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ORIGINAL ARTICLE

Development of a cream formulation containing bee venom and other bee products

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Abstract

This study aimed to develop a prototype skincare product with bee venom, propolis, honey, beeswax, and royal jelly. The prototype formulation contained 0.1% bee venom, 0.3% propolis extract, 0.45% honey, and 1.0% royal jelly. The prototype body cream was analyzed for stability, antioxidant activity, dermatological response, and cytotoxicity. In addition, a panel test evaluated the prototype for the claims such as skin smoothness, feelings of nourishment, moisturizing, skin tone, brightness, and visibility of wrinkles. According to the stability test, the prototype was stable for up to 90 days at room temperature and +40°C. The formulation was found to have a high antioxidant capacity at 85.45%. Cell viability detected over 70% indicated that the prototype body cream was not cytotoxic. The dermatological analysis revealed no irritation or allergic reaction in non-allergic individuals. Panel test showed that the prototype makes skin silky smooth, contributes to hydration, brightens and nourishes the skin, evens the skin tone, reduces the visibility of wrinkles, improves skin elasticity, and smoothes wrinkles. This prototype formulation requires further research to evaluate its effectiveness against skin aging on different skin types. Nevertheless, the side effects of such products need particular attention in developing a commercial product containing bee venom in susceptible individuals.

KEYWORDS
antiaging, bee venom, body cream, propolis, royal jelly

1 | INTRODUCTION

One of the pharmacology research areas is investigating the effects of natural drug-like products.[1] Numerous studies proved the positive effects of bee products such as bee venom, propolis, royal jelly, and honey on the skin.[2] Bee venom is a pharmacologically active hive product, synthesized in the venom glands of worker and queen honeybees, and stored in the poison reservoir.[3] Bee venom, also called apitoxin, acts when the needle is immersed, reaching the immersed place through a channel directly connected with the poison bag where it is stored. A worker bee produces approximately 0.3 mg of poison during its lifetime.[4]

Bee venom is a natural bee product showing a healing effect against skin diseases such as atopic dermatitis. Its antimicrobial activity against acne vulgaris highlighted its potential as an anti-acne agent in the pharmaceutical and cosmetic industries.[5-7] Bee venom is a photoprotective agent (Han et al., 2006) and effectively prevents deeper skin wrinkles.[8] Moreover, it has been proven that bee venom has a significant wound healing activity, which might be associated with the biological mechanisms of the expression of TGF-b1, fibronectin, VEGF, and collagen-I.[9] Bee venom can be an exceptionally beneficial natural ingredient for the cosmetics industry through its anti-inflammatory activity and wound healing properties.

Propolis is a strong adhesive, resinous substance collected from various plant sources, transformed, and used by bees to seal the holes in its honeycombs, fix the inner walls, and protect the entrance against intruders.[10] Propolis is known to have various biological activities such as anticancer, antioxidant, anti-inflammatory, antiviral,

and antifungal.[11] The phenolics and flavonoids of propolis supplying antioxidant activity and the ability to clean the free radicals from the cells are directly related to its efficacy for protecting the skin. These antioxidant compounds protect the skin against the harmful effects of UV light and free radicals occurring after penetration into the epidermis and dermis layers.[12] In addition to its skin protection activity, propolis also has wound healing properties.[13] Royal jelly, another beehive product, is a bee secretion product that is essential for the honeybee larva diet and plays a significant role in muscle differentiation. It is believed that the queen bee's longevity compared with other bees in the hive is due to the exclusive consumption of royal jelly throughout its life.[14] There is a substantial interest in the pharmacological properties of royal jelly.[15] Studies indicate that royal jelly can potentially protect the skin against UVB-induced photo and skin aging by increasing collagen production.[15,16] Like those bee products, honey also exhibits many beneficial effects on the skin, such as effects of softening, moisturizing, and soothing,keeping the skin young and delaying the formation of wrinkles; regulating the skin pH; and preventing pathogen infections.[17]

This study aimed to develop a prototype skincare formulation based on bee venom, propolis, honey, and royal jelly to effectively protect skin aging by analyzing various quality, stability, and safety parameters.

2 | MATERIALS AND METHODS

2.1 | Prototype formulation

Bee venom (Muğla, Turkey), royal jelly (Balıkesir, Turkey), honey (Bingöl, Turkey), and propolis (Düzce, Turkey) were obtained from the contracted beekeepers. In the beginning, raw materials of various skincare products available in the market were listed, and natural alternatives against the chemical ones were investigated. The prototype formulation was 0.1% bee venom, 0.3% propolis extract, 0.45% honey, and 1.0% royal jelly based on this preliminary evaluation. One of the main active ingredients of the formulation was bee venom, with 43.69% melittin, 1.87% apamine, and 12.18% phospholipase A2 content. The formulation also included propolis as a natural preservative, cetearyl alcohol and akoline GC as emulsifiers, locust bean gum to control viscosity, and glycerin as a moisturizer. The appearance and formulation of the prototype are given in Figure 1 and Table 1.

The skincare product designed as a body cream was prepared by mixing the locust bean gum and deionized water and heating at 90°C until the gum portion was melted. The mixture was allowed to cool down in a water bath, and glycerin and honey were added by controlling the temperature at 45–50°C. Finally, royal jelly and bee venom were added to the mixture, which was thoroughly mixed. The oil phase was prepared separately with stearyl alcohol, akoline GC, Lipex Shealight™, and jojoba oil. The oil phase was heated by mixing continuously until the temperatures reached 50°C. After obtaining a homogeneous, thoroughly melted mixture, it was removed from the heat source and added vitamin E. Then, the oil phase was homogenized with a homogenizer (IKA T25) at a constant speed of 2000 rpm (1153 *g*) for 10 min on a water bath. During this process, bee venom containing the first phase was added and homogenized thoroughly for 5 min. Following the formation of emulsion thoroughly, propolis and jasmine oil were also added and mixed, and then placed in containers.

FIGURE 1 Appearance of the prototype formulation

2.2 | Analysis of skincare prototype

2.2.1 | Stability analysis

The samples were kept in air-conditioned cabinets at room temperature and 40°C in triplicates for stability tests. The samples were analyzed for appearance, density, viscosity, pH, protective efficacy, and microbiological quality. For microbiological evaluations, aerobic mesophilic colony count (TS EN ISO 21149), *Pseudomonas aeruginosa* analysis (TS EN ISO 22717), *Staphylococcus aureus* analysis (TS EN ISO 22718), *Escherichia coli* analysis (TS EN ISO 21150), *Candida albicans* analysis (TS EN ISO 18416), and total mold-yeast count (TS EN ISO 16212) were carried out.

2.2.2 | Antioxidant activity

The antioxidant capacity of the prototype was evaluated by the free radical-scavenging activity (DPPH) based on the method given by Özdemir & Güven Çapanoğlu.[18] The radical scavenging activity of 2.2-diphenyl-1-picrylhydrazyl (DPPH) was quantified in terms of %

TABLE 1 Formulation of the prototype

Ingredients	INCI	%
Deionized Water	Aqua	77.40
Locust Bean Gum	Ceratonia Siliqua Gum	0.25
Glycerol	Glycerin	2.00
Royal Jelly	Royal Jelly Extract	1.00
Honey	Honey	0.45
Bee Venom	Bee Venom	0.10
Cetearyl alcohol	Cetearyl Alcohol	3.00
Akoline GC	Hydrogenated Vegetable Glycerides Citrate	5.00
Lipex Shealight	Shea Butter Ethyl Esters	5.00
Jojoba Oil	Simmondsia Chinensis (Jojoba) Seed Oil	4.00
Vitamin E	Tocopherol	0.50
Propolis Extract	Propolis Extract	0.30
Jasmine Oil	Jasminum Officinale (Jasmine) Oil	1.00
Total:		100.00

inhibition of the free radicals by the prototype formulation. In order to have a 2.0 mM DPPH, 19.7 mg of the DPPH radical was weighed and dissolved in ethanol, and then, the volume was completed to 25 ml. Subsequently, 2.7 ml of extract and 300 µl of DPPH solution were mixed in a test tube. For the blind test, ethanol was substituted for the extract. All the prepared mixtures were incubated for 15 min at room temperature in the dark. The absorbance against blind trial was measured with a UV-VIS spectrophotometer at a wavelength of 517 nm.[18] The inhibition value was calculated using Equation 1.

$$\%\ Inhibition = \frac{Blind\ Absorbance - Sample\ Absorbance}{Blind\ Absorbance} \times 100 \quad (1)$$

2.2.3 | Analysis of dermatologic response

Dermatological analysis examined the effect of the skincare prototype on sensitive skin by performing H-RIPT hypo-allergen tests on ten volunteers with sensitive skin, according to the regulation of the European Parliament and Council Regulation (EC) no 1223/2009 of 30 November 2009.

Volunteers participating in the research were selected based on current European and Polish law, Cosmetics Europe—The Personal Care Association and Declaration of Helsinki (1964–2013). All volunteers selected for the study met the requirements for inclusion and signed a consent form for their voluntary participation in the study. During the trials, a dermatologist monitored the volunteers for any adverse effects.

The research model used in trials was the skin test according to Jadassohn-Bloch, modified by Rudzki. The test consisted of applying the product to a selected skin area in triplicates and then observing the skin's condition at certain time intervals. The recording of the results and the classification of the product are based on the point classification (0–4) of the skin reaction (I04 / PO-08).

The average irritation index (x_{sr}) is calculated from the sum of the scores for erythema and edema. Based on the irritation index, the product is classified according to the scale given in Table 2.

2.2.4 | Analysis of cytotoxicity

Cytotoxicity analysis was performed *in vitro* according to TS EN ISO 10993–5 standard. L929 cell culture was exposed to the skincare prototype samples for 24 h in the test. The experimental protocol was based on calculating L929 healthy mouse fibroblast cell viability by metabolic activity. The yellow, water-soluble MTT [3- (4,5-dimethylthiazol-2-yl) −2,5-diphenyl tetrazolium bromide] is metabolically reduced to blue-violet, water-insoluble formazan in living cells. The number of viable cells was calculated by determining the color intensity after dissolving formazan in alcohol. Accordingly, L929 healthy mouse fibroblast cell was seeded in a 24-well plate and incubated until it formed a semi-confluent layer (24 h). Then, for direct contact, the samples were applied to the surface of a filter paper with a pore size of 0.45 µm and placed in the wells with the test substance on the cell surface. The filter papers were prepared to correspond to the 1:10 surface of the well area and were sterilized. After 24 h of incubation, formazan formation was determined for each sample and compared with the values obtained from control cultures. Cell viability is directly related to the amount of blue-purple formazan read as optical density at 570 nm. PBS (phosphate buffered saline) was used as the negative control group and SDS (0.4 mg/ml sodium dodecyl sulfate) as the positive control group. The decrease in cell viability compared with the negative control was calculated according to Equation 2.

$$cell\ viability\ (\%) = \frac{100 \times OD570e}{OD570b} \quad (2)$$

OD_{570e} is the mean value of the measured optical density of the bee venom containing prototype sample concentration. At the same time, OD_{570b} is the mean value of the measured optical density of the negative control group. Samples with cell viability below 70% are considered cytotoxic. The reaction degrees for the experiment made by direct contact are given in Table 3. Grading value greater than 2 specified in Table 3 was reported as the cytotoxic effect.

TABLE 2 Scale for classification of the irritation

Average irritation index (x_{sr})	Product classification
$x_{sr} < 0.5$	Non-irritating
$0.5 < x_{sr} < 2.0$	Slightly irritating
$2.0 < x_{sr} < 5.0$	Moderately irritating
$5.0 \leq x_{sr}$	Strongly irritating

TABLE 3 Definition of degree and reaction zone

Degree	Reaction	Reaction description of the reaction zone
0	None	No detectable zone around or under the specimen
1	Slight	Some malformed or degenerated cells under the specimen
2	Mild	Zone limited to area under the specimen
3	Moderate	Zone extending specimen size up to 1 cm
4	Severe	Zone extending farther than 1 cm beyond specimen

TABLE 4 Age and Skin types of the subjects

No	Sex	Age	Skin type
1	Woman	33	Combination
2	Woman	34	Combination
3	Woman	45	Normal
4	Woman	47	Dry
5	Woman	50	Dry
6	Woman	54	Dry
7	Woman	55	Combination
8	Woman	60	Combination
9	Woman	60	Combination
10	Woman	65	Dry

2.2.5 | Panel test

The in-use test aimed to assess how easy applying the prototype on the skin and verifying the product claims objectively. The study was conducted in accordance with Regulation of the European Parliament and Council Regulation (EC) No. 1223/2009 of November 30, 2009, and No. 655/2013 of July 10, 2013, on cosmetics and the recommendations of Cosmetics Europe—The Personal Care Association Guidelines: Product test guidelines for the Assessment of Human Skin Compatibility 1997—Guidelines for the Evaluation of the Efficacy of Cosmetic Products 2008. The product testing was carried out under the supervision of a qualified person and dermatologist on volunteers at home (house panel). A total of 10 women participants assessed the perceived effectiveness of the product and its cosmetic properties based on what they observed or felt. Age and skin types of the subjects are given in Table 4.

Participants in the studies were not instructed for any special requirements, assuming that tests carried out under normal consumption conditions would better imitate the conditions in real practice. Many factors could have influenced the results of user tests as type and condition of the skin, genetically determined individual characteristics, individual preferences, lifestyle, and environmental conditions.

The volunteer testers received one product package and asked to use it regularly for 3 weeks based on the instructions for applying it to the skin. The participants were informed that they should avoid using other products of identical or analogous during the trial. In addition, they were asked immediately to cease the use of the product in the case of any adverse symptoms or unexpected sensations at the location of the application and to report them to the supervisor. Confirmation of the declaration requires more than 50% of the positive answers from the respondents to the question regarding this declaration.

3 | RESULTS AND DISCUSSION

3.1 | Analysis of cream prepared

3.1.1 | Stability test

The stability test demonstrated that the prototype product maintained its homogeneous appearance for up to 90 days at room temperature (Table 5). Within 90 days, the density of the formulation changed between 1.143 and 1.179 g/ml, and pH was observed in the range of 6.4 – 7.6. Viscosity values ranged from 12.0×10^3 to 22.1×10^3 cP, indicating a stable emulsion structure. The microbiological tests and protective efficacy results were also acceptable (Table 5). According to these results, it is apparent that the

TABLE 5 Stability test results of the prototype product kept at room temperature

Control Parameters	0 day	15 days	30 days	60 days	90 days	Evaluation
Appearance	Homogeneous Beige Color	Homogeneous Beige Color	Homogeneous Beige Color	Homogeneous Beige Color	Homogeneous Beige Color	Appropriate
Density (g/ml)	1.179	1.143	1.165	1.168	1.169	Appropriate
Viscosity ($\times 10^3$ cP)	12.0	18.4	14.7	14.3	22.1	Appropriate
pH	6.4	7.1	7.6	7.0	7.6	Appropriate
Microbiological condition	Appropriate	Appropriate	Appropriate	Appropriate	Appropriate	Appropriate
Protective Activity	Appropriate	-	-	-	-	Appropriate

TABLE 6 Stability test results of the prototype product kept at +40°C

Control Parameters	0 day	15 days	30 days	60 days	90 days	Evaluation
Appearance	-	Homogeneous Beige Color	Homogeneous Beige Color	Homogeneous Beige Color	Homogeneous Beige Color	Appropriate
Density (g/ml)	-	1.141	1.161	1.153	1.155	Appropriate
Viscosity ($\times 10^3$ cP)	-	19.2	16.9	19.4	21.8	Appropriate
pH	-	7.6	7.8	7.0	6.7	Appropriate
Microbiological quality	-	Appropriate	Appropriate	Appropriate	Appropriate	Appropriate
Protective Activity	-	-	-	Appropriate	-	Appropriate

TABLE 7 Microbiological quality test results

Analysis	Method	Result	Unit	Limitation	Evaluation
Aerobic Mesophilic Colony Count	TS EN ISO 21149	<10	Cfu / ml	<1000	Appropriate
Pseudomonas aeruginosa Analysis	TS EN ISO 22717	Not Detected	Cfu / ml	0	Appropriate
Staphylococcus aureus Analysis	TS EN ISO 22718	Not Detected	Cfu / ml	0	Appropriate
Escherichia coli Analysis	TS EN ISO 21150	Not Detected	Cfu / ml	0	Appropriate
Candida albicans Analysis	TS EN ISO 18416	Not Detected	Cfu / ml	0	Appropriate
Total Mold-Yeast Count	TS EN ISO 16212	<10	Cfu / ml	<1000	Appropriate

TABLE 8 Results of dermatological test

Volunteer characteristics			1st application		2nd application		3rd application	
No	Sex	Age	Erythema	Edema/Swelling	Erythema	Edema/Swelling	Erythema	Edema/Swelling
1	F	24	0	0	0	0	0	0
2	F	21	0	0	0	0	0	0
3	F	27	0	0	0	0	0	0
4	F	61	0	0	0	0	0	0
5	F	30	0	0	0	0	0	0
6	F	46	0	0	0	0	0	0
7	F	56	0	0	0	0	0	0
8	F	58	0	0	0	0	0	0
9	F	39	0	0	0	0	0	0
10	F	22	0	0	0	0	0	0

prototype body cream remained stable at room temperature for 90 days. Similar to these findings, the stability test carried out at +40°C revealed that the prototype's appearance remained unchanged for 90 days (Table 6). The density of the body cream was between 1.141 and 1.155 g/ml, and the pH value remained in the neutral range (7.6–6.7). The viscosity remained reasonably stable at 19.2×10^3 – 21.8×10^3 cP, similar to the findings at room temperature. The prototype's microbiological and protective efficacy kept at 40°C was also appropriate (Table 6) according to the parameters given in Table 7.

Based on these findings, it is evident that the prototype product maintained its appearance, density, viscosity, and pH values for up to 90 days at room temperature and +40°C. In addition, the microbiological quality and protection efficacy were appropriate during storage for 90 days at both conditions.

3.1.2 | Antioxidant activity

According to the results of the free radical scavenging assay, the antioxidant capacity of the prototype was found to be 86.72%, which is compatible with the literature findings for cosmetic products. Mishra et al.[19] reported 87.51% antioxidant activity of o/w sunscreen cream containing herbal oil. Similarly, Lohani et al. (2010) evaluated the cosmetical potential of geranium and calendula essential oil, revealing a range of antioxidant activity between 85.51% ± 0.020% and 78.06% ± 0.04%, recorded after 30 min of the incubation period (Lohani et al.).[20] Therefore, the antioxidant activity of the prototype product is highly consistent with available literature findings.

The observed high antioxidant activity may be related to bee venom and propolis, which are the source of antioxidant activity in

the prototype formulation. Sobral et al.[20] investigated antioxidant, anti-inflammatory, and cytotoxic properties of bee venom collected in northeast Portugal. This study demonstrated antioxidant and anti-inflammatory properties of bee venom samples.[21] Another ingredient used to formulate the prototype body cream, propolis, is also known for its high antioxidant capacity. The polyphenolic molecular structure of flavonoids with its antioxidant activity supports that topical application of propolis to the skin may have beneficial light-protecting properties.[22]

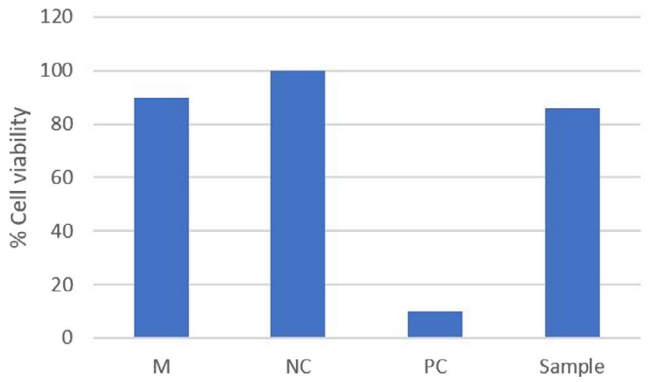

FIGURE 2 Comparison of % cell viability L929 cell with negative and positive control after 24 h exposure to test substance by direct contact. M, medium control; NC, negative control (PBS); PC, positive control (0.4 mg/ml SDS)

TABLE 9 Degree and reaction zone

Reaction zone	Degree
Negative control (PBS)	0
Positive control (SDS)	4
Prototype body cream	1

3.1.3 | Analysis of dermatologic response

Dermatological analysis of bee venom creams, performed as H-RIPT on 10 volunteers aged between 21 and 65, revealed no adverse reaction to their skins. The average irritation index for the tested product was found as "0" (Table 8). Based on the results, the bee venom containing prototype product was dermatologically suitable without causing any irritation or allergic reaction. On the contrary, You et al.[7], who applied an emollient containing bee venom for 4 weeks on 136 subjects diagnosed with atopic dermatitis, observed adverse reactions such as irritation and pruritus erythema, urticaria, and disease exacerbation on both the control and the experimental groups. However, the severity of adverse drug reactions was defined as mild, and it was emphasized that daily activities were unchanged and did not require any treatment.[7] Likewise, in a study examining the effects of bee venom and propolis on localized plaque psoriasis, general itching was experienced in 6 of 48

TABLE 10 Panel test results for the claims by the subjects

The tested product makes skin silky smooth			The tested product gives a feeling of nourished skin		
Answers	**count**	**%**	**Answers**	**count**	**%**
Definitely yes	2	18.2	Definitely yes	5	45.5
I suppose so	8	72.7	I suppose so	5	45.5
Not really	1	9.1	Not really	1	9.1
Definitely not	0	0	Definitely not	0	0
Affirmative answers: 90.9%			Affirmative answers: 90.9%		
The tested product gives feeling of hydration			**The tested product evens out the skin tone**		
Answers	**count**	**%**	**Answers**	**count**	**%**
Definitely yes	7	63.6	Definitely yes	2	18.2
I suppose so	3	27.3	I suppose so	5	45.5
Not really	1	9.1	Not really	4	36.4
Definitely not	0	0	Definitely not	0	0
Affirmative answers: 90.9%			Affirmative answers: 63.6%		
The tested product brightens the skin			**The tested product reduces the visibility of wrinkles**		
Answers	**count**	**%**	**Answers**	**count**	**%**
Definitely yes	2	18.2	Definitely yes	2	18.2
I suppose so	8	72.7	I suppose so	8	72.7
Not really	1	9.1	Not really	1	9.1
Definitely not	0	0	Definitely not	0	0
Affirmative answers: 90.9%			Affirmative answers: 90.9%		

patients as the side effects.[23] However, the authors reported that itching was not severe enough to leave the trial and disappeared spontaneously within a few weeks. During routine controls, it was concluded that bee venom and propolis cream did not have any systemic side effects on any patient.[10] Although these researches are on the dermal application of bee venom for specific diseases, there is a growing interest in the functions of bee venom in the cosmetics field, and particular attention is necessary to give information on the bee venom content and its specific components in products, considering any side effects.

3.1.4 | Analysis of cytotoxicity

Quantitative cytotoxicity analysis revealed that sample viability was 87.38% ± 3.77% compared to the negative control. The results of the cell viability of M (medium), NC (negative control), PC (positive control), and K1 (prototype body cream) groups are presented in Figure 2. The zone formation degree was 0 in the NC group and 4 in the PC group (Table 8). In the wells where bee venom body cream was applied directly, the zone formation degree was observed as 1. On the contrary, no zone formation was observed in the wells where the sample was applied directly in the qualitative analysis (Table 9).

According to the quantitative data of the prototype, the cell viability was detected over 70% compared with the NC; therefore, it was concluded that the sample was not cytotoxic. In the qualitative evaluation, the degree of reaction was observed less than 2, and it was presumed that the sample was not cytotoxic.

3.1.5 | Antiwrinkle efficacy test

The panel test results for the claims are given in Table 10. Accordingly, the tested product makes skin silky smooth, gives a feeling of hydration, brightens the skin, suggests a feeling of nourished skin, evens out the skin tone, reduces the visibility of wrinkles, improves skin elasticity, and smoothes wrinkles. Moreover, the cream is easy and pleasant to use with interpretations such as proper consistency, adequate intensity, fresh scent, and well absorbed. In general, the subjects' opinions highlighted that the prototype is a skincare product that is favorable and confidently recommended for others.

Based on the results and individual assessments of the subjects, the participants did not report any complaints, for example allergic or toxic—irritant effects on the skin such as itching, burning, or tightening. Since the participants are not allergic individuals, we have to keep in mind that these results do not apply to the persons showing any allergic reactions.

4 | CONCLUSION

This research developed and evaluated a prototype body cream formulation with bee venom, propolis, honey, and royal jelly as natural sources. According to the stability test, it was concluded that the cream could be used for 12 months after opening. A high antioxidant capacity contributes to the stability of the product in terms of color and appearance. In addition, the cytotoxicity results and dermatological tests confirm that the skin well tolerates the tested product without resulting in any irritating or allergenic reactions in non-allergic individuals. Therefore, the product is classified as non-irritating.

Panel test showed that the prototype body cream contributes to the disappearance of visible wrinkles and improves skin elasticity. The high antioxidant activity of the cream offering support against skin aging presents a significant advantage in developing similar products for the cosmetic sector. Therefore, the proposed skincare product is worth further research to elucidate its efficacy for UV protection and any potential to treat acne.

It is also recommended that the bee venom content of the formulations may require more testing to evaluate its effectiveness as an antiaging on different types of skins. Nevertheless, the side effects of such products need particular attention in developing a commercial product containing bee venom, such as declaring the amount and specific components of the product.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ETHICAL APPROVAL

The voluntary testing were carried out according to WMA Declaration of Helsinki—Ethical Principles for Medical Research Involving Human Subjects (1964–2013).

DATA AVAILABILITY STATEMENT

Research data are not shared.

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REFERENCES

1. Süzer PÖ. *Farmakoloji Ders Kitabı*. İstanbul Üniversitesi Cerrahpaşa Tıp Fakültesi; 2008.
2. Krell R. *Value-Added Products from Beekeeping*. Food and Agriculture Organization; 1996. No. 124.
3. Schmidt JO, Buchmann SL. Other products of the hive. In. Graham JM Ed. *The Hive and the Honey Bee* pp, 927-988. Dadant and Sons; 1992.
4. Tekeoğlu İ, Akdoğan M. "Bal Arısı Zehirinin Tamamlayıcı Tıptaki Güncel Yeri", Ankara Akupunktur ve Tamamlayıcı Tıp Dergisi. 2016. C. 2016;4, sayı 1:ss. 8–14.
5. An H-J, Lee W-R, Kim K-H, et al. Inhibitory effects of bee venom on Propionibacterium acnes-induced inflammatory skin disease in an animal model. *Int J Mol Med*. 2014;34(5):1341-1348.
6. Han SM, Lee KG, Pak SC. Effects of cosmetics containing purified honeybee (Apis mellifera L.) venom on acne vulgaris. *J Integr Med*. 2013;11(5):320-326.

7. You CE, Moon SH, Lee KH, et al. Effects of emollient containing bee venom on atopic dermatitis: a double-blinded, randomized, base-controlled, multicenter study of 136 patients. *Ann Dermatol*. 2016;28(5):593-599.
8. Han SM, Hong IP, Woo SO, et al. The beneficial effects of honeybee-venom serum on facial wrinkles in humans. *Clin Interv Aging*. 2015;10:1587.
9. Han SM, Lee K, Yeo J, Kim W, Park K. Biological effects of treatment of an animal skin wound with honeybee (Apis melifera. L) venom. *J Plast Reconstr Aesthet Surg*. 2011;64(3):e67-e72.
10. Burdock GA. Review of the biological properties and toxicity of bee propolis (propolis). *Food Chem Toxicol*. 1998;36(4):347-363.
11. Banskota AH, Tezuka Y, Kadota S. Recent progress in pharmacological research of propolis. *Phytother Res*. 2001;15(7):561-571.
12. Žilius M, Ramanauskienė K, Briedis V. Release of propolis phenolic acids from semisolid formulations and their penetration into the human skin in vitro. *Evid Based Complement Alternat Med*. 2013;2013:958717.
13. Gregory SR, Piccolo N, Piccolo MT, Piccolo MS, Heggers JP. Comparison of propolis skin cream to silver sulfadiazine: a naturopathic alternative to antibiotics in treatment of minor burns. *J Altern Complement Med*. 2002;8(1):77-83.
14. Pavel CI, Mărghitaş LA, Bobiş O, et al. Biological activities of royal jelly-review. *Sci Papers Anim Sci Biotechnol*. 2011;44(2):108-118.
15. Park HM, Hwang E, Lee KG, Han SM, Cho Y, Kim SY. Royal jelly protects against ultraviolet B–induced photoaging in human skin fibroblasts via enhancing collagen production. *J Med Food*. 2011;14(9):899-906.
16. Park HM, Cho MH, Cho Y, Kim SY. Royal jelly increases collagen production in rat skin after ovariectomy. *J Med Food*. 2012;15(6):568-575.
17. Burlando B, Cornara L. Honey in dermatology and skin care: a review. *J Cosmet Dermatol*. 2013;12(4):306-313.
18. Özdemir E, Güven Çapanoğlu E. *The Investigation of Antioxidant Properties of Propolis Products Obtained from Turkey (Master Thesis)*. Istanbul Technical University; 2018.
19. Mishra AK, Mishra A, Chattopadhyay P. Formulation and in-vitro evaluation of antioxidant activity of O/W sunscreen cream containing herbal oil as dispersed phase. *Inter J Biomed Res*. 2010;1:201-208.
20. Lohani A, Mishra AK, Verma A. Cosmeceutical potential of geranium and calendula essential oil: determination of antioxidant activity and in vitro sun protection factor. *J Cosmet Dermatol*. 2019;18(2):550-557.
21. Sobral F, Sampaio A, Falcão S, et al. Chemical characterization, antioxidant, anti-inflammatory and cytotoxic properties of bee venom collected in Northeast Portugal. *Food Chem Toxicol*. 2016;94:172-177.
22. Cole N, Sou PW, Ngo A, et al. Topical 'Sydney'propolis protects against UV-radiation-induced inflammation, lipid peroxidation and immune suppression in mouse skin. *Int Arch Allergy Immunol*. 2010;152(2):87-97.
23. Hegazi AG, Abd Raboh FA, Ramzy NE, Shaaban DM, Khader DY. Bee venom and propolis as new treatment modality in patients with localized plaque psoriases. *Int Res J Med Med Sci*. 2013;1(1):27-33.

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