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J Invest Dermatol. Author manuscript; available in PMC 2009 August 1.

Published in final edited form as:
J Invest Dermatol. 2009 February ; 129(2): 468–475. doi:10.1038/jid.2008.241.

Tumorigenic Effect of Some Commonly Used Moisturizing Creams when Applied Topically to UVB-Pretreated High-Risk Mice

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Abstract

Irradiation of SKH-1 mice with UVB (30 mJ cm^{-2}) twice a week for 20 weeks resulted in mice with a high risk of developing skin tumors over the next several months in the absence of further irradiation with UVB (high-risk mice). Topical applications of 100 mg of Dermabase, Dermovan, Eucerin Original Moisturizing Cream (Eucerin), or Vanicream once a day, 5 days a week for 17 weeks to these high-risk mice increased significantly the rate of formation of tumors and the rate of increase in tumor size per mouse. Additional studies indicated that treatment of high-risk mice with Dermabase, Dermovan, Eucerin, or Vanicream for 17 weeks increased the total number of histologically characterized tumors by 69% (average of two experiments; $P < 0.0001$ in each experiment), 95% ($P < 0.0001$), 24% ($P < 0.01$), and 58% ($P < 0.0001$), respectively. Topical applications of a specially designed Custom Blend cream to high-risk mice was not tumorigenic. The results indicate that several commercially available moisturizing creams increase the rate of formation and number of tumors when applied topically to UVB-pretreated high-risk mice. Further studies are needed to determine the effects of topical applications of moisturizing creams on sunlight-induced skin cancer in humans.

INTRODUCTION

Sunlight-induced nonmelanoma skin cancer is the most prevalent cancer in the United States, with more than one million cases per year (almost as many cases as for all of the other cancers combined; Scotto *et al*., 1996; Jemal *et al*., 2008). The incidence of these cancers is increasing, which is believed to be caused by the aging population, increased recreational exposure to sunlight, decreased clothing coverage, and the depletion of the atmospheric ozone layer (McKenzie *et al*., 1999; Wassberg *et al*., 2001; de Gruijl *et al*., 2003; Diffey, 2004; de Vries *et al*., 2006; Kojo *et al*., 2006; Norval *et al*., 2007; Ridky, 2007; Christenson *et al*., 2008). Although most nonmelanoma skin cancers (basal cell and squamous cell carcinomas) can be detected early and are cured by surgical removal, some people still die from these cancers—

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CONFLICT OF INTEREST
We received no funding for this study from Johnson and Johnson, but a patent application for the Custom Blend cream was filed on behalf of Rutgers and Johnson and Johnson. Funding for the study came from an NIH grant and supplemental departmental funds.

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particularly from squamous cell carcinomas. Because of the prevalence of sunlight-induced skin cancer, factors that influence the incidence of these cancers are of considerable importance. Recent research on UV carcinogenesis and factors influencing UV carcinogenesis are described in a special issue of Photochemistry and Photobiology (vol. 84, March/April 2008).

Large numbers of people worldwide are using moisturizing creams and ointments topically, but to the best of our knowledge most of these creams/ointments have not been tested for carcinogenic activity during the course of UVB irradiation in animals or when applied topically to UVB-pretreated animals after stopping irradiation with UVB in a model that resembles humans who receive extensive exposure to sunlight early in life and develop skin cancers later in life in the absence of further heavy exposure to sunlight. In earlier studies, we developed a mouse model for sunlight-induced skin cancer in humans by irradiating SKH-1 hairless mice with UVB (30 mJ cm^{-2}) twice a week for 20 weeks and then stopping UVB irradiation (Lou *et al*., 1999). These mice have a high risk of developing squamous cell papillomas, keratoacanthomas, and squamous cell carcinomas during the next several months in the absence of further UVB irradiation (high-risk mice; Lou *et al*., 1999).

In recent studies, we found that oral administration of caffeine or topical applications of caffeine or caffeine sodium benzoate enhanced UVB-induced apoptosis (Lu *et al*., 2000, 2002a, 2007) and inhibited carcinogenesis in UVB-pretreated high-risk mice in the absence of further UVB treatment (Lou *et al*., 1999; Lu *et al*., 2002b). Topical applications of caffeine also enhanced apoptosis in skin tumors in tumor-bearing mice (Lu *et al*., 2002b). Since our studies suggested the possible utility of caffeine and caffeine sodium benzoate as topical agents for inhibiting sunlight-induced skin cancer in humans, we started planning for human studies and initially selected Dermabase (the constituents in Dermabase and the other creams/ointments used in this study are given in Table 1) as a vehicle for topical caffeine studies in humans. However, we felt that it would be prudent to test Dermabase for carcinogenic activity before doing extensive studies in humans. Accordingly, we tested Dermabase for carcinogenic activity in UVB-pretreated SKH-1 mice that have no tumors but have a high risk of developing tumors after stopping UVB (high-risk mice).

Our initial study indicated that Dermabase was carcinogenic when applied topically once a day, 5 days a week for 17 weeks to UVB-pretreated high-risk mice after stopping UVB irradiation. Because of the carcinogenic activity of Dermabase in high-risk mice, we decided to test other commonly used moisturizing creams for tumorigenic activity as well as to develop a novel Custom Blend cream (The Custom Blend cream was prepared with the help of Johnson and Johnson Consumer and Personal Products Worldwide (Skillman, NJ)) that we hoped would not have tumorigenic activity. Substances that we worried about that were excluded from the Custom Blend cream at our request and prepared by Johnson and Johnson included sodium lauryl sulfate (an irritant; Bock *et al*., 2007; Slotosch *et al*., 2007) and mineral oil (a stimulator of UVB tumorigenesis; Kligman and Kligman, 1992). The present report describes the effects of topical applications of Dermabase, Dermovan, Eucerin Original Moisturizing Cream (Eucerin), Vanicream, and the Custom Blend cream on the formation of skin tumors in UVB-pretreated mice that have a high risk for developing skin tumors in the absence of further irradiation with UVB (high-risk mice). The constituents in these moisturizing creams, which are oil in water emulsions, are described in Table 1.

RESULTS

Experiment 1

Treatment of UVB-pretreated high-risk mice with 100 mg of Dermabase topically once a day, 5 days a week for 17 weeks increased the rate of increase in the formation of tumors per mouse

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($P < 0.001$) and tumor volume per mouse ($P = 0.023$) when compared with untreated control mice during the 17-week treatment period (Figure 1a).

Histology studies showed that topical applications of Dermabase to high-risk mice for 17 weeks increased the total number of tumors per mouse by 79% ($P < 0.0001$), the number of keratoacanthomas per mouse by 77% ($P < 0.0001$), and the number of squamous cell carcinomas per mouse by 127% ($P = 0.021$) when compared with untreated control high-risk mice (Table 2). The percentage of mice with squamous cell carcinomas was increased by 108% ($P = 0.043$) in the Dermabase-treated group (Table 2). Treatment of the mice with Dermabase increased the average tumor volume per mouse by 136% for total tumors, 64% for keratoacanthomas, and 262% for squamous cell carcinomas (Table 3). Tumor volume per mouse for all nonmalignant tumors was increased 63% ($P < 0.05$; Table 3).

Experiment 2

Water control versus untreated

Treatment of UVB-pretreated high-risk mice with 100 μl of water topically once a day, 5 days a week for 17 weeks did not have an effect on the rate or extent of tumor formation during the 17-week treatment period (Figure 1b) or on the formation or size of histologically defined tumors (Tables 4 and 5) when compared with untreated high-risk mice. Because the untreated and water-treated control groups were not different, they were combined into a single control group for the histology studies.

Studies with Dermabase

In the second experiment, topical applications of 100 mg of Dermabase once a day, 5 days a week to high-risk mice increased the rate of increase in the percent of mice with tumors ($P = 0.003$), tumors per mouse ($P < 0.0001$), and tumor volume per mouse ($P = 0.032$) when compared with control mice treated topically with water during the 17-week treatment period (Figure 1c).

Histology studies indicated that topical applications of Dermabase for 17 weeks to high-risk mice in experiment 2 increased the number of keratoacanthomas per mouse by 62% ($P < 0.0001$), the number of squamous cell carcinomas per mouse by 26%, and the total number of histologically characterized tumors per mouse by 59% ($P < 0.0001$) when compared with the combined control group (Table 4). Treatment of the mice with Dermabase increased the average tumor volume per mouse (for all mice) by 64% when compared with the combined control group (Table 5).

Studies with Dermovan

Treatment of high-risk mice with 100 mg of Dermovan topically once a day, 5 days a week for 17 weeks increased the rate of increase in the percent of mice with tumors ($P = 0.01$), tumors per mouse ($P < 0.0001$), and tumor volume per mouse ($P < 0.0001$) when compared with the control high-risk mice treated topically with water during the 17-week treatment period (Figure 1d).

Histology studies indicated that treatment of the high-risk mice with Dermovan for 17 weeks increased the percentage of mice with squamous cell papillomas by 342% ($P < 0.05$), the number of squamous cell papillomas per mouse by 244%, the number of keratoacanthomas per mouse by 90% ($P < 0.0001$), and the number of squamous cell carcinomas per mouse by 137% when compared with the combined control group (Table 4). The total number of histologically characterized tumors per mouse was increased 95% ($P < 0.0001$; Table 4).

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Treatment of the mice with Dermovan increased the average tumor volume per mouse (for all mice) by 88% (Table 5).

Studies with Eucerin

Treatment of high-risk mice topically with 100 mg of Eucerin once a day, 5 days a week for 17 weeks increased the rate of increase in the number of tumors per mouse ($P = 0.0005$) and tumor volume per mouse ($P < 0.0001$) when compared with the water control group (Figure 1e).

Histology studies indicated that topical treatment of high-risk mice with Eucerin for 17 weeks increased the number of keratoacanthomas per mouse by 21%, the number of squamous cell carcinomas per mouse by 100%, and the total number of histologically characterized tumors per mouse by 24% ($P < 0.01$) when compared with the combined control high-risk group (Table 4). Treatment of the mice with Eucerin increased the average size of tumors per mouse (for all mice) by 49% (Table 5).

Studies with Vanicream

Treatment of high-risk mice with 100 mg of Vanicream topically once a day, 5 days a week for 17 weeks increased the rate of increase in the number of tumors per mouse ($P < 0.0001$) and the tumor volume per mouse ($P = 0.013$) when compared with the water control group (Figure 1f).

Histology studies indicated that treatment of high-risk mice with Vanicream for 17 weeks increased the number of squamous cell papillomas per mouse by 89%, the number of keratoacanthomas per mouse by 61% ($P < 0.0001$), and the total number of histologically characterized tumors per mouse by 58% ($P < 0.0001$) when compared with the combined control group (Table 4). Treatment of the mice with Vanicream increased the average tumor size per mouse (for all mice) by 58% (Table 5).

Studies with Custom Blend cream

Treatment of high-risk mice topically with 100 mg of Custom Blend cream once a day, 5 days a week for 17 weeks did not have a significant effect on the rate of increase in the percent of mice with tumors, the number of tumors per mouse, or tumor volume per mouse when compared with the water-treated control group (Figure 1g).

Histology studies indicated that topical applications of the Custom Blend cream for 17 weeks did not increase the number of squamous cell papillomas, keratoacanthomas, or squamous cell carcinomas per mouse when compared with the combined control group (Table 4). Similarly, there was no statistically significant effect of treatment with Custom Blend cream on tumor size per mouse (Table 5).

DISCUSSION

Moisturizing creams and ointments used for the prevention and treatment of dry skin are generally tested for safety by determining irritant activity as well as for their effects on sensitization (an immunological response), but skin care preparations are generally not tested for carcinogenic activity *per se* or for carcinogenic activity in animals previously exposed chronically to UVB. Although mouse skin is widely used for carcinogenicity studies, it should be noted that mouse skin is much thinner and more permeable than human skin.

We have developed an animal model that resembles sunlight-induced skin cancer in humans who receive heavy exposure to sunlight early in life but develop skin cancer later in life in the

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absence of heavy sunlight exposure. In this albino animal model, we treat SKH-1 mice with UVB twice a week for 20 weeks and then stop UVB irradiation. These mice do not have tumors, but they do have a high risk of developing skin tumors over the next several months in the absence of further UVB irradiation (high-risk mice) (Lou *et al*., 1999; Lu *et al*., 2002b).

During studies to determine the safety of four commercially available and widely used moisturizing creams as possible vehicles for topical chemoprevention studies, we found that they all had tumorigenic activity when applied topically to UVB-pretreated high-risk mice. The mechanism of the tumorigenic effects of moisturizing creams in UVB-pretreated mice is not known but may be by a tumor-promoting type of mechanism that causes inflammation and proliferation in DNA-damaged skin, and further studies on this and other possible mechanisms are needed. During the course of our studies, we developed a Custom Blend cream that was not tumorigenic and was suitable for chemoprevention studies in humans.

In another study with moisturizing creams or excipients in these creams, topical applications of vasoline petroleum jelly or lanolin before each irradiation with UVB three times a week for 20 weeks inhibited tumorigenesis in SKH-1 mice, whereas similar applications of mineral oil enhanced tumorigenesis (Kligman and Kligman, 1992). In addition, topical applications of three proprietary vehicle formulations during the course of simulated sunlight irradiation 5 days a week for 40 weeks stimulated tumorigenesis in SKH-1 mice, whereas another three proprietary vehicles were inactive (Sambuco *et al*., 2003). Histological characterization of the tumors was not done in either of the above two studies. It should be emphasized that our study as well as the other studies described here were only done in hairless SKH-1 mice, and their significance for humans has not been established. Further studies are needed to determine the effects of the widespread use of moisturizing creams on the risk of sunlight-induced skin cancer in humans.

MATERIALS AND METHODS

Animals and exposure to UVB

Female SKH-1 hairless mice (6- to 7-week old) had free access to water and were fed Purina Laboratory Chow 5001 diet from the Ralston Purina Co. (St Louis, MO). The UV lamps used (FS72T12-UVB-HO; National Biological Corp., Twinsburg, OH) emitted UVB (280–320 nm; 75–80% of total energy) and UVA (320–375 nm; 20–25% of total energy). The studies described here were initiated under an institutionally approved protocol for treating high risk SKH-1 mice topically with acetone or certain chemicals in acetone once a day 5 days a week for 20 weeks. Procedures for studies in high risk SKH-1 mice treated topically with the various creams described in the present manuscript were institutionally approved after completion of the study.

Experiments 1 and 2

In experiment 1, we treated 60 female SKH-1 mice with UVB (30 mJ cm^{-2}) twice a week for 20 weeks. These mice have a high risk of developing skin tumors in the absence of further UVB irradiation (high-risk mice). UVB irradiation was stopped, and half of the mice were treated topically with 100 mg Dermabase once a day, 5 days a week for 17 weeks, and the control group was untreated. Dermabase (100 mg) was applied topically by lightly rubbing (massaging) the cream into the skin with a Q-tip. We used 3 g of Dermabase per 30 mice (or proportionately less cream for fewer mice) for each treatment session. All of the cream was distributed evenly among the different mice and was completely used up for each session. In experiment 1, there was no massage control and is the reason for having both an untreated control and a water-treated control in experiment 2 that controls for both the stress of removing the mice from their cages and the massage.

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In experiment 2, 210 female SKH-1 mice were irradiated with UVB (30 mJ cm^{-2}) twice a week for 20 weeks to obtain high-risk mice, and UVB irradiation was stopped. The mice (30 per group) were untreated or were treated topically with 100 μl water, or with 100 mg of Dermabase, Dermovan, Eucerin Original Moisturizing Cream (Eucerin), Vanicream, or Custom Blend cream once a day, 5 days a week for 17 weeks as described for experiment 1. The creams were massaged into the skin with a Q-tip after each application, and similar massaging was done in water-treated control mice. The compositions of the creams used are described in Table 1. The formation and size of tumors were measured throughout the 17-week treatment period in both experiments 1 and 2. Tumor volume was determined by measuring the three-dimensional size (height, length, and width) of each mass. The average of the three measurements was used as the diameter. The radius was determined and the volume was calculated by: volume = $4\pi r^3/3$. After the 17-week treatment period, the mice were killed and dorsal skins were taken to include each of the grossly observed masses in the treated areas of the mice. The skins were stapled flat to a plastic sheet and placed in 10% phosphate-buffered formalin at 4 °C for 24 hours followed by storage in ethanol until the preparation of sections of the epidermis and associated tumors for the histological characterization of tumors as described earlier (Lu *et al*., 2002b).

Statistical analysis

For the time-course analyses, the method of Kaplan–Meier estimation was used for the analyses of tumor-free distribution. The log-rank test was used to test homogeneity of the tumor-free distributions among all groups, and pair-wise comparisons of the tumor-free distributions between any of two groups. The repeated measurement (mixed effect) models (Lindsey, 1993; Diggle *et al*., 2003) without intercepts were used in the analyses of the treatment effects on the tumor number per mouse and tumor volume per mouse among the seven groups. The intercepts were not included in all the models so that the tumor number per mouse or tumor volume per mouse was zero at Day 0. The response was the tumor number per mouse or the tumor volume per mouse, and the covariates were time (weeks) and treatment together with the interaction. Time was treated as a continuous variable. Quadratic terms of time together with the interaction with treatment were included in the analyses to account for a possible quadratic trend. The first order autoregressive correlation structure was used for the within-mice correlation. The treatment effects were assessed based on the comparisons of slope (linear trend over time) of the regression lines and/or the quadratic trend over time. If the quadratic trend over time was not significant, it was not included in the final model. Multiplicity adjustment was not used for comparisons between treatment groups as this was a safety study and a conservative approach was used.

For the statistical analyses of histology studies, logistic regression models (Kleinbaum *et al*., 1998) were used for the analyses of the percent of mice with a specific type of tumor, and a Poisson regression model (Diggle *et al*., 2003) was used for the analyses of the tumor number per mouse for any tumor type. Since the tumor number per mouse was very small for some tumor types, Poisson regression was more appropriate in this situation. Linear regression (Kleinbaum *et al*., 1998) models were used for the analyses of the total tumor volume per mouse. Since there were no differences between water and untreated groups for any of the analyses, the two groups were combined and were called the control group. The comparisons of treatment groups with control groups were performed. The multiplicities of the comparisons were adjusted using Dunnett's method for all the analyses. When the normality assumption was not satisfied, a nonparametric test based on rank (Gibbons and Chakraborti, 2003) was used for the analyses. A 5% significance level was used for all the tests.

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Acknowledgements

This study was supported in part by NIH grant RO1 CA114442. We thank Ms Florence Florek for her excellent help in the preparation of this paper.

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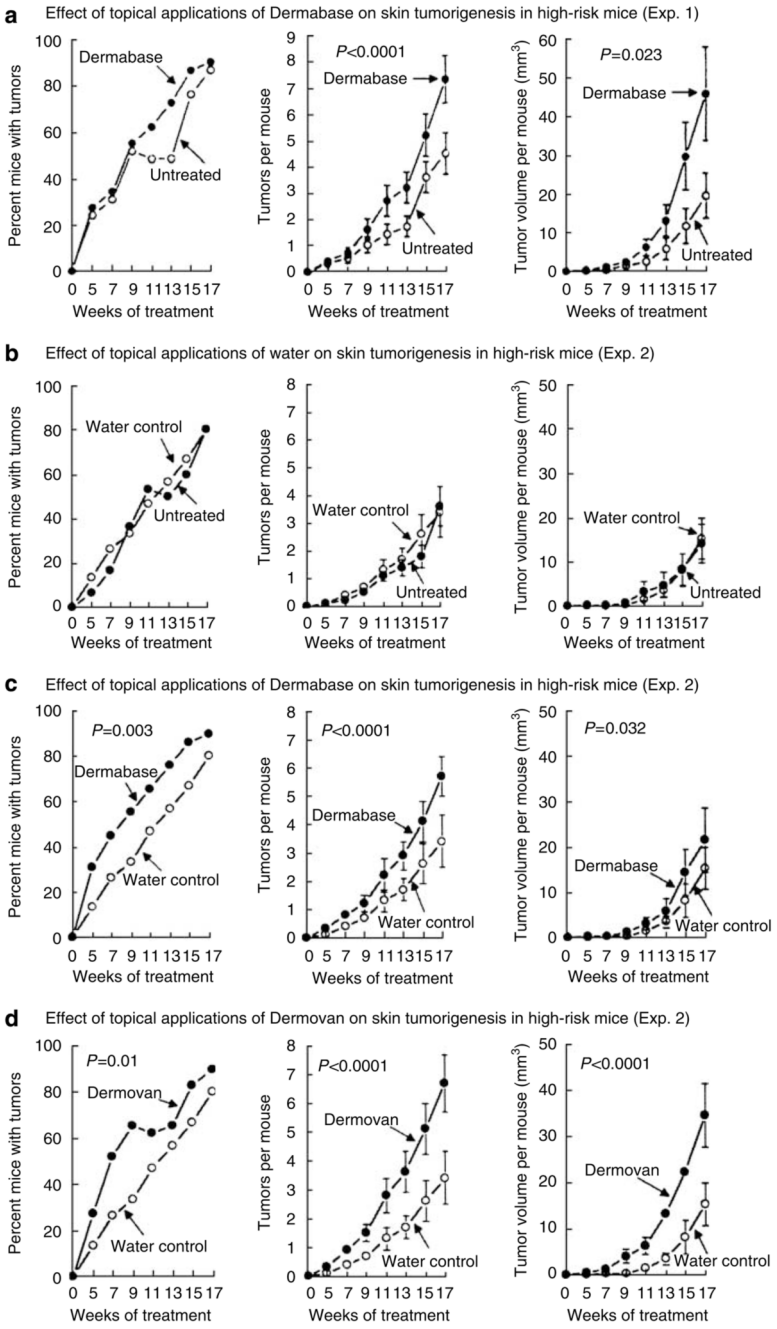

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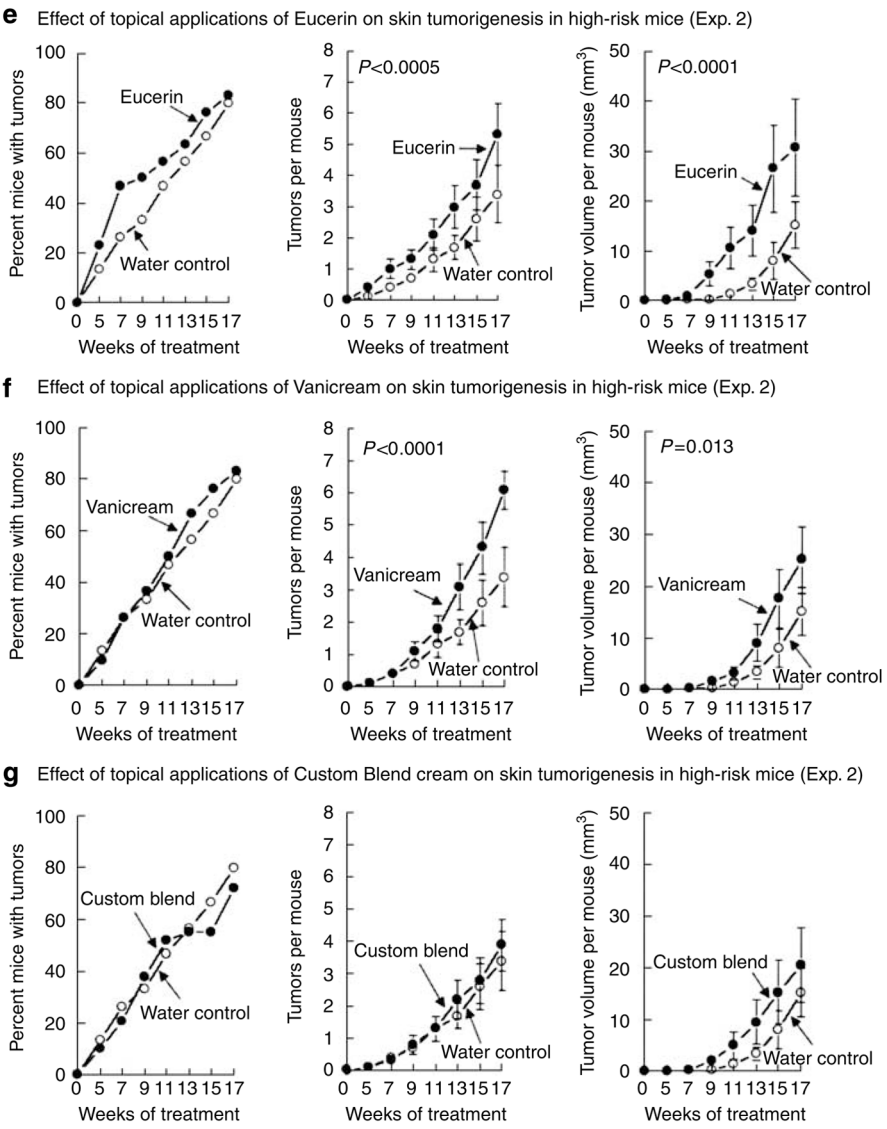

Figure 1. Time course for the effect of topical applications of different moisturizing creams on the formation of tumors in "high-risk" mice pretreated with UVB

Female SKH-1 hairless mice were treated with UVB (30 mJ cm^{-2}) twice a week for 20 weeks to obtain tumor-free "high-risk" mice. The mice were then untreated, treated topically with water (100 μl) or with the indicated cream (100 mg) once a day, 5 days a week for 17 weeks in the absence of further treatment with UVB. The data are expressed as the mean ± SE. Statistical analyses of differences in pair-wise regression slopes of rates of change with time were determined for tumors per mouse and for tumor volume per mouse as described in the Materials and Methods section. The statistical analysis of changes in the percent of mice with tumors versus time was based on a comparison of tumor-free distribution between the two groups by the log-rank test as described in the Materials and Methods section. Statistically significant differences from the water-treated control group ($P < 0.05$) are indicated.

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Table 1

Ointments and creams studied (oil in water emulsions)

Dermabase cream
Paddock Laboratories Inc.
(Minneapolis, MN)
Ingredients:
Purified water, mineral oil, petrolatum, cetostearyl alcohol, propylene glycol, sodium lauryl sulfate, isopropyl palmitate, imidazolidinyl urea, methylparaben, and propylparaben.

Dermovan
Healthpoint Ltd.
(Fort Worth, TX)
Ingredients:
Water, glyceryl stearate
(and) stearamidoethyl diethylamine, glycerin, mineral oil, cetyl esters, cetyl alcohol, butylparaben, methylparaben, and propylparaben.

Eucerin Original Moisturizing Cream (Eucerin)
Beiersdorf Inc.
(Wilton, CT)
Ingredients:
Water, petrolatum, mineral oil, ceresin, lanolin alcohol, methylchloroisothiazolinone, and methylisothiazolinone

Vanicream
Pharmaceutical Specialties Inc.
(Rochester, MN)
Ingredients:
Purified water, white petrolatum, cetearyl alcohol and ceteareth-20, sorbitol solution, propylene glycol, simethicone, glyceryl monostearate, polyethylene glycol monostearate, sorbic acid, and BHT.

Custom Blend
Johnson and Johnson Skin Research Center
(Skillman, NJ)
Ingredients:
Purified water, propylene glycol, stearyl alcohol, cetyl alcohol, polysorbate 20, isopropyl myristate, C12-15 alkyl benzoate, benzoic acid, glycerin, and sodium hydroxide
(final pH = 5.8)

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Table 2

Effect of topical applications of Dermabase cream on the incidence and multiplicity of histologically characterized skin tumors in high-risk SKH-1 mice previously treated with UVB light (exp. 1)

Treatment	No. of mice	Squamous cell papillomas		Keratoacanthomas		Total nonmalignant Tumors		Squamous cell carcinomas		Total tumors	
		Percent of mice with tumors	Tumors per mouse	Percent of mice with tumors	Tumors per mouse	Percent of mice with tumors	Tumors per mouse	Percent of mice with tumors	Tumors per mouse	Percent of mice with tumors	Tumors per mouse
Untreated	29	10	0.10 ± 0.06	86	6.41 ± 1.16	86	6.52 ± 1.19	24	0.41 ± 0.15	86	6.93 ± 1.28
Dermabase	28	7	0.11 ± 0.08	96	11.36 ± 1.37[1] (77)	96	11.46 ± 1.39[1] (76)	50[2] (108)	0.93 ± 0.22[2] (127)	96	12.39 ± 1.53[1] (79)

Female SKH-1 mice (7- to 8-week old) were irradiated with UVB (30 mJ cm^{-2}) twice weekly for 20 weeks, and UVB irradiation was stopped. These tumor-free mice with a high risk of developing skin tumors were untreated or treated topically with 100 mg of Dermabase cream once a day, 5 days a week for 17 weeks. The mice were killed at 18 weeks after the last dose of UVB, and all tumors were characterized by histopathology studies. Each value is the mean ± SE, and the numbers in parentheses represent percent increase. Statistical analysis was done as described in the Materials and Methods section. Statistically different from the untreated control group ([1]$P < 0.0001$, [2]$P = 0.021$).

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Table 3

Effect of topical applications of Dermabase cream on the size of tumors in high-risk SKH-1 mice previously treated with UVB light (exp. 1)

Treatment	No. of mice	Squamous cell papillomas	Keratoacanthomas	Total nonmalignant tumors	Squamous cell Carcinomas	Total tumors
		Tumor volume per mouse (mm^3)	Tumor volume per mouse (mm^3)	Tumor volume per mouse (mm^3)	Tumor volume per mouse (mm^3)	Tumor volume per mouse (mm^3)
Untreated	29	2.1 ± 1.8	29.9 ± 9.5	32.0 ± 9.9	18.8 ± 8.1	50.8 ± 14.7
Dermabase	28	3.1 ± 2.8 (48)	48.9 ± 10.6 (64)	52.0 ± 11.9 (63)	68.0 ± 24.5 (262)	120.0 ± 33.0 (136)

Female SKH-1 mice (7-to 8-week old) were irradiated with UVB (30 mJ cm^{-2}) twice weekly for 20 weeks, and UVB irradiation was stopped. These tumor-free mice with a high risk of developing skin tumors were untreated or treated topically with 100 mg of Dermabase cream once a day, 5 days a week for 17 weeks. The mice were killed at 18 weeks after the last dose of UVB, and all tumors were characterized by histopathology studies (Table 2) and the size of each tumor was determined. Each value is the mean ± SE, and the numbers in parentheses represent percent increase. None of the increases in tumor volume per mouse was statistically significant except for the increase in tumor volume per mouse for total nonmalignant tumors in the Dermabase group ($P < 0.05$) when analyzed by a nonparametric method as described in the Materials and Methods section.

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Table 4

Effect of topical applications of different creams and ointments on the incidence and multiplicity of histologically characterized skin tumors formed in high risk SKH-1 mice previously treated with UVB light (exp. 2)

Treatment	No. of mice	Squamous cell papillomas		Keratoacanthomas		Total nonmalignant tumors		Squamous cell carcinomas		Total tumors	
		Percent of mice with tumors	Tumors per mouse	Percent of mice with tumors	Tumors per mouse	Percent of mice with tumors	Tumors per mouse	Percent of mice with tumors	Tumors per mouse	Percent of mice with tumors	Tumors Per mouse
Water	30	6.7	0.07 ± 0.05	77	4.30 ± 1.12	77	4.37 ± 1.14	17	0.20 ± 0.09	77	4.57 ± 1.21
Untreated	27	7.4	0.11 ± 0.08	85	4.63 ± 0.94	85	4.74 ± 0.99	15	0.19 ± 0.09	85	4.93 ± 1.03
Combined control	57	7.0	0.09 ± 0.04	81	4.46 ± 0.28	81	4.54 ± 0.20	16	0.19 ± 0.06	81	4.74 ± 0.20
Dermabase	29	6.9 (0)	0.07 ± 0.05 (−22)	90 (11)	7.21 ± 1.15[1] (62)	90 (11)	7.28 ± 1.15[1] (60)	21 (31)	0.24 ± 0.09 (26)	90 (11)	7.52 ±1.18[1] (59)
Dermovan	29	31.0[2] (342)	0.31 ± 0.09[3] (244)	86 (6)	8.48 ± 1.64[1] (90)	90 (11)	8.79 ± 1.65[1] (94)	31 (94)	0.45 ± 0.16 (137)	90 (11)	9.24 ± 1.71[1] (95)
Eucerin	29	10.3 (47)	0.14 ± 0.08 (56)	79 (−2)	5.38 ± 1.18 (21)	79 (−2)	5.52 ± 1.22[2] (22)	21 (31)	0.38 ± 0.15 (100)	79 (−2)	5.90 ± 1.33[3] (24)
Vanicream	30	13.3 (90)	0.17 ± 0.08 (89)	83 (2)	7.17 ± 1.80[1] (61)	83 (2)	7.33 ± 1.83[3] (61)	17 (6)	0.17 ± 0.07 (−11)	83 (2)	7.50 ± 1.85[1] (58)
Custom Blend	25	4.0 (−43)	0.04±0.04 (−56)	72 (−11)	4.68±1.13 (5)	72 (−11)	4.72±1.13 (4)	12 (−25)	0.16±0.09 (−16)	72 (−11)	4.88±1.19 (3)

In experiment 2, female SKH-1 mice (7- to 8-week old) were irradiated with UVB (30 mJ cm^{-2}) twice weekly for 20 weeks, and these tumor-free mice with a high risk of developing skin tumors were untreated or treated topically with 100 μl of water or 100 mg of different types of creams or ointments once a day, 5 days a week for 17 weeks. The mice were killed at 18 weeks after the last dose of UVB. All tumors were characterized by histopathology studies. As there was no difference between the untreated and water-treated groups they were combined for comparisons with the groups treated with the various creams. Each value is the mean ± SE, and the numbers in parentheses represent percent increase. Statistical analysis was done as described in the Materials and Methods section.

[1] $P < 0.0001$,

[2] $P < 0.05$,

[3] $P \leq 0.01$.

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Table 5

Effect of topical applications of different moisturizing creams on the size of histologically characterized tumors in high-risk SKH-1 mice previously treated with UVB light (exp. 2)

Treatment	No. of mice	Squamous cell papillomas	Keratoacanthomas	Total nonmalignant tumors	Squamous cell carcinomas	Total tumors
		Tumor volume per mouse (mm^3)	Tumor volume per mouse (mm^3)	Tumor volume per mouse (mm^3)	Tumor volume per mouse (mm^3)	Tumor volume per mouse (mm^3)
Water	30	0.6 ± 0.5	15.3 ± 4.2	15.9 ± 4.3	7.4 ± 3.5	23.2 ± 6.6
Untreated	27	3.4 ± 3.4	13.7 ± 4.9	17.1 ± 6.5	14.9 ± 11.3	32.0 ± 12.6
Combined control	57	1.9 ± 1.6	14.5 ± 3.2	16.4 ± 3.8	10.9 ± 5.6	27.3 ± 6.9
Dermabase	29	0.3 ± 0.2 (−84)	15.0 ± 3.8 (3)	15.3 ± 3.9 (−1)	29.6 ± 22.5 (172)	44.9 ± 23.9 (64)
Dermovan	29	2.5 ± 1.6 (32)	23.7 ± 6.0 (63)	26.2 ± 5.9 (60)	25.1 ± 12.5 (130)	51.3 ± 14.0 (88)
Eucerin	29	2.6 ± 2.3 (37)	24.0 ± 8.3 (66)	26.6 ± 9.1 (62)	14.1 ± 10.8 (29)	40.6 ± 16.1 (49)
Vanicream	30	3.8 ± 2.6 (100)	32.4 ± 9.5 (123)	36.1 ± 9.6 (120)	7.0 ± 5.2 (−35)	43.0 ± 11.5 (58)
Custom Blend	25	1.3 (−32)	17.1 ± 5.3 (18)	18.5 ± 5.3 (13)	7.7 ± 5.9 (−29)	26.2 ± 9.8 (−4)

In experiment 2, female SKH-1 mice (7- to 8-week old) were irradiated with UVB (30 mJ cm^{-2}) twice weekly for 20 weeks, and these tumor-free mice with a high risk of developing skin tumors were treated topically with 100 μl of water or 100 mg of different creams or ointments once a day, 5 days a week for 17 weeks. The mice were killed at 18 weeks after the last dose of UVB. All tumors were characterized by histopathology studies (Table 4) and the size of each tumor was determined. Each value for tumor volume per mouse is the mean ± SE, and the numbers in parentheses represent percent increase in size when compared with the combined control group. None of the increases in tumor volume per mouse was statistically significant except for the increase in tumor volume per mouse for squamous cell papillomas in the Dermovan-treated mice ($P < 0.05$) when analyzed by a nonparametric method as described in the Materials and Methods section.