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New hopes on "SLU-PP-332" as an effective agent for weight loss with indirect kidney protection efficacy; a nephrology point of view

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Abstract
SLU-PP-332 activates estrogen receptor-related orphan receptors, increasing energy expenditure, fatty acid oxidation, and decreasing fat mass accumulation. The drug enhances mitochondrial function and cellular respiration in skeletal muscle cell lines, increases the expression of an estrogen receptor-related orphan receptor target gene, and enhances mitochondrial respiration in C2C12 myocytes. The drug also increases oxidative fibers in skeletal muscle and improves exercise endurance in C57BL/6J mice.

Keywords: SLU-PP-332, Exercise, Energy expenditure, Metabolism
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Introduction

SLU-PP-332 is a synthetic estrogen receptor-related orphan receptor (ERR) agonist, which activates an amplified aerobic exercise mode. This agent improves a natural metabolic route which typically happens in response to exercise, it amplifies energy expenditure and results in faster body fat metabolism (1). SLU-PP-332 enhances mitochondrial function and cellular respiration in skeletal muscle cell lines, increases the expression of an ERR target gene [pyruvate dehydrogenase kinase 4 (Pdk4)], and enhances mitochondrial respiration in C2C12 myocytes (1,2). The drug also increases oxidative fibers in skeletal muscle and demonstrated improvement in exercise endurance in C57BL/6J mice. This drug works on a group of proteins throughout the body organs called ERRs that activate some of the most significant metabolic pathways in the body, counting in the cardiac cells and the brain tissue (3-5). The drug can potentially transform the future of fitness and can facilitate weight loss by stimulating the body's muscles during exercise. The mechanism of action of SLU-PP-332 is to activate ERRs, leading to increased energy expenditure, fatty acid oxidation, and decreased fat mass accumulation (Figure 1) (1).

Search strategy

For this study, we searched PubMed, Web of Science, EBSCO, Scopus, Google Scholar, Directory of Open Access Journals (DOAJ), and Embase, using different keywords, including SLU-PP-332, exercise, energy expenditure, metabolism, and estrogen-related receptor.

Relationship of ERRs to metabolic pathways

Estrogen-related receptors are a group of proteins that play a central role in regulating metabolic genes and cellular energy metabolism. ERRs are transcription factors that regulate physiological processes by controlling the genes that will regulate many crucial events in the body (6). The estrogen-related receptor alpha (ERRα) and estrogen-related receptor gamma (ERRγ) isoforms are the most studied and have been shown to regulate various metabolic pathways, including glucose and fatty acid metabolism, mitochondrial biogenesis, and oxidative phosphorylation. Although less is known about estrogen-related receptor β (ERRβ), current findings have disclosed the significance of this isoform in maintaining embryonic stem cell pluripotency (7). The estrogen-related receptors are vital for several biological activities and their downstream metabolic pathways are disturbed in various diseases such as heart failure and diabetes. The estrogen-related receptors have also arisen as a potential therapeutic target for treating muscle atrophy, insulin resistance, osteoporosis, and other metabolic disorders (6,8).

Benefits of SLU-PP-332 compared to exercise

SLU-PP-332 does not affect food intake, appetite, or

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Implication for health policy/practice/research/ medical education

SLU-PP-332 is a drug that mimics the effects of exercise, directing to augmented energy expenditure and closer body fat metabolism.

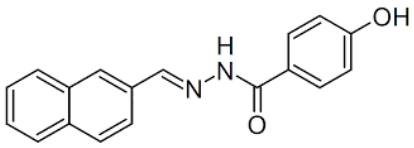

Figure 1. Structure of SLU-PP-332.

exercise initiation. This agent improves a natural metabolic pathway that characteristically reacts to exercise, resulting in amplified energy expenditure, and extra body fat metabolism. SLU-PP-332 enhances mitochondrial function and cellular respiration in skeletal muscle cell lines, increases the expression of an ERR target gene [pyruvate dehydrogenase kinase 4 (Pdk4)], and enhances mitochondrial respiration in C2C12 myocytes (9,10). Moreover, this agent focuses on a group of proteins in our body called ERRs that are accountable for triggering some of the most essential metabolic pathways in tissues. Furthermore, SLU-PP-332 can alter the prospect of fitness and help people lose weight simply by inducing the body's muscles to exercise. Of note, this agent did not generate any significant side effects during the experimental study (5,11,12). In this mini-review, we sought to describe the characteristics of this compound and describe its possible clinical use with possible kidney protective efficacy.

Benefits of exercise

Exercise has many benefits beyond weight loss, including amelioration of cardiovascular performance, improved muscle force and endurance, and improved mental health. Exercise can be tailored to individual needs and preferences and can be done in various settings. Exercise can be a social activity, providing opportunities for social interaction and support (13,14).

Short-term effects of taking SLU-PP-332

SLU-PP-332 is a drug still in the early stages of development, and its short-term effects are not yet fully understood. However, the agent did not create any side effects during the trial on mice, and it did not affect appetite or food intake. In contrast, this compound enhances a natural metabolic pathway that responds to exercise, resulting in increased energy expenditure and improved body fat metabolism. The drug makes the body act like it is training for a marathon (1,15). In the study by Billon et al, obese mice were treated with this compound twice daily over a month. Following 28 days, they weighed less than rodents who were not given the SLU-PP-332 notwithstanding the fact they were given the same amount of diet. On average, they gained ten times less fat than untreated mice and lost 12% of their body weight (15). This novel agent aims a cluster of proteins in the body recognized as ERRs, that activate several metabolic pathways in the body, including the cardiac and brain tissues. The drug can potentially treat diseases such as type 2 diabetes, obesity, nonalcoholic steatohepatitis, heart failure, kidney disease, and even cognitive dysfunction. Although the team has observed no severe side effects, safety considerations must be researched further. (16,17).

Long-term effects of taking SLU-PP-332

The long-term effects of taking SLU-PP-332 are unknown as the drug is still in the early stages of development. However, this medication has not produced any serious side effects during the study on mice, and the next step is to develop it into a drug candidate by refining its structure, ideally making it accessible as a pill instead of an injection (15,18). Then, the drug would be examined for side effects in more animal models before beginning human trials. According to the weight reduction effect of this drug, it can potentially treat diseases such as type 2 diabetes, obesity, nonalcoholic fatty liver disease, heart failure, kidney disease, and even cognitive dysfunction (1,15-19). Although the team has observed no severe side effects, safety considerations must be researched further. It is essential to establish healthy lifestyle habits, as the benefits of these compounds would wear off after discontinuation.

A nephrology point of view on clinical administration of SLU-PP-332

This drug can potentially treat diseases such as type 2 diabetes, obesity, nonalcoholic fatty liver disease, heart failure and kidney disease. Weight loss following administration of this agent will be accompanied by improvement of metabolic syndrome and type 2 diabetic which imply a kidney protective efficacy by this compound. However, it is essential to note that SLU-PP-332 needs more animal examination to evaluate probable side effects before it can be used for human trials (20).

Conclusion

SLU-PP-332 has some benefits compared to exercise, such as not affecting appetite or food intake but boosting a natural metabolic pathway that typically responds to movement. However, exercise has many benefits beyond weight loss and can be tailored to individual needs and preferences.

Conflicts of interest

The author is affiliated with Nickan Research Institute as a researcher; nevertheless, his professional role did not influence the peer-review process.

Ethical issues

Ethical issues (including plagiarism, data fabrication, and double

publication) have been completely observed by the author.

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