

# Topical metformin 30% gel in the treatment of acne vulgaris: A split face, placebo-controlled study

Nermeen Ibrahim Bedair MD1, Rehab Nabil Shamma PHD2, Nesma Moustafa Kamel Abdo MBBS3, Mohamed HM EL-Komy MD4

- 1: Associate professor, department of Dermatology, Andrology, Sexual Medicine and STDs, Faculty of Medicine, Helwan University, Helwan, Egypt
- 2: Professor, department of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmacy, Cairo University, Cairo, Egypt
- 3: Resident, department of Dermatology, National Hepatology and tropical medicine institute, Cairo, Egypt
- 4: Professor, department of Dermatology, Faculty of Medicine, Cairo University, Cairo, Egypt

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## Acne

A widely common disorder of the pilosebaceous unit

A recent suggested hypothesis for acne pathogenesis is that it comprises a cutaneous metabolic syndrome and is largely affected by western diet through hyperactivation of insulin, insulin-like growth factor 1 (IGF-1), mechanistic target of rapamycin complex 1 (mTORC1) and forkhead box transcription factor O1

Accumulating evidence suggests that the skin microbiome as well as gut microbiome alterations may play a role in acne pathogenesis.

## Metformin

One of the most prescribed antidiabetic medications worldwide. The exact mechanism of action is still to be elucidated.

Hypothetically acts through phosphorylation of Thr172 thus activates AMP-activated protein kinase (AMPK), causing inhibition of mechanistic target of rapamycin complex 1 (mTORC1) signaling pathway.

It also shifts composition of gut microbiota and disrupts cellular energy supply through the inhibition of mitochondrial complex1

**Patients and methods:** This split face study was designed to evaluate the efficacy and safety of 12 weeks application of daily topical metformin in comparison to placebo in the treatment of 21 adolescent female patients suffering from acne vulgaris.

Patients were assessed and lesions (comedones, papules, pustules and nodules) were counted at weeks 0,4,8,12,16

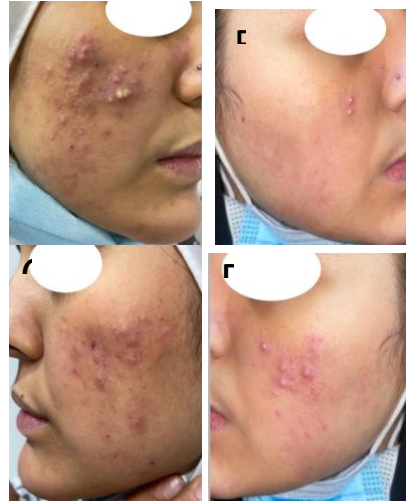
## Results

**Week 12 (end of the treatment):** the number of comedones, papules and nodules (but not pustules) decreased significantly on the metformin side compared to the placebo side

**Week 16 (end of the follow up):** a preserved significant difference in mean lesions counts for comedonal and papular lesions but not for pustules and nodules

Papules were the first lesions to start showing significant improvement by week 4, while comedones took 12 weeks to show significant improvement.

**On the metformin side:** no significant difference between improvement of inflammatory and non inflammatory lesions



**Figure1:** Patient at the baseline (A and C), at the end of treatment at week 12 (B= metformin side, D= placebo side)

Improvement	Lesion	Right side (metformin side) decrease in count Mean $\pm$ SD	Left side (placebo side) decrease in count Mean $\pm$ SD	P value	Significance
From W0 to W12	Comedones	-7.33 $\pm$ 6.143	-1.76 $\pm$ 6.371	0.002	S
	All inflammatory lesions	-7.00 $\pm$ 3.912	-3.57 $\pm$ 3.249	0.007	S
	Papules	-5.38 $\pm$ 3.232	-2.95 $\pm$ 3.626	0.046	S
	Pustules	-1.43 $\pm$ 1.832	-0.57 $\pm$ 1.748	0.196	NS
	Nodules	-0.19 $\pm$ 0.512	+0.14 $\pm$ 0.359	0.038	S
From W0 to W16	Comedones	-6.62 $\pm$ 6.786	+0.71 $\pm$ 7.676	0.015	S
	All inflammatory lesions	-6.43 $\pm$ 3.957	4.14 $\pm$ 3.525	0.055	NS
	Papules	-4.81 $\pm$ 3.076	-3.29 $\pm$ 3.913	0.075	NS
	Pustules	-1.57 $\pm$ 1.886	-0.81 $\pm$ 1.692	0.122	NS

**Table 1:** Change in lesions' count at the 2 endpoints (week 12 as the treatment ends and week 16 where the follow up ends)

## Conclusion

Topical metformin nanoemulsion gel can be a promising safe and effective treatment of acne vulgaris.

The improvement we observed could be attributed to the ability of metformin to decrease the follicular keratosis as well as decreasing the sizes of sebaceous glands and hair follicles, in addition to its anti-inflammatory effects.

While inflammatory acne showed significant improvement as early as 4 weeks of treatment, noninflammatory acne only improved by week 12. This may be related to a delayed effect of metformin on follicular keratinization in contrast to a faster anti-inflammatory impact.

We suggest that the effect of metformin on the different patho-mechanisms involved in acne vulgaris may vary in onset and potential.