Effectiveness of a Novel Poly(Urea-Urethane) as an Antimicrobial and in Reducing Inflammation and Pain

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Introduction: A new liquid bandage that consists of a non-toxic, poly(urea-urethane) liquid emulsion has been developed recently. This material (NUVADERM™)[1] adheres to the contours of the skin and forms a hydrophobic, elastomeric coating that provides a barrier against moisture, yet permeable to oxygen, thus reducing the chance of infection and further injury. The product has been shown to be biocompatible and an effective liquid bandage.[2] The goal of this study was to assess its a) antimicrobial activity and b) efficacy at reducing inflammation and pain.[3]

Materials and Methods: Liquid Bandage: The material was manufactured from a blend of a polytheramine, a secondary diamine, a modified diphenylmethane diisocyanate and a polyol in a carrier solvent/reactant mixed in a stoichiometrically balanced ratio.[4]

Antimicrobial Activity: NUVADERM™ was tested against five standard organisms from USP <51> (*S. aureus* (MRSA), *E. coli, P. aeruginosa, C. albicans, A. brasiliensis*) for its antimicrobial effectiveness. USP <1227> (Neutralization Validation) and ASTM E2315 (Standard Guide of Antimicrobial Activity Using a Time Kill Procedure) were used to measure the changes of a population (>10^7) of these microorganisms within 30 seconds and 30 minutes *in vitro*.

Pain/Edema Rat Model: See Table 1. A total of 55 albino rats (Sprague Dawley) were employed. **Group 1** comprised 15 animals whose both left and right hind paws were injected with bee venom (0.2 mg, *Apis millifera*). Cohort A (5 rats) received an application of the liquid bandage onto the left injected paw approximately 1 minute after bee venom administration, while the right paw received no application. Cohort B (5 rats) was similar to A except the liquid bandage was applied approximately 10 minutes after bee venom administration. Cohort C (5 rats) received an application of the liquid bandage onto the left and right injected paws approximately 1 and 10 minutes, respectively, after bee venom administration.

Table 1. Pain/Edema Rat Model

GROUP		NUMBER OF ANIMALS	INJURY INDUCTION		TREATMENT		ENDPOINT ASSESSMENT
			Left Paw	Right Paw	*Left Paw	Right Paw	
1	A	5	Bee Venom	Bee Venom	Test Article 1 minute	No Application	Edema
	B	5	Bee Venom	Bee Venom	Test Article 10 minutes	No Application	Edema
	C	5	Bee Venom	Bee Venom	Test Article 1 minute	Test Article 10 minutes	Edema
2	A	10	-	Bee Venom	No Application	No Application	Pain / Edema
	B	10	-	Bee Venom	No Application	Test Article 1 minute	Pain / Edema
	C	10	-	Bee Venom	No Application	Test Article 10 minutes	Pain / Edema
	D	10	-	Saline	No Application	No Application	Pain / Edema

Group 2 comprised 30 animals (cohorts A, B and C) and 10 animals (cohort D) whose only right hind paws received venom and saline injections (0.2 mg each), respectively. Cohorts A (10 animals) received no further treatment whereas cohorts B and C (10 animals each) received an application of the liquid bandage onto the injected paw approximately 1 and 10 minutes, respectively, after bee venom administration.

Pain assessment was derived by tallying the number of paw flinches every 5 minutes in the first hour.[5] Edema was assessed by the weight difference of the paw every 5 minutes in the first hour; every hour during the 2-8 hour interval; in 24 hours; and in 48 hours.

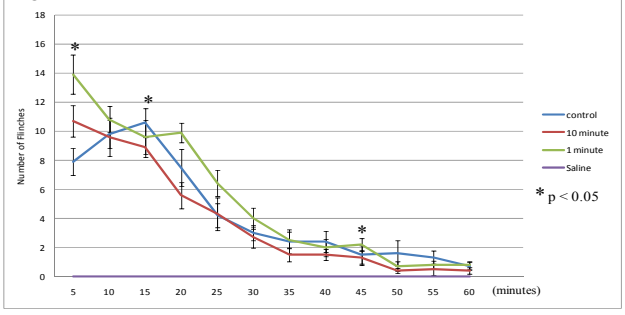
Results: Antimicrobial Activity: The liquid bandage consistently produced an average five-log kill of a $10^{7 \text{ to } 9}$ inoculum of all aforementioned organisms identified in USP <51> within 30 seconds of contact (Table 2).

Table 2: Antimicrobial Testing

Organism	Common	Neutralization (% Recovery)	Population Count	30 Second % Reduction	30 Minute % Reduction	Controls
Staphylococcus aureus (MRSA)	Bacteria	> 70%	> 10^8	> 99.99%	> 99.99%	No Reduction
Escherichia coli	Bacteria	> 70%	> 10^8	> 99.99%	> 99.99%	No Reduction
Pseudomonas aeruginosa	Bacteria	> 70%	> 10^8	> 99.99%	> 99.99%	8.33%-No Reduction
Candida albicans	Yeast	> 70%	> 10^8	> 99.99%	> 99.99%	No Reduction
Aspergillus brasiliensis	Mold	> 70%	> 10^7	> 99.99%	> 99.99%	No Reduction

Pain/Edema Rat Model: There were no adverse clinical observations throughout the course of the study. Significant pain reduction by the liquid bandage applied one minute post injection was reflected in the effect on the slopes of the mean pain scores for time points 5-10, 15-20 and 45-50 minutes after injection (Figure 1). Bee venom injections reached peak intensity within 15 minutes in the control animals and decreased continually thereafter. The one minute application decreased pain by 31% at 15 minutes post injection, while the no-application control produced a 34% increase in pain. There was no significant difference for the 10 minute application for any of the time points (for no obvious reasons) and, as expected, saline produced no behavior indicative of pain. As for edema scores, the liquid bandage rendered a slight reduction versus no application, though not statistically significant.

Figure 1. Mean Pain Scores for Rat Model



Conclusions: The results of this study demonstrated that NUVADERM™, a new poly(urea-urethane) liquid bandage, has a) antimicrobial properties and b) an analgesic effect toward bee venom and potentially other toxins.

References: (1) Manufactured for Chesson Laboratory Associates, Durham, NC (2) Product cleared by FDA, (K083913) July 2009, ISO 10993: Biological Evaluation of Medical Devices 2007 (3) A new submission has been made to the FDA (K093053), but it has not been cleared for this indication (4) Kovacs SG. US Patent 7,008,997, 2006(5) Lariviere LR. Pain 1996;66:271-277