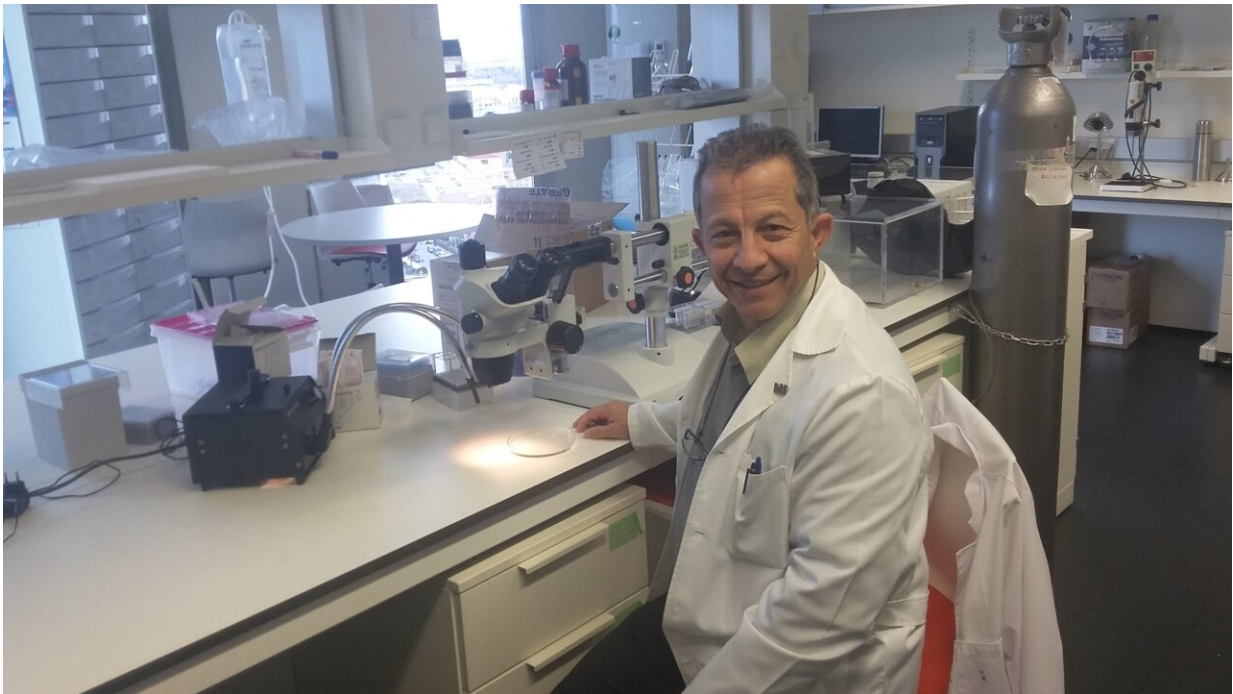


Melatonin shown to protect kidney damage caused by obesity with diabetes

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Dr. Ahmad Agil. Credit: University of Granada

Scientists from the University of Granada (UGR), the Hospital Universitario La Paz (Madrid), and the University of Texas (U.S.) have taken an important step in the fight against kidney damage and its progression toward kidney failure, which is closely related to diabetes (obesity with type 2 diabetes) and its complications.

Specifically, in two new studies recently published in the *Journal of Clinical Medicine* and *Pharmaceuticals*, researchers have developed an obese and diabetic rodent model and have shown that [melatonin](#) protects from [kidney](#) damage caused by diabetes.

The scientists have shown that chronic administration of melatonin at doses (10 mg/kg body weight/day) prevents mitochondrial and endoplasmic reticulum disruption, which play a critical role in the development and pathogenesis of kidney cell (nephron) damage, and its progression to [renal failure](#).

Thus, it has been shown that melatonin prevents the impairment of the function and dynamics of cellular mitochondria, decreasing the increased production of oxygen free radicals (responsible for [oxidative stress](#)). It also prevents pathological alteration in the function of the endoplasmic reticulum (another cell cytoplasmic organelle), which, in conditions of abnormally high oxidative stress, is related to an increase in programmed cell death (of the nephron) leading to the loss of renal functionality, as a preliminary step to the development of renal failure and the need for hemodialysis or transplantation.

The studies coordinated by the UGR show the efficacy of melatonin in halting the progression of renal damage mediated by mitochondrial damage and excess endoplasmic reticulum stress.

As the lead author of this study, Ahmad Agil, a researcher at the Department of Pharmacology of the UGR, says, "Kidney damage is caused by metabolic complications of obesity, such as diabetes, hypertension, blood lipid disorders or fatty liver disease. Given that the prevalence of these pathologies (collectively recognized as metabolic syndrome) continues to increase, kidney damage and its progression over time to [kidney failure](#) has become a health problem that affects millions of people worldwide, with a great socioeconomic cost, requiring

hemodialysis facilities and/or kidney transplant services, with the corresponding compatibility studies required."

The importance of the work lies not only in the efficacy of melatonin in counteracting the two proposed mechanisms of renal damage (based on the alteration of mitochondrial function and dynamics and the function of the endoplasmic reticulum (ER)), but they also propose an alternative preventive treatment that would improve this renal function with a well-studied drug with a very high safety profile such as melatonin, which is a drug that in the EU must be prescribed by a doctor and is already administered in the treatment of insomnia.

The new findings have also been associated with an improvement in [glomerular filtration rate](#) and renal damage of the nephron, manifested in a decrease in creatinine clearance levels (the best marker of renal function), proteinuria, and in the improvement of renal structure, observed after histopathological study of the kidney.

These results are in line with those previously published by these researchers in the last 10 years, demonstrating that the pharmacological administration of melatonin constitutes another new strategy in the therapeutic approach to diabetes (central obesity and its type 2 diabetes) and its complications (such as hepatic steatosis, hypertension, lipid alteration, etc.).

"Our main challenge is the application of melatonin and other strategies such as intermittent fasting in the field of medicine, especially to address the possibility of a treatment perspective for the aforementioned pathologies (diabetes and its complications) that involve an increase in oxidative stress, and mitochondrial damage and associated meta-inflammation (inflammation of metabolic origin)," Agil says.

According to the results, melatonin could help treat [kidney damage](#),

which establishes the need to develop new clinical trials to test its effectiveness in humans. The next step is to investigate how it helps in the maintenance of mitochondrial and endoplasmic reticulum homeostasis, and to a greater extent, if melatonin therapy would allow delaying or stopping progressive renal damage by promoting its chronic pharmacological use in kidney repair and regeneration.

More information: Ahmad Agil et al, Melatonin Improves Mitochondrial Dynamics and Function in the Kidney of Zucker Diabetic Fatty Rats, *Journal of Clinical Medicine* (2020). [DOI: 10.3390/jcm9092916](https://doi.org/10.3390/jcm9092916)

Samira Aouichat et al, Melatonin Improves Endoplasmic Reticulum Stress-Mediated IRE1 α Pathway in Zucker Diabetic Fatty Rat, *Pharmaceuticals* (2021). [DOI: 10.3390/ph14030232](https://doi.org/10.3390/ph14030232)

Provided by University of Granada

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