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ORIGINAL ARTICLE

# FREQUENCY OF CONSUMPTION OF SELECTED FOODS BY PEOPLE WITH ACNE VULGARIS

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#### **ABSTRACT**

**Background.** Acne is an inflammatory disease affecting adolescents during puberty, but also adults. Determinants of acne may include genetic predisposition as well as diet. The Western diet is rich in processed products with low nutrient density, resulting in a lack of supply of many essential minerals that are needed for the body to function properly.

**Objective.** The aim of this study was to assess the dietary behaviour of people with acne vulgaris and respondents' self-assessment of the severity of acne lesions after consumption of selected products.

**Material and Methods.** The study was carried out by means of an online, self-administered questionnaire, a link to which was inserted in group of people struggling with acne on a social network.

Results. More than half of the respondents said that acne was present in their parents. Almost 91% of the women surveyed said that acne lesions were exacerbated before menstruation. Respondents were most often treated by a dermatologist. The most common foods consumed by the respondents were milk and milk products and wheat bread. The least frequently consumed products were: sultanas, cornflakes, alcohol and fizzy drinks. Statistical analysis showed a strong strength of association between consumption of white rice, fast food, omega-6-rich oils on the severity of acne lesions, while sultana consumption was very strong correlated. In addition, the study showed an almost certain correlation regarding the consumption of white flour pasta on acne lesions.

**Conclusions.** Statistical analysis showed a relationship between the consumption of white rice, white flour pasta, fast food products, sultanas, oils rich in omega-6 fats and the exacerbation of acne lesions.

**Key words:** acne vulgaris, diet, eating behaviour

#### **STRESZCZENIE**

**Wprowadzenie.** Trądzik jest chorobą o charakterze zapalnym, dotykająca młodzież w okresie dojrzewania, ale także osoby dorosłe. Do czynników, warunkujących wystąpienie trądziku mogą należeć predyspozycje genetyczne, a także dieta. Dieta zachodnia bogata jest w produkty przetworzone o niskiej gęstości odżywczej, co skutkuje tym, że nie dostarcza ona wielu niezbędnych składników mineralnych, które są potrzebne do prawidłowego funkcjonowania organizmu. **Cel.** Celem pracy była ocena zachowań żywieniowych osób z trądzikiem pospolitym i samooceną ankietowanych nasile-

**Cel.** Celem pracy była ocena zachowań żywieniowych osób z trądzikiem pospolitym i samooceną ankietowanych nasilenia zmian trądzikowych po spożyciu wybranych produktów.

**Materiał i Metody.** Badanie przeprowadzono za pomocą internetowej, autorskiej ankiety, do której link został wstawiony w grupie osób borykających się z trądzikiem na portalu społecznościowym.

Wyniki. Ponad połowa ankietowanych stwierdziła, że trądzik występował u ich rodziców. Prawie 91% badanych kobiet stwierdziło, że zmiany trądzikowe nasilają się przed miesiączką. Ankietowani najczęściej leczyli się u dermatologa. Najczęstszą grupą spożywaną przez ankietowanych były: mleko i jego przetwory oraz pieczywo pszenne. Najrzadziej spożywanymi produktami były: rodzynki, płatki kukurydziane, alkohol, napoje gazowane. Analiza statystyczna wykazała silny związek między spożyciem białego ryżu, fast food, olejów bogatych w kwasy omega-6 na nasilenie zmian trądzikowych, podczas gdy spożycie sułtanki było bardzo silnie skorelowane. Ponadto badanie wykazało prawie pewną korelację między spożyciem makaronu z białej mąki a zmianami trądzikowymi.

Wnioski. Analiza statystyczna wykazała związek między spożyciem białego ryżu; makaronu z białej mąki; produktów typu fast food; rodzynek; olejów bogatych w tłuszcze omega-6 a zaostrzeniem zmian trądzikowych.

Słowa kluczowe: trądzik pospolity, dieta, zachowania żywieniowe

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## INTRODUCTION

Acne vulgaris is a chronic inflammatory skin disease that affects approximately 85% of people aged 12-25 years, and can persist into adulthood [6]. Negative effects of acne include the possibility of depression, anxiety, or insomnia [5]. Genetic factors, *Propionibacterium acnes*, androgenic activity, increased sebum production, keratinisation of the skin, as well as certain medicinal substances and cosmetics are cited as its main causes [4, 6]. The main hormones responsible for the development of acne are androgens, insulin and IGF-1 (insulin-like growth factor-1) [2].

The Western diet is also thought to influence the development of inflammatory skin lesions among other acne. In the past, groups such as the indigenous Canadian Inuit, the Japanese people of Okinawa, the Aché of Paraguay, the South African Zulus and the Kitavan Islanders of Papua New Guinea did not suffer from skin diseases. When they were introduced to Western dietary habits, processed foods, dairy products and refined sugars, cases of acne began to be reported in them [1]. The Western dietary model is deficient in many essential vitamins and nutrients, minerals [3].

Vitamins such as A, E, K, C, B vitamins and minerals such as selenium, zinc, copper and iron, as well as essential fatty acids (EFAs) are needed to maintain a healthy complexion [3]. Therefore, in order to treat acne lesions, a properly selected treatment, in combination with skin care and a correctly balanced nutrition, seems to be extremely important [4].

Studies show that a high glycaemic index contributes to hyperinsulinaemia, which affects androgen hormone secretion through IGF-1 stimulation, resulting in increased seborrhoea [12]. These factors contribute to a decrease in insulin-like growth factor binding protein IGFBP-3 that controls epidermal proliferation, as well as alterations in retinoid pathways [11].

Milk is a product that contains bioactive compounds such as insulin-like growth factor IGF-1, hormone precursors, transforming growth factor beta (TGF-β) in its composition [12]. Protein isolates in protein supplements have a higher insulin index than milk, due to the defatting of the product, isolation and increased concentration of selected essential amino acids. Insulin/IGF-1 levels are increased by whey protein, with a concomitant reduction in transcription factor elevated FoxO1 gene expression [1, 12].

Essential fatty acids (EFAs) have a positive effect on the complexion, reducing inflammation and inhibition of bacterial growth [4]. It has been proven that omega-3 fatty acids reduce IGF-1 levels [1]. The ratio of omega 3 and omega 6 fatty acids should be 1:3-1:5. However, disrupting this ratio and increasing the supply of omega-6 can lead to inflammatory

skin conditions, including the development of acne vulgaris [4].

The microbiota is related to the skin, which may mean that when the skin or microbiota is disturbed, increased activity of substance P and upregulation of P-containing nerve substances are observed. Substance P has been observed in acne and intestinal dysbiosis, and substance P can cause an increase in interleukin-6 levels and an increase in tumour necrosis factor-α which also contribute to acne formation [1]. Supplementation with *Lactobacillus rhamnosus* GG is thought to improve the complexion and reduce acne lesions due to a reduction in IGF-1 levels [1].

The aim of this study was to assess the dietary behaviour of people with acne vulgaris and the respondents' self-assessment of the severity of acne lesions after consumption of selected products.

## MATERIAL AND METHODS

The study was conducted using an anonymous, online, self-administered questionnaire, a link to which was posted in groups of people struggling with acne vulgaris on a social networking site. The author's questionnaire consisted of 16 questions and included single and multiple choice. The questionnaire consisted of a metric, questions about the prevalence of *acne vulgaris* and a dietary section. The exclusion criterion for the study was people who did not suffer from acne vulgaris. The sampling was voluntary, so that respondents decided for themselves whether they wanted to take part in the survey. Due to the nature of the implementation of the survey, fully anonymous, the approval of the bioethics committee was not required.

Sixty people (55 women and five men) took part in the study. The respondents were aged between 13 and 35 years. The average age of the people surveyed was 23.5 years. The survey was conducted between October 2022 and January 2023. Results were processed using Excel and Statistica 13. The strength of the relationship was determined using *Gamma* correlation. Statistical significance was determined at p<0.05. *Gamma* correlation strengths were determined using the classification according to J. Guilford.

## **RESULTS**

Among the group of respondents (n=60), the largest group consisted of people with secondary education (48.3%) and tertiary education (45%) and those studying (38.3%) or studying and simultaneously working (40%). The least, only 1.7% of respondents had a vocational education, while secondary education was held by 5% of respondents. Those only working accounted for 18.3% of those

surveyed. At the time of filling in the questionnaire, 3.3% were unemployed. The majority of respondents were urban residents (68.3%), while 31.7% were rural residents.

More than half (51.7%) of the respondents answered that their relatives (father, mother) had acne, while 21.7% declared that their parents did not have acne. The remainder of the respondents (26.7%) have no knowledge of this subject.

The most common location of acne among the respondents was the cheeks, forehead, jaw, and back. The question was multiple choice (Table 1).

Table 1. Location of acne

Location of acne	n	%	
Cheeks	53	88.3	
Mandible	41	68.3	
Forehead	45	75	
Nose	24	40	
Cleavage	17	28.3	
Back	32	53.3	
Chin	2	3.3	
Buttocks	2	3.3	
Arms	2	3.3	
Legs	2	3.3	
Other (arms, abdomen, neck, head)	1	1.7	

The majority of respondents – 75% did not complain of other illnesses, while the most frequently reported diseases were hypothyroidism (8.3%), polycystic ovary syndrome (5%) and atopic dermatitis (5%). The question was multiple choice.

Most (35%) respondents had been treated for acne lesions by a specialist, but had discontinued such treatment, while 33.3% were currently undergoing treatment. The remaining percentage (31.7%) of respondents responded negatively to this question. More than half of the respondents who were treated (58.3%) answered that they treated their lesions at a dermatologist, the second most treated among respondents was a gynaecologist (16.7%), followed by an endocrinologist (8.3%), a dietician (3.3%) and a general practitioner (1.7%). The question was multiple choice.

Almost all of the women surveyed (90.9%) responded that they noticed an increase in acne lesions before menstruation.

Respondents in the survey were asked about the use of any diet. 81.7% of the respondents were not on a diet, while the most frequently mentioned diets among respondents were plant-based diets: vegan (5%), vegetarian (3.3%). There were also responses mentioning a low glycaemic index diet (1.7%), as well

as a carbohydrate-restricted diet (3.3%) and a dairy-free diet (1.7%).

More than half of the respondents (56.7%) consumed 4-5 meals per day. Three meals a day were consumed by 38.30% of the respondents. The smallest number of respondents (1.70%) consumed 1-2 meals per day, while more than 5 meals per day were taken by 3.30% of respondents.

Table 2 examines the correlation of the effect of frequency of consumption of each food on self-assessment of skin condition (whether, and to what extent, there is an exacerbation of acne lesions according to them) after consumption of the food in question. Table 2 shows only those who have declared that they consume the product in question.

Respondents to the questionnaire were asked how often they consumed each product. They had the following answers to choose from: several times a day, once a day, several times a week, once a week, 1-3 times a month, I do not consume.

In the next question, respondents were asked to indicate in their evaluation how the consumption of a particular product affects their skin condition. Respondents were asked to rate on a 5-point scale, where 0 meant no difference, 1-slightly, 3-average, 5-very aggravated.

Those who answered 'I do not consume' in the question were not included in the statistical analysis. A *Gamma* coefficient was used to examine the correlation between the frequency of consumption of each individual product and its impact in the respondent's self-assessment on acne lesions (Table 2).

Responses that related to consumption and also to the severity of acne lesions were combined for statistical analysis as follows: one or mildly exacerbates (0-1 scale); moderately exacerbates (scale 2-3); severely exacerbates (scale 4-5) (Table 2). The largest number of people surveyed consumed products such as white rice (n=56) and white flour pasta (n=55). In contrast, the fewest people decried the consumption of sultanas (n=25). On the other hand, white bread (n=29) and milk and dairy products (n=27) were consumed daily by the largest number of respondents (Table 2).

There was a correlation between the consumption of: white rice (p=0.02); white flour pasta (p=0.007); fast food products (p=0.002); sultanas (p=0.045); oils rich in omega-6 fats (p=0.02) and the exacerbation of acne lesions (Table 2). The finding of a statistical relationship (p<0.05) between the consumption of: white rice, white flour pasta, fast food products, sultanas, oils rich in omega-6 fats and the exacerbation of acne lesions suggests that there is some association between the consumption of these products and the appearance of acne or its exacerbation. In practical terms, this means that diet can have a significant impact on skin health, and the consumption of the products mentioned may

Table 2. Exacerbation of acne lesions after consumption of food products

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Food products	Frequency of consumption	None or only slightly exacerbates	Moderately exacerbates	Severely exacerbates	Summary of those who have consumed (n)	p-value	Gamma correlation coefficient
Milk and milk products	Once or several times a day	17 (62.96%)	7 (25.93%)	3 (11.11%)			
	Once or several times a week	16 (69.57%)	6 (26.09%)	1 (4.35%)	53	0.74	0.05
	1-3 times a month	1 (33.30%)	0 (0%)	2 (66.70%)			
Wheat bread	Once or several times a day	23 (79.31%)	4 (13.79%)	2 (6.90%)	54	0.87	-0.04
	Once or several times a week	17 (80.95%)	4 (19.05%)	0 (0%)			
	1-3 times a month	3 (75%)	1 (25%)	0 (0%)			
Groats	Once or several times a day	0 (0%)	0 (0%)	1 (100%)	53	0.42	-0.23
	Once or several times a week	24 (96%)	1 (4%)	0 (0%)			
	1-3 times a month	25 (92.59%)	2 (7.41%)	0 (0%)			
White rice	Once or several times a day	0 (0%)	0 (0%)	1 (100%)	56	0.02	0.64
	Once or several times a week	28 (96.55%)	1 (3.45%)	0 (0%)			
	1-3 times a month	24 (92.31%)	2 (7.69%)	0 (0%)			
White flour pasta	Once or several times a day	1 (50%)	0 (0%)	1 (50%)	55	0.007	0.91
	Once or several times a week	37 (88.10%)	5 (11.90%)	0 (0%)			
	1-3 times a month	11 (100%)	0 (0%)	0 (0%)			
Cornflakes	Once or several times a day	0 (0%)	0 (0%)	1 (100%)	27	0.47	0.27
	Once or several times a week	5 (100%)	0 (0%)	0 (0%)			
	1-3 times a month	18 (85.71%)	3 (14.29%)	0 (0%)			
Fast food	Once or several times a day	0 (0%)	0 (0%)	1 (100%)	53	0.002	0.50
	Once or several times a week	3 (15.79%)	9 (47.37%)	7 (36.84%)			
	1-3 times a month	15 (45.45%)	11 (33.33%)	7 (21.21%)			
Sweeteners	Once or several times a day	5 (35.71%)	3 (21.43%)	6 (42.86%)			
	Once or several times a week	5 (21.74%)	13 (56.52%)	5 (21.74%)	46	0.16	-0.02
	1-3 times a month	4 (44.4%)	5 (55.6%)	0 (0%)			

Sweets	Once or several times a day	2 (20%)	2 (20%)	6 (60%)	55	0.29	0.16
	Once or several times a week	7 (21.21%)	15 (45.45%)	11 (33.33%)			
	1-3 times a month	3 (25%)	5 (41.67%)	4 (33.33%)			
Salty snacks	Once or several times a day	0 (0%)	1 (25%)	3 (75%)			
	Once or several times a week	11 (45.83%)	9 (37.50%)	4 (16.67%)	51	0.59	0.08
	1-3 times a month	8 (34.78%)	9 (39.13%)	6 (26.09%)			
	Once or several times a day	1 (33.33%)	0 (0%)	2 (66.67%)	37	0.64	0.09
Fizzy drinks	Once or several times a week	7 (43.75%)	6 (37.5%)	3 (18.75%)			
	1-3 times a month	9 (50%)	6 (33.33%)	3 (16.67%)			
	Once or several times a day	0 (0%)	0 (0%)	1 (100%)		0.14	
Alcohol	Once or several times a week	8 (57.14%)	3 (21.43%)	3 (21.43%)	30		0.32
	1-3 times a month	7 (46.67%)	3 (20%)	5 (33.33%)			
Hot spices	Once or several times a day	2 (33.33%)	2 (33.33%)	2 (33.33%)	42	0.31	
	Once or several times a week	11 (52.38%)	5 (23.81%)	5 (23.81%)			0.17
	1-3 times a month	6 (40%)	6 (40%)	3 (20%)			
Ripe banana	Once or several times a day	5 (83.33%)	0 (0%)	1 (16.67%)	52	0.86	0.04
	Once or several times a week	27 (87.1%)	4 (12.9%)	0 (0%)			
	1-3 times a month	13 (86.67%)	2 (13.33%)	0 (0%)			
	Once or several times a day	0 (0%)	0 (0%)	2 (100%)	39	0.08	
Fatty meat	Once or several times a week	19 (79.17%)	3 (12.50%)	2 (8.33%)			-0.38
	1-3 times a month	10 (76.92%)	3 (23.08%)	0 (0%)			
Sultanas	Once or several times a day	0 (0%)	0 (0%)	1 (100%)			0.71
	Once or several times a week	4 (100%)	0 (0%)	0 (0%)	25	0.045	
	1-3 times a month	19 (95%)	1 (5%)	0 (0%)			
Oils rich in omega-6 fats	Once or several times a day	7 (77.78%)	1 (11.11%)	1 (11.11%)			
	Once or several times a week	13 (100%)	0 (0%)	0 (0%)	42	0.02	0.64
	1-3 times a month	17 (85%)	2 (10%)	1 (5%)			

increase the risk of acne occurrence or worsening of acne symptoms. Therefore, people struggling with acne may benefit from reducing or eliminating these foods from their diet to help control symptoms.

There was no association between intake of: milk and milk products (p=0.74); wheat bread (p=0.87); groats (p=0.42); cornflakes (p=0.47); sweeteners (p=0.16); sweets (p=0.29); salty snacks (p=0.59); fizzy drinks (p=0.64); alcohol (p=0.14); hot spices (p=0.31); ripe banana (p=0.86); fatty meat (p=0.08) and exacerbation of acne lesions (Table 2). The finding that there was no correlation (p>0.05) between the consumption of the listed products and the exacerbation of acne lesions means that a diet containing these products is unlikely to have a significant effect on the occurrence of acne or its exacerbation. In practice, this means that consumption of milk and milk products, wheat bread, groats, cornflakes, sweeteners, sweets, salty snacks, fizzy drinks, alcohol, hot spices, ripe banana, fatty meat should not be responsible for worsening the skin condition in most people.

The strength of the association of statistical characteristics determining the consumption of: milk and dairy products; wheat bread; sweeteners; salty snacks; ripe banana; fizzy drinks with the exacerbation of acne lesions is negligible, suggesting that there is minimal or insignificant association between the consumption of these products and acne exacerbation (Table 2). In practical terms, this means that the consumption of milk and dairy products; wheat bread; sweeteners; salty snacks; ripe banana; fizzy drinks is unlikely to have a significant effect on the exacerbation of acne lesions in the subjects.

The strength of the association of statistical characteristics determining the consumption of groats, cornflakes, sweets with the exacerbation of acne lesions is weak, suggesting that there is a very weak association between the consumption of these products and acne exacerbation (Table 2). In practice, this means that the consumption of groats, cornflakes and sweets is unlikely to have a significant effect on the exacerbation of acne lesions.

The strength of the association of statistical characteristics determining the consumption of: alcohol; fatty meat and acne lesion exacerbation is medium, suggesting that there is an average association between the consumption of these products and acne exacerbation. Which may mean that among the subjects, it may influence, in part, the condition of the complexion (Table 2).

The strength of the association of statistical characteristics determining the consumption of: white rice; fast food; oils rich in omega-6 fats and exacerbation of acne lesions is strong (Table 2). In practice, this means that consumption of: white rice; fast food; oils rich in omega-6 fats may be a significant

risk factor for exacerbation of acne lesions in the study subjects. People with acne or who are concerned about the health of their skin may benefit from reducing their intake of these products to reduce acne symptoms, as found in a study in which less frequent consumption of these products resulted in less severe acne lesions.

The strength of the association of the statistical characteristics determining the consumption of sultanas and exacerbation of acne lesions is very strong (Table 2).

The strength of the association of the statistical characteristics determining the consumption of white flour pasta is almost certain, meaning that there is a very strong relationship. In practice, this means that the consumption of white flour pasta is very consistently and clearly related to the exacerbation of acne lesions in the subjects of the study.

Analyzing the data from the Table 2, it can be concluded that less frequent consumption of white flour pasta and omega-6-rich oils does not reduce the severity of acne lesions. For the products: milk and milk products, sweets, salty snacks, fizzy drinks, alcohol, hot spices that were most frequently selected with the highest lesion exacerbation, no reduction in lesion reduction was generally observed in those who consumed less frequently (Table 2).

#### **DISCUSSION**

According to the most recent English-language literature available in the Pubmed database, it is concluded that a high glucose intake and a high glycaemic index diet, promotes the development of acne vulgaris, while dairy intake shows a positive correlation among populations living in Europe, Australia and the United States [10].

In the study, more than half of the respondents answered affirmatively that acne was present in their parents, similar results were obtained in a 2015 study by Jakubczyk et al. [7] in which 51% surveyed adolescents aged 12 to 25 years from Szczecin confirmed the presence of acne in their parents. It is estimated that there is more than a 50% probability of acne occurrence in offspring whose parents both suffered from acne [7]. Among the adolescents studied, acne was most common on the face (85%), back (36%), and arms (22%) [7].

Similar to the study by Jakubczyk et al. [7], in our study, acne lesions most frequently affected respondents on the face. Similar results were obtained by Rokowska-Waluch et al. [13] in a 2009 study with 100 participants aged 11-55 years, where respondents also indicated the face (93%), back (54%), shoulders (39%), and décolleté (24%) most frequently [13].

In our study, almost all women, noticed an increase in lesions before menstruation. In the study

by Jakubczyk et al. [7], more than half of the women noted an increase in lesions, which also indicates a hormonal basis for the occurrence of acne.

In the study by Jakubczyk et al. [7], 71% of the surveyed adolescents noticed an exacerbation of changes after eating chocolate, 56% after chips and fast food, while 44% responded that they experienced an exacerbation of symptoms after eating spicy food. In our own study, respondents also identified sweets (chocolate, cocoa, chocolate bars, biscuits, cakes, ice cream, shake), fast food, salty snacks, fizzy drinks, hot spices and sweeteners as the products that most exacerbated their acne lesions. Also in the study by Rokowska-Waluch et al. [13], sweets were the main product that the subjects thought had an impact on acne lesions.

In a study by Akpinar Kara and Ozdemir [8] involving 53 acne patients and 53 non-acne patients, acne exacerbation was found to be exacerbated with carbohydrate consumption (p=0.007), whereas the authors did not associate exacerbation with fat consumption (p=0.69). In their own study, respondents rated milk as having an average effect on lesion exacerbation and did not notice any difference after oil consumption.

Also, in a study by LaRosa et al. [9] involving 225 participants (120 people with acne, 105 people without acne lesions), there were no statistical differences in the consumption of full-fat dairy (p=0.95) and reduced-fat dairy (p=0.36) between the study group and the control group. The authors of the same study showed no significant differences in mean glycaemic index values (5.09% acne subjects vs. 4.73% control group; p=0.7) or glycaemic load (73.37% vs. 50.69%; p=0.18) between the study groups [9]. The study authors concluded that their study shows that it is lowfat milk and skimmed milk (p=0.01) that are positively associated with moderate acne incidence, while fullfat milk has no statistically significant effect on acne (p=0.75) [9]. On the other hand, a study by Smith et al. [14] found that after a 12-week intervention, in groups of 16 and 15 participants, subjects who were on a lowglycaemic load diet showed an improvement in acne lesions (59%) compared to the control group (38%) (p=0.046).

For vegan and vegetarian diets with a reduced dairy supply, researchers Stewart and Bazergy [15] found in their study that adherence to a plant-based diet did not significantly differ between those with acne (n=8; 1.7%) and the control group (n=9; 3.6%) (p=0.13). In contrast, the study did not include a description of the meals and thus the glycaemic load and glycaemic index are unknown.

### CONCLUSIONS

Statistical analysis showed a relationship between the consumption of white rice (p=0.02); white flour pasta (p=0.007); fast food products (p=0.002); sultanas (p=0.045); oils rich in omega-6 fats (p=0.02) and the exacerbation of acne lesions.

It was observed that the consumption of products that are statistically significant and are in addition characteristics are highly correlated, less frequent consumption influences the reduction in severity, or lack of severity, of acne lesions after consumption of these products.

Respondents rated sweets, fast food, salty snacks, fizzy drinks, spicy condiments and sweeteners as exacerbating their acne lesions.

Those who have indicated that a particular product has exacerbated their lesions the most should observe whether reducing or eliminating such a product will help them improve their complexion.

It is important to raise patient awareness of the impact of diet on skin condition as an additional support for treatment. For patients with acne vulgaris, it is recommended to limit the following products: milk and milk products, hot spices, processed or high glycaemic index products.

More scientific studies need to be carried out in order to make clear recommendations.

#### **Conflict of interest**

The authors declare no conflict of interest.

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