

ORIGINAL RESEARCH

Efficacy of a Jellyfish Sting Inhibitor in Preventing Jellyfish Stings in Normal Volunteers

Alexa Boer Kimball, MD, MPH; Karina Zuelma Arambula, BA; Arlen Ray Stauffer, MD; Valeh Levy, MD; Valerie Weaver Davis, MD; Michael Liu, MD; Wingfield Ellis Rehmus, MD, MPH; Amit Lotan, PhD; Paul S. Auerbach, MD, MS

From the Department of Dermatology (Drs Kimball, Arambula, and Rehmus) and Division of Emergency Medicine (Drs Liu and Auerbach), Stanford University School of Medicine, Stanford, CA; the Bert Fish Medical Center, New Smyrna Beach, FL (Drs Stauffer, Levy, and Davis); and Nidaria Technology, Kinarot, Zemach, Jordan Valley, Israel (Dr Lotan).

Objective.—To evaluate the protective effects of a jellyfish sting inhibitor formulated in sunscreen lotion vs conventional sunscreen against *Chrysaora fuscescens* and *Chiropsalmus quadrumanus* jellyfish.

Methods.—Twenty-four healthy subjects at 2 research sites were randomly assigned to receive the jellyfish sting inhibitor (Nidaria Technology Ltd, Jordan Valley, Israel) to one forearm and conventional sunscreen to the other arm in a blinded fashion. Subjects were stung with jellyfish tentacles on each forearm for up to 60 seconds. Erythema and pain were assessed at 15-minute intervals over a 2-hour period.

Results.—In the *C fuscescens* group, all 12 arms pretreated with conventional sunscreen demonstrated erythema, and all subjects noted subjective discomfort. In contrast, no arm pretreated with the jellyfish sting inhibitor had objective skin changes ($P < .01$). Two subjects noted minimal discomfort in the arm treated with the sting inhibitor ($P < .01$). In the *C quadrumanus* group, discomfort was reported in 3 of the 12 inhibitor-treated arms compared with 10 of the 12 placebo-treated arms ($P < .05$). Erythema was noted on 1 arm treated with the inhibitor and 9 arms treated with the placebo ($P < .01$).

Conclusions.—The jellyfish sting inhibitor prevented sting symptoms of *C fuscescens* jellyfish in 10 of 12 subjects and diminished the pain of the jellyfish sting in the remaining 2 subjects. The jellyfish sting inhibitor also inhibited the more severe sting of the *C quadrumanus* jellyfish in the majority of subjects. The jellyfish sting inhibitor does not eliminate the sting from *C fuscescens* or *C quadrumanus* jellyfish but significantly reduces the frequency and severity of stings.

Key words: jellyfish, inhibitor, *Chrysaora*, *Chiropsalmus*, sting, nematocyst

Introduction

Envenomation by cnidarians, a common class of jellyfish found worldwide, is a problem that affects people in both recreational and occupational settings.¹

Chrysaora fuscescens jellyfish, also known as sea nettles, are scyphozoans. They are found worldwide, and various species are well known for stinging swimmers

and boaters in the Chesapeake Bay,² along the coastline of Florida, and over a broad expanse of waters along the West Coast of the United States³ (Figure 1). Contact with jellyfish tentacles usually causes immediate pain and blanching followed by erythema and induration at the sting site.⁴

The sting may be accompanied by a burning sensation and occasionally may result in blisters or skin necrosis.^{5,6} Although painful, the stings are not life-threatening to humans and typically resolve without treatment.⁷ In contrast, *Chiropsalmus quadrumanus* (box jellyfish or sea wasp) is cubozoan and causes more severe reactions including severe pain, redness, and swelling at the site of the reaction³ (Figure 2). This jellyfish is considered

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Corresponding author: Alexa Boer Kimball, MD, MPH, Director of Clinical Trials, Stanford University Department of Dermatology, 900 Blake Wilbur Dr, Stanford, CA 94305 (e-mail: akimball@stanford.edu).



Figure 1. *Chrysaora fuscescens* jellyfish.

to be dangerous to humans and may be of special danger, even life-threatening, to small children.^{7,8} It is prevalent in certain ocean waters of the United States, primarily in the Gulf of Mexico area and along the coastlines of Florida and Texas.

The stinging mechanism of cnidarians such as *Chrysaora* and *Chiropsalmus* is triggered when contact with foreign skin induces stinging cells (cnidocytes) to deliver a variety of toxins. The venom delivery mechanism of jellyfish is composed of millions of stinging organelles (nematocysts) that depend on several mechanical and chemical events.⁹

Each stinging cell consists of a dense capsule, within which is a highly folded harpoon. Hydrostatic (fluid) pressure of 150 atm is developed within the capsule just before the act of stinging¹⁰ (Figure 3). The capsule is

forced open by this pressure, allowing the harpoon to be released. The harpoon penetrates into the skin of a human or other species with acceleration of up to 40 000 times the force of gravity.^{11–13} The poisons are delivered into the skin within a fraction of a second, making a jellyfish sting one of the most rapid mechanical events found in nature.¹⁴ The venom contains histamine, histamine-releasing agents, and serotonin, which are injected into the skin upon penetration.¹⁵

Over 150 million people are exposed to jellyfish annually, and jellyfish cause many stings and several deaths each year. Whereas rash guards and stinger suits are excellent in preventing contact with jellyfish and are recommended for use in regions where lethal jellyfish are common, they are not widely used in areas inhabited by less toxic jellyfish. To provide practical and inexpen-



Figure 2. Thirteen-year-old surfer a day after a sting from a *Chiropsalmus quadrumanus* jellyfish.

sive protection for recreational and professional swimmers, a repellent cream was formulated. This repellent cream was compounded into a waterproof sunscreen containing octyl methoxycinnamate and zinc oxide, which would allow for single-application protection from both sting and sunburn.

This cream is already commercially available in many countries worldwide, including Japan, Spain, Italy, the United States, and Israel, and is promoted as protection against, not complete prevention of, the sting of most jellyfish. However, no data have been published evaluating its efficacy in preventing jellyfish stings.

The inhibitor was formulated to inactivate jellyfish

stinging cells in several ways. First, the inhibitor is hydrophobic and thus prevents the tentacles from making sufficient contact with the skin to sting it. Second, the inhibitor contains glycosaminoglycans that mimic the glycosaminoglycans of the jellyfish bell. Because this bell serves as part of the jelly's self-recognition system, the inhibitor can cause the jellyfish to recognize the user as self and prevents sting. Third, the inhibitor contains a competitive antagonist to nonselective receptors on jellyfish that bind to amino acids and sugar secretions from prey. Finally, calcium and magnesium within the inhibitor block transmembrane signaling channels of the jellyfish and work to reduce the osmotic forces required to

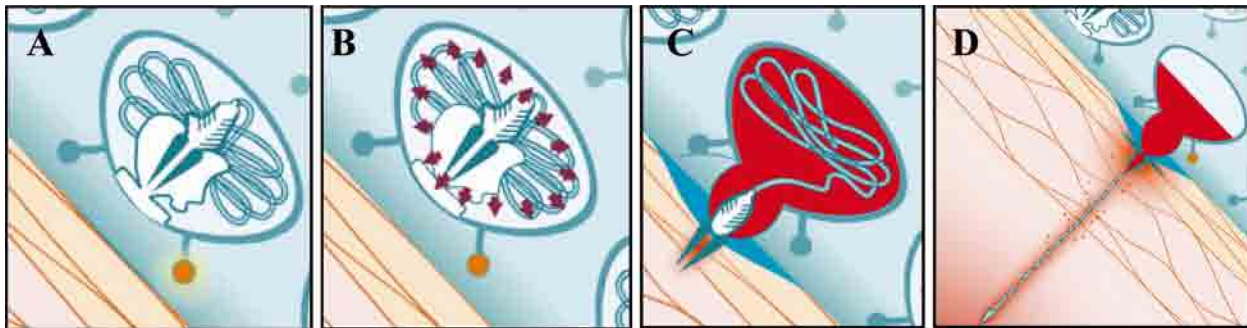


Figure 3. Jellyfish stinging mechanism. **A**, Stimulation from the skin initiates the stinging cell discharge process. **B**, High internal pressure of 150 atm develops within the stinging capsule. **C**, With acceleration of 40 000 times the force of gravity, the shaft drills a hole into the skin. **D**, A tubule follows the shaft and injects poison into the body.

create the necessary firing force within the capsule for the nematocyst.

Methods

Twenty-four adult subjects were enrolled in the study. Twelve subjects were enrolled in the study as normal volunteers in a protocol approved by Stanford's Panel on Human Subjects and were exposed to *C fuscescens* jellyfish. An additional 12 subjects were similarly in a protocol approved by the Institutional Review Board at Bert Fish Medical Center and were exposed to *C quadrumanus* jellyfish. Participation in the study was limited to adults because it was not felt appropriate to expose children to stings, and participants were not expected to have any personal gain as a result of their participation in the study. Each subject signed an informed consent, met inclusion and exclusion criteria, and underwent a physical examination before participating in the study. Subjects were randomized in a double-blind fashion to receive application of either the inhibitor lotion (Safe Sea, Nidaria Technology Ltd, Jordan Valley, Israel) or conventional sunscreen to the left forearm followed by an application of the other lotion to the right forearm. Coppertone SPF 15 was used as the placebo sunscreen because it contains similar chemical components found in the inhibitor lotion save the active inhibitor. It is also waterproof and is a widely used sunscreen for recreational use.

An area of 18 × 6 cm was marked on each forearm, and the inhibitor lotion and placebo sunscreen were identically applied in a thin layer (routinely recommended application) to the forearms according to the randomization protocol. After the substances were allowed to dry for 10 minutes, two marks were made in the center of the application area at a distance of 3 and 5 cm for *C quadrumanus* and *C fuscescens* jellyfish, respectively.

Tentacles were removed from live jellyfish in storage tanks and held vertically in the air to allow excess water to drip off. The tentacles were placed on the skin with the lower end of the tentacles applied to the distal mark and 3 or 5 cm of tentacle placed in a straight line on the left forearm until it reached the proximal mark (Figure 4). The tentacle was left in contact with the forearm for 10 and 30 seconds for *C quadrumanus* and *C fuscescens* jellyfish, respectively, at which time it was removed with tweezers. The same protocol was repeated on the right forearm. If the subject experienced no discomfort in either arm during the first application, fresh tentacles were applied a second time to each arm for a total of 15 to 20 additional seconds. In the *C fuscescens* experiment, the tentacles were placed for an additional 15 seconds for a total of 60 seconds if the subject had again noted no discomfort.

Subjects were examined and queried about pain at 0, 15, 30, 60, 90, and 120 minutes after completion of the tentacle application. Pain was scored on a 0 (no pain) or 1 (pain) scale. If discomfort was noted in both arms, but one arm was less severe than the other, that arm was given a score of 0.5 to distinguish it from the arm with more discomfort. The degree of inflammation was evaluated by a dermatologist according to the following criteria: 0 (no change), 1 (skin color change only), 2 (edema), and 3 (blister or ulcer formation). These measurements were taken at the same time points.

Additionally, digital and 35 mm photographs were taken of each arm at 0 and 15 minutes (Figure 5).

Statistical analyses were performed using SPSS for Windows 11.5 (SPSS, Chicago, IL). Mean pain and physician-assessed reaction were compared using 2-sided *t* tests. *P* values <.05 are noted in the tables and text.

Results

In the group of subjects exposed to *C fuscescens* jellyfish, all 12 enrolled subjects completed the protocol. The mean application time of tentacles was 37.5 seconds, with a minimum time of 30 seconds and a maximum of 60 seconds (Table 1). All 12 arms pretreated with the placebo sunscreen demonstrated erythema, and all 12 subjects noted discomfort in that arm. In contrast, no arm pretreated with the jellyfish sting inhibitor had clinically evident skin changes (*P* < .01). Two subjects noted some discomfort in the arm treated with the sting inhibitor, and in both cases, this discomfort was rated as less than in the placebo-treated arm (*P* < .01).

Similarly, all 12 enrolled subjects completed the protocol in the group exposed to *C quadrumanus* jellyfish. The mean application time of tentacles was 15 seconds, with a minimum time of 10 seconds and a maximum of 30 seconds (Table 2). Of the 12 enrolled subjects, only 3 noted discomfort in the arm treated with the sting inhibitor lotion. The mean and median measures of discomfort were 0.3 and 0, respectively. In contrast, 10 subjects noted discomfort in the arm treated with placebo. The mean and median measures of discomfort were 0.83 and 1, respectively, for the placebo treated arms (*P* < .05). Additionally, on medical examination performed by a blinded physician and scored as previously described, there was evidence of a reaction in only one arm treated with the inhibitor lotion. The arms treated with the placebo demonstrated visible or palpable evidence of stings in 9 of 12 cases (*P* < .01).

Discussion

The jellyfish sting inhibitor lotion prevented clinical symptoms of the sting of the *C fuscescens* jellyfish in

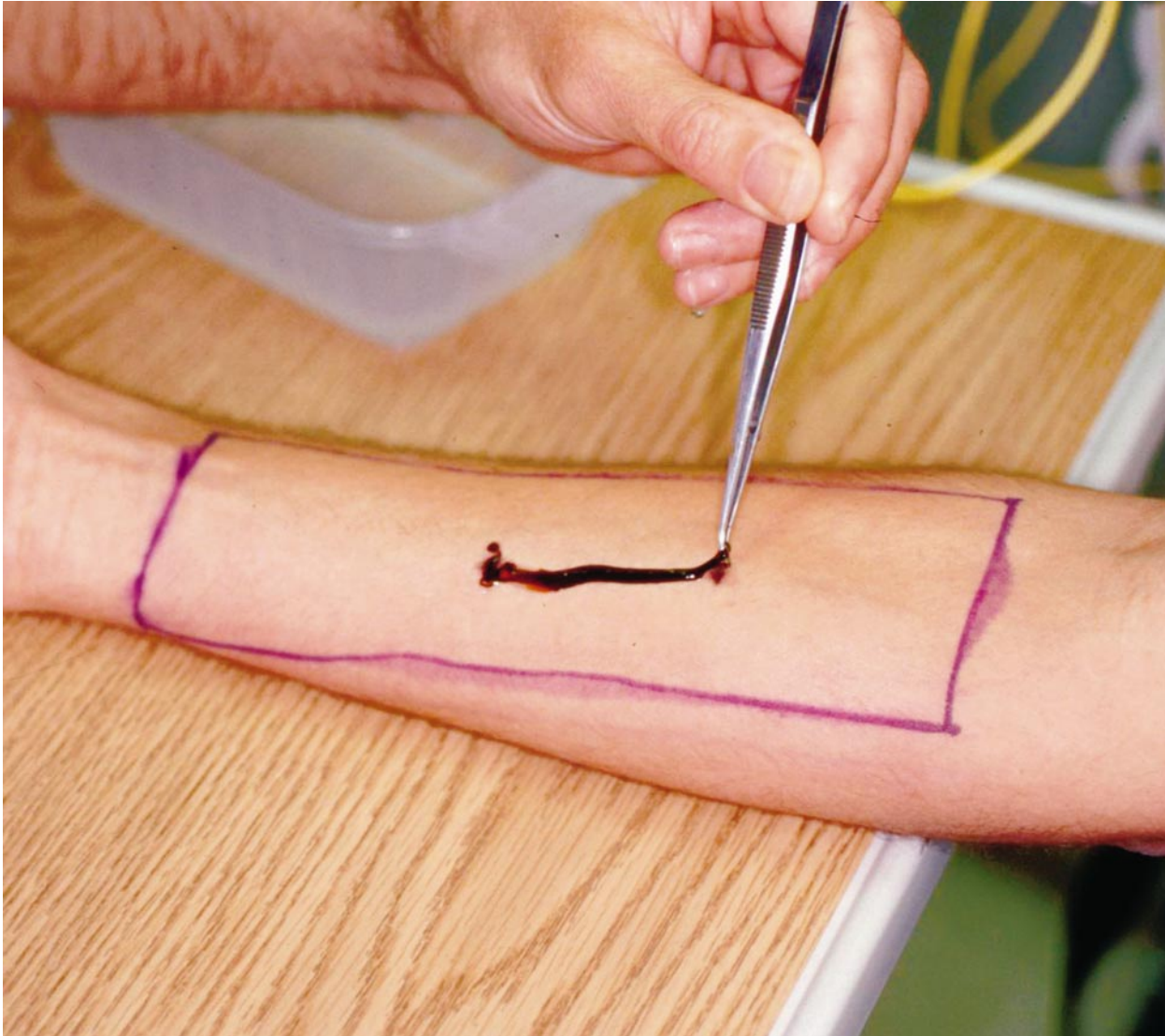


Figure 4. Application of *Chrysaora fuscescens* tentacles to the arm of a subject within the region treated with either placebo or a jellyfish sting inhibitor lotion.

10 of 12 subjects and diminished the pain of the jellyfish sting in the other 2 subjects. No visible sign of sting was noted in any of the arms treated with the inhibitor lotion, but erythema, edema, or both were present in all 12 arms treated with the placebo. The inhibitor also diminished the frequency and severity associated with the more severe sting of the *C. quadrumanus* jellyfish. Three of 12 subjects experienced discomfort in the inhibitor-treated arm compared with 10 subjects in the placebo-treated arm, and only 1 inhibitor-treated arm had clinical evidence of a sting compared with 9 placebo-treated arms. As has been noted in previous experiments, the maximum discomfort associated with the sting of the jellyfish was not always apparent immediately after the sting but

rather at a short time (approximately 15 minutes) later, and the clinical signs of the sting reached their maximum at approximately 30 minutes.

Stings from isolated jellyfish tentacles do not cause stings with the same frequency or intensity as live jellyfish in an open-water setting. It is possible that in an artificial setting, the effectiveness of the inhibitor might be overestimated because of an infrequency of stings. However, subjects did demonstrate signs and symptoms of the sting in all placebo-treated arms, suggesting that the jellyfish tentacles used in this study were capable of reliably causing stings and that some inhibition was clearly achieved. Anecdotal evidence suggests efficacy in open water, but future studies will be required to dem-



Figure 5. Erythema is notable on the arm treated with the placebo lotion and absent on the arm treated with the inhibitor lotion after exposure to a jellyfish tentacle.

onstrate efficacy in an underwater setting and after open-water contact with jellyfish. Additionally, whereas this inhibitor is formulated in a waterproof sunscreen, future research will be required to quantify the duration of protection afforded by the application of the inhibitor in an underwater setting.

In our study, the jellyfish sting inhibitor lotion did not completely inhibit all stings from the *C. fuscescens* or *C.*

quadrumanus jellyfish, but it did significantly reduce the frequency and severity of these stings. *C. fuscescens* (sea nettle) and *C. quadrumanus* (sea wasp) species were used in this study because of their prevalence in the waters of the United States. However, the mechanism of action of the inhibitor lotion and the results of similarly designed trials suggest that the lotion is likely to be effective against several other species of jellyfish, including

Table 1. Results from *C. fuscescens* group comparing severity of reaction (including both pain and clinical signs of reaction) and time to reach reaction after contact with tentacles in inhibitor and placebo treated arms

Subject No.	Total contact Time (s)	Inhibitor				Placebo			
		Max pain		Max reaction		Max pain		Max reaction	
		Amount of pain	Time (min)	Amount	Time (min)	Amount of pain	Time (min)	Amount	Time (min)
1	45	0	0	0	0	1	15	2	15
2	30	0	0	0	0	1	60	1	30
3	30	0	0	0	0	1	30	2	30
4	30	0	0	0	0	1	15	1	30
5	30	0	0	0	0	1	15	1	30
6	30	0	0	0	0	1	30	2	30
7	45	0	0	0	0	1	30	2	30
8	45	0	0	0	0	1	15	1	120
9	60	0	0	0	0	1	30	1	30
10	45	0.5	15	0	0	1	0	2	30
11	45	0	0	0	0	1	15	1	30
12	30	0	0	0	0	1	15	1	30
Median	37.50	0.00	0.00	0.00	0.00	1.00	15.00	1.00	30.00
Mean	38.75	0.04	1.25	0.00	0.00	1.00	22.50	1.42	36.25
P value						<.01		<.01	

* Max, maximum; min, minimum.

Table 2. Results from *C. quadrumanus* group comparing severity of reaction (including both pain and clinical signs of reaction) and time to reach reaction after contact with tentacles in inhibitor and placebo treated arms

Subject No.	Total contact Time (s)	Inhibitor				Placebo			
		Max pain		Max reaction		Max pain		Max reaction	
		Amount of pain	Time (min)	Amount	Time (min)	Amount of pain	Time (min)	Amount	Time (min)
1	10	0	0	0	0	1	0	1	30
2	10	0	0	0	0	1	15	1	90
3	20	0	0	0	0	1	15	2	120
4	10	0	0	0	0	1	15	1	120
5	10	0	0	0	0	1	60	1	60
6	20	1	15	0	0	1	30	2	30
7	10	0	0	0	0	1	0	0	0
8	10	1	0	0	0	0	0	0	0
9	20	0	0	0	0	1	30	1	30
10	20	1	15	1	90	0	0	0	0
11	30	0	0	0	0	1	60	2	60
12	10	0	0	0	0	1	15	1	30
Median	10	0	0	0	0	1	15	1	30
Mean	15	0.3	2.5	0.1	7.5	0.83	20	1	47.5
P value						<.05		<.01	

* Max, maximum; min, minimum.

Rhopilema nomadica and *Linuche unguiculata* (one causative agent of seabather's eruption, also known as sea lice) (unpublished data, Nidaria Technology, 1999). Consequently, use of this jellyfish sting inhibitor lotion may be an important preventive measure for people who are exposed to stinging jellyfish in recreational and occupational settings.

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