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The Director

of the United States Patent and Trademark Office has received an application for a patent for a new and useful invention. The title and description of the invention are enclosed. The requirements of law have been complied with, and it has been determined that a patent on the invention shall be granted under the law.

Therefore, this United States

Patent

grants to the person(s) having title to this patent the right to exclude others from making, using, offering for sale, or selling the invention throughout the United States of America or importing the invention into the United States of America, and if the invention is a process, of the right to exclude others from using, offering for sale or selling throughout the United States of America, products made by that process, for the term set forth in 35 U.S.C. 154(a)(2) or (c)(1), subject to the payment of maintenance fees as provided by 35 U.S.C. 41(b). See the Maintenance Fee Notice on the inside of the cover.

Katherine Kelly Vidal

DIRECTOR OF THE UNITED STATES PATENT AND TRADEMARK OFFICE



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(12) **United States Patent**
Hsin et al.

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(54) **8-PHENYL-ISOQUINOLINES AND PHARMACEUTICAL COMPOSITION THEREOF USED IN THE TREATMENT OF IRRITABLE BOWEL SYNDROME**

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 612 days.

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C07D 217/04 (2006.01)

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(52) **U.S. Cl.**

CPC **C07D 217/04** (2013.01); **A61P 1/00** (2018.01); **C07D 401/06** (2013.01)

(58) **Field of Classification Search**

CPC **C07D 271/04**; **C07D 401/06**; **A61P 1/00**
 See application file for complete search history.

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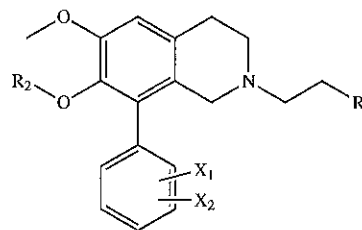
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(57) **ABSTRACT**

A series of 8-phenyl-isoquinoline derivatives (I) exhibit high binding affinity to 5-HT₇ receptor (5-HT₇R) and demonstrate potent antinociceptive activity in two animal models for Irritable Bowel Syndrome (IBS) by intraperitoneal injection (i.p.) or by oral administration (p.o.). These 5-HT₇ receptor antagonists are a new class of therapeutic agents for the treatment of IBS.



8 Claims, 12 Drawing Sheets