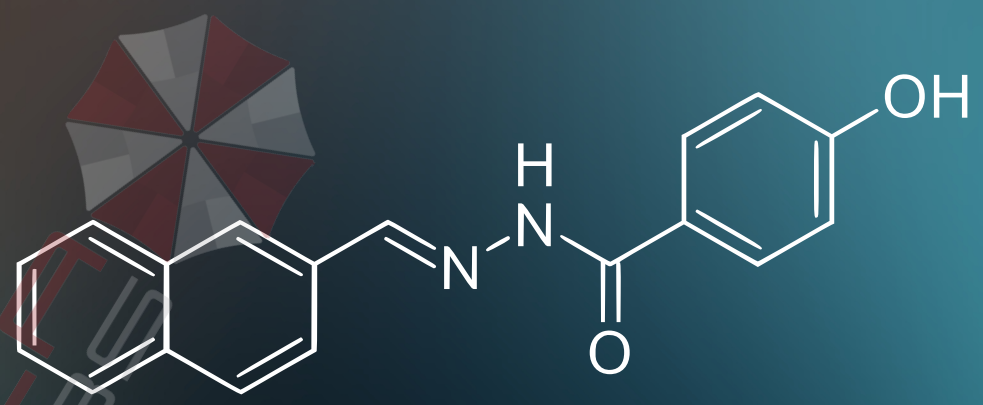

SLU-PP-332 - Unveiling the Multifaceted Benefits of an ERR Agonist in Preclinical Studies

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History

SLU-PP-332 is a member of the relatively new group of estrogen related receptor (ERR) agonists. It is not known which compound do bind to this receptor in the body, and little is known about its effects on human physiology. What is known is that the estrogen related receptors affect gene regulation, similar to other steroid receptors. It seems that the estrogen related receptors regulate energy metabolism and mitochondrial division in several tissues. At the present time, three different subtypes of the ERR are known, ERRα, ERRβ and ERRγ. SLU-PP-332 is reported to bind to all three subclasses but has the highest potency to ERRα.[1]

Cell Culture Experiments & Animal Studie

The first study on SLU-PP-32 was published in 2021.[2] It reported that mice with an lack of ERRs in the heart muscle died developed a deadly heart failure. Hence, the influence of SLU- PP-32 (and another ERR agonist named SLU-PP-915) in mice with ERR and mechanical manipulation to induce heart failure were investigated. SLU-PP-32 significantly improved heart function and mitochondrial structure. However, it was not able to prevent long term changes to the heart that eventually led to the death of the animals. Gene regulation analysis showed significant changes in genes influencing metabolism and to fatty acid breakdown.[2] A subsequent study claimed showed substantial normalization of metabolic profiles in fatty acid/ lipid and tricarboxylic acid/ oxidative phosphorylation metabolites in the mouse heart pressure overload. This study also found that out of the ERR subtypes, ERRγ is the main mediator of cardio-protection.[3]

Another study in mice showed SLU-PP-332 can increase the amount of type IIa muscle fibers, which have a high capacity to break down sugars and fats by oxidation and are resistant to fatigue. The researchers also observed that SLU-PP-332 induced an ERRα-specific acute aerobic exercise genetic program, and the ERRα activation was critical for enhancing exercise endurance in mice. These data indicate the feasibility of targeting ERRα as treatment of numerous metabolic disorders and to improve muscle function in the aging.[3]

In obese mice with metabolic syndrome, the administration of SLU-PP-332 increased a number of metabolic parameters such as increased energy expenditure and fatty acid oxidation. Additionally, the ERR agonist effectively reduced obesity and improved insulin sensitivity in models of metabolic syndrome.[4]

A study specifically on the impact of SLU-PP-332 on kidney failure in mice. They animals received 25mg/kg per day by i.p. injection for 3 weeks. The treatment reversed the increased inflammatory markers and the aging markers Cdkn1a, (PGC)-1α, ERRα, mitochondrial complexes, and medium chain acyl coenzyme A dehydrogenase (MCAD). This shows a significant anti-aging effect on mouse kidneys in this study.[5]

ERRs are also reported to induce autophagy, a process in which a cell digests itself partially. It is commonly believed that this process has regenerative potential, as the cell can get rid of old components through this mechanism. Hence, it has the potential to promote long-term health.[6]

In cell culture of skeletal muscle cells , SLU-PP-332 was reported to increase the mitochondrial function and cellular respiration.[1]

increased metabolic rate of muscle and fat tissue, which could be used to treat metabolic diseases in humans and facilitate weight loss. There are even some benefits of SLU-PP-332 intake over traditional exercise, namely that SLU-PP-332 does not affect food intake, appetite, or impede subsequent exercise initiation.[7] There is also some evidence suggesting SLU-PP-332 could be used as anti-aging compound.

However, there are no studies in humans and no preclinical toxicological studies, which means the safety profile and common side effects of SLU-PP-332 are unknown at the present time. It is very likely however, that studies either on SLU-PP-332 or other promising ERR agonists will be published in the near- and medium-term future.

A recent theoretical paper has postulated SLU-PP-332 may be an effective treatment option for Covid-19, no experimental evidence does exist to support this claim at the present time.[8]

Conclusion

As of now, some beneficial effects of SLU-PP-332 have been observed, particularly in terms of metabolic effects. The administration of SLU-PP-332 to mice (25-50 mg/kg injections twice per day) has shown repeatedly an

References

[1] Billon C, Sitaula S, Banerjee S, Welch R, Elgendy B, Hegazy L, Oh TG, Kazantzis M, Chatterjee A, Chrivia J, et al. Synthetic ERRα/β/γ Agonist Induces an ERRα- Dependent Acute Aerobic Exercise Response and Enhances Exercise Capacity. *ACS Chem Biol.* **2023**;18:756–771. doi: 10.1021/acschembio.2c00720.

[2] Xu W, Billon C, Li H, Nasiotis E, Fu C, Pei L, Wynshaw-Boris A, Burris TP, Zhang L. Abstract 9682: The Cardiac Protective Effects of Novel Synthetic Pan-Estrogen Related Receptor Agonists Slu-pp-332 and Slu-pp-915. *Circulation*. **2021**;144. doi: 10.1161/circ.144.suppl_1.9682.

[3] Xu W, Billon C, Li H, Wilderman A, Qi L, Graves A, Rideb JRDC, Zhao Y, Hayes M, Yu K, et al. Novel Pan-ERR Agonists Ameliorate Heart Failure Through Enhancing Cardiac Fatty Acid Metabolism and Mitochondrial Function. *Circulation*. **2024**;149:227–250. doi: 10.1161/CIRCULATIONAHA.123.066542.

[4] Billon C, Schoepke E, Avdagic A, Chatterjee A, Butler AA, Elgendy B, Walker JK, Burris TP. A Synthetic ERR Agonist Alleviates Metabolic Syndrome. *J Pharmacol Exp Ther.* **2024**;388:232–240. doi: 10.1124/jpet.123.001733.

[5] Wang XX, Myakala K, Libby AE, Krawczyk E, Panov J, Jones BA, Bhasin K, Shults N, Qi Y, Krausz KW, et al. Estrogen-Related Receptor Agonism Reverses Mitochondrial Dysfunction and Inflammation in the Aging Kidney. *Am J Pathol.* **2023**;193:1969– 1987. doi: 10.1016/j.ajpath.2023.07.008.

[6] Losby M, Hayes M, Valfort A, Walker J, Xu W, Zhang L, Billon C, Burris TP. The Estrogen Receptor-Related Orphan Receptors (ERRs) Regulate Autophagy through TFEB.

[7] Nasri H. New hopes on "SLU-PP-332" as an effective agent for weight loss with indirect kidney protection efficacy; a nephrology point of view. *J Ren Endocrinol.* **2024**;10:e25143. doi: 10.34172/jre.2024.25143.

[8] Hagiu B-A. Can SLU-PP-332 be a new drug to prevent COVID-19? *Medical Hypotheses.* **2024**;187:111362. doi: 10.1016/j.mehy.2024.111362.

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