TECHNOLOGY

Compositions and Methods to Evaluate Hepatobiliary/Gastrointestinal Health, Enterohepatic Circulation, and Drug Interactions

OVERVIEW

Summary

The patent describes a novel trifluorinated bile acid analogue, CA-sar-TFMA, designed for use as an imaging probe, diagnostic agent, or contrast agent in evaluating hepatobiliary/gastrointestinal health, enterohepatic circulation, and drug interactions. CA-sar-TFMA's is resistance to bacterial deconjugation and optimized for 19F MRI imaging offer and therefore offers unmatched stability, efficacy, and direct quantification capabilities. This innovation is especially suited in diagnostic imaging for hepatobiliary disorders, non-invasive gastrointestinal health assessments, drug interaction studies, and clinical research on bile acid malabsorption syndromes.

Market

The MRI segment is a dynamic and essential part of the medical imaging industry, currently experiencing significant growth. Valued at USD 1.76 billion in the U.S. in 2023, it's expected to reach USD 2.6 billion by 2030, growing at a compound annual rate of 6.3%.

Advanced MRI technologies, including imaging probes, diagnostic agents, or contrast agents, are crucial for accurately diagnosing and managing a range of conditions. These include non-alcoholic fatty liver disease (NAFLD), chronic liver diseases such as hepatitis and cirrhosis, bile acid malabsorption syndromes, gastrointestinal cancers, Crohn's disease, and irritable bowel syndrome (IBS). These innovations aim to boost diagnostic precision, track disease progression, and evaluate treatment efficacy effectively.

IBS, a widespread disorder affecting the large intestine, is characterized by symptoms like cramping, abdominal pain, and diarrhea. It's estimated to impact 10-15% of the global population, predominantly affecting women and those under 50. Bile acid malabsorption also varies widely in prevalence, often linked to Crohn's disease and sometimes overlooked. An estimated 1% of the adult population may experience primary bile acid diarrhea, a specific form of the condition.

Functional gastrointestinal disorders (FGIDs), now understood as disorders of gut-brain interaction, have a significant presence worldwide, affecting over 40% of the global population. These conditions notably degrade quality of life and healthcare accessibility.

NAFLD, a major global health challenge, affects approximately 25% of the global population, making it the most common chronic liver disease in the U.S., with 80-100 million Americans affected. Its prevalence is mirrored in Asia, with up to 30.3% of Korean adults impacted. The widespread occurrence of NAFLD emphasizes the critical need for advanced diagnostic and therapeutic options.

Technology

The patent in discussion introduces a groundbreaking trifluorinated bile acid analogue, designated as CA-sar-TFMA, innovated to serve as an imaging probe, diagnostic agent, or contrast agent for evaluating hepatobiliary/gastrointestinal health, enterohepatic circulation, and drug interactions.

CA-sar-TFMA is resistant to bacterial deconjugation, a substantial advancement that renders the compound stable in environments where similar agents might degrade. This stability is essential for accurate imaging and quantification in gastrointestinal environments and for maintaining the integrity of the imaging agent during enterohepatic circulation.

The technology utilizes trifluorination, which provides the molecule with three equivalent fluorine atoms. These atoms are pivotal in 19F magnetic resonance imaging (MRI), a modality chosen for its non-invasive nature and its avoidance of ionizing radiation. Unlike hydrogen MRI, 19F MRI does not have an endogenous background signal in biological tissues, enabling a higher signal-to-noise ratio and allowing for the direct quantification of the administered probe.

A notable aspect of the technology is the demonstration of in vitro and in vivo transport properties. CA-sar-TFMA acts as a substrate and inhibitor of sodium-dependent bile acid uptake transporters such as ASBT and NTCP, integral components in bile acid transport. It was shown to accumulate significantly in the gallbladders of mice in higher concentrations than in liver and plasma, and this was quantifiable via 19F MRI.

The primary applications of this technology include non-invasive diagnosis of bile acid malabsorption disorders and potential utility in clinical settings for the assessment of gastrointestinal health, particularly in conditions like idiopathic bile acid malabsorption (I-BAM) and chronic diarrhea predominant irritable bowel syndrome (IBS-D).

The novelty of this patent lies in the chemical structure of CA-sar-TFMA, which has been engineered to achieve a balance between biological compatibility, imaging efficacy, and chemical stability.

References

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Additional Information

Potential Fields of Application:

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  - Diagnostic imaging for hepatobiliary disorders
  - Non-invasive gastrointestinal health assessment
  - Drug interaction studies related to enterohepatic circulation.
  - Clinical research on bile acid malabsorption syndromes

Keywords:

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  - Trifluorinated bile acid analogue
  - 19F MRI imaging probe
  - Hepatobiliary health
  - Gastrointestinal diagnostics

- Enterohepatic circulation
- Bile acid malabsorption

Advantages:

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  - High stability against bacterial deconjugation
  - Effective as both a diagnostic agent and imaging probe
  - No endogenous background signal in 19F MRI
  - Capability for direct quantification of the imaging agent
  - Potential to enhance the diagnosis of gastrointestinal and hepatobiliary conditions

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PATENT STATUS

US 9,597,417 B2

LICENSE STATUS

Available for License

CATEGORIES

- Imaging

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ATTACHMENTS

- Download JP-2014-050 MRI Probe for BAM (Polli).pdf

EXTERNAL RESOURCES

- U.S. Magnetic Resonance Imaging Market Size Report, 2030
- Diagnostic Imaging Market Size, Share & Forecast [2033 Latest]
- • Wang, J.-H. Advances in Pathogenesis and Therapeutics of Hepatobiliary Diseases. Biomedicines 2023, 11,

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