice of foods, suggesting that sensory-specific satiety does not play a role here either.

By our count, the DLH has been cited as a potentially important factor in motivating diet mixing by at least 22 articles on marine herbivores (all of which cite Freeland and Janzen 1974). Among these, only four compared feeding rates or fitness on a mixed versus single diet (Cruz-Rivera and Hay 2000; Lyons and Scheibling 2007; Pennings et al. 1993; Poore and Hill 2006; see also Cruz-Rivera and Hay 2001). In no case were any of the hypothesized mechanisms that underlie the benefits of a mixed diet directly tested (DLH, nutritional complementarity or sensory-specific satiety). Clearly, we require greater mechanistic understanding of the physiology

of consumer resistance to prey secondary metabolites (DeBusk et al. 2008; Sotka et al. 2009; Vrolijk et al. 1995; Whalen et al. 2010), as has been seen among many terrestrial herbivores (Dearing et al. 2005; Foley and Moore 2005).

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