



Metformin for Systemic Lupus Erythematosus (SLE)

SUMMARY

Metformin is safe, inexpensive, and shows emerging promise in SLE. Metformin is an established therapy for type 2 diabetes with a 60+ year safety record. A growing body of research is exploring its potential as a repurposed therapy for systemic lupus erythematosus (SLE) due to its anti-inflammatory and immunomodulatory effects. Recent studies suggest that metformin may help improve outcomes for SLE patients.

MODE OF ACTION

Mechanistic studies [1-5] have identified several ways in which metformin may counteract pathways involved in SLE:

- Inhibition of the AMPK/mTOR/STAT3 pathway, affecting B and T cells
- Inhibition of oxidative phosphorylation
- Downregulation of NET mitochondrial DNA-activated plasmacytoid dendritic cell interferon pathways
- Reduction of mitochondrial dysfunction and oxidative stress

RECENT CLINICAL STUDIES

Evidence from recent studies suggests metformin may lower disease activity & flare rates in SLE:

2015 Study – Neutrophil Extracellular Traps (NETs)

Key finding: Metformin reduced NET formation and disease flares. A 2015 study identified that NETs, which stimulate inflammation and contribute to SLE activity, were reduced by metformin [6]. The study demonstrated a mechanistic pathway and showed that patients taking metformin experienced fewer flares and reduced corticosteroid need.

2020-22 Randomized Trials

Key finding: Metformin users showed lower flare rates at one year and increased remission. A multicenter randomized clinical trial in 140 non-diabetic SLE patients found that, while not all differences were statistically significant, metformin users had a lower proportion of disease flares at 12 months [7]. The authors pooled data from 201 people and found significantly fewer flares in the metformin (21%) vs. placebo (35%) group. Subgroup analyses suggested particular benefit for patients with negative anti-dsDNA antibodies and normal complement levels [8]. A 2022 report suggested that metformin, when added to standard SLE therapy, increased the proportion of patients achieving remission and maintaining low disease activity for longer periods compared with standard therapy alone [9].

2024 Retrospective Database Study

Key finding: Metformin was associated with a lower risk of major lupus complications. A large 2024 retrospective study found that SLE patients taking metformin had lower rates of lupus nephritis, chronic kidney disease, and major adverse cardiovascular events compared with non-users [10]

ROLE OF METFORMIN IN RELATION TO EXISTING TREATMENTS

Metformin has been studied as an adjunct to existing treatments for SLE. Better results have been achieved in patients taking metformin and hydroxychloroquine.

SAFETY AND DOSING

Metformin is an inexpensive, accessible medication used by over 150 million people worldwide for type 2 diabetes. The most common side effects involve gastrointestinal symptoms, which can be reduced with gradual dosing and taking with food.

Example of Gradual Dose Escalation

- Week 1: 500 mg with breakfast
- Week 2: 500 mg with breakfast + 500 mg with evening meal
- Week 3+: 500 mg with breakfast, 500 mg with lunch, 500 mg with evening meal

Extended-release formulations may further reduce gastrointestinal effects. Supplements of B12 and methylfolate can prevent deficiencies that may occur with metformin. Rare complications (such as lactic acidosis) are primarily relevant in individuals with significant kidney impairment.

Individual health history and risks must be evaluated by a prescribing physician to ensure that metformin is not contraindicated, and to determine an appropriate dose.

OVERCOMING SYSTEMIC BARRIERS TO PRESCRIBING

Metformin's most common use is to improve glycemic control for type 2 diabetes, although it has been prescribed off-label for a variety of health conditions. In medical systems with barriers to off-label prescribing, glycemic control may be a more readily accepted indication for SLE patients with iatrogenic (steroid-induced) changes in glycemic control.

REFERENCES:

¹ <https://doi.org/10.3390/cells8040323>

² <https://doi.org/10.3390/ijms25116162>

³ <https://doi.org/10.3390/diseases12090226>

⁴ <https://doi.org/10.1089/ars.2021.0070>

⁵ <https://doi.org/10.3904/kjim.2021.363>

⁶ <https://doi.org/10.1002/art.39296>

⁷ [https://doi.org/10.1016/S2665-9913\(20\)30004-7](https://doi.org/10.1016/S2665-9913(20)30004-7)

⁸ <https://doi.org/10.1136/lupus-2020-000429>

⁹ <https://doi.org/10.55563/clinexprheumatol/7y5ku8>

¹⁰ <https://onlinelibrary.wiley.com/doi/10.1002/acr2.11698>

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