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Pilot Study of Photoallergic Reactions to UV Filters among Dental Professionals

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Aims: To evaluate if there are photoallergic reactions to selected UV filters among dental professionals (dentists, nurses and attendants) and dental patients.
Study Design: In the study were included dental professionals, occupationally exposed to UV-filters containing dental materials, and randomly chosen dental patients of different gender, age and occupations, the main inclusion criteria being the lack of occupational exposure to dental materials.
Place and Duration of Study: Department "Oral and Image Diagnostic", Faculty of Dental Medicine, Medical University of Sofia, between July 2014 and March 2015.
Methodology: We included a total of 59 participants: 25 occupationally exposed dental professionals (15 women and 10 men; mean age 43.57±8.76) and 34 dental patients (14 women

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and 20 men; mean age 40.41±14.17). Skin photopatch testing with Benzophenone – 3, Benzophenone – 4, Para-aminobenzoic acid (PABA), BUTYL METHOXY-DIBENZOYL-METHANE, and 2,2-bis-[4-(2-hydroxy-3-methacrylo-xypropoxy)phenyl]-propane (BIS-GMA) (Chemotechnique Diagnostics) was performed, according to: Photopatch testing: a consensus methodology for Europe.

Results: Results for positive reactions to Benzophenone-3 and Benzophenone-4 showed no significant differences between the groups. A non-significant increase in the number of the reactions was observed among women (for Benzophenone-3 - 24.1% incidence after exposure to UV-irradiation vs 13.8% before - *P*=.23; for Benzophenone-4 - 13.8% after exposure to UV-irradiation vs 6.9% before, *P*=.63), and dental patients, (for Benzophenone-3 - 20.6% incidence after exposure to UV-irradiation vs 8.8% before - *P*=.75; for Benzophenone-4 - 14.7% after exposure to UV-irradiation vs 11.8% before, *P*=.54%). No reactions of photosensitization to PABA were observed in our study, no statistical significances between the studied groups were revealed. Concerning the positive skin patch test reactions to BUTYL METHOXY-DIBENZOYL-METHANE, no significant differences between the groups were revealed (*P*=.08). Results for positive reactions to Bis-GMA showed highest sensitization rates in all groups defined by us, but no significant differences between the groups were established (*P*=.40; *P*=.33).

Conclusion: The present pilot investigation failed to demonstrate any photosensitizing effect, but the sample is too small to determine if there is a tendency to increased activity of certain materials. Further work is needed to validate reliability.

Keywords: Photosensitization; dental professionals; photopatch skin testing; Benzophenone – 3; Benzophenone – 4; Para-aminobenzoic acid; BUTYL METHOXY-DIBENZOYL-METHANE; BIS-GMA.

1. INTRODUCTION

Dental materials are widely used, and some of their ingredients may give rise to health problems both for occupationally exposed dental professionals and for patients undergoing dental treatment.

Photosensitization reactions are a continuously growing area of research. Photosensitisation is the term used for reactions dependent on the presence of certain photochemicals and the action of optical radiation in the 320–800 nm range. The adverse reaction is initiated by visible light or UV induced excitation involving free radicals or reactive oxygen species. The photons deliver energy for either creating covalent bonds between hapten and endogenous protein (formation of antigenic photoadducts), or converting a prohapten into the actual sensitizing hapten. The mechanism of reaction is similar to that of allergic contact dermatitis, but absorption of irradiation is necessary for the formation of antigens. Photoallergic reactions usually occur within 24–48 h [1-3].

Photosensitisers can be of endogenous origin such as porphyrins and flavins, or exogenous such as those derived from tar, vegetable and plant products, and fragrance materials. In addition, a number of commonly used drugs, e.g. antimicrobials, are potential photosensitisers.

Modern techniques in dental cavity restorations, veneer- and orthodontic bonding and fissure sealing, depend on in situ polymerisation of monomers, most often brought about by light activation. UV absorbers in adhesives and other dental materials [4,5] absorb UV and visible light and can give rise to photosensitising reactions. In addition, leachables and degradation products from the dental materials as well as residuals from oral hygiene products and drugs may have radiation absorbing properties and, hence, may contribute to or be responsible for photoactivated reactions [6].

Photopatch testing is an effective approach for the diagnosis of photodermatitis or unclear photoreactions and helps in determining the sensitizing potentials of commonly used agents [7].

The purpose of the present pilot study was to evaluate if there are photoallergic reactions to selected UV filters among dental professionals (dentists, nurses and attendants) and dental patients.

2. MATERIALS AND METHODS

2.1 Studied Individuals

A total of 59 participants, divided into two groups, participated in the study: 25 dental professionals, the main inclusion criteria being occupational exposure to UV-filters containing dental materials; 34 randomly chosen dental patients of different gender, age and occupations, all of them with a history for treatment with UV-filters containing dental materials (e.g. dental composites) served as a control group, the the main inclusion criteria being the lack of occupational exposure in dentistry. Anti-allergic medication and age below 18 years constituted the main exclusion criteria for participation in the study.

The study was performed at the Department "Oral and Image Diagnostic", Faculty of Dental Medicine, Medical University of Sofia, between July 2014 and March 2015.

The study was granted by the Medical University – Sofia, Grant № 48/2014, and was approved the Medical Ethics Board at the Medical University of Sofia. All participants were informed about the purpose of the study and gave their written informed consent.

2.2 Skin Photopatch Testing

Skin photopatch testing with the following photoallergens, included in the European Photopatch Baseline Series (EP-1000 - Chemotechnique Diagnostics) - Benzophenone – 3 (10.0% pet), Benzophenone – 4 (2.0% pet), PABA (10.0% pet), BUTYL METHOXY-DIBENZOYL-METHANE (10.0% pet), as well as with BIS-GMA was performed, according to Photopatch testing: a consensus methodology for Europe [8], by application of the allergens in IQ-Ultra hypoallergenic patches of Chemotechnique Diagnostics (IQ Chambers®, Vellinge, Sweden) on the mid upper back skin, avoiding 3-5 cm on either side of the vertebrae. Duplicate sets on left and right side of the back of all participants were applyed for 48 h, after which both sets are removed. At this point, one set should be covered with an ultraviolet (UV) opaque material and the other irradiated with a calibrated metered broad-spectrum UVA source (UV-Therapy and Photodiagnosis system UV 236 PUVA) with a dose of 5 J/cm^2. Readings were recorded using the International Contact Dermatitis Research Group (ICDRG) scoring system with readings before irradiation, immediately after irradiation and also 48 and/or 72 h thereafter. Interpretation key based on recommendations by the ICDRG was applied (Table 1).

Table 1. Interpretation key of skin patch test results based on international contact dermatitis research group

Symbol	Meaning
(–)	negative reaction
?	doubtful reaction
+	weak positive reaction (non-vesicular)
++	strong positive reaction (oedematous or vesicular)
+++	extreme positive reaction (ulcerative or bullous)
IR	irritant reaction (discrete patchy erythema without infiltration)

2.3 Statistical Methods

The statistics were calculated with SPSS 19.0. Available for cross-tabulation statistics were used - Fisher Exact Test for statistical significance, and two-sample t-test. Values of $P<0.05$ were accepted as statistically significant.

3. RESULTS

Data regarding age and gender characteristics are presented in Table 2.

Distribution by gender was uniform. The mean duration of occupational exposure of dental professionals to photosensitizers as ingredients of dental materials is 18 years, and 68% of them were exposed up to 20 years.

Data concerning the incidence of positive skin patch test reactions to the tested substances, before and after UV-irradiation (distribution by gender and groups defined by occupational exposure in dentistry) are presented in (Table 3).

Results for positive reactions to Benzophenone-3 showed no significant differences between the groups. A non-significant increase in the number of positive reactions was observed in the following 2 subgroups: - the one of women, which showed a 24.1% incidence after exposure to UV-irradiation vs 13.8% before (P=.23), and the one of dental patients, which showed a 20.6% incidence after exposure to UV-irradiation vs 8.8% before (P=.75).

Table 2. General characteristics of the studied groups of individuals

Studied groups	Age (years) (M±SD)	Gender		Total
		Women n (%)	Man n (%)	
Dental patients	40.41±14.17	14 (79,5)	20 (20.5)	34
Dental professionals	43.57±8.76	15 (72.3)	10 (27.7)	25
Total	42.23±16.3	29 (49.2)	30 (50.8)	59

Table 3. Distribution of positive skin patch test reactions to tested substances, before and after UV-irradiation among the studied groups

Tested substances		Positive reactions - distribution by gender		Positive reactions - distribution by studied groups	
		Men n (%)	Women n (%)	Dental professionals n (%)	Dental patients n (%)
Benzophenone – 3	before UV-irradiation	3 (10.0%)	4 (13.8%)	4 (16,0%)	3 (8,8%)
	after UV-irradiation	4 (13.3%)	7 (24.1%)	4 (16,0%)	7 (20,6%)
BIS-GMA	before UV-irradiation	6 (20.0%)	4 (13.8%)	6 (24,0%)	4 (11,8%)
	after UV-irradiation	7 (23.3%)	5 (17.2%)	7 (28,0%)	5 (14,7%)
PABA	before UV-irradiation	5 (16.7%)	4 (13.8%)	5 (20,0%)	4 (11,8%)
	after UV-irradiation	4 (13.3%)	4 (13.8%)	5 (20,0%)	3 (8,8%)
Benzophenone – 4	before UV-irradiation	5 (16.7%)	2 (6.9%)	3 (12,0%)	4 (11,8%)
	after UV-irradiation	4 (13.3%)	4 (13.8%)	3 (12,0%)	5 (14,7%)
BUTYL METHOXY-DIBENZOYL-METHANE	before UV-irradiation	3 (10.0%)	-	-	3 (8,8%)
	after UV-irradiation	2 (6.7%)	3 (10.3%)	1 (4,0%)	4 (11,8%)

** All values had no statistical significant differences*

Similar were the results concerning positive reactions to Benzophenone-4 after UV-irradiation – no statistical significant differences between the groups were observed. A non-significant increase in the number of positive reactions was observed again among women (13.8% incidence after exposure to UV-irradiation vs 6.9% before, *P*=.63) and dental patients (14.7% incidence after exposure to UV-irradiation vs 11.8% before, *P*=.54%).

No reactions of photosensitization to PABA were observed in our study, no statistical significances between the studied groups were revealed.

Results from photopatch testing to BUTYL METHOXY-DIBENZOYL-METHANE are available in (Table 3). No statistical significances between the groups were revealed (*P*=.08). Interestingly, in the group of women and the one dental professional positive skin patch test reactions were observed only after application of UV-irradiation.

Finally, due to the wide use of Bis-GMA as an ingredient of a number of dental materials, in the present pilot study we studied the possible photosensitizing action of this substance. Results for positive reactions showed no significant differences between the groups (*P*=.40; *P*=.33).

4. DISCUSSION

Chemical ultraviolet (UV) filters have been increasingly used over the last few decades not only in conventional sunscreen products, but also in many cosmetics and toiletries. Allergic contact dermatitis as well as photoallergic contact dermatitis reactions were well documented as a consequence of such use [9].

Adhesives and other dental materials contain UV absorbers, and leachables and degradation products from the dental materials as well as residuals from oral hygiene products and drugs may have radiation absorbing properties and, hence, may contribute to or give rise to photosensitising reactions. According to our knowledge, no studies were performed to evaluate if there is a risk of photosensitization to UV filters among dental professionals. We

present the results from a pilot study to evaluate if there are photoallergic reactions among dental professionals to the presented most common UV filters, applicable in dentistry as well.

Benzophenones are ultraviolet light filters that have been documented to cause adverse cutaneous reactions, including contact and photocontact dermatitis, contact and photocontact urticaria, and anaphylaxis [9,10]. In recent years, they have become particularly well known for their ability to induce allergy and photoallergy. Topical sunscreens and other cosmetics are the sources of these allergens in most patients, but reports of reactions secondary to use of industrial products also exist. Benzophenones as a group have been named the American Contact Dermatitis Society's Allergen of the Year for 2014 to raise awareness of both allergy and photoallergy to these ubiquitous agents [10].

While UV filters can cause both allergic and photoallergic contact dermatitis [9], the latter condition occurs more frequently. It should be emphasized that considering the widespread use of sunscreens, contact and photocontact dermatitis is uncommon. Photoallergic dermatitis from sunscreens is caused by organic UV filters, with benzophenone-3 (also known as oxybenzone) being the most common cause [11-13].

Benzophenone-3 (Fig. 1) is used as UV-adsorber in topical sunscreens, moisturizers, shampoos, hair care products, lipsticks, lip balms, nail polish, etc. It is also common UV-adsorber and photostabilizer in dental composite materials, synthetic resins and other plastic materials [14,15].

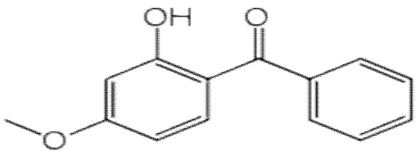

Fig. 1. Chemical structure of Benzophenone-3

It is one of the most widely used organic UVA filters today, providing broad-spectrum ultraviolet coverage, including UVB and short-wave UVA rays. As a photoprotective agent, it has an absorption profile spanning from 270 to 350 nm with absorption peaks at 288 and 350 nm. Despite its photoprotective qualities, much controversy surrounds Benzophenone-3 because of its possible hormonal and photoallergenic effects, leading many countries to regulate its use [16,17].

The substance is currently regulated in the Cosmetics Directive in Annex VII, part 1 ("List of permitted UV filters which cosmetic products may contain") in a concentration up to maximum 10%. The regulation demands a warning on the label "contains oxybenzone" due to the photo-allergenic potential of the substance [18,19]. By the current dossier, submitted in December 2007, the applicants apply for a maximum allowed concentration up to 6%.

Benzophenone-4 (Sulisobenzone) is an ingredient in various sunscreen products, moisturizers, nail polish, lipsticks, lip balms, as well as in textiles, plastics, paints and cosmetics, protecting the skin from damage by UVB and short-wave UVA ultraviolet light (Fig. 2) [20].

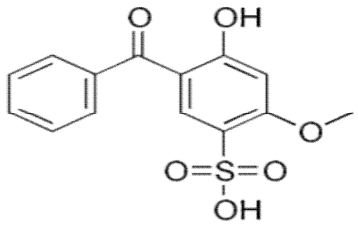

Fig. 2. Chemical structure of Benzophenone 4

Hughes and Stone (2007) investigated over a 3-year period whether any of selected chemical UV filters added to usual cosmetics/facial series produced positive patch test results in the absence of photostimulation. According to their results, benzophenone 4 produced significantly more positive patch test results than the other UV filters tested, and was the third most frequently positive result overall [21].

According to the results from the present study, dental material containing benzophenones do not elicit photosensitization. We could conclude that dental materials are not as sensitizing as dermatological products, but the study needs to be repeated with a larger (probably much larger) sample before a final statement to be given.

BUTYL METHOXY-DIBENZOYL-METHANE (Avobenzone) – (Fig. 3) is an oil soluble ingredient used in sunscreen cosmetics of the type creams, lotions, lipsticks, sun oils, etc., to absorb the full spectrum of UVA rays.

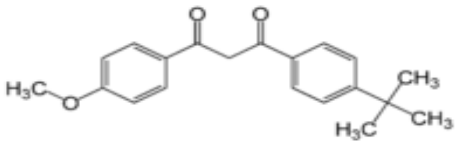

Fig. 3. Chemical structure of avobenzone

Its ability to absorb ultraviolet light over a wider range of wavelengths than many other sunscreen agents has led to its use in many commercial preparations marketed as "broad spectrum" sunscreens. Most sunscreens work by blocking UV rays and free radicals, but avobenzone works by absorbing the rays and converting them to energy that is less damaging to the skin. Avobenzone has an absorption maximum of 357 nm [22].

The results from the present study don't confirm the role of exposure to avobenzone for onset of photosensitization in dental practice. Since this is a pilot study, further investigations, with much more subject tested are needed before a categorical statement could be given. This substance seemed to play as a typical photosensitizer, since positive reactions were observed only after the application of UV-irradiation, in the group of women and the one of dental professionals.

Para-aminobenzoic acid (PABA) – (Fig. 4), is an intermediate in the synthesis of folate by bacteria, plants, and fungi. Many bacteria, including those found in the human intestinal tract such as E. coli, generate PABA.

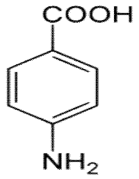

Fig. 4. Chemical structure of PABA

Patented in 1943, PABA was one of the first active ingredients to be used in sunscreen. It is a UVB absorber in wavelengths between 290 and 320 nm. In the past, PABA was widely used as a UV filter. Animal and in vitro studies in the early 1980s suggested PABA might increase the risk of cellular UV damage [23]. On the basis of these studies, as well as problems with allergies and clothing discoloration, PABA fell out of favor as a sunscreen. However, its water-insoluble derivatives, such as padimate O are currently used in some products. Other uses include its conversion to specialty azo dyes and crosslinking agents.

Allergic reactions to PABA can occur. It is formed in the metabolism of certain ester local anesthetics, and many allergic reactions to local anesthetics are the result of reactions to PABA [24].

According to Gao et al. [25], who investigated the prevalence of photoallergic contact dermatitis reactions to different photoallergens among 4957 patients during a 7-year period, para-aminobenzoic acid was among the most predominant photoallergens. Greenspoon et al. [26] completed a retrospective chart review of all patients who underwent photopatch testing between 2001 and 2010 in Canada. As most common relevant photoallergens they outlined benzophenone-3, PABA, and butylmethoxy-dibenzoylmethane.

Basing on the information above, we studied if photosensitization to PABA could be related with occupational exposures in dental practice.

We didn't observe statistically significant increase in positive reactions to PABA after UV-irradiation. According to the results achieved in our pilot investigation, doesn't seem to be photosensitizer in dental practice.

2,2-bis-[4-(2-hydroxy-3-methacrylo-xypropoxy)phenyl]-propane - Bis-GMA is a common monomer in composite fillings and fissure sealants, widely used in everyday dental practice. No data was found in the available literature concerning photosensitizing action of this compound, so we decided to include Bis-GMA in our test series. Sensitization rates to Bis-GMA were highest in all groups defined by us. Nevertheless, as groups at risk of sensitization could be outlined the one of dental professionals (sensitization rate 24%) and of men (sensitization rate 20%) - Table. 3. Regarding the incidence of positive skin patch test reactions after UV-irradiation, no statistical significances among the defined groups were observed. These findings require further investigations, with more participants included.

5. CONCLUSION

The present pilot investigation failed to demonstrate any photosensitizing effect. A slight photosensitizing action of Bis-GMA could be

suggested, but the sample is too small to determine if there is a tendency to increased activity of certain ingredients of dental materials. Further work is needed to validate reliability.

CONSENT

All authors declare that written informed consent was obtained from the participants in the present study.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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