PRESS RELEASE

Gwangju Institute of Science and Technology Researchers Discover Novel Drug Candidate to Combat Fatty Liver Disease

*Compound **11c (GM-60106)**, a novel 5HT$_{2A}$ antagonist, paves the way for advancing metabolic liver disease treatment.*

Scientists from Gwangju Institute of Science and Technology in Korea unveil compound 11c, a groundbreaking oral treatment for metabolic dysfunction-associated steatohepatitis. Their research signals a transformative leap in liver disease management, addressing both inflammation and fibrosis. 11c exhibits potent anti-inflammatory and fibrotic effects and remarkable safety attributes in animal models, propelling it to Phase 1 clinical trials by JD Bioscience. A potential game-changer in metabolic disorder treatment, it offers hope in the battle against rising liver diseases.

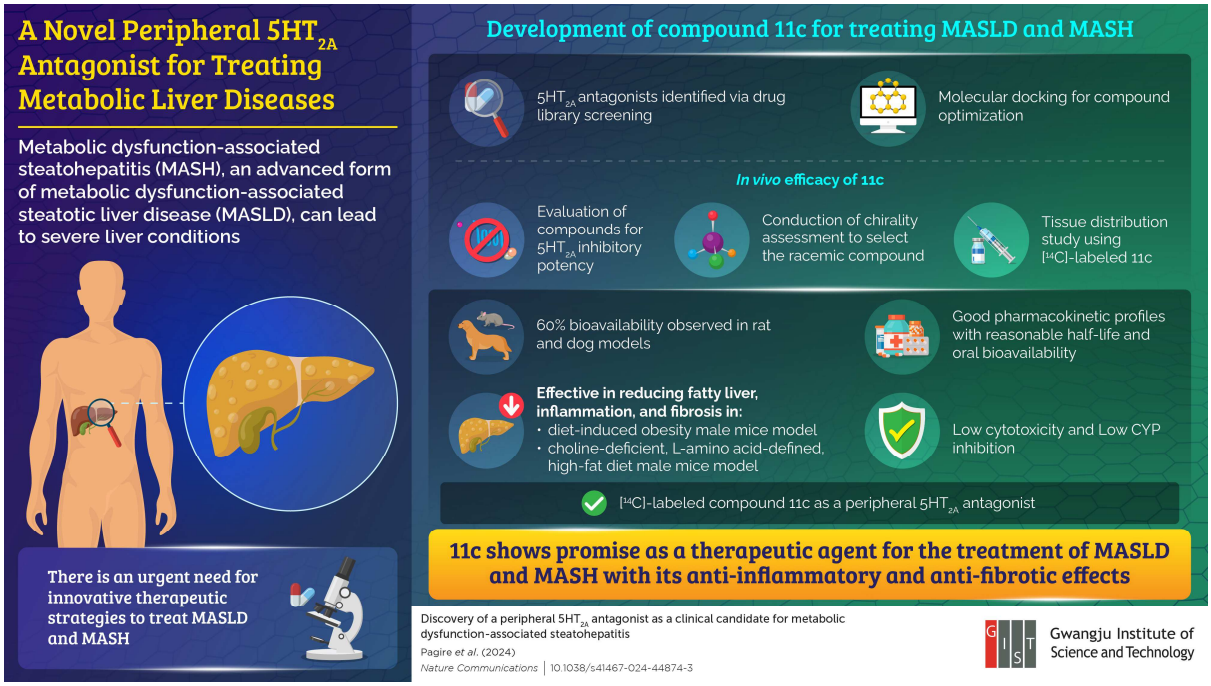

Image Title: A novel peripheral 5HT$_{2A}$ antagonist for treating metabolic liver diseases.
Image Caption: Researchers discovered a compound 11c, a peripheral 5HT2A antagonist, exhibits promising efficacy against metabolic dysfunction-associated steatohepatitis (MASH) and associated liver diseases, offering hope for improved treatment outcomes.
Image Credit: Jin Hee Ahn from GIST, Korea.
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Metabolic dysfunction-associated steatotic liver disease (MASLD) is a burgeoning global health concern, posing a significant threat to public health and escalating the burden on healthcare resources. Characterized by the accumulation of fat in the liver, MASLD increases

the risk of progressing to more severe conditions such as metabolic dysfunction-associated steatohepatitis (MASH), which is marked by inflammation, ballooning, and potential fibrosis.

In response to the pressing need of effective treatments for these metabolic disorders, researchers at the led by Prof. Jin Hee Ahn from Gwangju Institute of Science and Technology (GIST) meticulously developed compound **11c**, a novel peripheral $5HT_{2A}$ antagonist. This research was made available online on January 20, 2024, and was published in *Nature Communications*, highlighting a significant therapeutic breakthrough. The compound showcased a promising profile and demonstrated efficacy in preclinical models, positioning it at the forefront of groundbreaking advancements in the field.

11c exhibits promising attributes, including robust biological activity and a favorable safety profile. Dr. Haushabhau Shivaji Pagire, first author and senior researcher at the Medicinal Chemistry Laboratory at GIST, emphasizes, "*Our meticulous analyses have revealed a significant reduction in inflammatory and fibrosis markers, attesting to the potent anti-inflammatory and fibrotic effect of the compound. This action, targeting both inflammation and fibrosis, is a promising step forward in treating MASH*."

The journey for discovering the compound from drug library screening to its refined form involved the identification of Desloratadine, a peripheral agent, which showed promising inhibitory effects. Molecular docking techniques played a pivotal role in transforming Desloratadine into the potent compound **11c**.

" Based on in vitro, in vivo efficacy, tissue distribution data, DMPK and tox profiles, compound 11c shows promise as a therapeutic agent for the treatment of MASLD and MASH" highlights Prof. Ahn.

Beyond its therapeutic potential, compound **11c** displays an excellent safety profile, exhibiting hepatocyte and plasma stability, minimal cytotoxicity, and low cytochrome P450 inhibition. Noteworthy pharmacokinetic attributes, including over 60% oral bioavailability, position **11c** as a compelling candidate for advancing MASH treatment.

Obesity-associated MASH currently ranks as the third leading cause of liver transplantation and is poised to surpass hepatitis C in this critical medical intervention. Compound **11c**, identified as a promising oral treatment for MASH, holds profound implications for the future landscape of liver disease management. The researchers anticipate a transformative impact, signifying a pivotal advancement in the field.

Completing a successful preclinical study, compound **11c** now stands on the brink of a crucial milestone—the Phase 1 clinical trial. This phase holds the promise to reveal the compound's performance in humans, offering insights that could potentially reshape the treatment landscape for metabolic disorders. The successful outcome of these trials could potentially usher in a paradigm shift in the treatment of metabolic disorders.

In conclusion, **11c** stands as a beacon of hope against the rising tide of metabolic liver diseases. With its promising attributes and the anticipation surrounding the Phase 1 clinical trial, this compound represents a transformative prospect in liver disease management.

Reference

Title of original paper:	Discovery of a peripheral $5HT_{2A}$ antagonist as a clinical candidate for metabolic dysfunction-associated steatohepatitis
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About the Gwangju Institute of Science and Technology (GIST)

The Gwangju Institute of Science and Technology (GIST) was founded in 1993 by the Korean government as a research-oriented graduate school to help ensure Korea's continued economic growth and prosperity by developing advanced science and technology with an emphasis on collaboration with the international community. Since that time, GIST has pioneered a highly regarded undergraduate science curriculum in 2010 that has become a model for other science universities in Korea. To learn more about GIST and its exciting opportunities for researchers and students alike, please visit: http://www.gist.ac.kr/.

About the author

Dr. Haushabhau Shivaji Pagire is a Senior Researcher at the Medicinal Chemistry Laboratory at the Gwangju Institute of Science and Technology, Korea. Simultaneously, he serves as a Principal Scientist at JD Bioscience Inc. Dr. Pagire earned a Master of Science degree from the University of Pune, India and holds a PhD in Medicinal and Pharmaceutical Chemistry from UST and KRICT under the guidance of Prof. Jin Hee Ahn. He completed his postdoctoral training at Prof. Jin Hee Ahn's lab at GIST. His professional journey includes significant roles in global pharmaceutical companies like Glenmark Pharmaceuticals, MacLeod's Pharmaceuticals and Actavis. Currently, his team is dedicated to research on metabolic diseases.