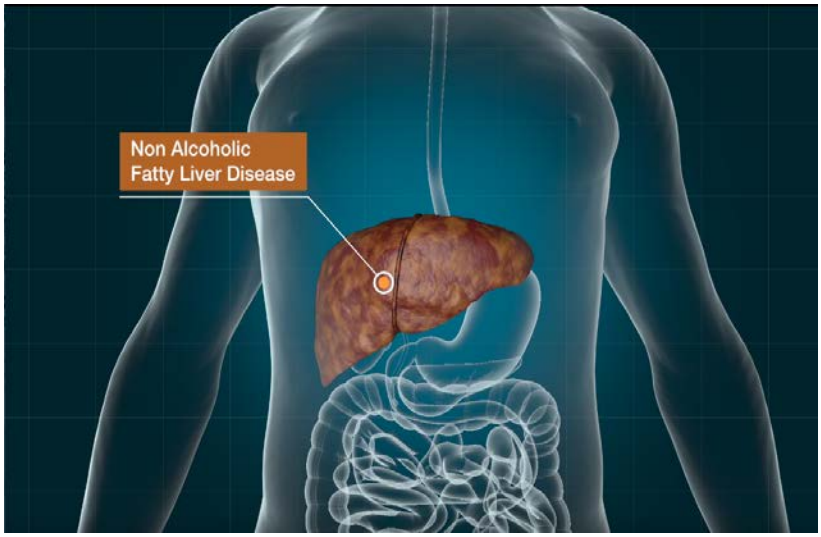
PRESS RELEASE

Modified Parkinson's Drug Shows Potential in Treating Nonalcoholic Fatty Liver Disease

Scientists spur advances in fatty liver disease therapy by modifying an existing neurological drug

Nonalcoholic fatty liver disease (NAFLD) severely impairs the quality of life in patients and often leads to various liver complications. Recently, scientists at Gwangju Institute of Science and Technology designed a novel compound that can potentially treat NAFLD by targeting peripheral serotonin, which regulates lipid metabolism in the liver. They achieved this by structurally modifying an existing neurological drug such that it targets peripheral serotonin by minimizing brain penetration.



Nonalcoholic fatty liver disease (NAFLD) often leads to various liver complications, but there is a lack of drugs for the treatment of NAFLD.

Nonalcoholic fatty liver disease (NAFLD) is a condition characterized by excessive fat accumulation in the liver. It can cause serious complications, including nonalcoholic steatohepatitis, cirrhosis, and cancer. Although prevalent, there is a dearth of drugs to treat NAFLD, with current therapies revolving around lifestyle interventions.

In a recent study published in *Journal of Medicinal Chemistry*, scientists from Gwangju Institute of Science and Technology, Korea, led by Prof Jin Hee Ahn, aimed to find new therapeutic options for NAFLD. Prof Ahn says, "*NAFLD is a serious public health problem worldwide. However, no pharmacological agents have been specifically approved for its treatment yet.*"

For their study, the scientists focused on a well-known neurotransmitter called serotonin. Serotonin is widely known as the "happy" neurotransmitter, and its deficiency in the central nervous system (CNS) can cause various brain disorders. But, not many know that it is also found in the gastrointestinal tract; here, it is called "peripheral" serotonin, which has different functions altogether, such as regulating lipid metabolism in the liver.

In a previous study published in *Nature Communication*, Prof Hail Kim, the co-corresponding author of this study, had investigated peripheral serotonin as a drug target with knockout mice models (mice lacking functional peripheral serotonin). This study reported that these mice showed reduction in liver weight, hepatic lipid accumulation, and hepatic triglyceride content and improved NAFLD activity.

These findings formed the basis of Prof Ahn's study and prompted the research group to identify new peripheral serotonin antagonists. The scientists selected a CNS drug approved for the treatment of Parkinson's, called pimavanserin. Pimavanserin acts as an "antagonist" to serotonin, mimicking its effect in the CNS. The scientists then structurally modified this drug such that it cannot permeate the blood-brain barrier, by adding different types of molecules to it. In this way, they generated an array of novel compounds. On testing these, the scientists found one compound in particular to show promising results: it showed very low blood-brain barrier permeation and thus had the potential to target peripheral serotonin systems.

The scientists tested this compound in obese mice with impaired liver function. Interestingly, the mice showed improvement in symptoms of fatty liver disease, such as improved glucose tolerance. Additionally, their body fat decreased while lean body mass increased. Prof Ahn says, "*Through the chemical optimization of an existing drug, pimavanserin, we identified a new peripheral agent for the possible treatment of NAFLD*."

Although this novel compound is yet to be tested in humans, these findings show that it has remarkable potential in treating fatty liver disease. Optimistic about these findings, Prof Ahn concludes, "*We hope that our novel drug candidate will offer relief to patients bearing the brunt of NAFLD*."

Reference

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About Gwangju Institute of Science and Technology (GIST)

Gwangju Institute of Science and Technology (GIST) is a research-oriented university situated in Gwangju, South Korea. One of the most prestigious schools in South Korea, it was founded in 1993. The university aims to create a strong research environment to spur advancements in science and technology and to promote collaboration between foreign and domestic research programs. With its motto, "A Proud Creator of Future Science and Technology," the university has consistently received one of the highest university rankings in Korea.

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About Prof Jin Hee Ahn

Prof Jin Hee Ahn is a Professor in the Department of Chemistry at Gwangju Institute of Science and Technology (GIST) and the CEO of JD Bioscience. He completed his postdoctoral training at University of California, Berkeley. In 1997, he received his PhD in the Department of Chemistry from Sogang University, Korea. Before joining GIST, Prof Ahn worked in the Drug Discovery Division of Korea Research Institute of Chemical Technology for 16 years. At GIST, his research group is focused on developing new drug candidates for fatty liver diseases. The group also aims to identify new small molecules for the treatment of metabolic diseases such as obesity and diabetes.