Clinical Letter

Clinical effects of omega-3 fatty acids on acne vulgaris

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Dear Editors,

There is growing evidence highlighting the impact of nutrition on the severity of acne [1, 2]. Dietary interventions for acne patients, in addition to pharmacotherapy are therefore being investigated. Yet, data on the impact of Omega-3 fatty acids (ω-3 FA), which may contribute to alleviate the clinical severity through reduced sebum production and keratinization of the pilosebaceous unit, is scarce [3, 4] (Figure 1 a, b).

A systematic review screening Cochrane, Embase and PubMed for "acne" and "omega-3-fatty acids" was conducted to assess all prospective, interventional clinical trials with oral supplementation of ω-3 FA evaluating the effects on acne based on clinical scores (Figure 2). Three trials were included in the present review (Table 1).

Rubin et al. conducted a study with five patients in 2008 [5]. After an eight-week supplementation of *eicosapentaenoic acid* (EPA), combined with micronutrients and a green tea antioxidant, a decrease in the lesion count from 62.8 to 40.4 was seen in 4/5 patients. Hereby, a reduction of inflammatory lesions was observed from 20.8 to 6.8. Furthermore, a mean improvement in patients' self-evaluated mental status by 24 % according to a standardized questionnaire was seen.

This pilot study may serve as a motivation to pursue future investigations; however, no clinical recommendations can be drawn from the presented cases. Results were not significant, possibly due to the extremely small patient collective. Notably, since patients took a combination of supplements, the described clinical improvement could not be attributed to ω-3 FA alone. Future trials should therefore include a larger patient cohort and focus on isolated supplementation.

In 2012, Khayef et al. investigated the effects of *docosahexaenoic acid* (DHA) and *docosapentaenoic acid* (DPA) in 13 males [6]. In addition to the lesion count, the authors investigated patients' skin redness and assessed a three-day food diary. No significant differences were found when comparing baseline lesion count to 12-week post-intervention. However, scores of 8/13 individuals improved, with 7/8 entering the study with moderate to severe appearances. In 4/13 patients, acne's grade worsened, with 3/4 patients presenting with mild acne at baseline. These findings raise the question whether patients with a more severe degree of acne might have lower blood levels of ω-3 FA compared to milder cases and might therefore profit more from an oral supplementation.

Limitations of this study are the small patient cohort without a control group and exclusion of female patients. Unfortunately, it could not be determined which acne treatment was allowed during the trial. It might only be speculated that "no intense treatment" might have excluded isotretinoin treatment. Future investigations should clearly state exclusion and inclusion criteria and prescription therapy should not be allowed to reduce bias.

Jung et al. conducted a randomized, double-blinded, controlled trial in 2014, with a male dominated study cohort of 46 patients [7]. The collective was divided into two treatment groups (ω-3 FA or ω-6 FA), and one control group. Apart from the lesion count, daily food reports, the extent of facial inflammation and patients' self-evaluated acne severity were assessed. Additionally, 2-mm punch biopsies were taken from inflammatory facial lesions.

Both treatment groups showed significant improvements compared to the control, but no significant differences were found between them. Patients' mean lesion counts and subjective ratings decreased. Immunohistology staining intensities diminished in both treatment groups, whereas no significant change was observed in the control group.

Out of the three reviewed trials, Jung et al. conducted the highest-quality study. Immunohistochemical analyses impressively demonstrated reduced inflammatory markers, bearing in mind that the location of a punch biopsy was examiner dependent. Interestingly, ω-3 and ω-6 FA both led to a clinical improvement, with no significant difference between the two groups. This finding contradicts preliminary data arguing that ω-6 FA foster inflammation. However, levels of FA as well as their bioavailability differ greatly between individuals, which might be a reason for the contradictory results [8]. Blood levels should therefore be regularly checked in future studies to establish baseline values, ensure sufficient availability and potentially even allow for adjustment of dosage throughout the study [9].

Despite the physiological anti-inflammatory mechanisms of ω-3 FA, the investigated trials showed inconclusive results possibly due to great limitations. Outlined conclusions should be implemented in future trials to elaborate whether ω-3 FA are effective in reducing acne severity.

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Conflict of interest

None.

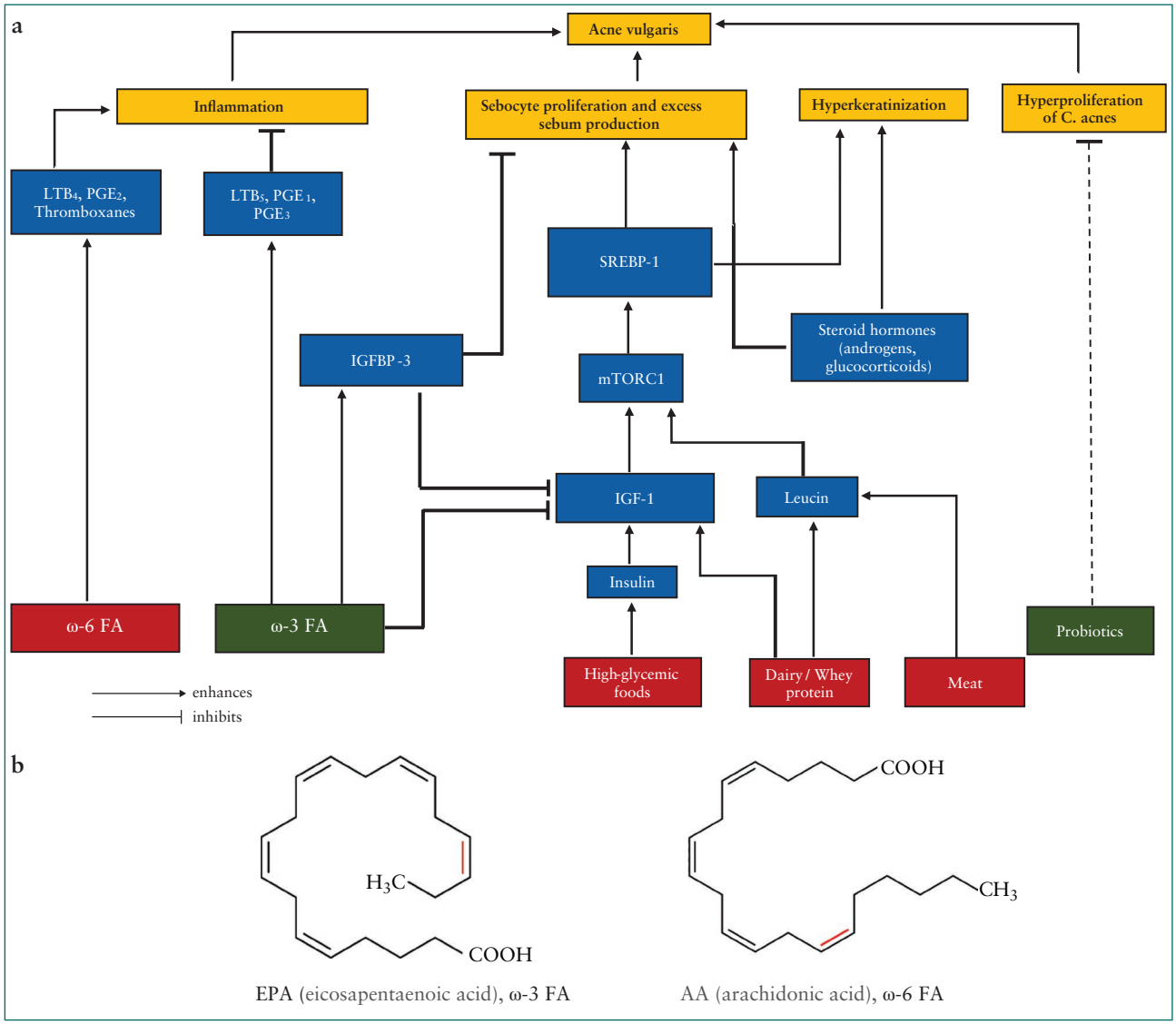

Figure 1 (a) Hyperglycemic foods and dairy products, especially whey protein, stimulate the synthesis of Insulin-like growth factor (IFG)-1, one of the central nutritive acne-inducers. IGF-1 activates the mammalian target of rapamycin complex 1 (mTORC1), which in turn triggers the transcription of Sterol response element-binding protein (SREBP)-1. SREBP-1 stimulates sebum production, hyperkeratinization of follicles and pro-inflammatory mediators. ω-3 FA inhibit IGF-1 and decrease inflammation by stimulating the production of PGE_1, PGE_3 and LTB_5. ω-6 FA are thought to foster inflammatory processes, e. g. via PGE_2 or LTB_4. *In vitro* and preliminary *in vivo* data show beneficials effects of probiotics on acne, including inhibitory mechanisms of C. acnes proliferation and reduced levels of IGF-1.

(b) Polyunsaturated fatty acids (PUFAs) including ω-3 FA with the first double bound in the third position of the carbon-carbon fatty acid chain and ω-6 FA with the first double bound in the sixth position. Sources of ω-3 FA (e. g., alpha-linoleic acid [ALA], eicosapentaenoic acid [EPA], docosahexaenoic acid [DHA]) are nuts, seeds (chia-, hemp-, linseeds) and algae (through algae intake also salmon, herring, sardines, seafood). ω-6 FA (e. g., arachidonic acid [AA], gamma-linoleic acid [GLA]) are found in sunflower oil and corn oil.

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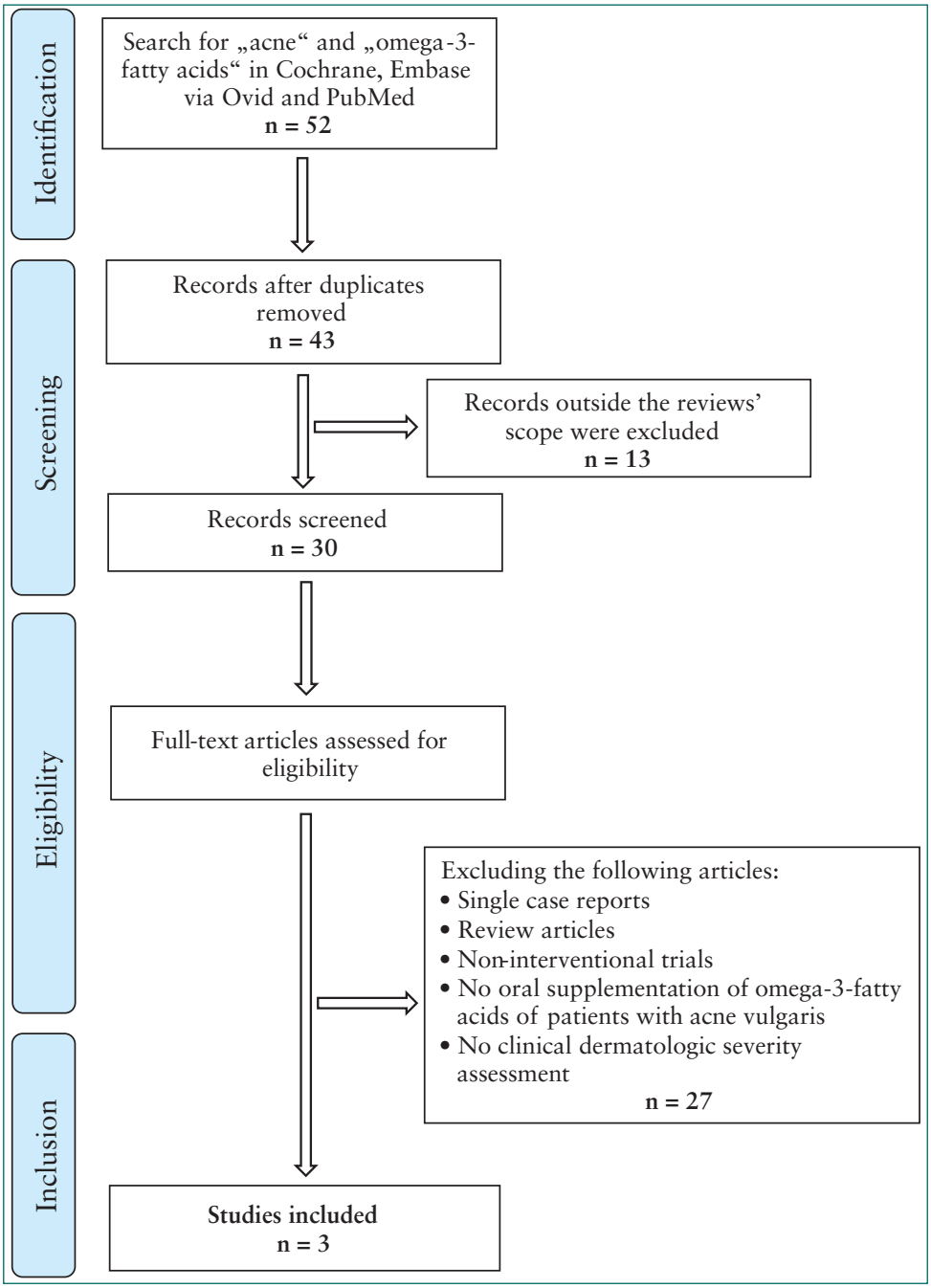

Figure 2 Review process based on PRISMA flow chart.

Table 1 Details of included prospective trials investigating the clinical effects of oral supplementation with ω-3 FA on acne vulgaris.

Title	Authors	Year of publication	Form of intervention	Supplements and origin	Daily Dosage	Time period of intervention	Study Visits	Number (n) and gender of patients	Age range (years)	Conditions during intervention	Primary study endpoint	Secondary study endpoints	Randomization?	Control group?	Evaluation of ω-3 FA level?
Acne vulgaris, mental health and omega-3 fatty acids: a report of cases.	Rubin MG, K Kim and A Logan	2008	Oral Supplementation	EPA (sardines, anchovies) Epigallocatechin gallate (EGCG, green tea extract) Zinc gluconate Selenium Chromium	250 mg 50 mg 3.75 mg 50 µg 50 µg	8 weeks	n = 2 (week 0, 8)	n = 5 3 males 2 females	18– 23	No prescribed acne treatments No other supplements or lifestyle changes	Lesion count	Mental health status via Arizona Integrative Outcomes Scale (AIOS)	No	None	No
Effects of fish oil supplementation on inflammatory acne.	Khayef G et al.	2012	Oral Supplementation	EPA (fish oil) DHA (fish oil) DPA (fish oil)	930 mg 720 mg 174 mg	12 weeks	n = 3 (week 0, 6, 12)	n = 13 13 males	18– 40	No "intense" acne treatment No additional intake of ω-3 FA-rich foods	Lesion count	Skin redness (L*a*b*color system; Commission Internationale de L'Eclairage)	No	None	No
Effect of dietary supplementation with omega-3 fatty acid and gamma-linolenic acid on acne vulgaris: a randomized, double-blind, controlled trial	Jung JY et al.	2014	Oral Supplementation	*Group 1:* EPA (fish oil) DHA (fish oil) *Group 2:* GLA (borage oil) *Group 3:* No supplementation	1000 mg 1000 mg 400 mg	10 weeks	n = 10 (week 0, 2, 5, 10)	n = 45 36 males 9 females *Group 1:* n = 15 *Group 2:* n = 15 *Group 3:* n = 15	18– 33	No prescribed acne treatment No other supplements No previous systemic acne treatment	Lesion count	Severity grading of facial inflammation based on color photographs (Cunliffe rating system) Patient self-assessment via visual analog scale (VAS) Staining intensity of Interleukin 8 (IL-8) and transforming growth factor (TGF) beta-1	Yes	Yes, but no placebo	No

Abbr.: EPA, eicosapentaenoic acid; EGCG, Epigallocatechin gallate; DHA, docosahexaenoic acid; DPA, docosapentaenoic acid; GLA, gamma-linoleic acid; ω-3 FS, omega-3 fatty acids

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