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Epidemiological Analysis of Allergic Contact Dermatitis Cases with Positive Patch-test Results Emerging After the COVID-19 Pandemic

COVID-19 Pandemisinden Sonra Alerjik Kontakt Dermatit Şikayetleri Başlayan Yama Testi Pozitif Hastaların Epidemiyolojik Olarak Değerlendirilmesi

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Abstract

Objective: Allergic contact dermatitis (ACD) is a common inflammatory skin disorder caused by extrinsic allergens that reach the skin through direct contact, airborne exposure, or systemic routes. Patch-testing is currently accepted as the gold-standard diagnostic method for ACD. Among the allergens included in the European standard patch-test series is propolis, and it has been suggested that the increased use of personal hygiene products and dietary supplements during the novel coronavirus (COVID-19) pandemic may have led to greater sensitization to this substance. This study aimed to evaluate the frequency of propolis allergy after the COVID-19 pandemic and to investigate possible associations between allergens and demographic or clinical variables.

Method: In this retrospective study, 152 patients who developed symptoms of ACD after the COVID-19 pandemic underwent the European standard patch-test series with 30 different allergens. Of these, 50 patients with at least one positive patch-test result were included in the further analysis. Data were recorded and evaluated according to age, sex, allergen frequency, occupation, hobbies, need for biopsy, and disease duration.

Results: In this study, one of the most striking observations was the notably high rate of propolis patch-test positivity, even surpassing that of nickel. Another key finding was the consistent visibility of propolis reactions: they appeared as early as the initial reading and persisted through day 7, underscoring the allergen's sustained reactivity.

Öz

Amaç: Alerjik kontakt dermatit (AKD), çoğunlukla deriye doğrudan temas, havadan veya sistemik maruziyetler yoluyla ekstrensek alerjenlerin neden olduğu yaygın bir enflamatuvar deri hastalığıdır. Yama testi, AKD tanısında günümüzde kabul edilen altın standart yöntemdir. Avrupa standart yama testi serisinde bulunan alerjenlerden biri propolistir ve yeni koronavirüs hastalığı-2019 (COVID-19) pandemisi döneminde kişisel hijyen ürünleri veya besin takviyelerinin kullanımındaki artış nedeniyle propolise karşı artan bir duyarlılık olabileceği düşünülmektedir. Bu çalışma, COVID-19 pandemisi sonrasında propolis alerjisinin görülme sıklığını ve alerjenler ile demografik/klinik değişkenler arasındaki olası ilişkileri değerlendirmeyi amaçlamaktadır.

Yöntem: Bu retrospektif çalışmada COVID-19 pandemisinden sonra AKD semptomları başlayan 152 hastaya 30 farklı alerjenle Avrupa standart test serisi uygulandı. Pandemi sonrası alerjik semptomları başlayan 152 hastadan yama testi pozitifliği olan 50 hasta ileri incelendi. Elli hastanın verileri yaş, cinsiyet, alerjen sıklığı, meslek, hobiler, biyopsi gerekliliği ve hastalık süresine göre epidemiyolojik dağılım olarak kaydedildi.

Bulgular: Bu çalışmanın en dikkat çekici bulgularından biri, propolis yama testi pozitifliğinin nikel pozitifliğini dahi aşacak düzeyde yüksek olmasıydı. Ayrıca propolis reaksiyonlarının ilk okumada ortaya çıkması ve 7. güne kadar devam etmesi, çalışmanın bir diğer önemli sonucu olarak değerlendirildi.

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Abstract

Conclusion: The findings suggest that the increased use of disinfectants and dietary supplements during the post-COVID-19 period may have contributed to sensitization to propolis. These results indicate that propolis is appearing more frequently as a positive allergen in patch-testing and should be carefully considered during evaluation. Prospective studies are needed to confirm these observations.

Keywords: Allergic contact dermatitis, COVID-19, incidence, nickel, patch-test, propolis

Öz

Sonuç: Bulgular, COVID-19 pandemisi sonrası dönemde dezenfektan ve besin takviyesi kullanımındaki artışın propolis duyarlanmasında rol oynamış olabileceğini düşündürmektedir. Bu durum, yama testlerinde propolisin giderek daha sık pozitifleştiğini ve değerlendirmelerde göz önünde bulundurulması gerektiğini göstermektedir. Prospektif çalışmalarla bu sonuçların desteklenmesi önemlidir.

Anahtar kelimeler: Alerjik kontakt dermatit, COVID-19, insidans, nikel, propolis, yama testi

Introduction

Allergic contact dermatitis (ACD) is a T-cell-mediated type IV hypersensitivity reaction and is common in the general population (1-3). Patch-testing is the gold-standard diagnostic method for ACD (4,5).

During the novel coronavirus disease-2019 (COVID-19) pandemic and its aftermath, various cutaneous manifestations and dermatological conditions have been associated with both vaccination and the infection itself. However, few studies have evaluated changes observed in patch-tests performed for allergic complaints. The existing literature on the COVID-19 pandemic primarily focuses on specific populations, such as healthcare workers, rather than the general population (6).

During the COVID-19 pandemic, people's daily routines have changed dramatically. In this context, the use of dietary supplements, cosmetics, and personal hygiene products increased significantly. Studies conducted in Turkey and various countries have demonstrated a notable increase in consumption of dietary supplements aimed at strengthening the immune system, particularly during the pandemic (7-9). The use of naturally sourced ingredients such as propolis has recently become highly popular in the cosmetics industry. Before the COVID-19 pandemic, the reported frequency of propolis contact allergy in European patch-test cohorts ranged from 1% to 3.5%, and the 2019 inclusion of propolis into the European baseline series (EBS) was based on an overall positivity rate of approximately 2-3% in multicenter studies (10,11). These findings indicate that propolis was a relatively uncommon allergen in the pre-pandemic period. However, during the COVID-19 pandemic, the widespread use of propolis-containing supplements, cosmetics, and hygiene products raised concerns about a potential increase in sensitization. This shift in public behavior formed the main rationale for the present study, which investigates post-pandemic propolis patch-test positivity in a tertiary dermatology center.

This study retrospectively evaluated patch-test positivity among patients from the general population who developed cutaneous complaints after the COVID-19 pandemic and were clinically suspected of ACD. This study aimed to assess patients with ACD who were patch-test–positive for propolis after the COVID-19 pandemic, focusing on epidemiological distribution, allergen frequency, and correlations with demographic and clinical factors.

Although the study does not include a pre-pandemic comparison group, the increased public use of propolis-containing supplements and hygiene products during the pandemic has raised concerns about a possible rise in sensitization. Therefore, the study focuses exclusively on post-pandemic cases and aims to contextualize the observed frequency within pre-pandemic rates reported in the literature.

Materials and Methods

Data from 152 patients whose symptoms began after the COVID-19 pandemic and who were clinically suspected of ACD and who underwent European Standard Patch-testing between March 1, 2023, and May 1, 2023, were retrospectively analyzed. Subsequently, data from fifty patients who tested positive for at least one allergen were examined.

No patient had received topical or systemic steroids or antihistamines on their backs within one month before the patch-test. None of the study participants had a history of atopic dermatitis, and patch-testing was not conducted on individuals with acute dermatitis. In addition, patients using systemic and/or topical immunosuppressive agents, pregnant women, and lactating women were excluded from the study.

Thirty allergens were applied under occlusion using Finn Chambers on the upper back. All patients provided consent and were instructed to avoid showering, wearing tight

clothing, exposure to ultraviolet radiation, exercising, and excessive sweating.

The patients' skin reactions were examined on days two, three, four, and seven. Any findings suggesting irritation were reported. Test readings were recorded as: (-) no reaction; (+/-) faint erythema; (+) mild reaction (erythema, infiltration, and possibly papules); (++) moderate reaction (erythema, infiltration, papules, and vesicles); (+++) severe reaction (erythema, infiltration, papules, vesicles, and bullae) according to the criteria of the International Contact Dermatitis Research Group (12).

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS) version 26.0 was used for statistical analysis of patient data; $p<0.05$ was considered significant. Descriptive statistics included the mean, standard deviation, minimum, maximum, frequency, and ratio values. Pearson's chi-square test was used to assess associations between categorical variables. Ethical approval for the study was obtained from the Local Ethics Committee of İstanbul Kent University (Scientific Research and Publication Ethics Committee of Health Sciences; approval number: E-10420511-050-26426, date: 02.10.2023), İstanbul, Turkey.

Results

All patients underwent patch-test evaluations on days 2, 3, 4, and 7. Among the 152 patients studied, 102 had negative results for all allergens included in the European baseline patch-test series. Patients who showed positive reactions to at least one allergen remained positive on days 3, 4, and 7. None of these 50 patients exhibited any irritant reactions.

No exacerbation or increase in symptoms or primary skin complaints was observed in any patient during the patch-test period.

Out of the 50 patients with positive patch-test results, 74% (n=37) were female and 26% (n=13) were male (Table 1). The mean age was 34.02±13.94 years; 12% (n=6) of patients were under 18 years, and the mean disease duration was 27.2±9.6 months (Table 1).

Among 50 patients with positive patch-test results, 32% (n=16) were stay-at-home spouses, 18% (n=9) were students, 12% (n=6) were teachers, 8% (n=4) were textile workers, 6% (n=3) cleaning workers, and the rest were other professions. Seventy-four percent (n=37) of the patients had no hobbies; among the 13 patients with a hobby, 76.9% (n=10) reported painting (Table 1).

Skin biopsies were performed in 18% of the 50 patients who tested positive on patch-tests, and no correlation was found between the severity and duration of ACD among those who underwent biopsy. Spongiotic dermatitis was observed in the histopathological examination of all biopsied patients.

Among patients with at least one allergen-positive patch-test, the most frequent allergens were propolis, nickel, fragrance mix I, colophonium, and fragrance mix II (Table 2).

Neomycin sulfate, caine mix III, mercapto mix, epoxy resin, bisphenol A, 2-mercaptobenzothiazole, quaternium-15, tixocortol-21-pivalate, methylisothiazolinone, and formaldehyde were negative in all patients (Table 2).

Pearson's chi-square tests were applied to examine the relationship between patch-test allergen status and patient gender. The patch-test allergen status of the participants did not differ by gender, age, profession, or hobby type ($p>0.05$ for all comparisons) (Table 3).

No statistically significant difference was found between participants' methyldibromo glutaronitrile allergen patch-test results and their age distribution ($p=0.14$).

Of the 50 patients, 17 had a positive propolis patch-test. The severity distribution among the 17 propolis-patch positive patients was as follows: 9 were mild (+), 5 were moderate (++), and 3 were severe (+++) (Table 4). Moreover, all propolis-positive patients continued to exhibit a positive propolis patch-test result on day 7,

Table 1. Frequency table of participants' demographic information

	Frequency	Percentage (%)
Gender		
Female	37	74.0
Male	13	26.0
Age		
<18 years	6	12.0
18-29 years	15	30.0
30-42 years	14	28.0
43-55 years	12	24.0
>55 years	3	6.0
Occupation		
Stay at-home spouse	16	32.0
Student	9	18.0
Teacher	6	12.0
Textile worker	4	8.0
Cleaning worker	3	6.0
Other	12	24.0

Table 2. Participants' allergen status in patch-test

		Negative	+	++	+++
Allergens		**f (%)**	**f (%)**	**f (%)**	**f (%)**
1	Potassium dichromate	48 (96.0)	2 (4.0)	0	0
2	P-phenylenediamine (PPD)	49 (98.0)	1 (2.0)	0	0
3	Thiuram mix	48 (96.0)	2 (4.0)	0	0
4	Neomycin sulfate	50 (100.0)	0	0	0
5	Cobalt (II) chloride hexahydrate	49 (98.0)	0	1 (2.0)	0
6	Caine mix III	50 (100.0)	0	0	0
7	Nickel (II) sulfate hexahydrate	34 (68.0)	5 (10.0)	8 (16.0)	3 (6.0)
8	2-hydroxy ethyl methacrylate	49 (98.0)	0	0	1 (2.0)
9	Colophonium	44 (88.0)	2 (4.0)	3 (6.0)	1 (2.0)
10	Paraben mix	49 (98.0)	1 (2.0)	0	0
11	N-isopropyl-n-phenyl-4-phenylenediamine (I PPD)	49 (98.0)	0	0	1 (2.0)
12	Lanolin alcohol	48 (96.0)	2 (4.0)	0	0
13	Mercapto mix	50 (100.0)	0	0	0
14	Epoxy resin, bisphenol a	50 (100.0)	0	0	0
15	Peru balsam	49 (98.0)	0	1 (2.0)	0
16	4-tert-butylphenolformaldehyde resin	49 (98.0)	1 (2.0)	0	0
17	2-mercaptobenzothiazole	50 (100.0)	0	0	0
18	Fragrance mix 1	44 (88.0)	3 (6.0)	3 (6.0)	0
19	Sesquiterpene lactone mix	49 (98.0)	0	1 (2.0)	0
20	Quatermuim-15	50 (100.0)	0	0	0
21	Propolis	33 (66.0)	9 (18.0)	5 (10.0)	3 (6.0)
22	Methylisothiazolinone + methylchloroisothiazolinone	48 (96.0)	1 (2.0)	0	1 (2.0)
23	Budesonide	49 (98.0)	0	0	1 (2.0)
24	Tixocortol-21-pivalate	50 (100.0)	0	0	0
25	Methyldibromo glutaronitrile	45 (90.0)	4 (8.0)	1 (2.0)	0
26	Fragrance mix II	46 (92.0)	4 (8.0)	0	0
27	Hydroxyisohexyl 3-cyclohexene carboxaldehyde	49 (98.0)	1 (2.0)	0	0
28	Methylisothiazolinone	50 (100.0)	0	0	0
29	Textile dye mix	48 (96.0)	0	0	2 (4.0)
30	Formaldehyde	50 (100.0)	0	0	0

Table 3. Relationship between propolis allergen severity and gender of participants

		Allergen severity					
		Negative	**+**	**++**	**+++**	χ^2	**p**
Allergens		**f (%)**	**f (%)**	**f (%)**	**f (%)**		
Propolis	Female	25 (75.8)	6 (66.7)	4 (80.0)	2 (66.7)	0.482	0.923
	Male	8 (24.2)	3 (33.3)	1 (20.0)	1 (33.3)		

p: Statistical significance

characterized by persistent erythematous papules on their upper back.

In these analyses, Pearson's chi-square tests were applied to examine associations between propolis allergen severity and gender, age, and profession. There were no differences in propolis allergen severity by gender (p=0.858; Table 3), age distribution (p=0.711; Table 4), or profession (p=0.458; Table 5) among the participants.

When the relationship between propolis allergen and rash localization was examined in patients, dermatitis

Table 4. Relationship between propolis allergen severity and age of participants

		Allergen severity					
		Negative	+	++	+++	χ^2	p
Allergens		f (%)	f (%)	f (%)	f (%)		
Propolis	<18	4 (12.1)	2 (22.2)	0	0	8.035	0.782
	18-29	9 (27.3)	3 (33.3)	2 (40.0)	1 (33.3)		
	30-42	10 (30.3)	2 (22.2)	2 (40.0)	0		
	43-55	8 (24.2)	2 (22.2)	1 (20.0)	1 (33.3)		
	>55	2 (6.1)	0	0	1 (33.3)		

p: Statistical significance

lesions were most frequently localized to the head and neck region. The Pearson chi-square test was applied to examine the relationship between patients' propolis allergen positivity and localization. Accordingly, no association was found between the participants' propolis allergy and localization (p=0.658). In addition, patients with positive patch-tests to propolis had involvement in all body regions, but none had genital complaints or lesions (Table 6).

An ANOVA was performed to evaluate the relationships among severity of sensitivity to propolis allergen, body mass index (BMI), and disease duration among participants. No statistically significant association was found between propolis allergen severity and either BMI (p=0.841) or disease duration (p=0.262) (Tables 7 and 8).

The Pearson's chi-square test was used to examine the association between propolis allergen severity and histopathological results. The severity of propolis allergen sensitivity did not differ significantly based on the histopathological results (p=0.247).

The Pearson chi-square test was used to assess the association between propolis allergen severity and types of hobbies. No significant difference in propolis allergen severity was observed among hobby types (p=0.879).

When examining other allergens that were positive alongside propolis in participants, 6% also tested positive for thiuram mix, cobalt (II) chloride hexahydrate, nickel (II) sulfate hexahydrate, paraben mix, 4-tert-butylphenol formaldehyde resin, sesquiterpene lactone mix, and methyldibromo glutaronitrile, while 12% tested positive for colophonium (Table 9).

Discussion

ACD is a common inflammatory skin disease characterized by a type IV hypersensitivity reaction. Clinical findings and history are essential in the diagnosis of ACD, but the allergen cannot be detected using clinical or histopathological methods (1,12,13). Patch-testing is currently considered the gold-standard diagnostic method for ACD (4,5). Propolis, a potent allergen, was added to the EBS patch-test as an allergen in 2019 (11).

The COVID-19 pandemic led to a significant increase in the use of systemic dietary supplements and personal hygiene products, including products containing propolis. This trend has raised concerns regarding their dermatological impacts, as highlighted by the increased propolis positivity observed in this study. During the COVID-19 pandemic, the consumption of propolis-

Table 5. Relationship between participants' propolis allergen severity and occupation

		Allergen severity					
		Negative	+	++	+++	χ^2	p
Allergens		f (%)	f (%)	f (%)	f (%)		
Propolis	Stay at-home spouse	12 (36.4)	1 (11.1)	2 (40.0)	1 (33.3)	12.677	0.627
	Student	6 (18.2)	3 (33.3)	0	0		
	Teacher	3 (9.1)	1 (11.1)	1 (20.0)	1 (33.3)		
	Textile worker	4 (12.1)	0	0	0		
	Cleaning worker	3 (9.1)	0	0	0		
	Other	5 (15.2)	4 (44.4)	2 (40.0)	1 (33.3)		

p: Statistical significance

Table 6. Relationship between propolis allergen and lesion localization of participants

		Negative	Positive	χ^2	p
Allergens		**f (%)**	**f (%)**		
Propolis	Head-neck	13 (39.4)	9 (52.9)	3.276	0.658
	Upper extremity	10 (30.3)	6 (35.3)		
	Trunk	3 (9.1)	0		
	Lower extremity	2 (6.1)	0		
	Head-neck and upper extremity	2 (6.1)	1 (5.9)		
	Upper and lower extremity	3 (9.1)	1 (5.9)		

p: Statistical significance

Table 7. Comparison of propolis allergen severity and BMI of participants

	Propolis allergen severity	n	Mean ± SD	M (min-max)	F	p
BMI	Negative	33	27.48±5.41	27.5 (16.71-40.82)	0.404	0.751
	+	9	25.07±7.19	22.06 (14.79-35.86)		
	++	5	26.18±8.82	23.44 (16.22-39.06)		
	+++	3	26.44±3.27	25.39 (23.83-30.11)		

BMI: Body mass index, SD: Standard deviation, M: Median, Min-max: Minimum-maximum, p: Statistical significance

Table 8. Comparison of propolis allergen severity and disease duration of participants

	Propolis allergen severity	n	Mean ± SD	M (min-max)	F	p
Disease duration	Negative	33	27.52±8.63	29 (6-36)	1.457	0.239
	+	9	28.67±12.48	36 (3-36)		
	++	5	19.40±10.51	19 (9-36)		
	+++	3	32.0±6.93	36 (24-36)		

SD: Standard deviation, M: Median, Min-max: Minimum-maximum, p: Statistical significance

Table 9. Concurrently positive allergens with propolis allergen positivity in participants

		Negative	Positive
Allergens		**f (%)**	**f (%)**
3	Thiuram mix	16 (94.1)	1 (5.9)
5	Cobalt (II) chloride hexahydrate	16 (94.1)	1 (5.9)
7	Nickel (II) sulfate hexahydrate	16 (94.1)	1 (5.9)
9	Colophonium	15 (88.2)	2 (11.8)
10	Paraben mix	16 (94.1)	1 (5.9)
16	4-tert-butylphenolformaldehyde resin	16 (94.1)	1 (5.9)
19	Sesquiterpene lactone mix	16 (94.1)	1 (5.9)
25	Methyldibromo glutaronitrile	16 (94.1)	1 (5.9)

containing dietary supplements and hygiene products markedly increased, reflecting the public's growing preference for natural, immune-supporting ingredients (8,14). Furthermore, the use of naturally sourced ingredients has become highly popular in the cosmetics industry. Propolis stands out as a key component, used both in natural cosmetic products and dietary supplements. Because of its antibacterial effects, this substance is also used as a preservative in the cosmetics industry (15,16).

Propolis is produced by bees through the combination of the tree resins they collect with beeswax and saliva, and is described in the literature as a potent contact allergen (10,17). The chemical composition of propolis varies depending on its geographical origin, water sources, and other factors. However, it is not known whether these differences affect the tendency of propolis to cause contact allergy. A 2021 study investigated the frequency of contact allergy to four types of propolis from different geographical origins and found similar frequencies across all types. However, for each propolis type, half of the patients who reacted did so exclusively to that type. Nevertheless, 50% of patients who developed contact dermatitis to a given propolis type reacted only to that type (10). In our study, the majority of patients who tested positive for propolis had unknowingly used over-the-counter products during the pandemic.

Published pre-pandemic patch-test studies have reported propolis sensitization rates generally ranging from 1% to

6% in European and Nordic cohorts. In a large Swedish multicenter analysis, propolis from different geographical origins produced positivity rates between 1.3% and 5.8% (10,18). Similarly, a retrospective study from Western Sweden conducted before 2020 reported a sensitization rate of 6.2% among 722 patch-tested patients (19). More recently, a 4-year retrospective evaluation following the inclusion of propolis in the EBS reported an overall positivity rate of 9.5% for 2019-2023 (11), still far below the rate observed in our post-pandemic cohort (34%). Although our study does not include a pre-pandemic comparison group, this sharp divergence from historical data suggests that increased pandemic-era exposure to propolis-containing supplements, disinfectants, and cosmetic products may have contributed to heightened sensitization. This interpretation aligns with global reports demonstrating a marked increase in public use of natural immune-boosting products, including propolis, during the COVID-19 pandemic (8,14). In our study, all patients with positive propolis patch-test results were asked whether they had used propolis systemically, topically, or both during the COVID-19 pandemic. None of the patients knew whether the cosmetic or personal hygiene products they used contained propolis. Among the 17 patients with positive propolis patch-test results, 10 (approximately 59%) reported purchasing over-the-counter products from pharmacies, markets, or online platforms during the COVID-19 pandemic to boost their immune systems. These products were reported to contain propolis. However, they could not recall the brand names or the dosage in milligrams. Consequently, no information could be obtained regarding the origin of the propolis. In addition, all patients reported using disinfectants and some antimicrobial sprays to increase their personal hygiene during the COVID-19 pandemic. Although they did not specify brand names, they reported using multiple brands and products.

The key finding of this study was that 17 patients had positive patch-test reactions to propolis. Propolis positivity among the patients was apparent at 48 hours and persisted through day 7. In Chaudhry's cohort, the patch-test, which had been negative on previous days, became positive on the seventh day (20). However, in our study, positivity was detected at the first reading and persisted for seven days. The underlying reason for this issue remains unclear, as the source and dosage of propolis used systemically by the patients were unknown. Furthermore, the patients were unaware of the composition of the topical product they applied.

Patch-test evaluations are routinely performed at 48 and 96 hours, with delayed readings if necessary. According to the literature, 7-14% of patients may exhibit delayed reactions to certain allergens, including metals (e.g., gold), topical antibiotics, preservatives (e.g., formaldehyde), compounds (e.g., cocamide diethanolamine and p-phenylenediamine), and topical corticosteroids. Therefore, delayed assessments on the seventh day may be conducted for some patients (20,21). In our study, all patients were routinely evaluated on the seventh day; no increase in the severity of positive reactions was observed. This situation may be explained by the synergistic topical and systemic effects of propolis (20). However, in our study, since the majority of patients used a combination of dietary supplements, cosmetic products, and disinfectants, it was impossible to determine exactly which factor contributed to this condition. Among our patients with positive reactions to propolis, one also reacted to thiuram mix; one to cobalt (II) chloride hexahydrate; one to nickel (II) sulfate hexahydrate; two to colophonium; one to paraben mix; one to 4-tert-butylphenol formaldehyde resin; and one to methyldibromo glutaronitrile. However, fragrances I and II were not detected in any patient with a positive patch-test to propolis. Numerous haptens have been identified in propolis, with caffeic acid and its ester derivatives suggested as the primary haptens. Because propolis is partly of botanical origin, it is common to observe concurrent positive patch-test reactions to both propolis and fragrances or plant-derived test preparations in the baseline series, which are often essential oils, colophonium, *M. pereirae* resin, and fragrances (10,11). Although propolis and colophonium were both positive in two of our patients, this finding did not apply to other substances. It is difficult to determine whether the reaction was solely due to propolis or cross-reactivity with these allergens. However, in our study, nine patients were exclusively allergic to propolis, with no sensitivity to other allergens. This shows that propolis alone can be a stimulus in ACD. Additionally, this finding highlights the importance of delayed readings on day seven, particularly in suspected cases, as the persistent positivity to this lesser-known substance warrants further investigation. Clinicians should specifically inquire about propolis-containing supplements or topical agents when evaluating ACD, particularly in post-pandemic cases.

In the case of propolis, the slow release of flavonoids and the prolonged retention of caffeic acid derivatives in the epidermis may contribute to prolonged and, in some cases, delayed positive reactions (22,23). Additionally, propolis has been extensively studied as a potent hapten that triggers an immune response (15,24). In our cohort, the persistent

positivity of propolis reactions at the day-7 reading provides important insights not only for clinical practice but also for the safety evaluation of propolis-containing cosmetic and food products. From an immunological perspective, T-cell-mediated sensitization to propolis may underlie the prolonged clinical course observed in some patients. The combination of an early reaction at the first reading and sustained positivity at day 7 in our patients is consistent with an initial release of allergenic compounds followed by their slower, continued release from the skin.

Especially during the pandemic, the widespread use of natural ingredients such as propolis for immune support may lead to sensitization in susceptible individuals, without their awareness. This emphasizes the importance of detecting propolis positivity in patch-tests at both early (48 hours) and late (day 7) time points. In our study, two patients had a history of propolis-induced systemic contact dermatitis related to prior systemic or topical exposure. No systemic reactions occurred during the patch-testing period. The patients' histories included use of multiple cosmetic products and dietary supplements. Therefore, a causal link between propolis and systemic contact dermatitis was not established. Cases related to systemic and local propolis use have been reported in the literature; however, these are case reports rather than studies (25,26). There is a need for large-scale studies to elucidate this condition.

It is known that systemic exposure, including from certain foods, and topical products (such as fragrances, powders, wet wipes, corticosteroids, personal-hygiene or perfumed sprays, or lubricants) may cause contact dermatitis in the anogenital area (3). In our study, 10 of the 17 patients with propolis positivity reported using propolis-containing products for immune support during the pandemic, suggesting that systemic use may have contributed to this sensitivity. However, the lack of information regarding the brands and contents of these products is a major limitation of our study. Additionally, our study found that the distribution of propolis-positive patients was homogeneous across age, gender, and occupational groups, and the severity of positivity was unrelated to these parameters. This finding suggests that propolis may be a common allergen across all segments of society. For instance, dermatitis lesions, frequently found in the head and neck area, may support the possibility that propolis was used both topically and via inhalation. The absence of anogenital involvement limits our ability to draw firm conclusions about the clinical impact of systemic exposure in our cohort. However, studies with a large number of participants, in which systemic and/or topical use is clearly defined at the patient level, are needed for confirmation.

In our study, eight allergens were positive alongside propolis; among them, colophonium and the sesquiterpene lactone mix were of plant origin and consistent with the literature. Because propolis is not among the allergens in the T.R.U.E.® test series but is included in another commonly used patch-test series, the observed propolis positivity rate—particularly after the COVID pandemic—suggests that propolis sensitization may have a higher incidence than nickel sensitization, as seen in our study.

An intriguing finding of this study is the lack of an association between propolis patch-test positivity and factors such as age, gender, BMI, occupation, hobbies, or disease duration. This observation suggests that propolis may be a potent allergen capable of affecting all populations equally, irrespective of these parameters. This is likely due to the increased use of disinfectants, personal hygiene products, and dietary supplements across all demographic groups during the COVID-19 pandemic (14,27-29). However, further multicenter studies are needed to substantiate the aforementioned hypothesis.

No studies in the literature have investigated positive patch-test reactions to propolis since the COVID-19 pandemic. Therefore, our study may raise awareness that substances such as nutritional supplements and disinfectants, whose use has increased significantly, especially during the COVID-19 pandemic, may not be innocuous.

An important aspect of our findings is that all propolis-positive reactions remained detectable on day 7. Although the evaluation of late readings was not originally defined as part of the primary aim, the consistent day-7 positivity emerged as an important complementary finding that provides additional clinical insight. This temporal persistence directly aligns with the goal of distinguishing true allergic responses from irritant or transient reactions. In standard patch-testing, allergic reactions typically intensify or persist at the day-7 reading, whereas irritant reactions resolve earlier. Therefore, the sustained positivity observed in our cohort strengthens the interpretation that the increased rate of propolis reactions reflects genuine ACD rather than irritant responses. This feature distinguishes our study from pre-pandemic series, in which late readings were either not routinely performed or, when performed, reported much lower persistence rates.

Study Limitations

This study has several limitations, including the lack of detailed data on the specific brands and compositions of propolis-containing products used by patients, the retrospective design, the small patient population, and the unknown duration of product use. We would like to emphasize once again that the findings should be supported by larger, prospective studies. Moreover, this study does not compare pre- and post-pandemic patch-test results; instead, it focuses solely on patients whose dermatological symptoms began after the COVID-19 pandemic. Therefore, the findings represent a cross-sectional evaluation of post-pandemic cases rather than a temporal comparison.

Conclusion

As expected, we observed that patients showed increased sensitivity to some allergens due to excessive use of disinfectants, cosmetic and personal hygiene products, and supplements since the start of the pandemic. We believe that sensitization to these allergens may still be on the rise over time.

The principal finding of this study is that increased sensitization to propolis was detected during the COVID-19 period; contrary to expectations, this was independent of occupation or hobbies. This study revealed a significant increase in positive patch-test reactions to propolis during the COVID-19 pandemic. Notably, positivity persisted from the first to the seventh day, emphasizing the need for delayed patch-test readings in suspected or borderline cases.

Ethics

Ethics Committee Approval: Ethical approval for the study was obtained from the Local Ethics Committee of İstanbul Kent University (Scientific Research and Publication Ethics Committee of Health Sciences; approval number: E-10420511-050-26426, date: 02.10.2023), İstanbul, Turkey.

Informed Consent: The study employed a retrospective design.

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Footnotes

Authorship Contributions

Surgical and Medical Practices: N.C., B.İ.D., Concept: N.C., B.İ.D., Z.T., Design: N.C., M.T., Z.T., Data Collection or Processing: N.C., B.İ.D., M.T., Analysis or Interpretation: N.C., B.İ.D., Z.T., Literature Search: N.C., B.İ.D., M.T., Writing: N.C., B.İ.D., Z.T.

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