Clin Exp Dermatol 2023; **00**:1–7
https://doi.org/10.1093/ced/llac027
Advance access publication date: 25 November 2022

CED
Clinical and Experimental Dermatology
Review Article

A systematic review of the uses of metformin in dermatology

Sami Raza[1,2] **Firas Al-Niaimi**[3] **and Faisal R. Ali**[4,5]

[1]Department of Medicine, Walsall Healthcare NHS Trust, UK
[2]Faculty of Medicine, Health and Life Science, Swansea University, UK
[3]University of Aalborg, Aalborg, Denmark
[4]Department of Dermatology, Mid-Cheshire NHS Foundation Trust, UK
[5]St John's Institute of Dermatology, Guy's and St Thomas' NHS Foundation Trust, London, UK

Correspondence: Faisal R. Ali, Dermatological Surgery and Laser Unit, Guy's Cancer Centre, Guy's and St Thomas' NHS Foundation Trust, London, UK. Email: f.r.ali.01@cantab.net

Abstract

Metformin is an established staple drug in the management of Type 2 diabetes mellitus. In this systematic review, we sought to establish the clinical utility of metformin in a range of dermatological conditions. The pathophysiology of acne vulgaris and polycystic ovarian syndrome (PCOS) is well suited to the pharmacological profile of metformin, and we found evidence for its efficacy in managing these conditions. We found some evidence for the use of metformin particularly in acne and PCOS; however, the evidence base is of mixed quality. There is scope for clinicians to consider metformin as an adjunct therapy in acne and PCOS. There is generally insufficient evidence to recommend metformin in other dermatological conditions.

Introduction

Metformin is a first-line therapy for Type 2 diabetes mellitus (T2DM) and is increasingly being used to help treat several dermatological conditions. It has a largely favourable safety profile. Reported dermatological adverse effects (AEs) include common AEs such as abdominal pain, decreased appetite and diarrhoea,[1] and cutaneous AEs such as leucocytoclastic vasculitis, bullous pemphigoid, lichen planus and psoriasiform drug eruption[2] (Table 1). In this systematic review, we assess the evidence for use of metformin in dermatology.

Search strategy

We performed a literature search for the past 15 years. Several databases, including MEDLINE and PubMed, were searched with key words including 'metformin' and 'dermatological conditions' (Figure 1). A summary of the evidence found is presented in Table 1.

Polycystic ovary syndrome and acne vulgaris

The role of insulin-like growth factor (IGF)-1 in androgen production and subsequent acne vulgaris is acknowledged, as IGF-1 is involved in the IGF-1 signalling pathway, which in turn can be induced by insulin. Metformin is an insulin-sensitizing agent. Androgens can also be affected by IGF-1[3] by stimulating comedonal production and sebogenesis by binding to receptors on the pilosebaceous unit.[4] In clinical practice, metformin is commonly prescribed (40%) for adolescents with polycystic ovarian syndrome (PCOS).[5]

Polycystic ovary syndrome

A Cochrane review[6] investigated the effectiveness of oral metformin against the oral contraceptive pill in PCOS. The review identified 44 randomized controlled trials (RCTs) ($n=2253$), with 39 of these RCTs assessing adults ($n=2047$) and 5 assessing adolescents ($n=206$). Evidence quality was noted to be low or very low, with the main limitations being risk of bias, imprecision and inconsistency. For hirsutism in adults, it was difficult to ascertain the efficacy of metformin against the oral contraceptive pill (OCP) in patients with body mass index (BMI) <25 [mean difference (MD) 0.38, 95% CI −0.44 to 1.19, $n=134$, $I^2=50\%$) or >30 (MD −0.38, 95% CI −1.93 to 1.17; $n=85$, $I^2=34\%$). For patients with BMI of 25–30, metformin was less effective in improving hirsutism than the OCP (Peto OR = 6.42, 95% CI 2.98–13.84, $n=602$, $I^2=0\%$). When metformin alone was compared with the combination of metformin and the OCP, metformin was found to be less effective at improving hirsutism (MD 1.36, 95% CI 0.62–2.11, $n=135$, $I^2=9\%$).

A continuing medical education article[4] assessed different therapies for treating the manifestations of PCOS. The authors found that there is inconsistent evidence for data for metformin use in the treatment of acne in PCOS. With

Accepted: 26 September 2022

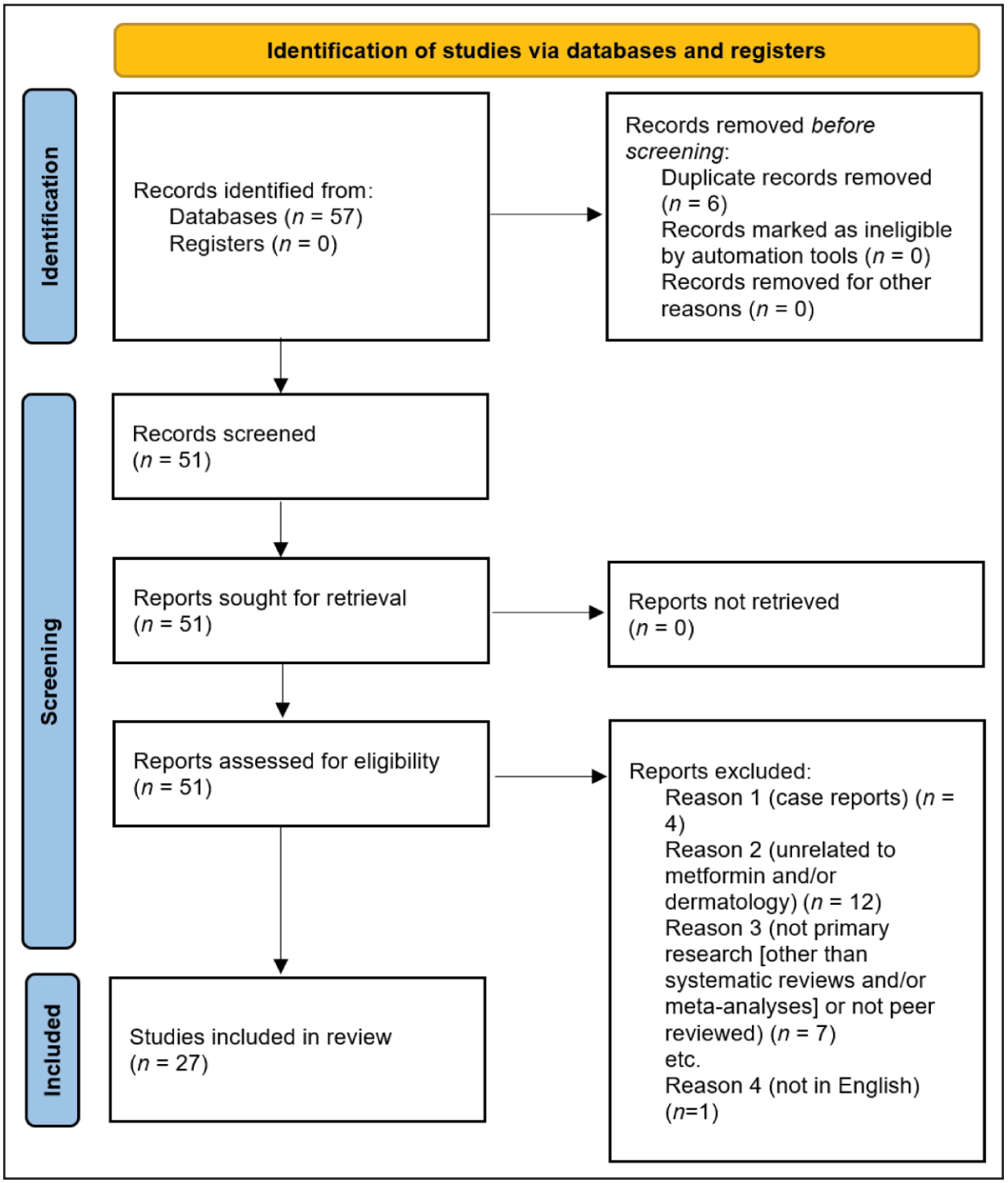

Figure 1 Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) diagram.

regards to hirsutism, metformin was less effective than combination flutamide and spironolactone, but the addition of flutamide to metformin was more effective than metformin monotherapy in four studies.[7–10]

One of the four papers quoted in the article was a systematic review[7] assessing metformin and thiazolidinedione (TZD) drugs for the treatment of hirsutism. Both spironolactone [pooled weighted mean difference (WMD) 1.3, 95% CI 0.03–2.6] and flutamide (WMD 5.0, 95% CI 3.0–7.0, $I^2 = 0\%$) were superior to metformin monotherapy. There was a small decrease in Ferriman–Gallwey (FG) score in women treated with insulin sensitizers (both metformin and TZD) relative to a placebo (WMD −1.5; 95% CI −2.8 to −0.2; $I^2 = 75\%$). The authors concluded that the data were imprecise and the inconsistent evidence of low to very low quality, suggesting that neither metformin nor TZD provided benefit for hirsutism treatment.

Another quoted study[8] was a single-blind study of 40 obese women with PCOS. Hirsutism was measured using the FG score before and at the end of the trial.

Table 1 Summary of metformin use in dermatology

Indications for which there is evidence	Strongest evidence of acne vulgaris and PCOS. Some evidence for HS, AN and melasma
Mechanism of metformin in AN[12]	Prevents GLUT-4 receptor endocytosis to facilitate peripheral glucose utilization, reducing hyperinsulinaemia and improving sensitivity to insulin. This prevents proliferation of dermal fibroblasts in keratinocytes
Dosing and route	
Acne and PCOS	850 mg twice daily orally[7]
HS	1.5 g daily total orally[10]
AN[20]	500–2000 mg daily orally, or weight-based dosing 25 mg kg^{-1} day^{-1}
Contraindications	eGFR $<$ 30 mL min^{-1} 1.73 m^{-2} Those at risk of lactic acidosis (including patients at risk of acute kidney injury, hepatic insufficiency and acute alcohol intoxication)
Caution in prescribing	Impaired renal function
Monitoring	Once yearly in those with normal renal function, twice yearly in patients with additional risk factors for renal failure (such as elderly patients)
Adverse effects	
Common[1]	Abdominal pain Decreased appetite Diarrhoea Gastrointestinal disorder Nausea Altered taste Vitamin B12 deficiency Vomiting
Cutaneous[2]	Leucocytoclastic vasculitis Bullous pemphigoid Lichen planus Psoriasiform drug eruption

AN, acanthosis nigricans; eGFR, estimated glomerular filtration rate; HS, hidradenitis suppurativa; PCOS, polycystic ovarian syndrome.

Following a 1-month diet, patients were allocated to one of four groups (placebo, metformin 850 mg twice weekly, flutamide 250 mg twice weekly or a combination of metformin 850 mg twice weekly and flutamide 250 mg twice weekly) for 6 months alongside a low-calorie diet. Following treatment, hirsutism scores significantly decreased in all three treatment groups but not in the placebo group, and the combination metformin and flutamide group produced a greater reduction in hirsutism compared with placebo ($P = 0.009$).

A third quoted study was a review article[9] assessing combination low-dose metformin and flutamide therapy for hyperinsulinaemic hyperandrogenism in nonobese women and adolescents. With a discontinuous regimen (21/28 days) and when combined with an oral contraceptive or a transdermal contraceptive, there were decreases of the hirsutism score.

The fourth article was another review,[10] which assessed two studies using antiandrogens alone and combination therapy with various drugs [pironolactone with combined (C)OCP; metformin with COCP; flutamide with metformin] is superior to metformin monotherapy and COCP monotherapy. The first study[11] assessed the efficacy of combination low-dose spironolactone 50 mg daily and metformin 1000 mg daily and either drug as monotherapy for a total of 6 months in managing 169 women with PCOS. At 6 months, the FG score in the combination group ($n = 62$) decreased significantly ($P < 0.05$) compared with either drug alone. The second study[12] was an RCT of 56 patients with PCOS treated for 6 months, with patients divided into two groups: Group A ($n = 28$) treated with metformin 1700 mg daily and Group B ($n = 28$) treated with a combination of metformin 1700 mg daily and spironolactone 25 mg daily. There was a statistically significant decrease in hirsutism (measured by FG score) in both groups, but this was greater in the combination Group B [15.1 (6.2) at baseline vs. 11.0 (5.0) at 6 months; $P < 0.001$] than the monotherapy Group A [12.2 (5.1) at baseline vs. 10.7 (4.9) at 6 months; $P < 0.001$].

Finally, a different study[13] assessed the effectiveness of adding either metformin or combined oral contraceptive pill (COCP) to laser hair removal in patients with PCOS. In total, 150 women with PCOS were randomized into three groups: Group 1 received laser hair removal only, Group 2 received metformin plus laser hair removal and Group 3 received COCP plus laser hair removal. The diode laser wavelength was 810 nm, and the protocol specified a total of six sessions in 1 month, followed by a further two sessions after 3 and 6 months. Outcomes were measured using visual analogue scale (VAS), Dermatology Life Quality Index and a customized questionnaire (Hirsutism Life Quality Index). All three patient groups showed improvement, but Group 3 (combination COCP plus laser) demonstrated better improvement than either Group 1 (laser monotherapy) or Group 2 (metformin plus laser).

Acne vulgaris

A systematic review and meta-analysis[14] compared metformin as an adjuvant therapy with OCP, statin, thiazolidinedione, vitamin D, myoinositol, or lifestyle change with therapy without metformin demonstrated a significant improvement in acne scores (standardized MD −0.256, 95% CI −0.439 to −0.074). There was also a significant decrease in the presence of post-treatment acne (OR = 0.362, 95% CI 0.271–0.485).

In treating moderate to severe acne vulgaris, a randomized, open-labelled study[15] aimed to assess the efficacy and safety of metformin as an adjunctive treatment. The cohort of 84 patients received either oral tetracycline 250 mg twice daily plus topical benzoyl peroxide 2.5%,

with or without metformin 850 mg daily. Participants who received metformin as an adjunctive treatment yielded higher treatment success rates than those who did not have metformin (66.7% vs. 43.2%, $P=0.04$). There was a greater mean percentage reduction from baseline in total lesion counts in the metformin group than in the nonmetformin group at 12 weeks (71.4% vs. 65.3%, $P=0.278$) and also a greater reduction in the Cardiff Acne Disability Index score (4.82 vs. 4.22, $P=0.451$).

Another study of 10 male patients[16] receiving a low-glycaemic diet (1500–2000 kcal) alongside metformin 500 mg twice daily for 6 months demonstrated a statistically significant improvement as assessed by the Global Acne Grading System [reduced from mean (SD), 25.10 (8.9) at T0 to 14.10 (10.4) at T1; $P<0.03$] compared with metformin alone [reduced from 24.90 (7.6) at T0 to 19.40 (7.4) at T1; $P=0.06$].

Hidradenitis suppurativa

A retrospective analysis[17] found a subjective clinical response of hidradenitis suppurativa (HS) to metformin in 68% of patients [36 of 53 patients; 4 patients (7%) had diabetes and 5 (9%) had PCOS], of whom 19% (7 of 36) achieved a complete response. Mean treatment duration was 11.3 months at a mean dose of 1.5 g day^{-1}.

A single-group open study of 25 patients[18] assessed the efficacy of metformin for patients with HS previously refractory to medical therapy. Patients were treated over 24 weeks with metformin, with clinical disease severity assessed at Weeks 0, 12 and 24 with evaluation by Sartorius score and DLQI. The study found a reduction in Sartorius score of 12.7 and DLQI score of 7.6, with a significant improvement in 16 of the 25 patients. The social benefit of metformin was reflected by a reduction in the number of working days lost, with a reduction from 1.5 to 0.4 days per month.

Acanthosis nigricans

A review of metformin in dermatology[19] suggested that metformin targets hyperpigmentary conditions by reducing expression of melanogenic proteins, including tyrosinase, tyrosine-related protein (TRP)-1, TRP-2, melanoma-associated antigen recognized by T cells-1 and protein kinase Cβ.

A systematic review[20] assessed the evidence surrounding metformin use in dermatological conditions, including psoriasis, HS, PCOS, acne, hirsutism and AN. For AN, the review noted the utility of metformin in treating AN in both male and female patients with ages ranging from 12 to 45 years old, based on five case reports, two prospective cohort studies, one RCT, one retrospective cohort study and one case series. Metformin was an efficacious treatment in 72.2% of patients.

Sett *et al.*[21] compared the effectiveness and safety of metformin 500 mg twice daily against Canthex (a capsule formulation of α-lipoic acid, biotin, chromium polynicotinate and zinc sulfate). Patients were randomly allocated to either treatment for 12 weeks. Both treatments performed similarly. With metformin, there was a statistically significant ($P<0.001$) reduction in the severity of neck lesions and skin texture from baseline.

Melasma

A study evaluated the efficacy of topical metformin compared with a triple combination cream (TCC) of hydroquinone 2%, tretinoin 0.025% and flucinolone acetonide 0.01%).[22] Patients were divided into two groups, with Group 1 ($n=20$) given 30% metformin lotion and Group 2 ($n=20$) given TCC for 8 weeks. Pigmentation was assessed with the Melasma Area and Severity Index at baseline and Week 8. In Group 1, 11 of the 20 patients demonstrated Grade 1 improvement (1% to < 25%) with 1 patient each having Grade 2 (25–50%) and Grade 3 (> 50–75%) improvement. In Group 2, 14 of the 20 patients showed Grade 1 improvement, with 2 patients showing Grade 2 and 1 patient each in Grades 3 and 4. However, the difference was not statistically significant.

Melanoma and nonmelanoma skin cancer

Tian and Zhao[23] demonstrated that metformin inhibits the proliferation of mouse melanoma cells and induces apoptosis through signalling pathways relative to a control. Metformin induces cell cycle arrest[24] and targets the mTOR signalling pathway to reduce growth of squamous cell carcinomas (SCCs) through enhanced apoptosis.[25]

A prospective study[26] found no clinical benefit of using metformin 1000 mg three times daily for 6 months in 17 patients with metastatic melanoma. It remains possible that metformin may have benefited if taken beyond 6 months or if combined with other treatments such as monoclonal antibodies, immunotherapy or chemotherapy.

A meta-analysis[27] found that metformin monotherapy was not significantly associated with a decreased risk of melanoma, SCC, basal cell carcinoma (BCC) or total nonmelanoma skin cancers (NMSCs) compared with controls.

One study[28] found that metformin conferred a lower risk of developing BCC in 4700 patients compared with 47 293 controls (OR = 0.71, 95% CI 0.61–0.83) but no altered risk of developing invasive SCC.

Psoriasis

Psoriasis is associated with metabolic syndrome, as metformin inhibits the upregulation of pro-interleukin (IL)-1β, a precursor of mature IL-1β, which is implicated in the pathogenesis of both psoriasis and T2DM.[29]

Despite promising preclinical studies, a systematic review[30] evaluating the effect of antidiabetic drugs on psoriasis found that metformin did not significantly reduce the ratio of 75% reduction in Psoriasis Area and Severity Index (PASI75), showing a risk difference (RD) of 0.50 (95% CI −0.15 to 1.15, $P=0.13$), whereas pioglitazone did (RD = 0.42, 95% CI 0.18–0.65, $P=0.0004$).

An observational, retrospective cohort study[31] divided patients with psoriasis and T2DM into metformin and nonmetformin groups to assess the safety of metformin. No significant difference was found in psoriasis-related admissions [hazard ratio (HR) = 1.32, 95% CI 0.90 to 1.93] or all-cause mortality (HR = 1.08, 95% CI 0.90 to 1.30).

A case–control study[32] assessing the use of antidiabetic drugs (thiazolidinediones, metformin, sulfonylureas

or acarbose) and the risk of developing first-time psoriasis found that metformin had lower odds of first-time psoriasis, with use of ≥15 prescriptions for metformin resulted in an adjusted OR of 0.77 (95% CI 0.62–0.96) compared with 1.07 (95% CI 0.88–1.31) for sulfonylureas.

Potential uses (from animal studies)

When metformin was given to irradiated mice, there was a significant reduction in radiation-induced skin thickening (a common AE of radiotherapy) and collagen accumulation.[33] A mouse study[34] showed that metformin downregulated proinflammatory factors, cytokines and fibrosis-inducing factors in scleroderma.

Another study[35] demonstrated efficacy of topical metformin 0.6% on the skin of ultraviolet B-irradiated mice by inhibiting cell death in keratinocytes.

Another study[36] further detailed the antifibrotic effect of metformin in mice as a potential therapeutic option for keloid scars. After dermal fibroblasts were stimulated and treated with metformin 10 mM, expression of extracellular matrix components was decreased.

Soydas *et al.*[37] proposed metformin as a potential antiageing treatment, based on its inhibition of human dermal fibroblasts.

Conclusion

The literature demonstrates the efficacy of metformin on dermatological conditions to be varied, with the evidence base having a wide-ranging basis of quality. The consensus is that for acne and PCOS, there is some reasonable evidence for the use of metformin, particularly as an adjunct, and clinicians may therefore consider using metformin as an adjunctive therapy in acne and PCOS. There is a general paucity of evidence to suggest use of metformin in other dermatological conditions, which warrants higher-quality trials.

Learning points

- The pharmacological profile of metformin is suited to treatment of the insulin-sensitive conditions of PCOS and acne vulgaris, as there is demonstrable evidence of metformin acting as both a treatment and as an adjuvant for these conditions.
- Clinicians may consider using metformin in HS, AN, PCOS and acne vulgaris.
- There is insufficient evidence to support using metformin for NMSC; preliminary data suggest that metformin may reduce the development of BCC; however, larger studies are needed.
- Data from animal studies suggest that metformin may have a role in the treatment of keloid scars and radiation-induced skin fibrosis, and as an anti-ageing option.

Acknowledgements

We are grateful to Kate Jones from Library and Knowledge Services at Walsall Healthcare NHS Trust for assisting with the literature search.

Conflict of interest

The authors declare that they have no conflict of interest.

Funding

None.

Ethics statement

Ethics approval: not applicable. The patient provided informed consent for publication of their case details and images.

Data availability

Data are available on request from the corresponding author.

References

1 National Institute for Health and Care Excellence. British National Formulary. Drugs. Metformin hydrochloride. Available at: https://bnf.nice.org.uk/drugs/metformin-hydrochloride/ (last accessed 23 September 2022).
2 Badr D, Kurban M, Abbas O. Metformin in dermatology: an overview. *J Eur Acad Dermatol Venereol* 2013; **27**:1329–35.
3 Dessinioti C, Dreno B. Acne treatments: future trajectories. *Clin Exp Dermatol* 2020; **45**:955–61.
4 Buzney E, Sheu J, Buzney C, Reynolds RV. Polycystic ovary syndrome: a review for dermatologists. Part II. Treatment. *J Am Acad Dermatol* 2014; **71**:859.e1–15.
5 Torres-Zegarra C, Sundararajan D, Benson J *et al.* Care for adolescents with polycystic ovary syndrome: development and prescribing patterns of a multidisciplinary clinic. *J Pediatr Adolesc Gynecol* 2021; **34**:617–25.
6 Fraison E, Kostova E, Moran LJ *et al.* Metformin versus the combined oral contraceptive pill for hirsutism, acne, and menstrual pattern in polycystic ovary syndrome. *Cochrane Database Syst Rev* 2020; **8**:CD005552.
7 Cosma M, Swiglo BA, Flynn DN *et al.* Insulin sensitizers for the treatment of hirsutism: a systematic review and metaanalyses of randomized controlled trials. *J Clin Endocrinol Metab* 2008; **93**:1135–42.
8 Gambineri A, Pelusi C, Genghini S *et al.* Effect of flutamide and metformin administered alone or in combination in dieting obese women with polycystic ovary syndrome. *Clin Endocrinol (Oxf)* 2004; **60**:241–9.
9 Ibáñez L, de Zegher F. Low-dose flutamide-metformin therapy for hyperinsulinemic hyperandrogenism in non-obese adolescents and women. *Hum Reprod Update* 2006; **12**:243–52.
10 Pasquali R, Gambineri A. Insulin-sensitizing agents in polycystic ovary syndrome. *Eur J Endocrinol* 2006; **154**:763–75.
11 Ganie MA, Khurana ML, Nisar S *et al.* Improved efficacy of low-dose spironolactone and metformin combination than either drug alone in the management of women with polycystic ovary syndrome (PCOS): a six-month, open-label randomized study. *J Clin Endocrinol Metab* 2013; **98**:3599–607.
12 Mazza A, Fruci B, Guzzi P *et al.* In PCOS patients the addition of low-dose spironolactone induces a more marked reduction of clinical and biochemical hyperandrogenism than metformin alone. *Nutr Metab Cardiovasc Dis* 2014; **24**:132–9.
13 Dorgham N, Sharobim A, Haggag H *et al.* Adding combined oral contraceptives or metformin to laser treatment in polycystic ovarian syndrome hirsute patients. *J Drugs Dermatol* 2021; **20**:302–6.

14 Yen H, Chang YT, Yee FJ, Huang YC. Metformin therapy for acne in patients with polycystic ovary syndrome: a systematic review and meta-analysis. *Am J Clin Dermatol* 2021; **22**:11–23.
15 Robinson S, Kwan Z, Tang MM. Metformin as an adjunct therapy for the treatment of moderate to severe acne vulgaris: a randomized open-labeled study. *Dermatol Ther* 2019; **32**:e12953.
16 Fabbrocini G, Izzo R, Faggiano A *et al.* Low glycaemic diet and metformin therapy: a new approach in male subjects with acne resistant to common treatments. *Clin Exp Dermatol* 2016; **41**:38–42.
17 Jennings L, Hambly R, Hughes R *et al.* Metformin use in hidradenitis suppurativa. *J Dermatol Treat* 2020; **31**:261–3.
18 Verdolini R, Clayton N, Smith A *et al.* Metformin for the treatment of hidradenitis suppurativa: a little help along the way. *J Eur Acad Dermatol Venereol* 2013; **27**:1101–8.
19 Bubna AK. Metformin – for the dermatologist. *Indian J Pharmacol* 2016; **48**:4–10.
20 Sung CT, Chao T, Lee A *et al.* Oral metformin for treating dermatological diseases: a systematic review. *J Drugs Dermatol* 2020; **19**:713–20.
21 Sett A, Pradhan S, Sancheti K *et al.* Effectiveness and safety of metformin versus CanthexTM in patients with acanthosis nigricans: a randomized, double-blind controlled trial. *Indian J Dermatol* 2019; **64**:115–21.
22 Banavase Channakeshavaiah R, Andanooru Chandrappa NK. Topical metformin in the treatment of melasma: a preliminary clinical trial. *J Cosmet Dermatol* 2020; **19**:1161–4.
23 Tian Y, Zhao L. Metformin induces apoptosis of melanoma B16 cells via PI3K/Akt/mTOR signaling pathways. *J BUON* 2020; **25**:2066–70.
24 Tseng HW, Li SC, Tsai KW. Metformin treatment suppresses melanoma cell growth and motility through modulation of microRNA expression. *Cancers* 2019; **11**:209.
25 Chaudhary SC, Kurundkar D, Elmets CA *et al.* Metformin, an antidiabetic agent reduces growth of cutaneous squamous cell carcinoma by targeting mTOR signaling pathway. *Photochem Photobiol* 2012; **88**:1149–56.
26 Montaudié H, Cerezo M, Bahadoran P *et al.* Metformin monotherapy in melanoma: a pilot, open-label, prospective, and multicentric study indicates no benefit. *Pigment Cell Melanoma Res* 2017; **30**:378–80.
27 Chang MS, Hartman RI, Xue J *et al.* Risk of skin cancer associated with metformin use: a meta-analysis of randomized controlled trials and observational studies. *Cancer Prev Res (Phila)* 2021; **14**:77–84.
28 Adalsteinsson JA, Muzumdar S, Waldman R *et al.* Metformin is associated with decreased risk of basal cell carcinoma: a whole-population case-control study from Iceland. *J Am Acad Dermatol* 2021; **85**:56–61.
29 Tsuji G, Hashimoto-Hachiya A, Yen VH *et al.* Metformin inhibits its IL-1β secretion via impairment of NLRP3 inflammasome in keratinocytes: implications for preventing the development of psoriasis. *Cell Death Discov* 2020; **6**:11.
30 Chi CC, Lee CY, Liu CY *et al.* Effects of antidiabetic drugs on psoriasis: a meta-analysis. *Eur J Clin Invest* 2021; **51**:e13377.
31 Su YJ, Chen TH, Hsu CY *et al.* Safety of metformin in psoriasis patients with diabetes mellitus: a 17-year population-based real-world cohort study. *J Clin Endocrinol Metab* 2019; **104**:3279–86.
32 Brauchli YB, Jick SS, Curtin F, Meier CR. Association between use of thiazolidinediones or other oral antidiabetics and psoriasis: a population based case-control study. *J Am Acad Dermatol* 2008; **58**:421–9.
33 Kim JM, Yoo H, Kim JY *et al.* Metformin alleviates radiation-induced skin fibrosis via the downregulation of FOXO3. *Cell Physiol Biochem* 2018; **48**:959–70.
34 Moon J, Lee SY, Choi JW *et al.* Metformin ameliorates scleroderma via inhibiting Th17 cells and reducing mTOR-STAT3 signaling in skin fibroblasts. *J Transl Med* 2021; **19**:192.
35 Xiao T, Chen Y, Song C *et al.* Possible treatment for UVB-induced skin injury: anti-inflammatory and cytoprotective role of metformin in UVB-irradiated keratinocytes. *J Dermatol Sci* 2021; **102**:25–35.
36 Jeon HB, Roh H, Ahn HM *et al.* Metformin inhibits transforming growth factor β-induced fibrogenic response of human dermal fibroblasts and suppresses fibrosis in keloid spheroids. *Ann Plast Surg* 2021; **86**:406–11.
37 Soydas T, Sayitoglu M, Sarac E *et al.* Metformin reverses the effects of high glucose on human dermal fibroblasts of aged skin via downregulating RELA/p65 expression. *J Physiol Biochem* 2021; **77**:443–50.

CPD questions

Learning objective

To demonstrate knowledge of the clinical utility of metformin across selected dermatological conditions.

Question 1

What effect does metformin have on pro-interleukin (IL)-1β (a precursor of mature IL-1β) in psoriasis?

(a) Metformin increases upregulation of pro-IL-1β.
(b) Metformin decreases upregulation of pro-IL-1β.
(c) Metformin inhibits the production of pro-IL-1β.
(d) Metformin increases upregulation of mature IL-1β.
(e) Metformin decreases upregulation of mature IL-1β.

Question 2

Which of the following is correct with regards to the efficacy of metformin and the oral contraceptive pill (OC), alone or in combination, compared with metformin alone in adult women with polycystic ovary syndrome (PCOS)?

(a) Metformin alone is less effective than the combination of metformin and the OCP in reducing hirsutism in adult women with PCOS.
(b) There is no difference in the effectiveness of metformin alone compared with the combination of metformin and the OCP in reducing hirsutism in adult women with PCOS.
(c) Metformin alone is more effective than he combination of metformin and the OCP in reducing hirsutism in adult women with PCOS.
(d) Metformin alone is more effective than the OCP alone in reducing hirsutism in adult women with PCOS with a body mass index (BMI) of 25–30.
(e) Metformin alone is equally as effective as the OCP alone in reducing hirsutism in adult women with PCOS with a BMI of <25.

Question 3

What is the effect of metformin on the risk of developing squamous cell carcinoma (SCC) and basal cell carcinoma (BCC)?

(a) When metformin is used as monotherapy, it increases the risk of both SCC and BCC.
(b) When metformin is used as monotherapy, it increases the risk of SCC but decreases the risk of BCC.

(c) When metformin is combined with 5-fluorouracil (5-FU), it decreases the risk of developing SCC and BCC.
(d) When metformin is combined with 5-FU, it increases the risk of developing SCC and BCC.
(e) When metformin is combined with 5-FU, it decreases the risk of developing SCC but increases the risk of developing BCC.

Question 4

What is the mechanism of action of metformin in hyperpigmentation disorders such as acanthosis nigricans?

(a) Metformin increases expression of melanogenic proteins.
(b) Metformin decreases expression of melanogenic proteins.
(c) Metformin inhibits the insulin-like growth factor (IGF)-1 pathway.
(d) Metformin upregulates the IGF-1 pathway.
(e) Metformin reduces keratinocyte proliferation.

Question 5

Compared with pioglitazone, how does metformin affect the ratio patients achieving 75% reduction in Psoriasis Area and Severity Index (PASI75)?

(a) Metformin significantly increases the PASI75 ratio.
(b) Metformin significantly decreases the PASI75 ratio.
(c) Metformin does not significantly decrease the PASI75 ratio.
(d) Metformin does not significantly increase the PASI75 ratio.
(e) Metformin has equal efficacy to pioglitazone.