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A novel topical ingredient derived from seaweed significantly reduces symptoms of acne vulgaris: A general literature review

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Synopsis

Currently, benzoyl peroxide, antibiotics, and retinoids are the mainstay topical treatments for acne vulgaris. However, potential benefits may be offered by natural, marine-derived ingredients, such as those derived from brown seaweed (*Laminaria digitata*). This article will review the available literature on two ingredients; "seaweed oligosaccharides," which are those derived from the polysaccharide membrane of *Laminaria digitata*, and a novel seaweed oligosaccharide–zinc complex (SOZC) (Phycosaccharide AC, The Mentholatum Company, East Kilbride, UK). Findings from a recent double-blind, placebo-controlled, randomized clinical trial (RCT) will also be reported and likely mechanisms discussed. The findings taken together suggest that SOZC can significantly ameliorate symptoms of acne vulgaris, particularly in terms of reducing sebum production and populations of *Propionibacterium acnes.*

INTRODUCTION

Acne vulgaris is a skin condition that affects about 80% of individuals during adolescence (1), persisting beyond the age of 25 years in 3% men and 12% women (2). The form of acne can range from simple comedones, papules, and pustules to severe inflammatory nodules and cysts on the face, chest, and back, which may cause long-term scarring (2,3). Symptoms can be persistent, often lasting for more than 12 months (4).

In addition to being a cosmetic nuisance, acne can lead to emotional and behavioral issues, especially in teenage girls and those with severe symptoms (5). One qualitative review of 16 studies found that acne had a significant impact on self-esteem and quality of life, often placing strains on family and social relationships (6). In one cross-sectional survey of 852 adolescents and young adults aged 12–25 years, 80.8% saw acne as a normal phase of adolescence, but 69.3% reported that it should be treated, preferably topically rather than systemically (4).

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Acne vulgaris is viewed as an inflammatory disease, but levels of sebum production and bacterial populations may also underpin causation, and should be targeted by treatment strategies (3,7). In particular, the gram-positive anaerobic bacteria, *Propionibacterium acnes* (*P. acnes*), are thought to contribute to the inflammatory phase of acne, although there is no consensus as on likely mechanisms (8,9).

Other factors can exacerbate the pathogenic process leading to the development of acne vulgaris, and these are described in detail elsewhere (10). Hormones, principally the androgenic-dependant hormone, testosterone, can increase sebum levels and trigger inflammatory processes (11). Poor quality diets, high in dairy foods, chocolate (12), and other lipid mediators, such as saturated fatty acids, are considered to be underlying risk factors, although the evidence base is currently weak (13). Research also suggests that emotional stress can stimulate immunoreactive nerve fibers, sebum synthesis, and the build up of bacteria, mainly in the form of *P. acnes* (14).

Cosmetic products are a popular treatment for acne but are not typically tested with the same rigor as medical treatments (15). However, this appears to be changing and a good example is the double-blind RCT published on the 'anti-aging' effects of niacinamide (16), which used the Kligman standards—three questions designed to test the scientific rationale behind cosmetic use (Table I; 17). As yet, these gold standard approaches have not been used to investigate treatment strategies for acne vulgaris.

Changes in today's modern society have led to greater pressures to have clear skin which have, in turn, have increased demand for cost–effective, noninvasive cosmeceutical products (15,18). There has also been increased interest in natural ingredients that were used to treat skin conditions in traditional cultures but remain untested in the clinical setting (19). Therefore, the aim of the present article is twofold: (i) to review studies which describe the potential role of seaweed oligosaccharides in the prevention and treatment of acne vulgaris and (ii) to review the results from a recent published RCT that used a novel seaweed ingredient.

SEAWEED OLIGOSACCHARIDES

Oligosaccharides can be extracted from the brown seaweed *Laminaria digitata (L. digitata).* The plant is a rich source of potassium, sodium, magnesium, and iodine (Table II), although seasonal changes are known to affect the composition and ratio of the polysaccharides (20). Brown seaweeds are also a good source of anti-inflammatory omega-3 fatty acids, with the algal blade containing more omega-3 fatty acids than the other parts of the plant (21).

Extracting the oligosaccharides involves a four-stage process beginning with the harvesting of *L. digitata* from sustainably managed seabeds. This is done using a curved iron hook, called a scoubidou, which is suspended from a hydraulic arm mounted on a boat and lowered into the seabeds. The hook is then rotated to draw the seaweed out of the sea (22).

In the next stage, aqueous extraction methods are used to remove long-chain polysaccharides (between 200 and 2500 sugar components) from the algae. This is followed by enzymatic depolymerization that breaks the polysaccharide into oligosaccharides, smaller polymers with 3–10 sugar components. The final process involves chelating the

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Table I
Kligman Standards (Ref. 17)

1	Can the active ingredient penetrate the stratum corneum and be delivered in sufficient concentrations to its intended target in the skin?
2	Does the active ingredient have a known specific biochemical mechanism of action in the target cell or tissue in human skin?
3	Are there published, peer-reviewed, double-blind, placebo-controlled, statistically significant, clinical trials to substantiate the efficacy claims?

oligosaccharide with zinc sulfate (0.1% zinc-pyrrolidone), forming a zinc complex (Phycosaccharide® AC, The Mentholatum Company, East Kilbride, United Kingdom) that actively crosses the skin barrier, even when the skin is greasy (22).

Formerly, zinc has been used in combination with erythromycin to treat acne, but has limited efficacy on its own (23). In general, zinc has an important role in promoting wound healing and reducing inflammation (24,25). It also helps to control levels of skin sebum by inhibiting the enzyme 5-α-reductase that converts testosterone into its biologically active form, 5-α-dihydrotestosterone, which stimulates sebaceous gland activity (26). In addition, zinc can inhibit bacterial lipases from converting sebum triglycerides to fatty acids, which are potent mediators of acne (27). Scientific evidence on the likely impact of marine-derived oligosaccharides on symptoms of acne vulgaris will be evaluated in section "Evidence for Benefit."

EVIDENCE FOR BENEFIT

Marine organisms offer a host of biological activities including antibacterial, anti-inflammatory, and antioxidative properties that could be used in preparations (28) with a view to alleviating symptoms of acne vulgaris. In particular, sulfated polysaccharides extracted from edible brown seaweeds have strong antioxidant properties (29), which may deliver anti-inflammatory benefits.

Until recently, most evidence has been arisen from animal trials, in vitro tests, or phase I clinical trials. One animal study showed that topical application of brown algae polyphenols to the skin of hairless mice inhibited cyclooxygenase-2 activity and rates of cell division, protecting against oxidative stress, inflammation, and cell proliferation (30). A later study, similar in design, showed that seaweed polysaccharides promoted skin regeneration and prevented infections when applied to the skin of mice using sponge dressings (31).

If an ingredient is to be useful against acne, it must also show antimicrobial properties. In one animal experiment, dietary supplementation with *L. digitata* led to significant reduction in gut enterobacteriaceae populations (32), suggesting antimicrobial properties. Equally, in vitro tests revealed that a 5.6% preparation of a patented seaweed oligosaccharide–zinc

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Table II
Composition of L. *digitata* (Brown Algae) (Ref. 45)

Component	Amount in *L. digitata* (g per 100 g dry matter)
Water (%)	73–90
Ash	73–90
Total carbohydrate	—
Other carbohydrates	1–2
Protein[a]	8–15
Fat	1–2
Alginic acid	20–45
Laminaran	0–18
Mannitol	4–16
Fucoidan	2–4
Potassium	1.3–3.8
Sodium	0.9–2.2
Magnesium	0.5–0.8
Iodine	0.3–1.1

[a]Key: Should be treated with caution as value depends on levels of free nitrate that is found in variable amounts in brown algae.

complex (SOZC) reduced *P. acnes* counts by 74% (22). In a human trial, a reduction in *Staphylococcus aureus (S. aureus)* was noted in 58% of volunteers after 28 days of use (22). Additional tests carried out on skin samples showed that use of SOZC increased levels of interleukin 1 alpha (IL1α) by 11.1% in the active versus the control comparator, indicating that the product may have soothing effects (22).

Turning to Phase I clinical trials, cutaneous sebum levels reduced by 67% after a group of 12 volunteers used a gel containing 5% SOZC for 28 days (22). Results from an anti-prickling test carried out on day 28 in a subgroup of these volunteers ($n = 8$) suggested a significant reduction in the skin's reactivity threshold (by 36%), indicating reduced sensitivity and improved skin healing. Another clinical trial ($n = 10$) reported that a preparation containing SOZC and the preservative phenoxyethanol, improved levels of hydration in surface layers of the skin for 4 h following application (33). These results indicate that, in addition to reducing skin sensitivity, the active agent may have hydrating properties ultimately helping to seal the skin and epidermis barrier (33).

A double-blind RCT of a SOZC preparation has been published recently, involving 60 males with mild acne recruited from an acne clinic (34). After providing informed consent, the males (mean age 18.4 years) were randomly allocated to receive an active (containing SOZC) or placebo treatment for 56 days. Both treatment vehicles comprised a topical wash and balm. Examination of the skin, including photographs, was undertaken by two dermatologists at baseline, then on days 3, 14, 28, and 56. At each visit, comedones and inflammatory lesions (papules, pustules) were counted, desquamation and erythema were measured according to a standard four-point severity scale, while a sebumeter was used to estimate sebum production 3 h after use of the wash.

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Table III
Effect of Active and Placebo Treatments on Lesion Numbers and Sebum Production (Ref. 34)

	Treatment	Baseline	Day 3	Day 14	Day 28	Day 56
Comedones (mean number)	Active	48.2 ± 24	48 ± 24	34.1 ± 24	28.1 ± 17	19.7 ± 13
	Placebo	58.4 ± 23	58 ± 23	49.3 ± 22	45.1 ± 20	38.4 ± 18
Inflammatory lesions (mean number)	Active	37.7 ± 4	37 ± 4	26.9 ± 4	17.3 ± 5	13.6 ± 6
	Placebo	42.6 ± 4	42.2 ± 4	34.4 ± 6	31.6 ± 6	20.3 ± 6
Sebum production ($\mu g/cm^2$)	Active	154 ± 12	153 ± 12	146 ± 14	123 ± 15	101 ± 5
	Placebo	150 ± 12	148 ± 12	144 ± 12	130 ± 18	106 ± 11

Between baseline and day 56, there was a statistically significant reduction in the number of papules/pustules and comedones in the placebo and active treatment groups. However, when the percentage change from baseline was considered, the active group had a statistically greater reduction in papules/pustules and comedones, even after only 14 days of continued use. Levels of sebum production reduced in both groups, as did the number of inflammatory lesions (Table III). Neither product was found to cause irritation to the skin or desquamation.

DISCUSSION

Acne vulgaris is a common inflammatory skin disorder affecting mainly adolescents (35), but sometimes continuing into adulthood (2). Although considered to be a condition rather than a disease, acne impacts on social and psychological wellbeing, particularly if scarring occurs (36).

Although topical agents, such as benzoyl peroxide, antibiotics, and retinoids, are popular treatments (37), interest in the use of natural ingredients is growing (19), including botanical compounds, such as chamomile, green tea, and curcumin (38). However, few have been tested rigorously in human trials.

The present review evaluated evidence for the therapeutic effects of brown seaweed and its bioactive compounds on markers of skin health and symptoms of acne vulgaris. More recent evidence is provided by a double-blind RCT that tested the effects of a novel seaweed ingredient, SOZC, on symptoms of mild acne over 56 days of use. This trial found significant improvements in acne vulgaris symptoms by 14 days of use. While the placebo-treated subjects showed similar improvements up to day 14, but not beyond, this may have been because of the 1.8% lactic acid present in the product vehicle. Facial peels contain 35% to 50% lactic acid and are known to improve comedonal acne (39). Smaller clinical trials have showed a 67% reduction in skin sebum levels and increased levels of IL1α following treatment with SOZC, suggesting that the ingredient has soothing effects (22). Seaweed extracts may also help to hydrate the skin, thus sealing the epidermis barrier and supporting the healing process (33).

Acne vulgaris is influenced by the growth of *P. acnes* (8), which has traditionally been treated with antibiotic therapies (37). However, concerns have been raised about bacterial resistance, particularly when topical and oral antibiotic treatments are combined (40).

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Consequently, marine-derived bioactive ingredients could be a safe, natural alternative. There is good evidence that application of SOZC helps to reduce populations of *P. acnes* and *S. aureus* by 67% and 58%, respectively, after 28 days of use (22). Natural, topical therapies may also cause fewer potential side effects than conventional drug or laser treatments (41). In the most recent published RCT (34), skin sensitivity was reduced but no side effects, e.g., skin irritation or desquamation, were reported.

The likely mechanisms of action are not fully known but may include antibacterial (22,32), antioxidant and anti-inflammatory effects related to the nutrient profile of brown seaweed (21,29). Alginates, also found in *L. digitata* (see Table II), have been found to promote wound healing, possibly by modulating levels of growth factors and collagen (42). Although zinc has been reported to promote wound healing and may have anti-inflammatory effects (24,25), it is thought to have limited efficacy on its own (23). It is therefore likely that the reduced levels of inflammation and comedone formation in the aforementioned studies were due to a combined effect of seaweed oligosaccharides and zinc complex (22).

There is now increased expectation for cosmetic products to prove efficacy using properly controlled trials (43), as is already the case for medical products (15). The double-blind RCT reported here (34) is one of the first to apply methods in line with Kligman standards to over-the-counter skincare (17). In the future, applying Consolidated Standards of Reporting Trials (CONSORT) guidelines or registered trials prospectively on public databases could help to strengthen the evidence for skincare products (44). It is important to reassure consumers that over-the-counter products are supported by high-quality data.

In conclusion, the use of seaweed oligosaccharides and associated novel ingredients, such as a patented oligosaccharide–zinc complex, appear to offer an effective, natural alternative for the treatment of acne vulgaris. Future research is needed to confirm how marine oligosaccharides exert their therapeutic actions, and to compare the efficacy of seaweed extracts with standard prescription treatments for acne.

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