# Acne and diet: a review

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## Abstract

Acne is one of the most frequent dermatological afflictions especially for people in their first 30 years of age. Several studies have shown that nutrition is one of the key factors involved in acne pathogenesis. Data show that a high glycemic index diet may be a trigger in acne pathogenesis, while patients with a low glycemic index diet have fewer acne lesions. Milk and chocolate are also involved in the exacerbation of acne. However, foods rich in omega-3 fatty acids suppress the production of inflammatory cytokines with therapeutic effect. Additionally, docosapentaenoic acid and γ-linolenic acid have demonstrated improved acne lesions. The aim of this review was to summarize current knowledge on the association between acne and diet with special attention to the most frequently discussed factors involved in its pathogenesis: milk, chocolate, omega-3 fatty acids, hyperglycemia, hyperinsulinism, and IGF-1.

## Introduction

Acne vulgaris is a chronic inflammatory disease influenced by numerous genetic and hormonal factors. The role of diet, among environmental factors, is still uncertain. A correlation between acne onset and exacerbation and a high-glycemic diet, milk, and chocolate consumption has been postulated. This association might be explained by the fact that a high glycemic index can lead to hyperinsulinemia, which results in endocrinological imbalance.[1] Furthermore, high insulin levels determine an increase in biological parameters such as androgens, insulin-like growth factor-1 (IGF-1), and insulin-like growth factor-3 (IGF-3), which also lead to acne onset and worsening.[2] Additionally, insulin, sex hormone binding protein (SHBP), sterol regulatory element binding protein-1 (SREBP-1), and inflammatory mediators play an important part in acne development.[3] The aim of this review was to examine the biological link between acne and diet, focusing on different types of food and their effects on acne pathogenesis (Table 1).

## Materials and methods

A systematic search of the PubMed and Science.gov databases was performed for the period 2000-2020 using the terms: *acne* and *acne vulgaris* in combination with each of the following: *diet, nutrition, milk, chocolate, Omega-3 fatty acids, hyperglycemia, hyperinsulism, IGF-1*. Other potentially relevant articles were identified by manually checking the references of

**Table 1** Effects of foods in inflammatory and endocrinological mechanisms related to acne

| Foods | Effects |
|---|---|
| Milk | • Promotes anabolic mTORC1 signaling;<br>• Promotes the IGF-1 synthesis and stimulates lipogenesis of sebaceous glands;<br>• Inhibits mRNA expression of PTEN, which downregulates nuclear FoxO1. |
| Chocolate | • Increases cytokine production. |
| Omega-3 fatty acids | • Suppresses the production of inflammatory cytokines;<br>• Decreases IGF-1 level;<br>• Inhibits the dimerization of TLR-1 and TLR-2 signaling;<br>• Inhibits mTORC1 signaling;<br>• Downregulates the SREBP-1c pathways. |
| Carbohydrates with a high glycemic index | • Increases IGF-1 level. |
| Fish, resveratrol, curcumin, genistein, and silymarin | • Decreases inflammation;<br>• Inhibits SREBP-1;<br>• Suppresses sebaceous lipogenesis; |

FOXO1, forkhead box O1; IGF-1, insulin-like growth factor-1; mRNA, messenger ribonucleic acid; mTORC1, mammalian target of rapamycin complex 1; PTEN, phosphatase and tensin homolog; SREBP-1c, sterol regulatory element-binding protein transcription 1; TLR, toll-like receptor.

the included literature. Only articles in English were selected. The last search was run on March 17, 2021. We included reviews and meta-analyses, pooled analyses, cohort studies, observational studies, and case reports. Independent extraction of articles was performed by two investigators using predefined criteria for assigned sub-chapters. Disagreement was resolved by a discussion between the two review authors.

## Results

### Omega-3 fatty acids and acne

Omega-3 polyunsaturated fatty acids (PUFAs) are known for their anti-inflammatory properties and might beneficially influence acne development.[4] However, omega-3 PUFAs are usually lost or oxidized through food processing.[5] Their beneficial effect in acne might be through a decrease in IGF-1 level, which, in turn, determines a reduction in proinflammatory cytokine expression in human sebocytes: IL-1β, IL-6, IL-8, TNF-α, and matrix metallo proteinases (MMPs).[6] Another inflammatory pathway upon which Omega-3 PUFAs have an inhibitory effect is through toll-like receptor-1 (TLR-1) and TLR-2 dimerization.[7] Conversely, *C. acnes* increases TLR expression in both keratinocytes and macrophages, thus leading to keratinocyte proliferation and inflammation. Keratinocyte TLR-2 and TLR-4 expression leads to nuclear factor kappa-light-chain-enhancer of activated B cells (NF-kB) and mitogen-activated protein kinase (MAPK) pathway activation and subsequent inflammation through IL-1, IL-6, IL-8, TNF-α, human β-defensin-2, granulocyte-macrophage colony-stimulating factor (GM-CSF), and MMP production.[8] Furthermore, NLR family pyrin domain containing NLRP3-inflammasome activation in antigen-presenting cells is inhibited by omega-3 PUFAs and stimulated by C. acnes. NLRP3-inflammasome determines caspase-1 activation, which further leads to monocyte-derived IL-1β release.[7] IL-1β promotes Th17 activation, inflammation, and keratinization. This process is regulated by the generation of reactive oxygen species (ROS) and proteases.[9] Moreover, omega-3 FAs inhibit the mammalian target of rapamycin complex 1 (mTORC1) signaling, downregulating the sterol regulatory element-binding transcription 1 (SREBP-1c) pathways.[10]

Jung et al. investigated the influence of dietary habits on acne development in Koreans and found that acne was correlated with a high intake of "junk food," as compared to individuals with healthy eating habits.[11] A limited case series on five patients with acne showed a reduction in acne inflammation and an improvement in the overall appearance after intake of eicosapentaenoic acid (EPA) and antioxidant nutrients for a minimum period of two months.[12] Another study conducted on an Italian population demonstrated that fish consumption had a protective effect on moderate and severe acne.[9] Similarly, Khayef et al. demonstrated that fish oil, which is rich in EPA, docosahexaenoic acid (DHA), and docosapentaenoic acid (DPA), improved acne severity.[13] Additionally, foods rich in GLA (γ-linolenic acid) may improve acne lesions.[5]

### Chocolate

The amount of scientific evidence to support the negative impact of chocolate intake on the sebum production is low. Chocolate consumption has been associated with the appearance of new acne lesions.[14] In a study conducted on acne patients aged between 13 and 18 years, 66% of the respondents mentioned chocolate as an aggravating factor.[15] The pathogenetic explanation might lie in an elevated post-consumption glycemic index.[4] One study involving 10 male patients who consumed chocolate daily for one week found a statistically significant increase in the mean number of acneiform lesions at day 4 and at day 7, as compared to baseline. Also, there was a strong correlation between the amount of chocolate ingested and the number of new acne lesions.[16] Cocoa percentage might also be an influential factor, since dark chocolate, which is richer in antioxidants, has less comedogenic effects. However, cocoa percentage is rarely mentioned in scientific papers.[14–16]

### Role of insulin, insulin resistance, and IGF-1 in acne

Sebaceous glands have a central role in acne pathogenesis.[17] Carbohydrate-rich diets, such as the Western diet, are associated with hyperglycemia, reactive hyperinsulinemia, and increased levels of IGF-1.[2] Additionally, an association between

IGF-1 gene polymorphism, high levels of IGF-1, and acne severity has been demonstrated.[18] In a study by Jung et al, patients who reported acne aggravation after food intake had higher IGF-1 serum levels, as compared to patients unaffected by food intake.[11] IGF-1 has a dual role: it stimulates androgen receptor (AR) transcriptional activity and inhibits AR nuclear coregulator forkhead box O1 (FoxO1).[3,17] Additionally, stronger comedogenic reactions secondary to the insulin/IGF-1 signaling pathway might be because of different CAG trinucleotide repeats in the N-terminal domain (NTD) region of the AR.[3] FoxO1 suppresses AR by binding to the NTD region, which makes individuals with shorter CAG repeats more prone to stronger comedogenic reactions.[2]

### SREBP-1 and mTORC1 variation because of hyperglycemic food intake

The role of high glycemic load diets on the induction and aggravation of acne has been confirmed by several placebo and case-controlled studies.[3,19] Hyperglycemia is correlated with low levels of sex hormone binding globulin (SHBG).[19,20] This is further confirmed by a study by Kwon et al, who observed a decrease in sebaceous gland size and SREBP-1 expression in facial acne after 10 weeks of a low glycemic load diet in 17 patients.[21] SREBP-1 is a key regulator of stearoyl-CoA desaturase and Δ6-desaturase gene expression. Δ6-desaturase converts palmitic acid (16:0) to sapienic acid (16:1).[22] The latter acts as a natural antimicrobial agent and is involved in epidermal host defenses.[23] Additionally, low levels of SREBP-1 decrease total sebum production and might also have a part in reducing the rate of sebum triglyceride fatty acid desaturation.[19]

Another major role in diet-induced acne is played by mTORC1 signaling.[24] Its role includes regulation of anabolism and nutrient-dependent cell cycle progression, as well as lipogenesis activation.[19] Insulin/IGF-1-mediated activation of AKT results in mTORC1 activation, which implies that mTORC1 expression is also influenced by diet.[19] Moreover, FoxO1 is a negative regulator of mTORC1.[25] The saying of Kapahi et al, "with TOR less is more," originally concocted for its role in the aging process, apparently applies in the treatment and prevention of acne as well.[19,26]

### Milk and acne

The impact of milk consumption on acne pathogenesis depends on its ability to promote anabolic mTORC1 signaling.[27] Milk can stimulate IGF-1 synthesis in the liver, thus increasing serum IGF-1 levels.[19,27] Furthermore, milk protein contains high levels of glutamine.[19] This amino acid is responsible for promoting cellular leucine uptake, and it is also the precursor of the glutaminolysis pathway, which has a critical role in mTORC1 activation, sebaceous lipogenesis, and sebocyte proliferation.[19] Cow's milk is known to transfer exosomal bioactive microRNAs,[28] enclosed by membranous microvesicles (exosomes).[29] Moreover, bovine microRNA-21 is identical to human microRNA-21,[30] responsible for inhibiting mRNA expression of phosphatase and tensin homolog (PTEN), thus promoting phosphatidylinositol 3-kinase/protein kinase B (PI3K/AKT) signaling pathway and downregulating nuclear FoxO1.[19] Furthermore, recent evidence suggests that microRNA-21 can also directly target FoxO1 mRNA, which leads to acne onset and worsening.[19] Finally, milk protein, whey, and casein are excessively used as part of fitness and bodybuilding workouts and are frequently associated with acne onset and exacerbations in consumers.[31] Further randomized controlled studies are warranted before any milk restrictions are implemented as beneficial in acne patients.[32]

## Acne nutrition therapy

Populations exposed to a paleolithic diet with a low glycemic index, no milk or dairy consumption, are generally acne-free: the Kitavan islanders of Papua New Guinea, the Ache hunters in Paraguay, the Inuit and adolescents of rural areas of Brazil.[2,19] The effects of diet on acne development are further demonstrated in the cases of Inuits, Okinawa islanders, and Chinese who transitioned to Westernized diets.[19] In a cohort consisting on New York young adults, acne severity was associated with the following: a hyperglycemic diet, the number of daily milk servings, and the amount of saturated fat and *trans*-fatty acid (TFA) intake.[33] Conversely, both diet and pharmacological supplements like EPA, DHA, or borage oil, which contains 400 mg γ-linoleic acid, have anti-inflammatory effects on acne by limiting inflammasome activation, thus improving acne lesions.[10,13,34]Furthermore, in a study by Jung et al, 2000 mg daily doses of omega-3 fatty acid (1000 mg eicosapentaenoic acid and 1000 docosahexaenoic acid), as well as 400 mg γ-linoleic acid significantly improved acne lesions after 10 weeks.[10] Additionally, green tea polyphenol epigallocatechin-3-gallate (EGCG) and stilbenol resveratrol might improve acne lesions[19] by EGCG inhibition of SREBP-1 in SEB-1 sebocytes and mTORC1 activity,[35] thus suppressing sebaceous lipogenesis.[36] Finally, it is advisable to use nutrients that contain plant-derived natural mTORC1 inhibitors like green tea (EGCG), resveratrol, curcumin, genistein, and silymarin.[35,37]

## Conclusions

Several studies have shown there is a correlation between acne and a high glycemic index diet by means of increased IGF-1 production. These results are further supported in a publication by Bronsnick et al where, on the basis of level IB evidence, a low glycemic load diet is recommended for acne patients.[32] Chocolate may also worsen acne lesions, but there is a difference between milk and dark chocolate. In fact, it has been observed that dark chocolate has fewer comedogenic effects given its antioxidant properties. Additionally, milk is implicated in sebaceous lipogenesis by promoting anabolic signaling of

mTORC1, thus exacerbating acne lesions. Moreover, a paleolithic dietary approach consisting of a low glycemic load diet and no milk consumption is linked to acne-free populations. Furthermore, the consumption of foods rich in omega-3 fatty acids, docosapentaenoic acid, and γ-linolenic acid can have a therapeutic effect on acne through their anti-inflammatory properties. Other factors, like green tea polyphenol epigallocatechin-3-gallate, stilbenol resveratrol, curcumin, genistein, and silymarin remain to be further investigated.

## True or False Questions (answers provided after references)

**1** The role of diet in acne pathogenesis is still uncertain.
**2** Omega-3 polyunsaturated fatty acids have anti-inflammatory properties especially through a decrease in IGF-1 level.
**3** Intake of fish oil rich in eicosapentaenoic acid, docosahexaenoic acid, and docosapentaenoic acid demonstrated no effect on acne lesions.
**4** Daily consumption of chocolate has been proven to significantly increase the mean number of acneiform lesions.
**5** Dark chocolate has less comedogenic effects than milk chocolate.
**6** Carbohydrate-rich diets have no effect on IGF-1 production.
**7** A low glycemic load diet improved acne lesions by decreasing sebaceous gland size and sex hormone binding globulin expression.
**8** mTORC1 signaling is not implicated in acne pathogenesis.
**9** Milk intake has no influence on the production of IGF-1.
**10** Populations with a low glycemic index diet and no dairy consumption are generally acne-free.

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## Answers to questions

1 True, 2 True, 3 False, 4 True, 5 True, 6 False, 7 True, 8 False, 9 False, 10 True