Effectiveness of topical antibiotics in treating corals affected by Stony Coral Tissue Loss Disease

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Since 2014, Stony Coral Tissue Loss Disease (SCTLD) has led to mass mortality of the majority of hard coral species on the Florida Reef Tract. Following the successful treatment of SCTLD lesions on laboratory corals using water dosed with antibiotics, two topical pastes were developed as vehicles to directly apply antibiotic treatments to wild corals. These pastes were tested as placebos and with additions of amoxicillin on active SCTLD lesions on multiple coral species. The effectiveness of the pastes without antibiotics (placebo treatments) was less than 10%, no different from untreated controls. Adding amoxicillin to both pastes significantly increased effectiveness to 70% and 84%. Effectiveness with this method was seen across five different coral species, with success rates of the more effective paste ranging from 67% (*Colpophyllia natans*) to 90% (*Orbicella faveolata* and *Montastraea cavernosa*). Topical antibiotic application is a viable and effective tool for halting disease lesions on corals affected by SCTLD.

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2 **Disease**

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13 **Abstract**

14 Since 2014, Stony Coral Tissue Loss Disease (SCTLD) has led to mass mortality of the majority

15 of hard coral species on the Florida Reef Tract. Following the successful treatment of SCTLD

16 lesions on laboratory corals using water dosed with antibiotics, two topical pastes were

17 developed as vehicles to directly apply antibiotic treatments to wild corals. These pastes were

18 tested as placebos and with additions of amoxicillin on active SCTLD lesions on multiple coral

19 species. The effectiveness of the pastes without antibiotics (placebo treatments) was less than

20 10%, no different from untreated controls. Adding amoxicillin to both pastes significantly

21 increased effectiveness to 70% and 84%. Effectiveness with this method was seen across five

22 different coral species, with success rates of the more effective paste ranging from 67%

23 (*Colpophyllia natans*) to 90% (*Orbicella faveolata* and *Montastraea cavernosa*). Topical

24 antibiotic application is a viable and effective tool for halting disease lesions on corals affected

25 by SCTLD.

26

27 **Introduction**

28 Beginning in 2014, a disease since named Stony Coral Tissue Loss Disease (SCTLD) appeared

29 on scleractinian corals near Miami, Florida (Precht et al. 2016). It has since spread throughout

30 the Florida Reef tract with a spatial pattern following a contagious model of transmission (Muller

31 et al. 2020). Beginning in 2017, SCTLD began appearing in other regions of the Caribbean

32 (Alvarez-Filip et al. 2019; Weil et al. 2019). The disease is known to affect over 20 species of

33 corals and is characterized by multifocal acute lesions that in some cases are preceded by a

34 bleaching margin (FKNMS/DEP 2018). It is highly virulent, and capable of being transmitted by

35 physical contact and also through seawater (Aeby et al. 2019). Progression of lesions across a

36 colony is rapid compared to most other coral diseases, and in the majority of cases, lesions result

37 in complete colony mortality. Ecosystem impacts are substantial and include significant

38 decreases in coral cover, colony density, and biodiversity (Precht et al. 2016; Walton et al. 2018).

39 Fulfillment of Koch's postulates for coral diseases is particularly difficult (Richardson 1998) and

40 definitive pathogen identification for SCTLD has not been successful. However, efforts to

41 identify the cause of the epidemic are ongoing and have identified differences in bacterial

42 communities between healthy and diseased corals (Meyer et al. 2019; Rosales et al. 2020).

43 Additionally, early laboratory work noted that water dosing with antibiotics resulted in disease

44 cessation (O'Neil et al. 2018; Aeby et al. 2019), suggesting a bacterial component. Though both

45 amoxicillin and ampicillin water baths were effective, ampicillin was preferred as it dissolved

46 more easily. Follow up efforts by NOAA's Coral Disease and Health Consortium (C Woodley,

47 pers comm) developed a modified dental paste that could be applied to disease margins; this

48 product is still in use by laboratories and aquariums treating SCTLD-affected corals (O'Neil et al.

49 2018). However, the use of the modified dental paste requires patting the coral dry and

50 maintaining it in low water flow for 18 hours, making it impracticable on wild corals. To resolve

51 this, partnerships between the authors, the Florida Aquarium, and a pharmaceutical formulation

52 and manufacturing company (Ocean Alchemists LLC and CoreRx Pharmaceuticals) led to the

53 development of topical pastes that could be used in field applications to determine whether

54 SCTLD could be stopped on in situ colonies with active lesions.

55 This study compared the effectiveness of untreated controls, two placebo topical pastes (here

56 termed Base 2b and New Base), and both pastes with amoxicillin additives to determine whether

57 disease lesions could be halted.

58

Materials & Methods

60 Corals affected with Stony Coral Tissue Loss Disease were selected for treatment at Sand Key

61 (Fig. 1) in the lower Florida Keys (permit from Florida Keys National Marine Sanctuary #2019-

62 115). Colonies were located within a 4000 m^2 area ranging in depth from 5 to 13 meters.

63 A total of 61 corals representing five species were selected for experimental treatment in October

64 2019. Each colony had between 1 and 12 active SCTLD lesions, and a total of 171 lesions were

65 treated (Table 1). Due to the limited availability of suitable colonies and the varying number of

66 lesions on each, the numbers of colonies and lesions were not the same across species and

67 treatments. Three species (*Colpophyllia natans, Montastraea cavernosa, Orbicella faveolata*)

68 were represented across all treatments. *C. natans* has been identified as a highly susceptible

69 species, while *M. cavernosa* and *O. faveolata* have been classed as intermediately susceptible

70 species (FKNMS/DEP 2018). Two additional highly susceptible species, *Diploria*

71 *labyrinthiformes* and *Pseudodiploria strigosa,* were compared between just two treatment types.

72 Selected colonies all had visibly active and rapidly progressing SCTLD disease lesions as

73 identified by at least 1 cm of bright white bare skeleton adjacent to live tissue. Colonies had

74 maximum linear dimensions ranging from 12 to 432 cm. Each colony was tagged and mapped

75 for future identification. A masonry nail (2") was hammered into each lesion to identify the

76 location and progression of the disease margin.

77 Colonies were randomly assigned one of five treatments.

78   1. Control. Colony was tagged and nails were affixed at the disease margin, but no

79   treatment was applied.

80   2. "Base 2b" Placebo. A proprietary (CoreRx/Ocean Alchemists) silicone-based paste that

81   included polymers to mimic coral mucus consistency was applied directly to the disease

82   margin(s).

83   3. Base 2b + Amoxicillin. The silicone-based paste was hand mixed with powdered

84   amoxicillin (sourced from Phytotechnology Laboratories. 98.1% purity) in an 8:1

85   (base:amoxicillin) by weight ratio. The paste included time-release products that regulate

86   release of the amoxicillin over a three-day time period.

87   4. "New Base" Placebo. A proprietary (CoreRx/Ocean Alchemists) biodegradable

88   hydrophobic ointment designed to hold and release antibacterial compounds.

89   5. New Base + Amoxicillin. The New Base Placebo was mixed with powdered amoxicillin

90   in an 8:1 by weight ratio. Release modifiers in the base facilitated amoxicillin release

91   over three days.

92 Treatments were prepared less than 6 hours before application by mixing amoxicillin into

93 treatments 3 and 5, and by packing treatments 2 – 5 into 60cc catheter syringes. At each affected

94 coral, a treatment was squeezed from the syringe and pressed by hand onto the length of the

95 disease margin in a band approximately 1 cm wide. Half (0.5 cm) of the application overlaid and

96 anchored on to the dead skeleton while 0.5 cm covered adjacent live tissue. If there were

97 multiple lesions on a coral, they all received the same treatment. The amount of treatment

98 product applied to each coral varied with the number and the size of lesions but averaged 12.3

99   mL (±11.2 mL SD) per treated coral. Among the 28 amoxicillin-treated colonies, an average of

100 1.6 g (±1.7 g SD) of amoxicillin was applied for a total application of 39.6 grams at the site.

101 Corals were monitored four weeks after the initial treatment. At each coral, the number of

102 effective and ineffective treatments were tallied. Photographs were also taken and arranged so

103 before and after photos of each lesion could be compared (representative samples: Fig. 2). All

104 analyses were based on the photographic comparisons because more lesions could be positively

105 identified. Effectiveness was defined as the cessation of disease progression at the treatment line.

106 Ineffectiveness was defined as the lesion continuing unimpeded across the colony. After the one-

107 month monitoring, all lesions on all surviving corals were treated with Base 2b + Amoxicillin. A

108 total of 55 retreated lesions (5 *C. natans*, 19 *M. cavernosa*, and 31 *O. faveolata*) were reassessed

109 two months later for effectiveness.

110 The proportion of halted lesions were compared across treatments using Fisher's exact test

111 (α=0.05), which is suitable for unequal as well as small sample sizes. Lesions on the same coral

112 were considered independent because:

   1. Microbiome studies of SCTLD colonies identify healthy regions of tissue adjacent to
113   diseased regions (Meyer et al. 2019)
114
   2. Field observations of lesion development on individual colonies over time note
115   asynchronous appearance, suggesting independent development.
116

117 Additional analyses that do not assume lesion independence were conducted by comparing the

118 proportion of halted lesions on each colony across species and treatments. Sample sizes were

119 small, (between one and six colonies per species per treatment), unequal, and failed normality

120 tests (Kolmogorov-Smirnov), so One-Way ANOVA on Rank tests were used to compare

121 treatments.

122

123 **Results**

124 The percentage of effective lesion treatments varied by treatment type and, to some extent,

125 species (Fig. 3). Across all species, 0% of the control (untreated) lesions halted. Overall

126 effectiveness of New Base Placebo and Base 2b Placebo treatments on lesions were 4% (1/27)

127   and 9% (4/47) respectively. When amoxicillin was added, effectiveness increased to 70% (16/23)

128   for the New Base and 84% (49/58) for the Base 2b.

129   Because the treatments varied in the number of lesions on different species, analyses were

130   further broken down by species (Table 2). *Colpophyllia natans* treatments showed the least

131   difference between placebo and amoxicillin treatments; when amoxicillin was added to both the

132   New Base and the Base 2b, effectiveness increased by 29%. On *Orbicella faveolata*,

133   effectiveness increased 78% when amoxicillin was added to the New Base and 91% when added

134   to the Base 2b. On *Montastraea cavernosa*, the addition of amoxicillin increased effectiveness

135   by100% in New Base and 89% in Base 2b as compared to their placebo counterparts. Because of

136   species rarity, *Diploria labyrinthiformes* and *Pseudodiploria strigosa* lesions treatments were

137   restricted to Base 2b Placebo and Base 2b + Amoxicillin treatments; effectiveness was 0% with

138   placebo treatments, while 88% (7/8: *D. labyrinthiformes*) and 73% (11/15: *P. strigosa*) of

139   amoxicillin treated lesions were effective.

140   Fisher's exact tests identified similarities and differences among treatments (Table 2). On *O.*

141   *faveolata, M. cavernosa*, and *C. natans*, there were no significant differences between untreated

142   controls, New Base Placebo, and Base 2b Placebo. On *C. natans*, there were no significant

143   differences between any treatments (controls, placebos, and non-placebos), although the p-value

144   between untreated controls and Base 2b + Amoxicillin was 0.055. On both *O. faveolata* and *M.*

145   *cavernosa*, there were significant differences between controls and both amoxicillin products.

146   There were also significant differences between both placebo bases and their amoxicillin

147   counterparts. There were no significant differences in effectiveness between New Base +

148   Amoxicillin and Base 2b + Amoxicillin. On *D. labyrinthiformes* and *P. strigosa*, effectiveness of

149   Base 2b + Amoxicillin was significantly higher than the Base 2b Placebo (p = 0.001). Across

150   five of the six tested species, the percentage of lesions halted using both amoxicillin bases was

151   between 73% - 90%. However, amoxicillin treatments on *Colpophyllia natans* were less

152   effective, particularly with the New Base (29%).

153   Treatments were also analyzed at a colony level in consideration that host genotype may play a

154   role in treatment effectiveness. The percentage of halted lesions on each colony was compared

155   across treatments for each species (Fig. 4). For all species, the percentage of halted lesions was

156   higher for New Base + Amoxicillin or Base 2b + Amoxicillin treatments than for placebo-treated

157   colonies and controls. Statistically, ANOVA on Rank tests across all treatment types had

158   extremely low power and could not detect post-hoc differences between treatments by species

159   (Table 3). However, individual ANOVA on Rank tests did detect significant differences on *P.*

160   *strigosa* between Base 2b + Amoxicillin and Base 2b Placebo (p = 0.038), and also on *O.*

161   *faveolata* between Base 2b + Amoxicillin compared to both Base 2b Placebo and New Base

162   Placebo (p = 0.008 and < 0.001 respectively).

163   One month after treatment, one of the control colonies and six of the Base 2b Placebo colonies

164   had died completely. Of the surviving colonies, new lesions had developed on: 40% of the

165   controls, 50% of the New Base placebo, 29% of the Base2b placebo, 29% of the New Base +

166   Amoxicillin, and 33% of the Base2b + Amoxicillin. Failed and new lesions from all surviving

167   colonies were treated with Base 2b + Amoxicillin. Fifty-five of those retreatments were re-

168   surveyed after two months; 80% of *C. natans* lesions, 77% of *O. faveolata* lesions, and 58% of

169   *M. cavernosa* lesions had halted.

170

171   **Discussion**

172   Past uses of antibiotics on diseased corals have included utilization as a diagnostic tool to help

173   identify bacteria as a presumptive pathogen in white band disease (Kline and Vollmer 2011;

174   Sweet et al. 2014) as well as water dosing to halt SCTLD lesion progression in laboratory and

175   aquarium work (C Woodley, K O'Neil, C Lewis, pers comm). The use of skin wound treatment

176   patches containing antiseptics, antioxidants, and/or antibiotics have also shown promise in

177   helping mechanically damaged corals to heal (Contardi et al. 2020). However, the results

178   presented here represent the first known use of topical antibiotics as a disease treatment tool to

179   preserve wild populations. Effectiveness of placebos was no greater than for untreated controls,

180   but the addition of amoxicillin significantly increased the percentage of lesions halted.

181   Antibiotic application was successful at halting lesions on all tested species, but effectiveness on

182   *C. natans* was lower, particularly for the New Base + Amoxicillin treatment. We suggest that the

183   deep polyp grooves of *C. natans* create gaps where the treatment is not in contact with coral

184   tissue. Divers noted that the New Base had poorer adherence to the coral colonies than the Base

185   2b, which may have been particularly pronounced in the highly rugose *C. natans*, thus creating

186   ineffective treatment barriers. Careful application into grooves to ensure physical contact with

187   the coral tissue is suggested.

188   Antibiotic effectiveness is likely to remain localized within the region of application rather than

189   spreading throughout the colony; this is evidenced by the appearance of new lesions on some

190   amoxicillin-treated corals. To minimize mortality, coral colonies require one-month revisitation

191   in order to retreat any failed margins and to treat any new lesions. Longer-term studies are

192   recommended and currently underway to determine appropriate visitation intervals and long-

193   term maintenance requirements. Physiological studies determining the spread of the amoxicillin

194   throughout the colony and the mechanism for effectiveness are also recommended.

195   Treatment of SCTLD-affected colonies using topical amoxicillin paste is an option for SCTLD

196   disease intervention. The methodology has already been utilized to save laboratory and aquaria

197   corals (Florida Aquarium, Keys Marine Lab, Frost Museum of Science), offshore nursery corals

198   (Coral Restoration Foundation and Florida Keys National Marine Sanctuary), corals targeted for

199   assisted reproduction efforts (Mote Marine Lab), and the preservation of over 2000 large reef-

200   building corals on the Florida Reef Tract (Nova Southeastern University, Harbor Branch

201   Oceanographic Institute). Such actions have been and should continue to be weighed in a risk

202   management scenario that considers unknown factors such as impacts on the treated corals'

203   microbiomes as well as potential antibiotic resistance. Though requiring an investment of time

204   and resources for initial treatment as well as repeated visitation, topical antibiotic treatment is a

205   viable tool for preserving high-value corals.

206

207   Conclusions

208   Topical amoxicillin treatments successfully arrested disease lesion progression on multiple

209   species of stony corals affected by Stony Coral Tissue Loss Disease. As this disease spreads

210   throughout already affected reefs as well as new regions of the Caribbean, this type of in-water

211   intervention is an option to be considered within management response strategies. Follow-up

212   studies on the physiological mechanisms, potential risks, and long-term trajectory of treated

213   corals are recommended.

214

215   **Acknowledgements**

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217   2019-115. Use of antibiotics was approved by the US Food and Drug Administration's Office of

218   Minor Use and Minor Species. We are grateful to the editor and three reviewers for

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257

258 **Figure Legends**

259 Figure 1. Map showing research site (star) at Sand Key, Florida Keys. Grey indicates land, pink

260 represents patch reefs, and red indicates spur and groove reefs.

261

262 Figure 2. Representative photos of placebo (progressing) treatments and amoxicillin (halted)

263 treatments. Species codes are: PSTR – *Pseudodiploria strigosa*, DLAB – *Diploria*

264 *labyrinthiformes*, OFAV – *Orbicella faveolata*. Photos show the corals immediately before

265 treatment was applied, immediately after treatment was applied, and one month after treatment.

266 The exception is the "1 month" photo of the placebo DLAB (*), which was taken two weeks

267 after treatment; the colony was totally dead at one month.

268

269 Figure 3. Number of halted (A) and progressing (B) lesions one month after treatments. Colors

270 represent different species. Total percentage of lesions that halted under each treatment regime

271 are shown above the halted lesion bars.

272

273 Figure 4. The average percentage of lesion treatments that were halted on each coral colony,

274 separated by species and treatment type. Error bars indicate standard error.

275

Figure 1

Map of research site at Sand Key, Florida Keys

Figure 1. Map showing research site (star) at Sand Key, Florida Keys. Grey indicates land, pink represents patch reefs, and red indicates spur and groove reefs.

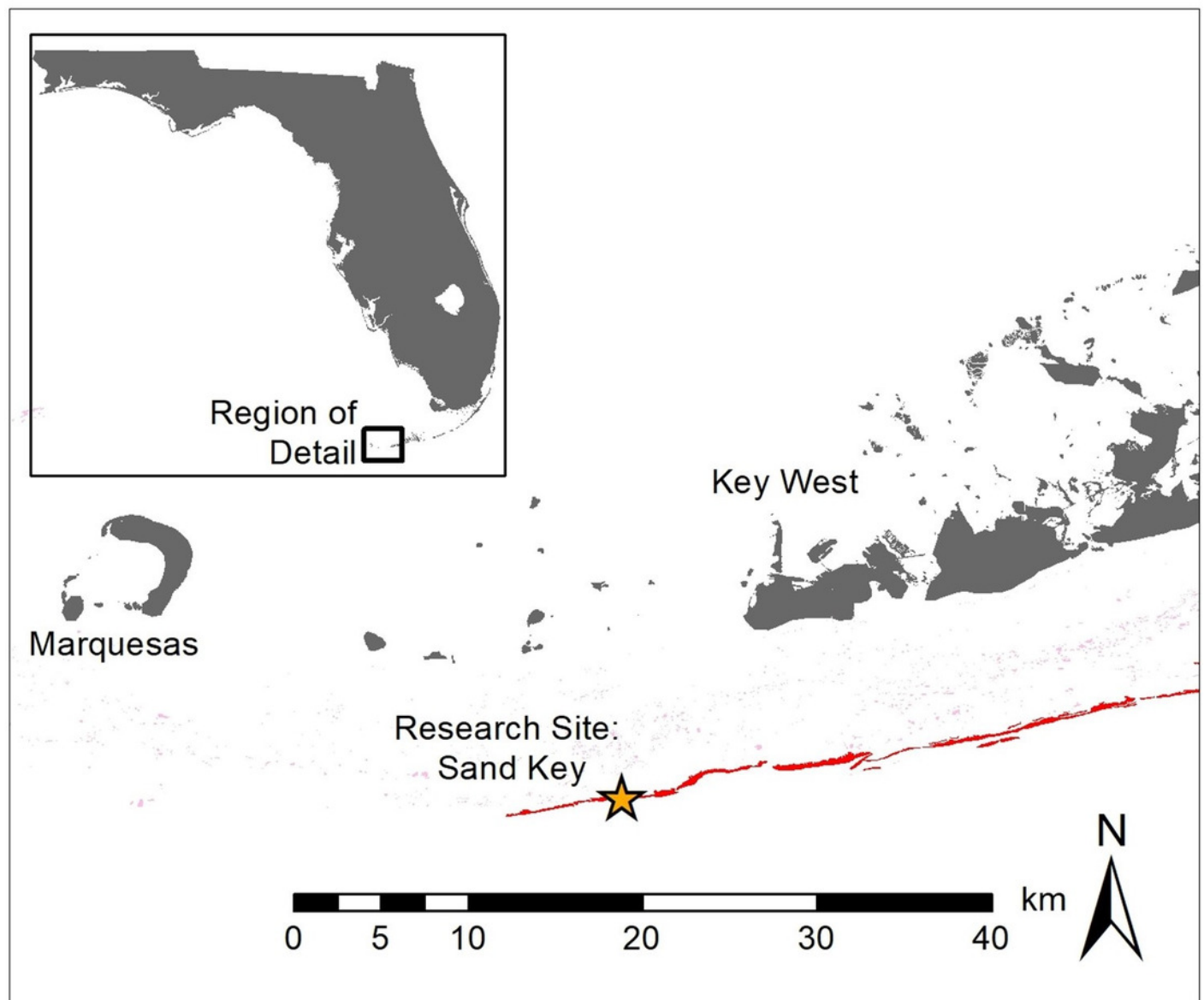



Figure 2

Representative photos of placebo and amoxicillin-treated SCTLD lesions

Figure 2. Representative photos of placebo (progressing) treatments and amoxicillin (halted) treatments. Species codes are: PSTR – *Pseudodiploria strigosa*, DLAB – *Diploria labyrinthiformes*, OFAV – *Orbicella faveolata*. Photos show the corals immediately before treatment was applied, immediately after treatment was applied, and one month after treatment. The exception is the "1 month" photo of the placebo DLAB (*), which was taken two weeks after treatment; the colony was totally dead at one month.

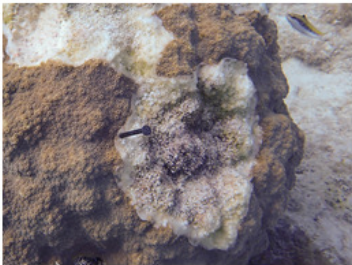
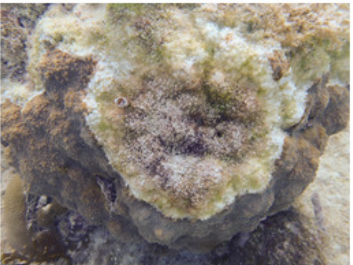



Figure 3

Number of halted and progressing lesions for each treatment type

Figure 3. Number of halted (A) and progressing (B) lesions one month after treatments. Colors/patterns represent different species. Total percentage of lesions that halted under each treatment regime are shown above the halted lesion bars.

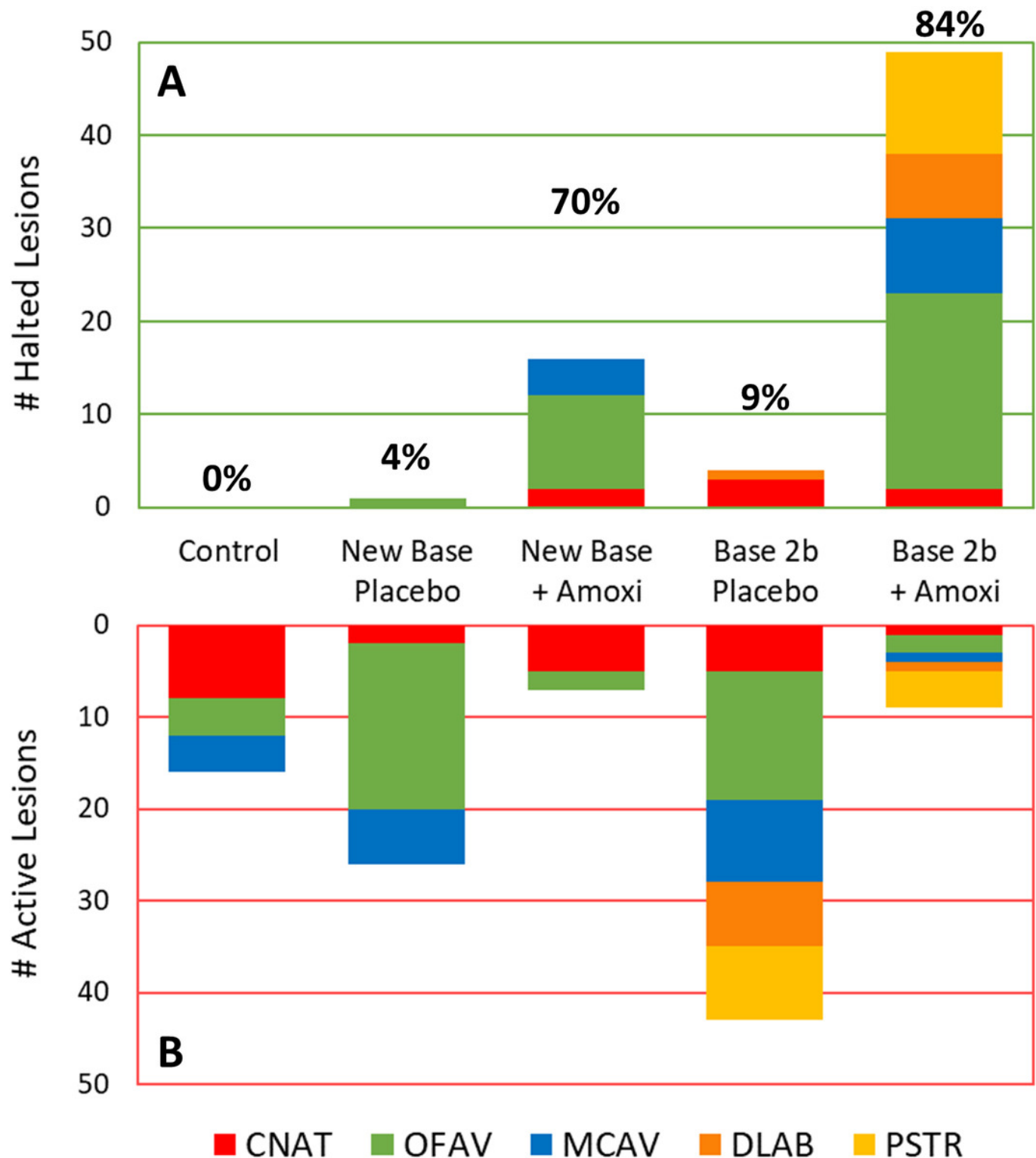



Figure 4

Percentage of effective lesion treatments per colony

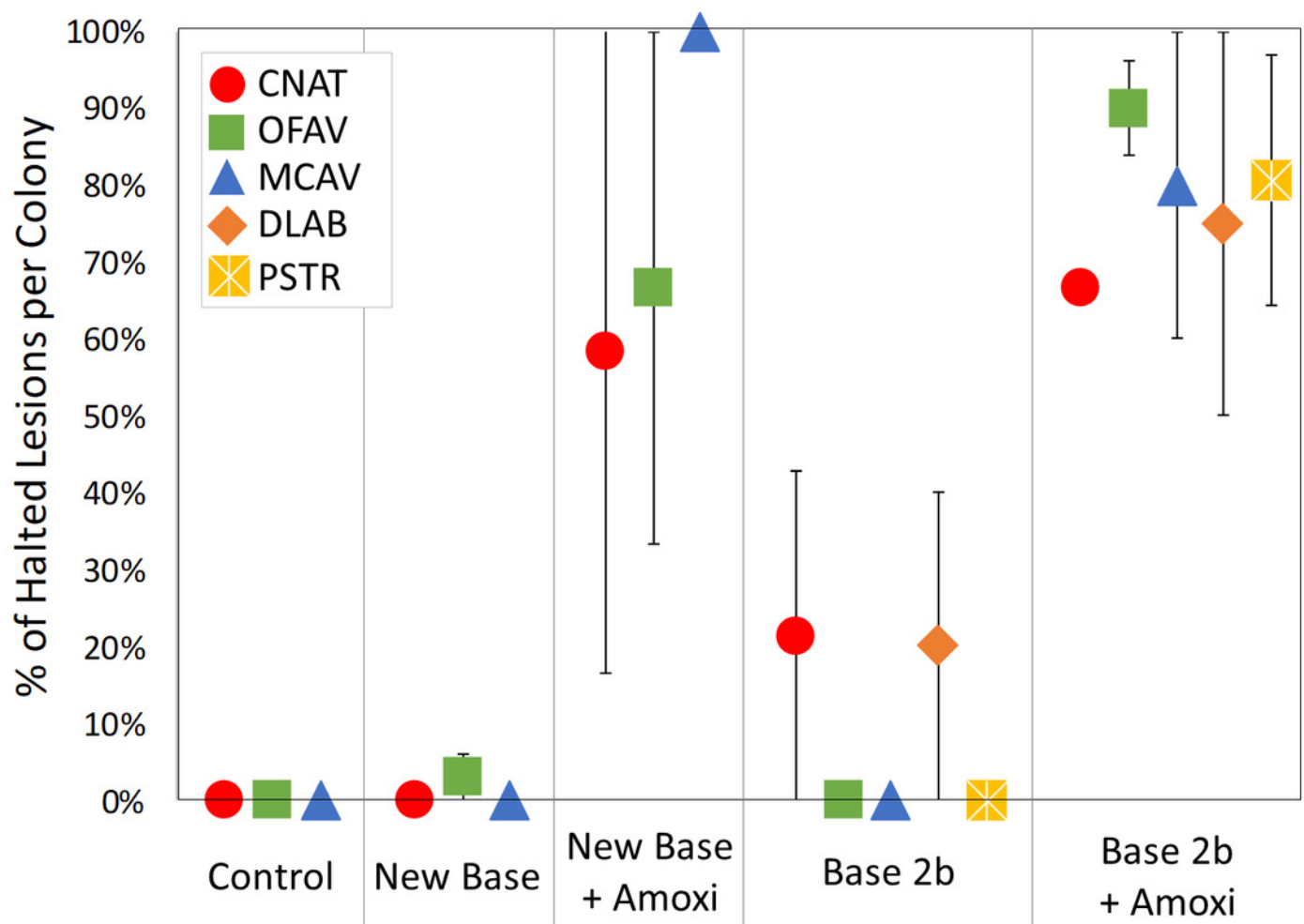
Figure 4. The average percentage of lesion treatments that were effective on each coral colony, separated by species and treatment type. Error bars indicate standard error.

Number of colonies and lesions receiving each treatment.

Table 1. Number of colonies (top) and lesions (bottom) receiving each treatment ("Amoxi" represents addition of powdered amoxicillin). Four-letter species codes represent: *Colpophyllia natans* (CNAT), *Montastraea cavernosa* (MCAV), *Orbicella faveolata* (OFAV), *Diploria labyrinthiformes* (DLAB), and *Pseudodiploria strigosa* (PSTR).

1   Table 1. Number of colonies (A) and lesions (B) receiving each treatment ("Amoxi" represents

2   addition of powdered amoxicillin). Four-letter species codes represent: *Colpophyllia natans*

3   (CNAT), *Montastraea cavernosa* (MCAV), *Orbicella faveolata* (OFAV), *Diploria*

4   *labyrinthiformes* (DLAB), and *Pseudodiploria strigosa* (PSTR).

A — # Colonies

A		Control	New Base Placebo	New Base + Amoxi	Base 2b Placebo	Base 2b + Amoxi
	CNAT	2	2	2	2	1
	MCAV	2	3	2	3	5
	OFAV	2	3	3	5	5
	DLAB				5	4
	PSTR				4	6

B — # Lesions

B		Control	New Base Placebo	New Base + Amoxi	Base 2b Placebo	Base 2b + Amoxi
	CNAT	8	2	7	8	3
	MCAV	4	6	4	9	9
	OFAV	4	19	12	14	23
	DLAB				8	8
	PSTR				8	15

Number of effective and ineffective lesion treatments with statistical comparisons.

Table 2. Number of effective and ineffective lesion treatments for each species and treatment type (first row of each species) and p-values from Fisher's exact test comparisons between treatments for each species (comparison matrix). Statistically significant results are highlighted in green.

1   Table 2. Number of effective and ineffective lesion treatments for each species and treatment type (first row of each species) and p-

2   values from Fisher's exact test comparisons between treatments for each species (comparison matrix). Statistically significant results

3   are highlighted in green.

A - CNAT	Control	New Base Placebo	New Base + Amoxi	Base 2b Placebo	Base 2b + Amoxi
Effective:Ineffective	0:8 (0%)	0:2 (0%)	2:5 (29%)	3:5 (38%)	2:1 (67%)
Control		N/A (both zero)	0.2	0.2	0.055
New Base	N/A (both zero)		1	1	0.4
New Base + Amoxi	0.2	1		1	0.5
B2B	0.2	1	1		0.54
B2B + Amoxi	0.055	0.4	0.5	0.54	

B - OFAV	Control	New Base Placebo	New Base + Amoxi	Base 2b Placebo	Base 2b + Amoxi
Effective:Ineffective	0:4 (0%)	1:18 (5%)	10:2 (83%)	0:14 (0%)	21:2 (91%)
Control		1	0.008	N/A (both zero)	< 0.001
New Base	1		< 0.001	1	< 0.001
New Base + Amoxi	0.008	< 0.001		< 0.001	0.594
B2B	N/A (both zero)	1	< 0.001		< 0.001
B2B + Amoxi	< 0.001	< 0.001	0.594	< 0.001	

C - MCAV	Control	New Base Placebo	New Base + Amoxi	Base 2b Placebo	Base 2b + Amoxi
Effective:Ineffective	0:4 (0%)	0:6 (0%)	4:0 (100%)	0:9 (0%)	8:1 (89%)
Control		N/A (both zero)	0.029	N/A (both zero)	0.007
New Base	N/A (both zero)		0.005	N/A (both zero)	0.001

New Base + Amoxi	0.029	0.005		0.001	1
B2B	N/A (both zero)	N/A (both zero)	0.001		< 0.001
B2B + Amoxi	0.007	0.001	1	< 0.001	

D - DLAB			Base 2b Placebo	Base 2b + Amoxi
Effective:Ineffective	p = 0.001		1:7 (13%)	7:1 (88%)

E - PSTR			Base 2b Placebo	Base 2b + Amoxi
Effective:Ineffective	p = 0.001		0:8 (0%)	11:4 (73%)

Percentage of effective lesions on corals, with statistical comparisons.

Table 3. Average percentage (± standard error) of effective lesions on corals, separated by species and treatment (first row of each species), and p-values from One-Way ANOVA on Ranks comparing treatments (comparison matrix). Statistically significant results are highlighted in green.

1   Table 3. Average percentage (± standard error) of effective lesions on corals, separated by species and treatment (first row of each

2   species), and p-values from One-Way ANOVA on Ranks comparing treatments (comparison matrix). Statistically significant results

3   are highlighted in green.

A - CNAT	Control	New Base Placebo	New Base + Amoxi	Base 2b Placebo	Base 2b + Amoxi
Average % (± SE)	0 ± 0	0 ± 0	58 ± 42	21 ± 21	67 ± N/A
Control		1		0.667	N/A
New Base	1		0.333	0.667	N/A
New Base + Amoxi	0.333	0.333		0.667	N/A
B2B	0.667	0.667	0.667		N/A
B2B + Amoxi	N/A	N/A	N/A	N/A	

B - OFAV	Control	New Base Placebo	New Base + Amoxi	Base 2b Placebo	Base 2b + Amoxi
Average % (± SE)	0 ± 0	3 ± 3	67 ± 33	0 ± 0	90 ± 6
Control		0.495	0.136	1	0.095
New Base	0.495		0.24	0.57	<0.001
New Base + Amoxi	0.136	0.24		0.143	0.399
B2B	1	0.57	0.143		0.009
B2B + Amoxi	0.095	<0.001	0.399	0.009	

C - MCAV	Control	New Base Placebo	New Base + Amoxi	Base 2b Placebo	Base 2b + Amoxi
Average % (± SE)	0 ± 0	0 ± 0	100 ± 0	0 ± 0	80 ± 20

Control		1	0.333	1	0.19
New Base	1		0.33	1	0.19
New Base + Amoxi	0.333	0.33		0.2	0.857
B2B	1	1	0.2		0.07
B2B + Amoxi	0.19	0.19	0.857	0.07	

D - DLAB			Base 2b Placebo	Base 2b + Amoxi
Average % (± SE)	p = 0.27		20 ± 20	75 ± 25

E - PSTR			Base 2b Placebo	Base 2b + Amoxi
Average % (± SE)	p = 0.03		0 ± 0	81 ± 16