Received: 5 August 2017 | Revised: 27 October 2017 | Accepted: 30 October 2017

DOI: 10.1111/dth.12576

REVIEW ARTICLE

WILEY DERMATOLOGIC THERAPY

The role of zinc in the treatment of acne: A review of the literature

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Abstract

Acne vulgaris is a chronic disease of the pilosebaceous units presenting as inflammatory or noninflammatory lesions in individuals of all ages. The current standard of treatment includes topical formulations in the forms of washes, gels, lotions, and creams such as antibiotics, antibacterial agents, retinoids, and comedolytics. Additionally, systemic treatments are available for more severe or resistant forms of acne. Nevertheless, these treatments have shown to induce a wide array of adverse effects, including dryness, peeling, erythema, and even fetal defects and embolic events. Zinc is a promising alternative to other acne treatments owing to its low cost, efficacy, and lack of systemic side effects. In this literature review, we evaluate the effectiveness and side-effect profiles of various formulations of zinc used to treat acne.

KEYWORDS

acne, inflammatory disorders, systemic therapy, therapy topical, zinc

1 | INTRODUCTION

Acne vulgaris is a chronic inflammatory disease of the skin that affects the individuals of all ages, especially adolescents and young adults (Fox, Csongradi, Aucamp, du Plessis, & Gerber, 2016; Gollnick, Finlay, Shear, & Global Alliance to Improve Outcomes in Acne, 2008). Although the pathogenesis is complex and multifactorial, a few theories are widely accepted (Zaenglein et al., 2016). Notably, the stimulation of sebaceous glands by androgens, along with hyperkeratinization, results in the obstruction of sebaceous follicles (Toyoda & Morohashi, 2001). *Propionibacterium acnes* (*P. acnes*) proliferates in this environment, recruits inflammatory cells to the area, and metabolizes triglycerides in the sebum to form free fatty acids that in combination with other inflammatory mediators leads to the hastening of irritation (Muizzuddin, Giacomoni, & Maes, 2008).

Current treatments for acne vulgaris aim to inhibit one or more of the steps in pathogenesis. The choice of therapy depends on the severity of disease, site of involvement, age of the patient, and personal preference (Zaenglein et al., 2016). Topical formulations, including washes, gels, lotions, and creams, are the most widely used. Antibiotics, antibacterial agents, retinoids, and comedolytics are common options (Fox et al., 2016). Systemic treatments are reserved for more severe or resistant forms of acne. These include oral isotretinoin, oral antibiotics, and hormonal mediators such as spironolactone and oral contraceptives (Katsambas & Papakonstantinou, 2004). Both topical and systemic treatments are widely used; however, both incur several risks and disadvantages. Topical retinoids induce dryness, peeling, erythema, and irritation, which may make patients less likely to use them. Oral isotretinoin is teratogenic and hence requiring frequent monitoring and enrollment in the iPLEDGE program (McElwee et al., 1991). Overuse of antibiotics is a growing concern worldwide, contributing to the development of resistant bacterial strains and decreased efficacy (Humphrey, 2012; Ventola, 2015). Fetal defects and embolic events remain a risk for hormonal modulators. For these reasons and more, alternative treatments are often sought.

Zinc, a divalent cation, is an essential micronutrient for the proper functioning of several processes in the human body. Among these, zinc appears to play a role in a number of skin disorders. The utility of zinc in acne vulgaris was first recognized in the 1970s when Fitzherbert (1977) noted the improvement of acne after its administration to zinc-deficient patients with acrodermatitis enteropathica. It was later determined that zinc levels in those with acne were significantly lower than controls (Michaëlsson, Vahlquist, & Juhlin, 1977). Although the exact mechanism by which zinc exerts its effects to improve acne vulgaris is

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not fully understood, current knowledge suggests multiple mechanisms (Azzouni, Godoy, Li, & Mohler, 2012; Chow, 2009; Gupta, Mahajan, Mehta, & Chauhan, 2014; Kitamura et al., 2006; Ozuguz et al., 2014; Sardana, Chugh, & Garg, 2014; Sugimoto, López-Solache, Labrie, & Luu-The, 1995):

1. Regulation of protein, lipid, and nucleic acid metabolism owing to its role as an essential cofactor in more than 300 metalloenzymes and 2,000 transcription factors.
2. Regulation of gene transcription through involvement in histone deacetylation reactions and via zinc-finger motif-containing proteins and factors such as those in steroid and thyroid hormone receptors.
3. Regulation of DNA and RNA polymerases, thymidine kinases, and ribonucleases and hence assisting in the maintenance of proper cell replication, immune activity, and wound repair.
4. Maintenance of immunologic response by preserving macrophage and neutrophil function and stimulating natural killer cell and complement activity.
5. Inflammatory regulation by inhibition of IL-6 and TNF-α production.
6. Inhibition of inflammatory mediator production, such as nitric oxide (owing to its presence in Zn-Cu prosthetic groups in superoxide dismutase).
7. Inhibition of integrin and toll-like receptor expression by keratinocytes, thus acting as an anti-inflammatory agent (Kitamura et al., 2006) (Note: *P. acnes* induces cytokine production through a toll-like receptor-dependent pathway) (Sardana et al., 2014).
8. Direct inhibition of *P. acnes* proliferation (Ozuguz et al., 2014).
9. Inhibition of 5α-reductase thus blocking conversion of testosterone to dihydrotesterone (DHT) and suppressing sebaceous gland activity (Note: DHT plays a key role in the development of acne as it stimulates sebaceous gland activity.) (Azzouni et al., 2012; Sugimoto et al., 1995).

Zinc has shown promise in the treatment of acne vulgaris in a number of clinical trials. Herein, we examine the role of zinc in the treatment of acne vulgaris and summarize the current published literature to further conclude on zinc's efficacy.

2 | METHODS

A number of investigations have been conducted to assess the efficacy of zinc as a treatment modality for acne vulgaris. Searching through the PubMed/MEDLINE and Clinicaltrials.gov database without a language or publishing-time restriction, we identified 161 articles using the keyword "Zinc AND Acne AND treatment." We included case reports and clinical trials with male and female patients diagnosed with acne vulgaris. Two reviewers independently determined the eligibility of the studies and performed the methodological quality assessment. Following our inclusion/exclusion criteria, we excluded 129 studies and included 32 original studies in this review.

Inclusion Criteria includes:

- Studies must directly involve subjects with at least mild acne.
- Studies must use a human model.
- Studies must use topical or oral zinc formulations.

For each study, we report on the sample size, degree of disease, dosing protocols, study length, follow-up periods, adverse effects, outcome measures, and results. Treatments containing only zinc are referred to as "single-agent products" (Table 1), whereas the treatments containing zinc in addition to other components are referred to as "combination products" (Table 2). Furthermore, we report on the studies comparing zinc to other treatment modalities (Table 3), such as clindamycin and erythromycin. Quantitative and qualitative assessments of acne lesions were used by most studies and are summarized in Tables 1–3.

3 | RESULTS

3.1 | Single-agent products

A total of 12 studies (Cochran, Tucker, & Flannigan, 1985; Dreno, Amblard, Agache, Sirot, & Litoux, 1989; Dreno et al., 2005; Göransson, Lidén, & Odsell, 1978; Hillström et al., 1977; Kobayashi, Aiba, & Tagami, 1999; Lidén, Göransson, & Odsell, 1980; Meynadier, 2000; Orris, Shalita, Sibulkin, London, & Gans, 1978; Verma, Saini, & Dhamija, 1980; Weimar, Puhl, Smith, & tenBroeke, 1978; Weismann, Wadskov, & Sondergaard, 1977) (Table 1) tested the efficacy of zinc as a single agent on acne vulgaris; 11 studies tested oral zinc (Dreno et al., 1989, 2005; Göransson et al., 1978; Hillström et al., 1977; Kobayashi et al., 1999; Lidén et al., 1980; Meynadier, 2000; Orris et al., 1978; Verma et al., 1980; Weimar et al., 1978; Weismann et al., 1977) (zinc gluconate [3], zinc sulfate [8]) and one study tested topical zinc sulfate (Cochran et al., 1985). Most studies (9/12) used a control group consisting of lactose placebo capsules or topical vehicle placebo (Cochran et al., 1985; Dreno et al., 1989; Göransson et al., 1978; Hillström et al., 1977; Lidén et al., 1980; Orris et al., 1978; Verma et al., 1980; Weimar et al., 1978; Weismann et al., 1977). All studies, except the case report by Kobayashi et al. (1999), used quantitative outcome measures, such as inflammatory lesion count, noninflammatory lesion count, and acne load/score. One study assessed sebum production and found that 58.6% of patients (17/29) experienced a decrease in facial oiliness, compared to 0% of patients taking lactose placebo (Verma et al., 1980). Qualitative outcome measures, such as examiner's and patient's subjective opinion of acne severity, were assessed by nine studies (Cochran et al., 1985; Dreno et al., 1989; Göransson et al., 1978; Hillström et al., 1977; Kobayashi et al., 1999; Lidén et al., 1980; Meynadier, 2000; Weimar et al., 1978; Weismann et al., 1977).

A total of eight studies concluded that zinc was an efficacious treatment for acne vulgaris (Dreno et al., 1989, 2005; Göransson et al., 1978; Hillström et al., 1977; Kobayashi et al., 1999; Lidén et al., 1980; Meynadier, 2000; Verma et al., 1980), out of which five found a statistically significant improvement compared to controls (Dreno et al., 1989; Göransson et al., 1978; Hillström et al., 1977; Lidén et al., 1980;

TABLE 1 Overview of the studies that used zinc as a single-agent treatment

Author (year)	Study type Sample size [completed study] (zinc, control)	Acne severity (classification/ grading system)	Zinc treatment group (dosing)	Control group (dosing)	Follow-up period	Zinc adverse effects (%/# of patients)	Outcome measure	Results	Summary (zinc compared to baseline/ control/other)
Dreno et al. (2005)	Open trial 30 [20] (20,0)	Inflammatory (resistant to ERY during the previous 12 months)	Group A: **Zn gluconate** (oral, effervescent, 100 mg, BID, 2 months)	N/A	60 Days	Nausea, vomiting, stomach cramps (5)	#1= Inflammatory[a] lesion count	Compared to baseline[b] Group A: SS reduction in #1 ($p < .001$)	+ To baseline
Dreno et al. (1989)	Multicenter double-blind, controlled trial 66	Inflammatory	Group A: **Zn gluconate** (oral, effervescent, 100 mg, 2 capsules QD, 2 months)	Group B: Lactose **placebo** (oral, 2 capsules QD, 2 months)	2 Months	Nausea (3), slight gastralgia (3), abdominal pain (2)	#1 = Inflammatory lesion count/ score #2 = Examiner's subjective opinion #3 Patient's subjective opinion	Compared to control (Group B): Group A: SS reduction of #1 ($p < .02$) & improvement of #2 ($p < 10^{-4}$) and #3 ($p < .002$)	+ To control
Meynadier (2000)	Multicenter, double-blind, randomized, comparative study 67 [67] (32/35, 0)	Inflammatory	Group A: **Zn gluconate** (Rubozinc) (oral, 60 mg, 3 weeks → 30 mg, 4 weeks → 15 mg, 6 weeks) (loading dose regimen) Group B: **Zn gluconate** (Rubozinc) (oral, 100 mg, 2 capsules, 13 weeks)	N/A	91 Days	Nausea, gastric pain (57%)	#1 Superficial inflammatory lesion count #2 Deep inflammatory lesion (nodule/macrocysts) count #3 Physician's overall opinion	Compared to baseline: Groups A and B: SS reduction in #1 ($p < .001$), but no SS difference in #2–3 Group comparison: No SS difference between groups in reduction of #1–2 or improvement of #3 throughout the study	+ To baseline = To loading dose regimen
Orris et al. (1978)	Double-blind, parallel-group RCT 30 [22] (12,10) Only males were studied	Moderate, Grades 2 & 3 (Pillsbury)	Group A: **Zn sulfate monohydrate** (oral, 137 mg, 1 capsule, TID, 8 weeks) Began with a 4-week "wash-out period" = lactose placebo (oral, 1 capsule, TID, 4 weeks)	Group B: Lactose **placebo** (oral, 1 capsule, TID, 12 weeks)	12 Weeks	Not mentioned	#1 Papule, pustule, and open/closed comedone count	Compared to baseline: Both groups had NS reduction in #1 (except for open comedones) from weeks 4 to 12 Both groups had SS reduction in #1 from weeks 0 to 4 ("wash-out period") ($p < .05$) Compared to control (Group B):	= To baseline = To control

(Continues)

TABLE 1 (Continued)

Author (year)	Study type Sample size [completed study] (zinc, control)	Acne severity (classification/ grading system)	Zinc treatment group (dosing)	Control group (dosing)	Follow-up period	Zinc adverse effects (%/# of patients)	Outcome measure	Results	Summary (zinc compared to baseline/ control/other)
								No SS difference in #1 between groups from weeks 4 to 12	
Weimar et al. (1978)	Double-blind, RCT 52 [40] (18,22)	Mild to moderate	Group A: **Zn sulfate** (oral, 220 mg, 1 capsule, TID, 12 weeks)	Group B: Lactose, cornstarch, and magnesium stearate **placebo** (oral, 1 capsule, TID, 12 weeks)	12 Weeks	Nausea/vomiting (40%), diarrhea (10%)	#1 Comedone, papule, pustule, infiltrate, and cyst count #2 Severity index #3 Patient's subjective impression	Compared to baseline: Group A: slight NS in reduction of pustule count and #2 Compared to control (Group B): No SS difference between groups	= To baseline = To control
Hillström et al. (1977)	Multicenter, double-blind RCT 112 [91] (48, 43)	Grades 2 & 3 (Pillsbury)	Group A: **Zn sulfate** (oral, 200 mg, 1 capsule, BID, 12 weeks)	Group B: **Placebo** (oral, BID, 12 weeks)	12 Weeks	GI side effects, pruritus and mouth dryness (8)	#1 Papule and pustule count #2 Physician's subjective opinion #3 Patient's subjective opinion	Compared to control (Group B): Group A: SS superior in #2 ($p < .01$) and #3 ($p < .05$).	+ To control
Göransson et al. (1978)	Double-blind, RCT 59 [54] (27, 27)	Grades 1 to 3 (Pillsbury)	Group A: **Zn sulfate** (oral, 200 mg, TID, 6 weeks)	Group B: **Placebo** (oral, TID, 6 weeks)	4 Months	Indigestion (2)	#1 Total acne lesion count #2 Acne load/ score (using severity index) #3 Percent change in #2 #4 Patient's subjective opinion #5 Investigator's subjective evaluation	Compared to baseline: Group A: SS reduction in #1, #2 and #3 ($p < .001$) Neither group had a SS difference in #4 or #5 Compared to control (Group B): Group A: SS superior in reduction of #1–2 ($p < .05$) and #3 ($p < .01$).	+ To baseline + To control
Verma et al. (1980)	Double-blind placebo-controlled clinical trial 56 [56] (29,27)	Inflammatory	Group A: **Zn sulfate** (oral, 300 mg, 1 capsule, BID, 12 weeks)	Group B: Lactose **placebo** (oral, 1 capsule, BID, 12 weeks)	12 Weeks	Nausea (4) Vomiting (1)	#1 Papule count #2 Pustule count #3 Infiltrate and cyst count #4 Facial oiliness	Compared to baseline: Group A: SS reduction in #1 ($p < .05$) and #3–4 ($p < .001$); SS increase in #5	+ To baseline + To control

(Continues)

TABLE 1 (Continued)

Author (year)	Study type Sample size [completed study] (zinc, control)	Acne severity (classification/ grading system)	Zinc treatment group (dosing)	Control group (dosing)	Follow-up period	Zinc adverse effects (%/# of patients)	Outcome measure	Results	Summary (zinc compared to baseline/ control/other)
							#5 Serum vitamin A levels	($p < .01$); no SS reduction in #2 Group A (17/29 patiens) reported a decrease in #4, whereas no patients in Group B had such change Compared to control (Group B): Group A was SS superior to Group B in reduction of #1, 3, and 4 and in increase of #5	
Kobayashi et al. (1999)	Case report 1	Acne conglobata/ cystic acne (+dissecting cellulitis)	**Zn sulfate** (oral, 135 mg, TID, 12 weeks; BID/QD, 1 year)	N/A	1 Year	Nausea	Overall acne appearance	After 4 weeks, nodules regressed and became flat. Lesions diminished within 8 weeks and were well controlled for 1 year	+ To baseline
Weismann et al. (1977)	Double-blind, RCT 39 [39] (20,19)	Inflammatory	Group A: **Zn sulfate** (oral, 200 mg, TID, 4–12 weeks)	Group B: Lactose **placebo** (oral, TID, 4–12 weeks)	12 Weeks	Nausea (5) Vomiting (1)	#1 Inflammatory count #2 Infiltrate count #3 Patient's and physician's evaluation of overall clinical effect	Compared to baseline: Both groups had SS reduction in #1 and improvement in #3; No SS reduction in #2 Compared to control (Group B): No SS difference in #1 and #2 between groups ($p > .05$)	+ To baseline = To control

(Continues)

TABLE 1 (Continued)

Author (year)	Study type Sample size [completed study] (zinc, control)	Acne severity (classification/ grading system)	Zinc treatment group (dosing)	Control group (dosing)	Follow-up period	Zinc adverse effects (%/# of patients)	Outcome measure	Results	Summary (zinc compared to baseline/ control/other)
Lidén et al. (1980)	Double-blind, RCT 59 [54] (27,27)	Grades 1–3	Group A: **Zn sulfate** (oral, 600 mg, QD, 6 weeks)	Group B: **Placebo** (oral, QD, 6 weeks)	6 Weeks	NR	#1 Total lesion count #2 Acne severity score #3 Investigator's photographic assessment #4 Patient's subjective evaluation	Compared to baseline: Group A has SS reduction in #1–2 ($p < .05$) and #3–4 ($p < .001$) Compared to control (Group B): Group A: SS superior to group B in #1–2 ($p < .05$) and percentage change in #2 ($p < .01$);No SS difference between groups in #3 and #4	+ To baseline + To control
Cochran et al. (1985)	Double-blind placebo-controlled study [30]	Mild to moderate	Group A: **Zn sulfate** (topical solution, 2% elemental Zn, TID, 12 weeks) Average daily topical dose was 20 mg	Group B: Vehicle **placebo** (topical, TID, 12 weeks)	12 Weeks	Erythema, scaling, burning, itching	# 1 Acne lesion count/type #2 Acne severity score # 3 Patient's and physician's rate of progress	Compared to Control (Group B): No SS difference in #1–3 between groups ($p > 0.05$)	= To control

[a]Inflammatory lesion count refers to papule and pustule count, unless otherwise specified.
[b]Baseline refers to the patient's acne severity/counts prior to treatment.

TABLE 2 Overview of the studies that use zinc in a combination treatment

Author (year)	Type of study Sample size [completed study] (zinc, control)	Acne severity (classification/ grading system)	Zinc treatment group (dosing)	Control group (dosing)	Follow-up period	Zinc adverse effects (%/# of patients)	Outcome measure	Results	Summary (zinc combinations compared to baseline/ control/other)
Schachner, Eaglstein, et al. (1990)	Double-blind comparative cross-over study 73 [57](38,19) Only females were studied	Grade ≥3 (Cook)	Group A: **Zn acetate** (1.2%) + **ERY** (4%) (topical, BID, 12 weeks)	Group B: Vehicle **Placebo** (topical, BID, 12 weeks)	12 Weeks	NR	#1 Acne severity grade (Cook grading scale) #2 Papule and pustule count #3 Total comedone count #4 Total inflammatory lesion count	Compared to control (Group B): Group A: SS superior in #1 ($p < .05$) and in reduction of #1 ($p < .001$), #2 and #4 ($p < .01$) and #3 ($p < .05$)	+ To control
Strauss and Stranieri (1984)	Double-blind, RCT 22 [21] (11,10)	Mild to moderate acne vulgaris	Group A: **Zn acetate** (1.2%) + **ERY** (4%) (topical, solution, BID, 10 weeks)	Group B: Vehicle **Placebo** (topical, solution, BID,10 weeks)	10 Weeks	NR	#1 Propionibacterium count #2 Free fatty acid on skin surface count #3 Inflammatory lesion count	Compared to baseline: Group A: SS reduction in #1–3 ($p < .05$) Compared to control (Group B): Group A was SS superior to Group B in reduction of #2 and #3 ($p < .05$)	+ To baseline + To control
Fluhr et al. (1999)	Double-blind randomized comparison study 32 [28]	Acne papulo-pustulosa	Group A: **Zn acetate dehydrate** (1.2%) + **ERY** (4.0%) (topical, BID, 7 days) Group B: **Zn acetate dehydrate** (1.2%) (topical, BID, 7 days)	N/A	7 Days	None	#1 Infundibular Antibacterial activity (reduction of propionibacteria and *Micrococcaceae* via the cyanoacrylate method)	Compared to baseline: Both groups had SS improvement in #1 ($p < .0001$) Group comparison: Group A was not SS superior to Group B	+ To baseline = to Zn acetate dehydrate
Shalita et al. (2012)	Multicenter, open-label prospective study 235 [235] (235,0)	Moderate to severe	Group A: **NicAzel®** (nicotinamide [600 mg], azelaic acid [5 mg], Zn oxide [10 mg], pyridoxine [5 mg], copper [1.5 mg], folic acid [500 μg]) (oral, 1–4 tablets, QD, 8 weeks) in addition to current acne regimen	N/A	8 Weeks	None	# 1 Lesion count reduction #2 Patient's subjective opinion of acne improvement #3 Patient's subjective opinion of global satisfaction	Compared to baseline (current acne regimen): Group A: SS improvement in #1–3 ($p < .001$)	+ To baseline
Sardana and Garg (2010)	Observational clinical trial 60 [48]	Mild to moderate	**APC complex™** (methonine-bound zinc complex 75 mg	N/A	12 Weeks	Abdominal pain, diarrhea, urti-	#1 Global acne count	Compared to baseline: Group A: SS improvement in #1 ($p < .05$),	+ To baseline

(Continues)

TABLE 2 (Continued)

Author (year)	Type of study Sample size [completed study] (zinc, control)	Acne severity (classification/ grading system)	Zinc treatment group (dosing)	Control group (dosing)	Follow-up period	Zinc adverse effects (%/# of patients)	Outcome measure	Results	Summary (zinc combinations compared to baseline/ control/other)
			[equivalent to zinc 15 mg], ascorbic acid 60 mg, *Dunaliella salina* extract [providing mixed carotenoids 6 mg], D-alpha tocopheryl acetate 11.53 mg [equivalent to natural vitamin E 15 IU], and chromium picolinate 1.04 mg [equivalent to chromium 0.13 mg]) (oral, 600 mg, TID, 3 months)			carial (2)	#2 Pustules, papules, and closed comedone count #3 Nodule and open comedone count #4 Patient and investigator overall acne severity evaluation and global assessment of effectiveness	#2 ($p < .001$), and #4 ($p < .001$); no SS difference in #3 throughout the study ($p > .05$)	
Capitanio et al. (2012)	Double-blind, RCT 60 [60](30,30) Only men were studied	Mild (Leeds)	Group A: **Zn pyrrolidone** (0.1%) + ***L. digitata*-derived oligosaccharide** (topical cream, BID, 56 days)	Group B: Vehicle **placebo** (topical cream, BID, 56 days)	56 Days	NR	#1 Comedone and inflammatory lesion count #2 Sebum production (Sebumeter) #3 Desquamation and erythema	Compared to baseline: Both groups had SS reduction in #1 (Group A reached greater reduction) Both groups had equal reduction in #2, without SS Group comparison: Group A: SS superior to Group B in reduction of #1 after day 14 ($p < .01$). Neither product produced #3	+ To baseline + To control

Abbreviations: NA = not applicable; BID = twice daily; QD = once daily; TID, three times daily; NR = not reported; SS = statistically significant; ERY = erythromycin; Zn = zinc; RCT = randomized controlled trial; NS = numerically significant/significantly (significant result, as determined by the investigators, without reaching statistical significance).

TABLE 3 Overview of the studies that compared zinc with other treatment groups

Author (year)	Type of study Sample size [completed study] (zinc, other tx, control)	Acne severity (classification/ grading system)	Zinc treatment group (dosing)	Other treatment group (dosing)	Control group (dosing)	Follow-up period	Zinc adverse effects (%/# of patients)	Outcome measure	Results	Summary (zinc combinations compared to baseline/control/ other)
Schachner, Pestana, et al. (1990)	Randomized comparative clinical trial 103 [92] (48,44,0)	Grade ≥3 (Cook)	Group A: **Zn acetate** (1.2%) + **ERY** (4%) (topical, BID, 12 weeks)	Group B: **CDP** (topical, 1%, BID, 12 weeks)	N/A	12 Weeks	Facial burning and redness (1)	#1 Acne severity grade #2 Papule count #3 Pustule count #4 Combined inflamm lesion count #5 Open and closed comedone count	Compared with baseline: Both groups had SS improvement in #1–5 Group Comparison: Group A was SS superior to Group B in improvement of #1 ($p < .001$) and reduction of #2–5 ($p < .05$)	+ To baseline + To CDP
Cunliffe et al. (2005)	Multicenter, observer-blind, randomized, parallel-group, comparative clinical study 246 [223] (73/73,77,0)	Mild to moderate, Grades 2–7	Group A: **Zn acetate dihydrate** (0.516%) + **CDP** (1%) (topical gel, QD, 16 weeks) Group B: **Zn acetate dihydrate** (0.516%) + **CDP** (1%) (topical gel, BID, 16 weeks)	Group #C: **CDP** (topical lotion, 1%, BID, 16 weeks)	N/A	16 Weeks	Mild irritant dermatitis	#1 Total lesion count #2 Inflamed lesion count #3 Noninflamed lesion count #4 Acne grade #5 Skin surface and follicular propionibacterium spp. and Micrococcaceae count #6 Patient's and investigator's global assessment	Compared to baseline: All groups had NS reductions in #1–5 and improvement in #6 Group comparison: No SS difference between groups in reduction of #1–5 or improvement of #6 throughout the study ($p > .05$)	+ To baseline = To CBP
Langner et al. (2007)	Multicenter, single-blinded, randomized parallel group comparison 148 [148] (75,68, 0)	Mild to moderate, Grade <7	Group A: **Zn acetate** (1.2%) + **ERY** (4%) (topical solution, BID, 12 weeks)	Group B: **CDP** (1%) + **BPO** (5%) (Topical gel, QD, 12 weeks)	N/A	12 Weeks	≥1 Adverse effect (30.7%)	#1 Total lesion count #2 Inflamm lesion count #3 Noninflamm lesion count #4 Acne grade (Leeds Revised Acne Grading System) #5 Global change from baseline assessed by physician	Compared to baseline: Groups A and B: NS decline in #1–3; Both groups had NS improvement in #4–6 (more so and earlier onset for group B)and Group comparison: Group B: SS superior to Group A in reduction of #1 ($p = .029$) and #2 ($p = 0.017$), in % of patients with ≥30% improvement	= To baseline – To CDP/BPO

(Continues)

TABLE 3 (Continued)

Author (year)	Type of study Sample size [completed study] (zinc, other tx, control)	Acne severity (classification/ grading system)	Zinc treatment group (dosing)	Other treatment group (dosing)	Control group (dosing)	Follow-up period	Zinc adverse effects (%/# of patients)	Outcome measure	Results	Summary (zinc combinations compared to baseline/control/ other)
								#6 Patient's self-assessment of improvement	in #2 ($p = .018$), and in improvement of #1 ($p = .014$), #3 ($p = .047$), #5 ($p = .004$), and #6 ($p = .007$)	
Habbema et al. (1989)	Multicenter, double blind, randomized comparative study 122 [102]	Moderate to severe, mean Grade 3.7	Group A: **Zn acetate** (Zineryt) + **ERY** (4%) (topical, BID, 12 weeks)	Group B: **ERY** (Eryderm) (topical, 2%, BID, 12 weeks)	N/A	12 Weeks	Dryness of the skin, itching, burning, and/or erythema (13)	#1 Acne grade #2 Comodone, papule, and pustule count #3 Nodule and macule count	Compared to baseline: Both groups had SS reduction of #1 and #2 ($p < .001$) throughout the study; Group A: SS reduction in #3 ($p < .01$) Group comparison: Group A: SS superior to Group B in #1–3 (except pustule count)	+ To baseline + To ERY
Bojar et al. (1994)	Double-blind study 52 [45] (20,25,0)	Mild to moderate, Grades 0.5–3 (Burke and Cunliffe scale)	**Zn acetate** (1.2%) + **ERY** (4%) (topical, BID, 12 weeks)	**ERY** (topical, 4%, BID, 12 weeks)	N/A	12 Weeks	NR	#1 Total Propionibacterium count #2 ERY-resistant Propionibacterium count #3 Acne grade (Burke and Cunliffe scale) #4 Inflamed and noninflamed lesion count	Compared to baseline: Both groups had SS reduction in #1–4 ($p < .001$) after 4 weeks Group omparison: No SS difference in #1–4 between groups	+ To baseline = To ERY
Cunliffe et al. (1979)	Double-blind RCT 48 [40] (20,20,0)	Moderate to severe	Group A: **Zn sulfate/ citrate complex** (oral, 1 capsule, TID, 3 months) Dosage not reported	Group B: **Tetracycline hydrochloride** (oral, 1 capsule, 250 mg BID, 3 months)	N/A	3 Months	Nausea and abdominal pain (2), and deterioration of acne (2)	#1 Acne severity grade #2 Comedone, papule, small pustule, deep pustule, and nodule count #3 Patient's assessment	Compared to baseline: Group A: SS reduction only in pustule count; Group B: SS improvement in #1–3 ($p < .05$)	+ To baseline – To tetracycline
Feucht et al. (1980)	Double-blind, RCT	Grades 3.5–4.5	Group A: **Zn acetate** (1.2%) +	Group C: **Tetracycline** (oral,	Group D: **Placebo** (topical vehicle and	10 Weeks	Erythema, dryness, and irritation	#1 Acne severity grade (Cook grading scale)	Compared to control (Group D):	+ To control = To tetracycline Liquid Zn = to gel Zn

(Continues)

TABLE 3 (Continued)

Author (year)	Type of study Sample size [completed study] (zinc, other tx, control)	Acne severity (classification/ grading system)	Zinc treatment group (dosing)	Other treatment group (dosing)	Control group (dosing)	Follow-up period	Zinc adverse effects (%/# of patients)	Outcome measure	Results	Summary (zinc combinations compared to baseline/control/ other)
	149 [141] (38/35,38,30) Only males were studied	(Cook grading scale)	**ERY** (4%) (topical liquid) + Placebo (oral, cornstarch) (BID, 10 weeks) Group B: **Zn octoate** (1.2%) + **ERY** (4%) (topical gel) + Placebo (oral, cornstarch) (BID, 10 weeks)	250 mg, BID, 10 weeks) + **Placebo** (topical, vehicle)	oral [cornstarch] [BID, 10 weeks])			#2 Papule count #3 Pustule count #4 Comedone count/grade	Groups A and B: SS reduction and percent reduction in #1 ($p < .001$) and #2 ($p < .01$) Group C: SS reduction and percent reduction in #1 ($p < .05$) and #2 ($p < .001$) Group A: SS better in reduction of #4 ($p < .05$). All other groups showed NS reduction of #4, without SS No SS difference in #3 for any group throughout the study Group comparison: Groups A and B were as effective as Group C in reduction of #1 and #2 throughout the study	
Michaëlsson, Juhlin, and Ljunghall (1977)	Double-blind study 40 [37]	Moderate to severe acne vulgaris of acne score, >40	Group A: **Zn sulfate** (oral, 200 mg, 1 capsule, TID, 12 weeks) 45 mg of Elemental Zn	Group B: **Oxytetracycline** (oral, 250 mg, 1 capsule, TID, 2 weeks then BID, 2 weeks, then QD, 8 weeks)	N/A	12 Weeks	None	#1 Lesion (papules, pustules, and comdedone) count #2 Physician and patient's subjective evaluation of acne severity and degree of improvement	Compared to baseline: All groups had NS reduction in #1–2 Group comparison: No SS difference between groups	= To baseline = To oxytetracycline
Papageorgiou and Chu (2000)	Double-blind, parallel group RCT 45 [41] (13,13,15)	Mild—Grade 1	Group A: **Nels® cream** (chloroxylenol + Zn oxide)	Group B: **BPO** (topical, cream, 5%, BID, 8 weeks)	Group C: Vehicle **placebo** (topical, BID, 8 weeks)	8 Weeks	Acne flare up (1), dryness, and peeling (1)	#1 Inflamm lesion (papule/pustule) count	Compared to control (Group C): Groups A and B: SS superior in reduction of #1 ($p < .05$) and	+ To control = To BPO

(Continues)

TABLE 3 (Continued)

Author (year)	Type of study Sample size [completed study] (zinc, other tx, control)	Acne severity (classification/ grading system)	Zinc treatment group (dosing)	Other treatment group (dosing)	Control group (dosing)	Follow-up period	Zinc adverse effects (%/# of patients)	Outcome measure	Results	Summary (zinc combinations compared to baseline/control/ other)
			(topical, cream, BID, 8 weeks)					#2 Noninflamm lesion (comedone) count #3 Patient and investigator's grading of response and efficacy	#2 ($p < .01$), a and SS superior in #3 ($p < .01$) Group comparison: No SS difference between Groups A and B in reduction of #1 and #2 or improvement of #3 Group A was NS superior to Group C in improvement of #3	
Chu et al. (1997)	Evaluator-blinded, randomized, parallel comparison study 72	Grades 2–3 (Pillsbury)	Group A: **Zn** (1.2%) + **ERY** (4%) (topical, solution, BID, 10 weeks)	Group B: **BPO** (5%) + **ERY** (3%) (topical, gel, BID, 10 weeks)	N/A	10 Weeks	Dryness (1), irritation (2), botchy redness (1), itching (2), scratching (1), scaling (1), and soreness (1)	#1 Physical global evaluation/ improvement score #2 Inflammatory lesion count #3 Comedone count #4 Patient efficacy (global improvement and cosmetic acceptability) evaluation #5 Facial skin condition profile (facial oiliness, erythema, and peeling)	Compared to baseline: Both groups had NS improvement in #1–4 at each visit Group comparison: Group B: SS superior to Group A in #1 ($p \leq .05$) and in #4 ($p \leq .001$) Group B: SS superior to Group A in reduction of #2 ($p \leq .005$) and reduction of #3 ($p \leq .001$) No SS difference in #5 between groups	= To baseline – To BPO/ERY
Michaëlsson (1980)	RCT 64 [64]	Grades 3–4, acne vulgaris	Group A: **Zn** (oral, 45 mg, 1 tablet, TID, 4 weeks) Group B: **Zn** (oral, 45 mg, 1 tablet, TID) + **Vitamin A** (drops,	Group C: **Vitamin A** (drops, 150,000 IU/ml, 25 drops, BID, 4 weeks)	Group D: **Placebo** (oral, 1 tablet, TID, 4 weeks)	12 Weeks	NR	#1 Lesion (papule, pustule, and comedone) count #2 Acne score #3 Patient's and investigator's opinion of degree of improvement	Compared to baseline: All groups had NS reduction in #2 Group comparison: Groups A and B had SS reduction in #1 compared to Groups C and D	= To baseline + To control + To vitamin A

(Continues)

TABLE 3 (Continued)

Author (year)	Type of study Sample size [completed study] (zinc, other tx, control)	Acne severity (classification/ grading system)	Zinc treatment group (dosing)	Other treatment group (dosing)	Control group (dosing)	Follow-up period	Zinc adverse effects (%/# of patients)	Outcome measure	Results	Summary (zinc combinations compared to baseline/control/ other)
			150,000 IU/ml, 25 drops, BID, 4 weeks)							
Michaëlsson, Juhlin, and Vahlquist, (1977)	RCT 64 [64]	Grades 2–4, acne vulgaris (Pillsbury scale)	Group A: **Zn sulfate** (oral, 200 mg, TID, 4 weeks) Group B: **Zn sulfate** (oral, 200 mg, TID, 4 weeks) + **Vitamin A palmitate** (drops, 150,000–200,000 IU/ml, BID, 4 weeks)	Group C: **Vitamin A palmitate** (drops, 150,000–200,000 IU/ml, BID, 4 weeks)	Group D: **Placebo** (oral, 1 tablet, TID, 4 weeks)	12 Weeks	None	#1 Open comedone, closed comedone, papule, pustule, infiltrates, and cyst count #2 Total severity score #3 Patient's opinion of improvement	Compared to baseline: Groups A and B had SS reduction in #1 (except cysts) and #2 Group comparison: Group A was SS superior to Group D No SS difference in #1 and #2 between Groups A and B Groups A and B had SS higher percentage improvement in #3 than in Groups C and D ($p < .001$)	+ To baseline + To control + To vitamin A palmitate Zn sulfate = to Zn sulfate + vitamin A palmitate
Dreno et al. (2001)	Multicenter double-blind, RCT 332 [288] (143,145,0)	Inflamm acne vulgaris with ≥20 superficial papules or pustules	Group A: **Zn gluconate** (oral, 2 capsules QD, 3 months)	Group B: **Minocycline hydrochloride** (oral, 100 mg, 1 capsule [+1 placebo capsule], QD, 3 months)	N/A	90 Days	Moderate nausea, vomiting, abdominal pain (55, [33.7%]), severe seborrheic dermatitis (1)	#1 Clinical success rate (% with ≥−2/3 decrease in inflamm lesion count) #2 Superficial inflamm lesion count #3 % With ≥20% decrease in open/closed comedone count #4 Investigator's overall opinion on clinical efficacy #5 Patient's overall opinion on clinical efficacy	Compared to baseline: Group A had 31.2%, whereas Group B had 63.4% for #1 Groups A and B: SS reduction in #2 ($p < .001$) Group A had 49.4%, whereas Group B had 67.3% for #3 Group comparison: Group B was SS superior to Group A in reduction of #2 ($p < .002$) and improvement of #3 ($p < .02$) and #4–5 ($p < .001$)	+ To baseline – To minocycline hydrochloride

Abbreviations: tx = treatment; CDP = clindamycin phosphate; BPO = benzoyl peroxide; inflamm = inflammatory; RCT = randomized controlled trial; NS = numerically significant/significantly (significant result, as determined by the investigators, without reaching statistical significance).

Verma et al., 1980). Four studies (Cochran et al., 1985; Orris et al., 1978; Weimar et al., 1978; Weismann et al., 1977) concluded that zinc was not a therapeutic option for acne vulgaris. These results may be attributed to the limited number of patients or zinc dosage used in these investigations. It is worth noting that although Weismann et al. (1977) did not favor the use of zinc, their results did show a statistically significant reduction in inflammatory and infiltrate count as early as 4 weeks after treatment when compared to baseline. Their rationale for not recommending zinc stems from the lack of statistical significance when comparing treatment to placebo. However, as described by the authors, there was an unexplained rise in serum zinc levels in the controls which likely masked the differences between groups.

3.2 | Combination products

Six studies evaluated zinc in combination with other compounds (Capitanio, Sinagra, Weller, Brown, & Berardesca, 2012; Fluhr, Bösch, Gloor, & Hoffler, 1999; Sardana & Garg, 2010; Schachner, Eaglstein, Kittles, & Mertz, 1990; Shalita et al., 2012; Strauss & Stranieri, 1984) (Table 2). Only half of these studies (3/6) (Capitanio et al., 2012; Schachner, Eaglstein, et al., 1990; Strauss & Stranieri, 1984) compared the results with a control group, all of which utilized topical vehicle solution. Three studies combined topical zinc with topical erythromycin (Fluhr et al., 1999; Schachner, Eaglstein, et al., 1990; Strauss & Stranieri, 1984). Schachner, Eaglstein, et al. (1990) and Strauss and Stranieri (1984) evaluated this combination in comparison to vehicle and both demonstrated a statistically significant improvement in acne compared to placebo. Fluhr et al. (1999) compared zinc plus erythromycin to zinc alone and demonstrated a significant improvement in infundibular antibacterial activity compared to baseline in both groups, yet found no significant difference between the groups.

Two studies evaluated an oral supplemental compound containing zinc for effectiveness against acne (Sardana & Garg, 2010; Shalita et al., 2012). Shalita et al. (2012) examined NicAzel®, a combination containing 10 mg of Zn, and demonstrated a significant improvement in all study endpoints compared to baseline. Sardana and Garg (2010) compared the APC complex™, containing 15 mg of Zinc, to baseline and found a statistically significant improvement in global acne count, inflammatory counts, closed comedone count, and patient and investigator overall acne severity evaluation, but not in nodule or open comedone count.

Finally, Sardana & Garg (2010) studied the use of zinc pyrrolidone combined with *Laminaria digitata*-derived oligosaccharides in men with mild acne and favorably reported that this combination was statistically more effective in acne lesion reduction than vehicle placebo.

3.3 | Zinc compared to other treatments

Fourteen studies compared a zinc-containing product to other available treatments for acne vulgaris (Bojar, Eady, Jones, Cunliffe, & Holland, 1994; Chu, Huber, & Plott, 1997; Cunliffe, Burke, Dodman, & Gould, 1979; Cunliffe et al., 2005; Dreno et al., 2001; Feucht, Allen, Chalker, & Smith, 1980; Habbema, Koopmans, Menke, Doornweerd, & De Boulle, 1989; Langner, Sheehan-Dare, & Layton, 2007; Michaëlsson, 1980; Michaëlsson, Juhlin, & Ljunghall, 1977; Michaëlsson, Juhlin, & Vahlquist, 1977; Papageorgiou & Chu, 2000; Schachner, Pestana, & Kittles, 1990; Sharquie, Noaimi, & Al-Salih, 2008) (Table 3), out of which only four were controlled (Feucht et al., 1980; Michaëlsson, 1980; Michaëlsson, Juhlin, & Vahlquist, 1977; Papageorgiou & Chu, 2000). Ten studies compared a zinc-containing compound to an antibiotic. Schachner, Pestana, et al. (1990) and Cunliffe et al. (2005) compared topical zinc combinations to topical clindamycin. Schachner, Pestana et al. (1990) determined that topical zinc combined with erythromycin was statistically superior to topical clindamycin in all endpoints, whereas Cunliffe et al. (2005) determined that there was no statistically significant difference between topical zinc combined with clindamycin and topical clindamycin alone. These results suggest that the combination of zinc with erythromycin might be more therapeutic than that of zinc with clindamycin although these two treatment groups were not compared to each other and therefore there is a lack of scientific evidence. Langner et al. (2007) compared zinc plus erythromycin to clindamycin plus benzoyl peroxide and reported no statistical difference in either group when compared to baseline. The clindamycin/erythromycin combination statistically outdid the zinc/erythromycin regimen for most endpoints, causing authors to favor its use. The zinc/erythromycin combination did, however, show an earlier onset of action when compared to the other treatment group.

Two studies evaluated topical zinc plus erythromycin against topical erythromycin alone. Habbema et al. (1989) demonstrated that zinc plus erythromycin was statistically superior to erythromycin alone in all endpoints, with the exception of pustule count. Bojar et al. (1994) revealed that both groups significantly improved all endpoints, but were not significantly different from one another. Three studies examined oral tetracycline against a zinc-containing compound. Cunliffe et al. (1979) examined oral tetracycline versus an oral zinc sulfate compound. The results demonstrated that zinc only statistically reduced pustule count, whereas tetracycline statistically improved all treatment endpoints. Feucht et al. (1980) studied oral tetracycline in comparison to a zinc plus erythromycin topical treatment (applied in either liquid or gel form). The analysis of acne severity grade and papule count showed that the zinc/erythromycin combination, in liquid and gel formulations, was statistically better than placebo and as effective as oral tetracycline. Only the liquid formulation of zinc/erythromycin resulted in a statistically significant reduction in comedone count. Finally, Michaëlsson, Juhlin, and Ljunghall (1977) compared oral oxytetracycline to oral zinc sulfate and found no significant difference in lesion count or subjective improvement between groups or compared to baseline. Both groups experienced an average decrease in acne score of about 70% after 12 weeks of treatment.

Chu et al. (1997) evaluated a zinc/erythromycin combination against a benzoyl peroxide/erythromycin combination and revealed that benzoyl peroxide/erythromycin was significantly superior. Papageorgiou and Chu (2000) studied Nels® cream, a zinc oxide-containing compound, in comparison with benzoyl peroxide and revealed that both groups significantly improved acne. However, they found no significant difference between the two groups. Two studies by Michaëlsson et al. (Michaëlsson, 1980; Michaëlsson, Juhlin, & Vahlquist, 1977) compared oral vitamin A with oral zinc. Both studies showed that zinc alone and zinc plus

vitamin A significantly outdid vitamin A monotherapy and placebo. Sharquie et al. (2008) evaluated topical zinc sulfate versus topical tea lotion and concluded that tea lotion was superior to topical zinc. Finally, Dreno et al. (2001) studied oral zinc gluconate in comparison to oral minocycline. Although both significantly improved acne, minocycline proved to be significantly better than zinc.

4 | DISCUSSION

4.1 | Overview

This review, on the efficacy and safety of zinc for acne vulgaris, includes a total of 31 studies, featuring 9 randomized clinical trials, 17 controlled trials, 13 noncontrolled clinical trials, and 1 case report. These studies collectively analyzed the treatment response of 2,356 patients with varying treatment regimens and follow-up times. Zinc was evaluated as a single-agent product in 12 studies, in combination products in 6 studies, and compared to alternative treatments in 13 studies. The single-agent product and combination product studies suggest that zinc is effective in treating acne vulgaris. The comparative studies, however, revealed conflicting results. The combination treatment may be a more effective therapeutic option than zinc as a single agent, as all combination product studies, including zinc with topical erythromycin, zinc in the NicAzel® oral supplement, zinc in the APC complex™ oral supplement, and zinc pyrrolidone plus *L. digitata*-derived oligosaccharide concluded that these combinations significantly improve acne. In contrast, only 8 of the 12 single-agent studies concluded that zinc was an efficacious treatment modality for acne vulgaris. Additionally, single-agent products containing zinc appear to be less tolerable than combination treatments, for a large majority of these studies reported at least one adverse effect after the treatment. Nevertheless, additional studies are warranted before a definitive conclusion can be made of the efficacy and safety profiles of combination studies compared with those of single-agent product studies, for twice as many single-agent product investigations as combination product investigations were included in this review.

Fourteen studies were comparative, evaluating the efficacy and safety of zinc in its oral and topical forms with other therapeutic modalities used for acne vulgaris. Ten of these studies compared a zinc compound with an antibiotic containing compound such as clindamycin, oral tetracycline, erythromycin, and minocycline. The results demonstrated that zinc was equally as effective or less effective than oral tetracycline, equally as effective or more effective than erythromycin and clindamycin, and less effective than oral minocycline. Thus, although zinc may be compared favorably to erythromycin and clindamycin, oral tetracycline and minocycline are likely to be more effective acne therapies. Additionally, the studies show that zinc may be superior to vitamin A, yet inferior to tea lotion.

4.2 | Study length

The studies involving zinc as a single agent evaluated the treatment effects from 30 days to 1 year. The studies involving combination treatments were conducted from 7 days to 12 weeks. Finally, comparative studies were conducted from 8 to 12 weeks. Except for the study by Göransson et al. (1978), no other study explicitly mentioned follow-up time after treatment or recurrence of acne after the completion of treatment. It is worth noting that data on topical acne products, such as clindamycin and retinoid, showed effectivity only after an average of 8–12 weeks. Of the 12 studies that examined topical product, only 7 followed patients for this period or longer. Oral treatments, such as oral antibiotics or isotretinoin, are generally recommended for a course of 3–6 months. Of the 17 studies examining oral agents, 16 followed patients for up to 3 months, indicating that an insufficient amount of time was given to realize the true results of these therapies.

4.3 | Outcome measures

Different outcome measures were used to measure the response to treatment including both qualitative and quantitative methods. Most studies used a quantitative grading scale that includes the numbers and type of acne lesions, disease severity, and scarring. Although many studies were able to declare statistical significance (or insignificance), several acne severity grading scales were used and these scales are not always comparable to one another. Future studies should assess the best and most representative scale for acne vulgaris, helping to streamline the plethora of data in this field. Other quantitative outcome measures such as antibacterial effects and sebum production could help better quantify the results of the treatment.

4.4 | Side effects

Of the 32 studies analyzed, 11 reported at least one adverse effect secondary to zinc treatment. Most of the studies reporting adverse effects (10/11) used zinc as a single-agent treatment, as opposed to a combination regimen or in comparison with other treatments. All but one of the 11 studies reported primarily gastrointestinal adverse effects, the most common being nausea. In a 25-patient study analyzing zinc sulfate, five (25%) patients experienced nausea and one patient experienced vomiting (Weismann et al., 1977). In another study, 13.8% (4/29) of patients on zinc sulfate complained of nausea; one patient had to discontinue the treatment owing to accompanied vomiting (Verma et al., 1980). In a similar manner, 25% (5/20) of the patients on zinc gluconate presented with digestive side effects, including nausea, vomiting, and/or stomach cramps, causing two patients to withdraw from the study (Dreno et al., 2005). Additional adverse effects included pruritus in one patient treated with zinc sulfate (Hillström et al., 1977) and urticaria in another patient treated with a methionine-based zinc complex (Sardana & Garg, 2010). Another notable adverse effect of topical zinc is the increased level of irritation, erythema, burning, and itching, attributed to zinc's potential role in the conversion of linoleic acid to prostaglandins (Cochran et al., 1985).

5 | CONCLUSIONS

Zinc is an inexpensive, over-the-counter mineral with a well-established safety profile. Limited studies have suggested that it is

effective in treating acne vulgaris, but several study design limitations need to be addressed before zinc is widely introduced as an alternative or adjunct treatment in the clinical setting. Given the small sample size, short follow-up periods and lack of standardization in most of the studies reviewed, additional large-scale double-blind, randomized controlled studies are needed to determine the optimal treatment regimen for high efficacy of zinc in acne vulgaris.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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How to cite this article: Cervantes J, Eber AE, Perper M, Nascimento VM, Nouri K, Keri JE. The role of zinc in the treatment of acne: A review of the literature. *Dermatologic Therapy*. 2018;31:e12576. https://doi.org/10.1111/dth.12576