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Integrated Metabolic and Topical Therapy for Cellulite in Women With Metabolic Syndrome and Insulin Resistance: A Protocol Using Tirzepatide and G21 Topical Formulation

Metabolic syndrome (MetS) represents a cluster of metabolic abnormalities including insulin resistance, central obesity, hypertension, and dyslipidemia, and is strongly associated with an increased risk of cardiovascular disease and type 2 diabetes. In our previous study entitled Exploring the Link Between Metabolic Syndrome and Cellulite (Cureus. 2024 Jun 29;16(6):e63464), we examined the potential association between MetS and cellulite by focusing on the shared pathophysiological mechanisms underlying both conditions. Cellulite, characterized by a dimpled skin appearance predominantly affecting women, has traditionally been considered a cosmetic concern; however, emerging evidence suggests that it may reflect deeper metabolic and structural alterations within adipose and connective tissue.

Our earlier review highlighted several overlapping biological pathways between MetS and cellulite, including chronic low-grade inflammation, microcirculatory dysfunction, extracellular matrix remodeling, adipocyte hypertrophy, and hormonal imbalance. These mechanisms suggest that cellulite may serve as a clinical marker of underlying metabolic dysregulation rather than merely a superficial dermatologic condition.



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In the present work, we report newer clinical observations derived from the follow-up of 101 patients treated with a combined therapeutic protocol consisting of tirzepatide and CRMP-based G21 topical gel. Particular emphasis was placed on inflammatory markers, hormonal modulation, and changes in adipose tissue remodeling. Rapid weight loss induced by substantial subcutaneous fat reduction, such as that observed with tirzepatide therapy, may lead to tissue laxity and skin sagging due to the loss of structural support previously provided by adipose tissue. This highlights the need for targeted anti-laxity and anti-cellulite interventions.

The EU-patented G21 topical formulation, when used concomitantly with tirzepatide, may provide complementary therapeutic benefits. Tirzepatide appears to exert metabolic and potential antifibrotic effects, including modulation of extracellular matrix stiffness and reduction of chronic adipose tissue inflammation, while G21 gel may promote dermal remodeling and tissue tightening. This combined approach may therefore improve the clinical appearance of cellulite while simultaneously addressing underlying metabolic dysfunction. A deeper understanding of the interaction between metabolic syndrome and cellulite may contribute to improved prevention, diagnosis, and therapeutic strategies.

Keywords: Metabolic syndrome; Cellulite; Tirzepatide; Adipose remodeling; Inflammation; Skin laxity

Biography

Dr. Sotirios Adamidis, MD, PhD, is an expert in diabetes, obesity, and cardiometabolic diseases. He graduated from the National and Kapodistrian University of Athens, School of Medicine, and is board certified in Internal Medicine. He is Director of the Internal Medicine and Lifestyle Medicine Departments at Athens Medical Center and President of the European Society of Diabetes, Metabolic Syndrome and Obesity. Dr. Adamidis is a member of the American Diabetes Association and the Southern Medical Association and serves on several editorial boards. Author of scientific articles and books on metabolic health, he frequently appears in the media and shares educational content on diabetes, obesity, exercise, and metabolic health online.