Quach M, Chang YF, Lee I (Tai L, Choi F, Bodemer A. Inositol for Treating Dermatological Disorders: A Systematic Review. *Journal of Integrative Dermatology*. Published online September 3, 2024.

Review Article

Inositol for Treating Dermatological Disorders: A Systematic Review

Myiah Quach[1a], Yu-Feng Chang[2,3b], Irene (Tai-Lin) Lee[4,5c], Franchesca Choi[6], Apple Bodemer[6]

[1] University of Wisconsin School of Medicine and Public Health, Madison, WI, USA, [2] Department of Dermatology, Beth Israel Deaconess Medical Center, Boston, MA, USA, [3] Harvard Medical School, Boston, MA, USA, [4] Department of Radiology, Emory University, Atlanta, Georgia, USA, [5] Center for Global Health, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA, [6] Department of Dermatology, University of Wisconsin, Madison, WI

Keywords: inotisol, Myo-inositol, Skin disorders

Journal of Integrative Dermatology

Relevance

Inositol is a natural compound widely used to treat metabolic conditions, hormonal regulation, and neurodegenerative diseases. However, its implication in dermatological disorders is unknown.

Objective

To comprehensively assess evidence on inositol supplementation for treating dermatological disorders and discuss its mechanism of action.

Methods

PubMed, MEDLINE, and EMBASE databases were searched to include randomized controlled trials, case series, and case reports addressing inositol treatment in skin disorders.

Results

Thirteen studies met the inclusion criteria. Inositol demonstrates promising effectiveness for the treatment of polycystic ovarian disease (PCOS) or non-PCOS-related acne and hirsutism. Limited evidence for seborrheic dermatitis, hidradenitis suppurativa, psoriasis, trichotillomania, and melanoma were available. No serious adverse effects were reported.

Conclusion

Inositol is a safe and effective adjunctive therapy for acne and hirsutism.

INTRODUCTION

The benefits of natural supplementation in medicine has stimulated the development of functional and integrative dermatology.[1] Inositol (Ins) is a family of naturally occurring cyclohexanehexol (myo-, scyllo-, muco-, neo-, and D-chiro-Inositol) and its derivatives (L-chiro-, allo-, epi-, cis-Inositol) that has received much interest.[2] Myo-inositol (MI) and D-chiro-Inositol (DCI) have been shown to improve insulin resistance and decrease total testosterone, granting their utility in patients with polycystic ovarian syndrome (PCOS) and hyperandrogenism.[3-5]

Over the past years, MI was used for the treatment of metabolic syndrome, reproductive diseases, and pregnancy development. Given the intricate link of skin health to hormones and metabolism,[6] this systematic review will explore the potential roles of Ins in skin diseases, including acne vulgaris, hirsutism, psoriasis, seborrheic dermatitis (SD), hidradenitis suppurativa (HS), trichotillomania, and melanoma.

MATERIALS AND METHODS

LITERATURE SEARCH

This study was performed in accordance to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[7] A primary literature search was conducted with MEDLINE, EMBASE, and Cochrane Library databases on December 20, 2021, with no limitation on date. The search

a Authors contributed equally

b Authors contributed equally

c Authors contributed equally

terms included: ("Acne Vulgaris" OR "Acne" OR "Dermatitis" OR "Skin Diseases" OR "Skin" OR "Skin Physiological Phenomena" OR "Skin Abnormalities" OR "Dermatology" OR "Cutaneous") AND ("Myo-inositol" OR Inositol). The full list of the search terms is available in online supplementary materials (**Table S1**).

STUDY SELECTION AND APPRAISAL

Two reviewers (T.L and Y.C) independently screened all articles to include clinical trials and case series written in English or Chinese on Ins and skin disorders. Any discrepancies were resolved with a third reviewer (F.C). Animal studies, reviews, and those not discussing skin diseases were excluded. Additional studies meeting the criteria were identified from references and included if the above-mentioned criteria were met.

DATA EXTRACTION AND QUALITY ASSESSMENT

Quality of evidence was determined per the Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence.[8] The Cochrane Risk of Bias tool was used for randomized controlled trials (RCTs),[9] the Risk of Bias in Non-randomized Studies of Interventions was used for non-RCTs,[10] and the National Institute of Health quality assessment tool was used for case reports and case series.[11]

RESULTS

The initial search identified 1,181 records non-duplicate articles from the database. A total of 282 studies met the inclusion criteria. After full-text review, 13 studies including 6 randomized controlled trials (RCTs),[12-17] five non-RCTs,[18-22] one case series,[23] and one case report[24] were included in this systematic review (Figure 1).

HYPERANDROGENISM: ACNE AND HIRSUTISM

ACNE

Oral Ins as a treatment for acne has been described in four clinical trials (total n = 204) and one study using topical MI (n = 40). In a study by Fruzzetti et al, 38% of PCOS females who consumed 4 g MI plus 400 mcg folic acid daily reported improvement in acne symptoms.[12] Although these PCOS women had a higher average testosterone level, Ins did not consistently affect patients' androgen levels. Advani et al assessed the effect of twice daily oral combined 600 mg Ins (MI+DCI) on 51 PCOS women with normal (≤23) or high (>23) body mass index (BMI).[18] They revealed a larger decrease in acne scores in overweight or obese subjects compared to lean individuals (-10.05 vs -4.38), although both groups achieved significant acne clearance within a 12-week treatment course. Another study assessing 2 g Ins twice daily in 50 PCOS women found decreased numbers of papulopustular lesions.[13] Ramanan et al conducted a trial on 32 females with mild-to-moderate acne and hirsutism but no comorbid endocrine and metabolic diseases.[20] Their result revealed a significant reduction of the modified Cook's acne scale from 4.34±0.33 to 1.3±0.17 after 24 weeks of twice daily 2 g MI. Lastly, Fabbrocini et al tested topical Ins on 40 women with adult female acne.[22] Participants were instructed to apply 4% MI peel-off mask every other night for 2 months. The study reported a 45-69% reduction in mean acne counts.[22]

HIRSUTISM

We identified three clinical trials on hirsute women with or without PCOS using oral Ins (n = 129). Minozzi et al prescribed 2 g MI twice daily for 6 months to 46 women with mild to moderate hirsutism and found a significant decrease in hirsutism scores (-2.3±0.9, $p < 0.001$) and total androgens (-13±2.6, $p < 0.002$) from baseline.[21] Another study by Ramanan et al followed 32 women with the same inclusion criteria and intervention and found a time-dependent reduction in modified Ferriman-Gallwey hirsutism score from 10 to 5.8.[20] Additionally, 60% fewer patients were complaining of hair loss at the end of the study. The other study by Advani et at reported a reduction in hirsutism score of (-0.45, $p < 0.01$) in obese PCOS women and (-0.25, $p < 0.05$) in lean PCOS women.[18]

INFLAMMATORY DERMATOSES: PSORIASIS, SEBORRHEIC DERMATITIS, AND HIDRADENITIS SUPPURATIVA

PSORIASIS

The use of Ins in psoriasis has been reported in two randomized controlled trials (n = 69). Allan et al published a study on 23 patients with concomitant plaque psoriasis and bipolar disorder using the oral preparation of 6 g Ins daily for 2.5 months.[16] Improvement of psoriasis, as measured by Psoriasis Area and Severity Index score (PASI), was seen in the subgroup of patients taking lithium but not in the other non-lithium treated subgroup. There was no difference in treatment of bipolar disorder appreciated in patients with use of Ins. Another study by Owczarczyk-Saczonek et al investigated topical 0.25% and 1% DCI for the treatment of chronic plaque psoriasis on 46 patients and showed subjective and clinical improvement of psoriasis as measured with PASI.[14] In addition, the high-dose group showed improvement objective measurement of transepidermal water loss while patients in the low-dose group achieved better clinical outcomes seen in PASI improvement.

SEBORRHEIC DERMATITIS

A topical gel containing glycerol-phospho-Inositol (GPI) was tested on 25 patients with mild-to-moderate facial SD in an uncontrolled clinical trial.[19] They demonstrated a significant reduction in the investigator's global assessment scale and an excellent response with more than 80% improvement reported in nearly 50% of the cases. However, it was unclear whether the effect was due to GPI or other ingredients in the product. More studies are required to further look at topical inositol as a potential treatment for seborrheic dermatitis.

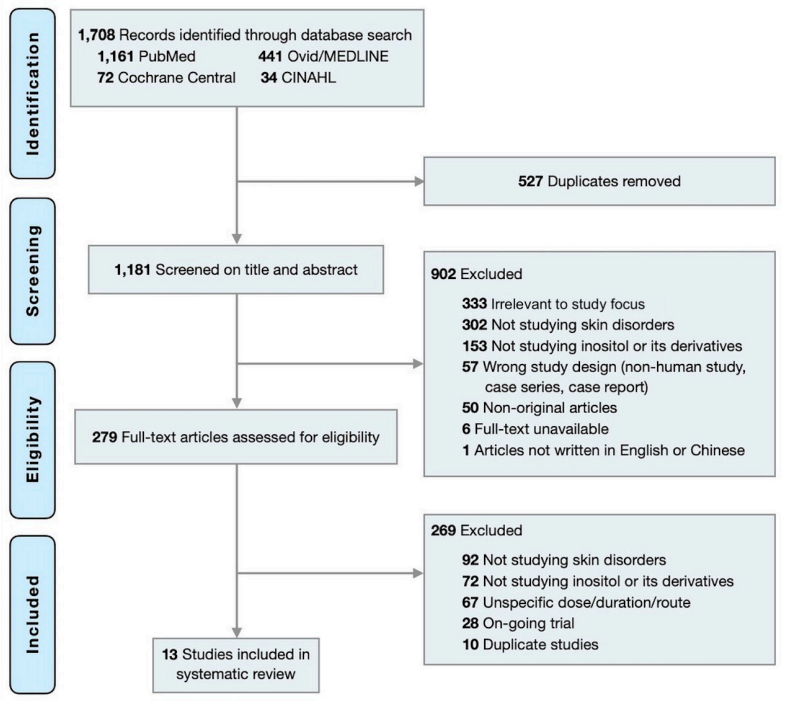

Figure 1. PRISMA Flow Diagram.

HIDRADENITIS SUPPURATIVA

Donnarumma et al evaluated the effectiveness of additional oral MI (2 g daily) in 20 hidradenitis suppurativa (HS) patients taking concurrent antimicrobials.[15] The study reported a significant reduction of the Sartorious Score in the dual therapy group from 38.3±7.75 to 27.3±8.02 (p < 0.04). On the contrary, the antibiotic monotherapy group improved from 38.4±7.88 to 31.1±8.02 (p = 0.55). This was the only study available looking at inositol as an adjunctive treatment for the treatment of hidradenitis suppurativa.

TRICHOTILLOMANIA

Two studies using Ins in patients with psychodermatoses (n = 22) were identified. Seedat et al, reported successful treatment of refractory trichotillomania and compulsive skin picking with Ins in 3 cases using daily dose of 18 g/d administered in white powder form.[23] The other study was a randomized controlled trial assessing 19 patients with trichotillomania.[17] In this study, 42.1% of the 19 patients reported "much or very much improved" with oral Ins 6 to 18 g/day, while 35.3% of the 19 patients on placebo reporting clinical improvement. These studies did not show statistically significant effects of Ins therapy (p > 0.05). Further studies are required to conclude the potential use comorbid psychiatric disorder.

NEOPLASM – MELANOMA

Khurana et al reported a stage IV melanoma patient who had preferred treatment with inositol hexaphosphate (IP6) plus MI (800 mg/220 mg) over standard of care treatment.[24] The patient received a total dose of 8 g IP6 and 2.2 g Ins daily for 2 years and when complete, clinical and radiological remission was achieved and no relevant side effects reported. However, this is the only case report reported in the literature.

DISCUSSION

Inositol is a polyol widely distributed in animal and plant cells as phosphorylated derivates and in cell membranes and serves as a fundamental component for cellular membranes and intracellular messengers.[16] Inositol's function in cellular signaling transduction is postulated to be insulin-like in quality,[22] and comprising a major role in cellular growth and survival, metabolic regulation, nerve functionality, and reproductive activity.[5] Due to its ubiquitous nature, the average human consumes one gram per day of Ins. It also is available without prescription as an oral nutritional supplement but can also be used in topical forms.[3, 16]

Through this systematic review, we have provided quantitative estimates of the efficacy of Ins as adjunctive treatment for various dermatologic pathologies with inflammatory, psychiatric, and neoplastic etiologies. The wide breadth of pathologies highlighted in this review suggest the diverse roles that inositol possibly plays as a cell signal transducer.

Inositol is known to have positive systemic effects consistently found on reproductive disturbance and insulin resistance in populations with PCOS.[5] This androgen-lowering property of Ins was investigated as a possible adjunct to acne and hirsutism topical therapy, as acne arises from the interplay between sebaceous glands, skin flora, and androgenic hormones.[25] Like most current regimens, effect of Ins on acne may involve multiple mechanisms other than hormonal regulation, including anti-inflammatory ef-

fects.[26,27] Hirsutism is characterized by excessive male-pattern hair growth in women. Like acne, hirsutism can also be hormonal or idiopathic.[25] Ins may improve PCOS-related hirsutism in the same fashion as PCOS-related acne. Two out of three studies investigated hirsutism in non-PCOS women. Thus, synergistic hormonal balance and inflammatory cytokine down-regulation could have contributed to the improvement in either type of hirsutism. Overall, topical Ins may be considered as an adjunctive treatment in acne and hirsute women with PCOS or non-PCOS-related due to its promising reported efficacy and safety profile.

Psoriasis is characterized partly by an overproduction of TNF-α, a key inflammatory cytokine underlying the formation of skin and joint lesions.[28] Studies have reported some anti-inflammatory and antioxidant properties of MI and DCI.[27] In particular, TNF-α was found significantly suppressed by pinitol, a methylated form of DCI.[26] Despite these plausible mechanisms, the role of Ins in psoriasis requires further elucidation. Different responses between the two groups in the study reported by Allan et al's[16] the authors suggested that endogenous Ins, which is inhibited by lithium, may be a sufficient but not necessary molecule for psoriasis pathogenesis.[29] Therefore, the efficacy of Ins may depend on patient characteristics and route of administration, more research is warranted to identify possible underlying mechanism.

SD is a common multifactorial inflammatory skin condition associated with aberrant hormone levels, skin flora composition, fatty acid metabolism, and neurogenic factors.[30] Recently, *Malasseszia* was reported to trigger a Type 17 response mediated by IL-17 and IL-23 that exacerbates cutaneous inflammation.[31] Future studies should look at the potential role of inositol and immunity against fungal related cutaneous disorders.

HS is a relapsing-remitting inflammatory dermatosis characterized by painful nodules, abscesses, and sinus tract formation.[32] Interactions between innate immunity and skin microbiota, and genetic factors have all been linked to the development of HS.[33] The inflammatory cytokines at play are very similar to psoriasis, including TNF-α, IL-17, and IL-23.[34] Therefore, a detailed understanding of its pharmacodynamics may shed light on the possible roles of Ins in treating both conditions.

MI regenerates hydrolyzed phosphoinositides (PI), the first messenger in multiple neurotransmitter pathways, making it an emerging therapeutic treatment for psychiatric disorders.[35] Trichotillomania, characterized by repetitive hair pulling leading to hair loss, is not uncommonly seen in this population. Although selective serotonin reuptake inhibitors were proposed to treat comorbid skin diseases, concerns about worsening psychological stability have limited their use. More studies are required to improve the understanding on the relationship between psychodermatology disorders with inositol.

MI and its derivative IP6 have been demonstrated to be involved in a wide range of physiological and pathological settings, including cell cycle progression, apoptosis, and differentiation.[36] Ins inhibits RB protein phosphorylation, preventing cell cycle progression through the RB/E2F pathway. It was also proposed that MI significantly reduces PI3K/Akt pathway activity.[37] Downstream inhibition of molecular pathways supporting epithelial-mesenchymal transition prohibits possible transformation of cells into aggressive carcinomas.[38] Ins has been shown to inhibit the proliferation of other types of cancer in vitro, including breast cancer, colon cancer, and lung cancer. However, its efficacy for melanoma requires further investigation.

There are wide variety of isoforms, dosing, and treatment duration employed among the included studies. Out of a total of 371 patients included in this study, mild gastrointestinal distress was reported in 11 patients, and headaches were reported in 3 patients. None of the adverse events were severe and they usually wore off with continual use. However, Seedat et al,[23] reported that psychiatric patients are more prone to neurological side effects.

CONCLUSIONS

Integrative treatment for dermatology is on the rise. Our study highlighted the existing utilities of Ins in acne and hirsutism. Limited studies were available to demonstrate utility in dermatoses such as SD, HS, psoriasis, trichotillomania, and melanoma, which highlights the need for future well-designed clinical studies on alternative and adjunctive treatments are required to provide additional evidence to the field.

FUNDING SOURCES

This article has no funding source.

CONFLICTS OF INTEREST

The authors have no conflict of interest to declare.

Submitted: June 24, 2024 PDT, Accepted: July 25, 2024 PDT

Table 1. Summary of included studies.

Author, Year	Study design, LOE*	Participants	Regimen	Route	Primary outcome	AE (s)	FU (weeks)
Hyperandrogenism – acne, hirsutism							
Pezza et al,[13] 2015	RCT, 1b	50 PCOS women with acne	Inositol, 2 g, BID	Oral	Decreased number of papulopustular lesions	None	6
Fabbrocini et al,[22] 2017	Uncontrolled clinical trial, 2b	40 women with adult female acne	4% MI and 1% trehalose-loaded liposomes, overnight every other day	Peel-off facial mask	1. Significantly reduced mean count of comedones (-3.9), papule (-6.1), pustule (-2.0), and nodular (-0.5) lesion (P<0.001) 2. Global acne grading score reduced from 16.8±5.3 to 9.8±4.6 (P<0.001) 3. Sabotage score decreased from 3.4±0.6 to 1.8±0.2 (P<0.001)	None	2
Fruzzetti et al,[12] 2017	RCT, 1b	25 PCOS women	MI, 4 g, QD plus folic acid, 400 mcg, QD	Oral	Patient-self assessment, 1. 20% felt a slight improvement in hirsutism, the remaining reported no change 2. 38% felt a slight improvement in acne, 12% reported worsening, the remaining reported no change	None	6
Minozzi et al,[21] 2008	Uncontrolled clinical trial, 2b	46 women with mild to moderate hirsutism	MI, 2 g, BID	Oral	Hirsutism score decreased by -2.3±0.9 (P<0.001)	None	6
Advani et al,[18] 2020	Controlled clinical trial, 2b	Obese (35) or lean (16) PCOS women*	Trazer F Forte, BID: Inositol (MI:DCI) 600 mg, NAC 300 mg, Biotin 5 mg, 10% Lycopene 5 mg, Chromium picolinate 200 mcg, Folic Acid 120 mcg, Vitamin D 400 IU	Oral tablet	In the obese and lean group, 1. Acne score scores -10.05 (P<0.001) and -4.38 (P<0.01), respectively 2. Hirsutism score scores -0.45 (P<0.01) and -0.25 (P<0.05), respectively	None	3
Ramanan et al,[20] 2020	Uncontrolled clinical trial, 2b	32 females with mild-to-moderate acne and hirsutism	Tracnil, BID: MI, 2 g; folic acid 1 mg, vit D3 1000 IU	Oral powder sachets	1. GA scores reduced from 4.34±0.33 to 1.3±0.14 by Weeks 24 2. Modified Ferriman-Gallwey hirsutism score reduced to 8.6, 7.4,	Mild GID in some patients	6

Author, Year	Study design, LOE*	Participants	Regimen	Route	Primary outcome	AE (s)	FU (weeks)
					and 5.8 by Weeks 4, 12, and 24, respectively		
Inflammatory dermatosis – seborrheic dermatitis, hidradenitis suppurativa, psoriasis							
Allan et al,[16] 2004	Crossover RCT, 1b	Patients on lithium who developed chronic plaque psoriasis (15) or patients not on lithium with psoriasis (8)	Inositol, 6 g, QD	Oral	1. Patients on lithium: PASI scores -1.7 in the inositol group compared to +1.9 in the placebo group (P>0.05) 2. Patients not on lithium: PASI scores +0.7 in the inositol group compared to -0.75 in the placebo group (P=0.015)	None	2.5
Dall' Oglio et al,[19] 2017	Uncontrolled clinical trial, 2b	25 patients with mild-to-moderate SD	GPI, piroctone olamine, lactoferrin, and Aloe vera, BID	Topical gel	1. Excellent response (IGA = 4) in 47.9% of patients and no case of worsening (IGA = 0) 2. Significant reduction in desquamation, erythema, and pruritus (P<0.001)	None	1.5
Donnarumma et al,[15] 2020	RCT, 1b	10 patients with HS	Antibiotics with MI 2 g, liposomal magnesium and folic acid, BID	Oral	Reduction of Sartorius scores from 38.3±7.5 to 27.3±13.53 (P<0.04)	None	6
Owczarczyk-Saczonek et al,[14] 2021	RCT, 1b	46 patients with mild plaque psoriasis (PASI<10, BSA<10%)	1% (B) or 0.25% (C) DCI, 1 fingertip unit, BID, or placebo applied to three different psoriatic plaques	Topical cream	1. Visual analogue scale reduced by 22% and 33% in the B and C group; and 23% in the placebo group (P<0.05) 2. Plaque severity index reduced by 30% and 45% in the B and C group; and 28% in the placebo group (P<0.05)	Not reported	1.5
Psychodermatoses – skin picking, trichotillomania							
Seedat et al,[23] 2001	Case series, 4	3 patients with trichotillomania and compulsive skin picking	Inositol, 6 g, TID (primary treatment in two and adjunct to SRI in one)	Oral powder dissolved in water or juice	Two patients reported a CGI-I score of 2 (much improved), and 1 (adjunct to SRI) reported CGI-I of 1 (very much improved)	Mild GID (2) and headache (1)	2-3
Leppink et al,[17] 2017	RCT, 1b	19 patients with trichotillomania	Incrementing inositol from 6 to 12 to 18 g, QD, every 2 weeks	Oral powder	Patients were "much or very much improved"	Mild GID (9) and headache (2); one	2.5

Author, Year	Study design, LOE*	Participants	Regimen	Route	Primary outcome	AE (s)	FU (weeks)
			for a total duration of 10 weeks			hospitalization due to ectopic pregnancy	
Neoplasm							
Khurana et al,[24] 2019	Case report	A patient with stage IVB melanoma	IP6+inositol (800 mg/220 mg), 5 tablets, BID	Oral tablets	Restaging scans showed significant improvement after 6 months, complete clinical and radiological remission after 2 years	None	24

Abbreviations: AE: adverse event; FU: follow-up; PCOS: polycystic ovarian syndrome; MI: myo-Inositol; DCI: d-chiro-Inositol; QD: once daily; BID: twice daily; TH: trehalose; TIW: thrice weekly; PASI: psoriasis area and severity index; TID: thrice daily; GID: gastrointestinal disturbance; CGI-I: clinical global impressions-improvement scale; IGA: investigator global assessment; SD: seborrheic dermatitis; GPI: glycero-phospho-Inositol; IP6: inositol-6 phosphate; HS: hidradenitis suppurativa; LOE: level of evidence; SRI: serotonin reuptake inhibitor; Hexopal : inositol nicotinate.
*Obese/overweight: BMI >23; non-obese/lean: BMI ⩽23.

Table 2. Quality assessment of included studies.

Risk of Bias Tool									
Randomized Controlled Trial	**Random Sequence Generation**	**Allocation Concealment**	**Blinding of Participants and Personnel**		**Blinding of Outcome Assessment**		**Incomplete Outcome Data Addressed**		**Selective Reporting**
Allan et al,[16] 2004	Low	Low	Low		Low		Low		Low
Pezza et al,[13] 2015	Low	Low	Low		Moderate		Low		Low
Fruzzetti et al,[12] 2017	Low	Low	Low		Low		Low		Low
Leppink et al,[17] 2017	Low	Low	Low		Low		Low		Low
Donnarumma et al,[15] 2020	Low	Low	High		High		Low		Low
Owczarczyk-Saczonek et al,[14] 2021	Low	Low	Low		Low		Low		Low
Risk of Bias in Non-randomized Studies of Interventions									
Uncontrolled Trials	**Confounding**	**Selection bias**	**Classification of Intervention**		**Intended intervention**		**Missing data**	**Measurement of outcome**	**Reported results**	**Overall**
Minozzi et al,[21] 2008	Moderate	Low	Low		Low		Low	Low	Low	Low
Dall' Oglio et al,[19] 2017	Moderate	Low	Low		Low		Low	Moderate	Low	Moderate
Fabbrocini et al,[22] 2017	Moderate	Low	Low		Low		Low	Low	Low	Low
Advani et al,[18] 2020	Moderate	Low	Low		Low		Low	Moderate	Low	Moderate
Ramanan et al,[20] 2020	Moderate	Low	Low		Low		Low	Low	Low	Low
National Institute Health Tool										
Clinical Studies	**Q1**	**Q2**	**Q3**	**Q4**	**Q5**	**Q6**	**Q7**	**Q8**	**Q9**	**Quality Rating**
Seedat et al,[23] 2001	Yes	Yes	Unclear	Unclear	Yes	No	Yes	Unclear	Yes	Fair
Khurana et al,[24] 2019	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	Unclear	Yes	Fair

Q1: Question/Objective Stated; Q2: Population Specified and Defined; Q3: Consecutive Cases; Q4: Subject Comparability; Q5: Intervention Clearly Described; Q6: Outcome Measures Defined, Valid, Reliable, and Consistently Implemented; Q7: Sufficient Length of Follow-up; Q8: Statistical Methods Well Described; Q9: Results Well Described; Q10: Quality Rating (Good/Fair/Poor)

REFERENCES

1. Tirant M, Lotti T, Gianfaldoni S, Tchernev G, Wollina U, Bayer P. Integrative Dermatology – The Use of Herbals and Nutritional Supplements to Treat Dermatological Conditions. *Open Access Maced J Med Sci*. 2018;6(1):185-202. doi:10.3889/oamjms.2018.041

2. Antonowski T, Osowski A, Lahuta L, Górecki R, Rynkiewicz A, Wojtkiewicz J. Health-Promoting Properties of Selected Cyclitols for Metabolic Syndrome and Diabetes. *Nutrients*. 2019;11(10). doi:10.3390/nu11102314

3. Unfer V, Facchinetti F, Orrù B, Giordani B, Nestler J. Myo-inositol effects in women with PCOS: a meta-analysis of randomized controlled trials. *Endocr Connect*. 2017;6(8):647-658. doi:10.1530/EC-17-0243

4. Zhao H, Xing C, Zhang J, He B. Comparative efficacy of oral insulin sensitizers metformin, thiazolidinediones, inositol, and berberine in improving endocrine and metabolic profiles in women with PCOS: a network meta-analysis. *Reprod Health*. 2021;18(1):171. doi:10.1186/s12978-021-01207-7

5. Miñambres I, Cuixart G, Gonçalves A, Corcoy R. Effects of inositol on glucose homeostasis: Systematic review and meta-analysis of randomized controlled trials. *Clin Nutr*. 2019;38(3):1146-1152. doi:10.1016/j.clnu.2018.06.957

6. Chen Y, Lyga J. Brain-Skin Connection: Stress, Inflammation and Skin Aging. *Inflamm Allergy Drug Targets*. 2014;13(3):177-190. doi:10.2174/1871528113666140522104422

7. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. The BMJ. Accessed August 14, 2022. https://www.bmj.com/content/372/bmj.n71

8. Oxford Centre for Evidence-Based Medicine: Levels of Evidence (March 2009). Centre for Evidence-Based Medicine (CEBM), University of Oxford. Accessed August 14, 2022. https://www.cebm.ox.ac.uk/resources/levels-of-evidence/oxford-centre-for-evidence-based-medicine-levels-of-evidence-march-2009

9. RoB 2: A revised Cochrane risk-of-bias tool for randomized trials | Cochrane Bias. Accessed August 18, 2022. https://methods.cochrane.org/bias/resources/rob-2-revised-cochrane-risk-bias-tool-randomized-trials

10. Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ*. Published online October 12, 2016:i4919.

11. Study Quality Assessment Tools. NHLBI, NIH. Accessed August 18, 2022. https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools

12. Fruzzetti F, Perini D, Russo M, Bucci F, Gadducci A. Comparison of two insulin sensitizers, metformin and myo-inositol, in women with polycystic ovary syndrome (PCOS). *Gynecol Endocrinol Off J Int Soc Gynecol Endocrinol*. 2017;33(1):39-42. doi:10.1080/09513590.2016.1236078

13. Pezza M, Carlomagno V, Casucci G. Inositol and acne. *G Ital Dermatol E Venereol Organo Uff Soc Ital Dermatol E Sifilogr*. 2015;150(6):649-653.

14. Owczarczyk-Saczonek A, Czerwińska J, Wygonowska E, Kasprowicz-Furmańczyk M, Placek W. D-chiro-inositol as a treatment in plaque psoriasis: A randomized placebo-controlled clinical trial. *Dermatol Ther*. 2021;34(1):e14538. doi:10.1111/dth.14538

15. Donnarumma M, Marasca C, Palma M, Vastarella M, Annunziata MC, Fabbrocini G. An oral supplementation based on myo-inositol, folic acid and liposomal magnesium may act synergistically with antibiotic therapy and can improve metabolic profile in patients affected by Hidradenitis suppurativa: our experience. *G Ital Dermatol E Venereol Organo Uff Soc Ital Dermatol E Sifilogr*. 2020;155(6):749-753. doi:10.23736/S0392-0488.18.06012-1

16. Allan SJR, Kavanagh GM, Herd RM, Savin JA. The effect of inositol supplements on the psoriasis of patients taking lithium: a randomized, placebo-controlled trial. *Br J Dermatol*. 2004;150(5):966-969. doi:10.1111/j.1365-2133.2004.05822.x

17. Leppink EW, Redden SA, Grant JE. A double-blind, placebo-controlled study of inositol in trichotillomania. *Int Clin Psychopharmacol*. 2017;32(2):107-114. doi:10.1097/YIC.0000000000000156

18. Advani K, Batra M, Tajpuriya S, Gupta R, Saraswat A, Nagar HD, et al. Efficacy of combination therapy of inositols, antioxidants and vitamins in obese and non-obese women with polycystic ovary syndrome: an observational study. *J Obstet Gynaecol J Inst Obstet Gynaecol*. 2020;40(1):96-101. doi:10.1080/01443615.2019.1604644

19. Dall' Oglio F, Tedeschi A, Fusto CM, Lacarrubba F, Dinotta F, Micali G. A novel cosmetic antifungal/anti-inflammatory topical gel for the treatment of mild to moderate seborrheic dermatitis of the face: an open-label trial utilizing clinical evaluation and erythema-directed digital photography. *G Ital Dermatol E Venereol Organo Uff Soc Ital Dermatol E Sifilogr*. 2017;152(5):436-440. doi:10.23736/S0392-0488.17.05539-0

20. Ramanan EA, Ravi S, Anbu KRR, Michael M. Efficacy and Safety of TracnilTM Administration in Patients with Dermatological Manifestations of PCOS: An Open-Label Single-Arm Study. *Dermatol Res Pract*. 2020;2020:7019126. doi:10.1155/2020/7019126

21. Minozzi M, D'Andrea G, Unfer V. Treatment of hirsutism with myo-inositol: a prospective clinical study. *Reprod Biomed Online*. 2008;17(4):579-582. doi:10.1016/S1472-6483(10)60248-9

22. Fabbrocini G, Capasso C, Donnarumma M, Cantelli M, Le Maître M, Monfrecola G, et al. A peel-off facial mask comprising myoinositol and trehalose-loaded liposomes improves adult female acne by reducing local hyperandrogenism and activating autophagy. *J Cosmet Dermatol*. 2017;16(4):480-484. doi:10.1111/jocd.12340

23. Seedat S, Stein DJ, Harvey BH. Inositol in the treatment of trichotillomania and compulsive skin picking. *J Clin Psychiatry*. 2001;62(1):60-61. doi:10.4088/JCP.v62n0112f

24. Khurana S, Baldeo C, Joseph RW. Inositol hexaphosphate plus inositol induced complete remission in stage IV melanoma: a case report. *Melanoma Res*. 2019;29(3):322-324. doi:10.1097/CMR.0000000000000577

25. Lucky AW. Hormonal correlates of acne and hirsutism. *Am J Med*. 1995;98(1A):89S-94S. doi:10.1016/S0002-9343(99)80064-3

26. Pandi A, Sattu K, Kalappan VM, Lal V, Varikasuvu SR, Ganguly A, et al. Pharmacological effects of D-Pinitol – A comprehensive review. *J Food Biochem*. Published online October 2022. doi:10.1111/jfbc.14282

27. Baldassarre MPA, Di Tomo P, Centorame G, Pandolfi A, Di Pietro N, Consoli A, et al. Myoinositol Reduces Inflammation and Oxidative Stress in Human Endothelial Cells Exposed In Vivo to Chronic Hyperglycemia. *Nutrients*. Published online June 27, 2021. doi:10.3390/nu13072210

28. Singh R, Koppu S, Perche PO, Feldman SR. The Cytokine Mediated Molecular Pathophysiology of Psoriasis and Its Clinical Implications. *Int J Mol Sci*. 2021;22(23):12793. doi:10.3390/ijms222312793

29. Yu W, Greenberg ML. Inositol depletion, GSK3 inhibition and bipolar disorder. *Future Neurol*. 2016;11(2):135-148. doi:10.2217/fnl-2016-0003

30. Schwartz RA, Janusz CA, Janniger CK. Seborrheic dermatitis: an overview. *Am Fam Physician*. 2006;74(1):125-130.

31. Sparber F, De Gregorio C, Steckholzer S, Ferreira FM, Dolowschiak T, Ruchti F, et al. The Skin Commensal Yeast Malassezia Triggers a Type 17 Response that Coordinates Anti-fungal Immunity and Exacerbates Skin Inflammation. *Cell Host Microbe*. 2019;25(3):389-403.e6. doi:10.1016/j.chom.2019.02.002

32. Coates M, Mariottoni P, Corcoran DL, Kirshner HF, Jaleel T, Brown DA, et al. The skin transcriptome in hidradenitis suppurativa uncovers an antimicrobial and sweat gland gene signature which has distinct overlap with wounded skin. *PloS One*. 2019;14(5):e0216249. doi:10.1371/journal.pone.0216249

33. Jiang SW, Whitley MJ, Mariottoni P, Jaleel T, MacLeod AS. Hidradenitis Suppurativa: Host-Microbe and Immune Pathogenesis Underlie Important Future Directions. *JID Innov*. 2021;1(1):100001. doi:10.1016/j.xjidi.2021.100001

34. Del Duca E, Morelli P, Bennardo L, Di Raimondo C, Nisticò SP. Cytokine Pathways and Investigational Target Therapies in Hidradenitis Suppurativa. *Int J Mol Sci*. 2020;21(22):8436. doi:10.3390/ijms21228436

35. Mukai T, Kishi T, Matsuda Y, Iwata N. A meta-analysis of inositol for depression and anxiety disorders. *Hum Psychopharmacol Clin Exp*. 2014;29(1):55-63. doi:10.1002/hup.2369

36. Bizzarri M, Dinicola S, Bevilacqua A, Cucina A. Broad Spectrum Anticancer Activity of Myo-Inositol and Inositol Hexakisphosphate. *Int J Endocrinol*. 2016;2016:2016. doi:10.1155/2016/5616807

37. Liu G, Song Y, Cui L, Wen Z, Lu X. Inositol hexaphosphate suppresses growth and induces apoptosis in HT-29 colorectal cancer cells in culture: PI3K/Akt pathway as a potential target. *Int J Clin Exp Pathol*. 2015;8(2):1402-1410.

38. Dinicola S, Fabrizi G, Masiello MG, Proietti S, Palombo A, Minini M, et al. Inositol induces mesenchymal-epithelial reversion in breast cancer cells through cytoskeleton rearrangement. *Exp Cell Res*. 2016;345(1):37-50. doi:10.1016/j.yexcr.2016.05.007