

# Prospective Examination of the Efficacy of 2 Topical Over-the-counter Cosmeceutical Creams for Rapid Treatment of Facial Rhytids

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**Objective:** To examine the efficacy of 2 over-the-counter cosmeceutical creams in reducing facial rhytids—Freeze 24/7 Anti-Wrinkle Cream (Freeze 24/7 International LLC, New York, New York) and LiftFusion Micro-Injected M-Tox Transdermal Face Lift (Fusionbeauty, Inc, Boca Raton, Florida)—against placebo (Nutraderm Therapeutic Lotion; Healthpoint, Inc, San Antonio, Texas).

**Methods:** A prospective, blinded clinical trial was performed on 42 subjects, comparing 2 cosmeceutical creams that each represent a class of purported rapid rhytid reduction formulas with placebo. Independent analysis by 2 facial plastic surgeons was performed as well as completion of self-assessment questionnaires by the participants.

**Results:** No complications occurred. Self-evaluation of cream effectiveness was no different for test creams compared with placebo. Neither cream produced substantial reduction of rhytids when examined critically by 2 independent facial plastic surgeons. Stratification by Glogau (photoaging) class did not reveal increased effectiveness based on rhytid severity.

**Conclusion:** Two typical over-the-counter rhytid reduction products are ineffective at substantially reducing facial rhytids.

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THE DEMAND FOR LESS INVASIVE techniques for facial rejuvenation over the past decade is well known.<sup>1</sup> As surgeons have developed less invasive rejuvenescent techniques, several over-the-counter products have been introduced that purport facial enhancement that is equivalent to those available in physicians' offices. These have included topical lip enhancement and facial stimulation devices.<sup>2,3</sup>

Recently, over-the-counter alternatives to botulinum toxin type A injection have come to market. Several of these cosmeceutical creams claim improvement of facial wrinkles within minutes. While many of the products do cite clinical studies demonstrating their effectiveness, a PubMed search revealed no such studies indexed on Medline (as of March 2007). The present study examined the efficacy of 2 such creams—Freeze 24/7 Anti-Wrinkle Cream (Freeze 24/7 International LLC, New York, New York) and LiftFusion Micro-Injected M-Tox Transdermal Face Lift (Fusionbeauty, Inc, Boca Ra-

ton, Florida)—both of which claim to reduce rhytids within minutes and are marketed as alternatives to botulinum toxin type A injection, the efficacy of which is well documented.<sup>4,5</sup>

## METHODS

All study protocols were approved by the Stanford University School of Medicine Human Subjects Committee, Stanford, California. Participants who had undergone any facial surgical or resurfacing procedure, botulinum toxin type A injection, or filler injection in the past 12 months were excluded from this study. Participants were assigned randomly to 1 of 3 study groups, and received plain, number-coded vials containing (1) Freeze 24/7 Anti-Wrinkle Cream, (2) LiftFusion Micro-Injected M-Tox Transdermal Face Lift, or (3) Nutraderm Therapeutic Lotion (Healthpoint, Inc, San Antonio, Texas) (placebo). Participants were photographed prior to application of the assigned cream to the forehead, infraorbital, lateral orbital, and glabellar areas. Photographs were then taken 15 and 30 minutes later. Participants then used the creams twice a day for 7 days, and follow-up photographs were taken. A self-assessment questionnaire was administered af-

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ter 7 days of application. In addition, 2 independent blinded facial plastic surgeons were asked to rate rhytids in pretreatment and posttreatment photographs. Statistical analysis was performed using a *t* test. Statistical significance was set at  $P < .05$ .

## RESULTS

Forty-two patients completed the initial portion of the study, including assessments at 15 and 30 minutes after application. Thirty-eight returned for the second portion of the study, including 7-day assessment and questionnaire. The average age for participants was 55 years; all patients were female. The average Glogau class of all enrolled participants was 2.9 (range, 1-4). No patients experienced any significant discomfort with the study creams or placebo. Overall satisfaction was the same for the 2 tested creams and placebo (**Table 1**). Several patients who used the Freeze 24/7 Anti-Wrinkle Cream noted a “sticky” feeling (data not shown). Several patients noted “tingling” on application of either Freeze 24/7 Anti-Wrinkle Cream or LiftFusion Micro-Injected M-Tox Transdermal Face Lift (data not shown). Global self-evaluation of facial rejuvenation was similar for the 2 test creams and placebo. Self-assessment of the lateral orbital, lower eyelid, forehead, and glabellar areas individually revealed no trends or statistical differences between the 2 test creams or placebo (Table 1).

To objectively quantify any changes in facial rhytids, full-face photographs of the subjects were reviewed in blinded fashion by 2 facial plastic surgeons. Subjects were rated by Glogau class at time zero. The mean age and Glogau class for each test group were similar (**Table 2**). Photographs at various time points were rated based on a wrinkle score of 1 (minimal or no rhytids) through 10 (severe rhytids). The forehead, glabella, and lateral orbital areas were each rated separately.

To examine the effect each cream may have over time, the wrinkle scores were compared with baseline after 15 and 30 minutes, and after 7 days following initiation of treatment. A trend toward decreased wrinkle score was noted in the group using Freeze 24/7 Anti-Wrinkle Cream, particularly on the forehead, but no statistical significance was noted in comparison to baseline (Table 2). To compare the creams with each other, the change in wrinkle score (in comparison to baseline) at each time point was calculated and compared across treatment creams. No statistical difference in change in wrinkle score was noted at any time point for each test cream in comparison to placebo (**Table 3**). However, Freeze 24/7 Anti-Wrinkle Cream was noted to have a greater effect on rhytids than LiftFusion Micro-Injected M-Tox Transdermal Face Lift in the glabella at 15 and 30 minutes after treatment, although this effect was lost by day 7 (Table 3). Once again, a trend was noted in Freeze 24/7 Anti-Wrinkle Cream users toward a greater effect, but no statistical significance was achieved.

To examine the effectiveness of the tested creams by wrinkle severity, study participants were stratified by Glogau class into 2 groups: one group included only those participants who were assigned to Glogau classes 1 and 2, and the other group consisted of those participants who

**Table 1. Self-assessment of Facial Antiwrinkle Creams<sup>a</sup>**

Query	Freeze 24/7 (n=12)	LiftFusion (n=13)	Placebo (n=13)
1. Did you experience any discomfort?	1.3±0.6	1.2±0.6	1.1±0.3
2. Overall satisfaction	2.7±1.1	2.8±1.2	2.6±1.2
3. Would you consider buying this on your own?	2.5±1.1	3.0±1.4	2.6±1.4
4. Did you notice any changes in your face during this period?	1.9±1.1	2.2±1.2	2.0±1.3
5. Would you characterize ANY aspect of your face as more youthful appearing now than before you started using the cream?	1.9±1.0	2.2±1.2	1.7±1.0
6. How would you rate the improvement in the crow's feet?	1.8±1.1	2.0±1.3	1.8±1.2
7. How would you rate the improvement in under-eye circles?	1.6±0.8	1.7±1.2	1.6±1.3
8. How would you rate improvement in the forehead?	1.8±1.2	1.8±1.0	1.8±1.0
9. How would you rate improvement in the frown lines?	1.8±1.0	1.8±1.2	1.7±1.0

Abbreviations: Freeze 24/7, Freeze 24/7 Anti-Wrinkle Cream (Freeze 24/7 International LLC, New York, New York); LiftFusion, LiftFusion Micro-Injected M-Tox Transdermal Face Lift (Fusionbeauty, Inc, Boca Raton, Florida); placebo (Nutraderm Therapeutic Lotion; Healthpoint, Inc, San Antonio, Texas).

<sup>a</sup>Data are given as mean±SD rated on a scale of 1 (no or none) to 5 (yes or significant improvement).

were assigned to Glogau classes 3 and 4. Once stratified this way, the same examinations noted earlier were performed. Participants in Glogau classes 1 and 2 had no differences among the 3 test creams (data not shown). In those classified as being in Glogau classes 3 and 4, it was once again noted that those using the Freeze 24/7 Anti-Wrinkle Cream had a greater effect on rhytids than those using LiftFusion Micro-Injected M-Tox Transdermal Face Lift in the glabella (**Table 4**). However, once again no substantial difference was noted in comparison to placebo.

## COMMENT

As the quest for noninvasive facial rejuvenation continues, so does the introduction of various over-the-counter remedies. While in the past most such products were clearly of nonmedical grade, the lines have begun to blur. For example, many products are marketed with names that are clearly meant to invoke the names of medically administered agents. One clear example is the use of the suffix *tox*, which is added to many products. One of the products studied herein has trademarked the term *M-Tox* (**Figure**). Indeed, the manufacturer's product notes contained in the box cite clinical studies that demon-

**Table 2. Mean Wrinkle Scores Over Time for Antiwrinkle Creams and Placebo<sup>a</sup>**

Variable	Wrinkle Score After Application			
	0 min	15 min	30 min	7 d
<b>Freeze 24/7 (n=15)</b>				
Mean age of participants, 57.2 y				
Mean Glogau classification, 2.9				
Region				
Glabella	4.8±1.7	4.4±1.5	4.5±1.5	4.4±1.6
Forehead	4.5±1.7	4.0±1.6	4.0±1.7	3.8±1.6
Periorbital	5.6±1.7	5.0±1.5	5.1±1.5	5.0±1.7
<b>LiftFusion (n=14)</b>				
Mean age participants, 54.0 y				
Mean Glogau classification, 2.8				
Region				
Glabella	4.2±1.7	4.1±1.7	4.3±1.7	4.1±1.6
Forehead	4.5±1.7	4.4±1.6	4.4±1.6	4.4±1.6
Periorbital	4.7±1.8	4.5±1.7	4.5±1.7	4.3±1.6
<b>Placebo (n=13)</b>				
Mean age, 52.3 y				
Mean Glogau classification, 2.7				
Region				
Glabella	4.6±2.0	4.4±1.9	4.4±1.9	4.6±2.0
Forehead	4.2±1.5	4.2±1.5	4.2±1.5	4.2±1.6
Periorbital	5.2±1.7	5.1±1.5	5.0±1.9	5.1±1.6

Abbreviations: Freeze 24/7, Freeze 24/7 Anti-Wrinkle Cream (Freeze 24/7 International LLC, New York, New York); LiftFusion, LiftFusion Micro-Injected M-Tox Transdermal Face Lift (Fusionbeauty, Inc, Boca Raton, Florida); placebo (Nutraderm Therapeutic Lotion; Healthpoint, Inc, San Antonio, Texas).

<sup>a</sup>Data are given as mean±SD. Full-face photographs of participants were examined by independent, blinded reviewers and rated on a scale of 1 (none) through 10 (most severe) as described in the "Methods" section. Pretreatment Glogau classification was noted. No statistical significance was found at any time point after treatment in comparison to the zero time point for any cream.

**Table 3. Comparison of Change in Wrinkle Scores Over Time for Antiwrinkle Creams and Placebo for 42 Participants<sup>a</sup>**

Facial Region and Test Cream	Change in Wrinkle Score at Each Time Point		
	15 min	30 min	7 d
Glabella			
Freeze 24/7 (n=15)	0.4±0.4	0.3±0.5	0.1±0.4
LiftFusion (n=14)	0.1±0.3 <sup>b</sup>	0.0±0.2 <sup>b</sup>	0.1±0.3
Placebo (n=13)	0.2±0.6	0.2±0.6	0.0±0.1
Forehead			
Freeze 24/7	0.5±0.8	0.5±0.9	0.4±0.8
LiftFusion	0.1±0.2	0.1±0.2	0.1±0.2
Placebo	0.04±0.1	0.04±0.1	0.0±0.0
Lateral orbital			
Freeze 24/7	0.6±0.8	0.6±0.7	0.3±0.5
LiftFusion	0.3±0.4	0.3±0.6	0.4±0.4
Placebo	0.1±0.3	0.2±0.4	0.1±0.5

Abbreviations: Freeze 24/7, Freeze 24/7 Anti-Wrinkle Cream (Freeze 24/7 International LLC, New York, New York); LiftFusion, LiftFusion Micro-Injected M-Tox Transdermal Face Lift (Fusionbeauty, Inc, Boca Raton, Florida); placebo (Nutraderm Therapeutic Lotion; Healthpoint, Inc, San Antonio, Texas).

<sup>a</sup>Data are given as mean±SD. Full-face photographs of subjects were examined by independent, blinded reviewers and rated on a scale of 1 (none) through 10 (most severe) as described in the "Methods" section. Pretreatment Glogau classification was noted. Change in score in comparison to baseline is shown.

<sup>b</sup>P<.05 in comparison of Freeze 24/7 Anti-Wrinkle Cream and LiftFusion Micro-Injected M-Tox Transdermal Face Lift.

strate the improved effectiveness of its formulation containing M-Tox over botulinum toxin type A (Botox; Allergan Inc, Irvine, California). Interestingly, the efficacy

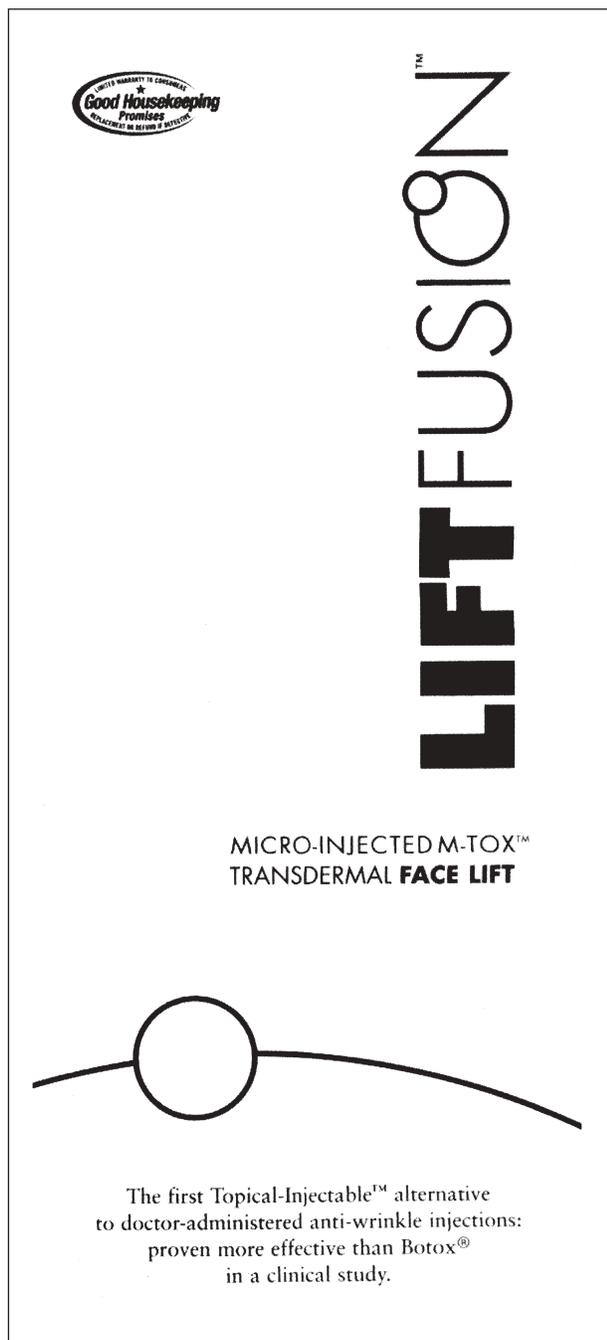
**Table 4. Change in Wrinkle Scores Over Time for Antiwrinkle Creams and Placebo for 23 Participants With Glogau Classes 3 and 4<sup>a</sup>**

Facial Region and Test Cream	Change in Wrinkle Score at Each Time Point		
	15 min	30 min	7 d
Glabella			
Freeze 24/7 (n=9)	0.6±0.5	0.3±0.6	0.1±0.5
LiftFusion (n=7)	0.0±0.0 <sup>b</sup>	0.0±0.3	0.1±0.3
Placebo (n=7)	0.3±0.8	0.3±0.8	0.0±0.3
Forehead			
Freeze 24/7	0.7±0.9	0.6±1.0	0.6±0.9
LiftFusion	0.07±0.2	0.07±0.2	0.07±0.2
Placebo	0.07±0.2	0.07±0.2	0.0±0.0
Lateral orbital			
Freeze 24/7	0.8±0.9	0.7±0.8	0.4±0.6
LiftFusion	0.2±0.4	0.6±0.5	0.5±0.5
Placebo	0.4±0.3	0.4±0.4	0.1±0.5

Abbreviations: Freeze 24/7, Freeze 24/7 Anti-Wrinkle Cream (Freeze 24/7 International LLC, New York, New York); LiftFusion, LiftFusion Micro-Injected M-Tox Transdermal Face Lift (Fusionbeauty, Inc, Boca Raton, Florida); placebo (Nutraderm Therapeutic Lotion; Healthpoint, Inc, San Antonio, Texas).

<sup>a</sup>Data are given as mean±SD. Comparison of change in wrinkle scores over time for antiwrinkle creams and placebo. Only patients rated as having Glogau (photoaging) class 3 or 4 rhytids were included. Full-face photographs of subjects were examined by independent, blinded reviewers and rated on a scale of 1 (none) through 10 (most severe) as described in the "Methods" section. Pretreatment Glogau classification was noted. Change in score in comparison to baseline is shown.

<sup>b</sup>P<.05 in comparison of Freeze 24/7 Anti-Wrinkle Cream and LiftFusion Micro-Injected M-Tox Transdermal Face Lift.



**Figure.** View of the manufacturer's package insert for LiftFusion Micro-Injected M-Tox Transdermal Face Lift, Fusionbeauty, Inc, Boca Raton, Florida.

of these 2 products is compared at 10 minutes and 72 hours after application. A reduction in wrinkles is noted in the eye area at 10 minutes by 30% of the participants and 72 hours by 60% of the participants after application, while no effect of botulinum toxin type A is noted. To the lay public this may seem impressive, unless one realizes the mechanism of botulinum toxin type A and its typical time to onset.<sup>4,5</sup> The use of charts and citation of clinical studies invokes the notion that the user is using a true pharmaceutical when this is not the case. Indeed, the makers of LiftFusion Micro-Injected M-Tox Trans-

dermal Face Lift have trademarked the term *topical-injectable* and use it prominently on the product packaging. At cosmetic counters around the country, data like these are touted as proof of effectiveness.

Of the approximately 35 ingredients listed for LiftFusion Micro-Injected M-Tox Transdermal Face Lift, the first 3 are water, cyclopentasiloxane (a silicone emollient that does not penetrate the skin), and ethylehexyl palmitate (also an emollient). As demonstrated in this study, no effect on wrinkles was noted with this formulation when compared with either baseline or placebo.

Freeze 24/7 Anti-Wrinkle Cream is representative of a host of freeze-creams that purport muscle relaxation by direct application of the inhibitory neurotransmitter  $\gamma$ -aminobutyric acid (GABA) directly through the skin. The penetration of GABA through the skin is poor, so formulations of such creams contain various plant extracts that are included to enhance penetration of GABA, but no scientific evidence of such penetration exists. While such evidence is awaited, creams such as this are sold in an unregulated fashion, with little or no clinical evidence as to their efficacy. In the present study, a trend toward some mild effect was noted. However, Freeze 24/7 Anti-Wrinkle Cream was most effective immediately after drying. Indeed, many participants noted a sticky feeling, and many compared the sensation to that of "dried egg white" on the skin. The thick, pastelike quality of this cream (when dried) probably contributed to some mild softening of wrinkles at the early time points, and thus long-lasting effects were lost after face washing, as noted herein.

In conclusion, the study herein presents objective data on 2 classes of facial creams that purport near-instant wrinkle reduction. Many more such products remain without such testing. Fortunately, it appears the only harm that comes from use of these products is financial. However, as the envelope is pushed and more naturopathic medicines are introduced as cosmeceuticals, the chances of untoward events increases. In this milieu, it is ever-important for physicians to be armed with knowledge regarding the efficacy and safety of such products.

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