



US008048860B2

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

(10) **Patent No.:** **US 8,048,860 B2**
(45) **Date of Patent:** **Nov. 1, 2011**

(54) **BUTANOL EXTRACT OF *BIDENS PILOSA***

(75) Inventors: **Wen-Chin Yang**, Taichung County (TW); **Shu-Lin Chang**, Hsin-Chu (TW); **Lee-Tian Chang**, Taichung (TW); **Yi-Ming Chiang**, Taipei County (TW); **Lie-Fen Shyur**, Nankang (TW)

(73) Assignee: **Academia Sinica**, Taipei (TW)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 382 days.

(21) Appl. No.: **12/263,896**

(22) Filed: **Nov. 3, 2008**

(65) **Prior Publication Data**

US 2009/0062216 A1 Mar. 5, 2009

Related U.S. Application Data

(62) Division of application No. 11/219,503, filed on Sep. 2, 2005, now abandoned.

(51) **Int. Cl.**
A61K 31/7032 (2006.01)
C07G 3/00 (2006.01)
C07H 15/10 (2006.01)

(52) **U.S. Cl.** **514/25**; 536/4.1

(58) **Field of Classification Search** None
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

2007/0053998 A1 3/2007 Yang et al.
2010/0204166 A1* 8/2010 Yang 514/25

FOREIGN PATENT DOCUMENTS

JP 2002205954 7/2002
JP 2004083463 3/2004
WO WO 95/23214 8/1995

OTHER PUBLICATIONS

Machine translation of JP2004-083463, published Mar. 2004, downloaded from www.ipdl.inpit.go.jp.*

Van den Berg et al., "Amelioration of established murine collagen-induced arthritis with anti-IL-1 treatment" *Clin Exp Immunol.* (1994) vol. 95, pp. 237-243.*

"Tolbutamide", downloaded from PubMed Health at <http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0000692/>, revised Jul. 1, 2010.*

Christiansen et al., "Discovery of Potent and Selective Agonists for the Free Fatty Acid Receptor 1 (FFRA1/GPR 40), a Potent Target for the Treatment of Type II Diabetes," *J. Med. Chem.* 61: 7061-7064 (2008).

Ren et al., "Synthesis and Structure-Activity Relationship Study of Antidiabetic Penta-O-Gallyol-D-Dlucopyranose and its Analogurd," *J. Med. Chem.* 49:2829-2837 (2006).

Neogi et al., "Synthesis and Structure-Activity Relationship Studies of Cinnamic Acid-Based Novel Thiazolidinedione Antihyperglycemic Agents," *Bioorganic & Medicinal Chemistry*, 11:4059-4067 (2003).

Kim et al., "Design, Synthesis and Structure-Activity Relationship of Carbamate-Tethered Aryl Propanoic Acids as Novel PPAR Alpha/Gamme Dual Agonists," *Bioorganic & Medicinal Chemistry Letters*, 17:3595-3598 (2007).

Miura et al., "Hypoglycemic Activity and Structure-Activity Relationship of Iridoidal Glycosides," *Bio Pharm. Bull.* 19(1): 160-161 (1996).

Bell, "Type 2 Diabetes Mellitus: What is the Optimal Treatment Regimen?" *The American Journal of Medicine* vol. 116: 23S-29S (2004).

Verspohl, E.J., "Recommended Testing in Diabetes Research," *Planta Med.* 61:581-590 (2002).

Wicksteed et al., "Glucose-Induced Translation Control of Proinsulin Biosynthesis is Proportional to Preproinsulin mRNA Levels in Islet B-Cells But Not Regulated via a Positive Feedback of Secreted Insulin," *The Journal of Biological Chemistry*, vol. 278, 43:42080-42090 (2003).

Henquin, "Perspectives in Diabetes Triggering and Amplifying Pathways of Regulation of Insulin Secretion by Glucose," *Diabetes* 49:1751-1760.

Leibiger et al., "Exocytosis of Insulin Promotes Insulin Gene Transcription via the Insulin Receptor/PI-3 Kinase/p70 s6 kinase and CaM Kinase Pathways," *Molecular Cell*, 1:933-938 (1998).

Oubré et al., "From Plant to Patient: An Ethnomedical Approach to the Identification of New Drugs for the Treatment of NIDDM" *Daibetologia*, 40:614-617 (1997).

Habeck, M., "Diabetes Treatments Get Sweet Help from Nature," *Nature Medicine*, 9:1228 (2003).

Alarcon-Aguilar et al., "Investigation on the hypoglycaemic Effects of Extracts of Four Mexican Medicinal Plants in Normal and Alloxan-diabetic Mice," *Phytotherapy Research*, 16:383-386 (2002).

Krettli et al., "The Search for New Antimalarial Drugs from Plants Used to Treat Fever and Malaria or Plants Randomly (sic) Selected: A Review," *Mem Inst Oswaldo Cruz*, 96(8): 1033-1042 (2001).

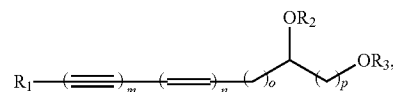
(Continued)

Primary Examiner — Eric S Olson

(74) *Attorney, Agent, or Firm* — Occhiuti Rohlicek & Tsao LLP

(57) **ABSTRACT**

A method of treating a Th1-mediated disorder includes administering to a subject in need of the treatment an effective amount of a compound of the formula I:



wherein R₁ is H, alkyl, aryl, or cyclyl; R₂ is pyranose; R₃ is H or alkyl; m is 2, 3, 4, 5, or 6; n is 0, 1, 2, or 3; o is 0, 1, 2, 3, 4; p is 1, 2, 3, or 4; and the Th1-mediated disorder is non-obese diabetes, Crohn's colitis, autoimmune hemolytic anemia, rheumatoid arthritis, autoimmune encephalitis, multiple sclerosis, or autoimmune myocarditis. Also disclosed is a pharmaceutical composition including a compound of formula I above and a pharmaceutically acceptable carrier.

17 Claims, No Drawings