

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
26 June 2003 (26.06.2003)

PCT

(10) International Publication Number
WO 03/051348 A2

(51) International Patent Classification⁷: **A61K 31/132**,
A61P 25/28

(21) International Application Number: PCT/US02/40732

(22) International Filing Date:
18 December 2002 (18.12.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
10/017,235 18 December 2001 (18.12.2001) US

(63) Related by continuation (CON) or continuation-in-part
(CIP) to earlier application:
US 10/017,235 (CIP)
Filed on 18 December 2001 (18.12.2001)

(71) Applicant and

(72) Inventor: **MURPHY, Michael, A.** [US/US]; 5619
Chelsea Avenue, La Jolla, CA 92037 (US).

(74) Agents: **CHARMASSON, Henri, J., A.** et al.; 1545 Hotel
Circle South, Suite 150, San Diego, CA 92108-3426 (US).

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,
CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG,
SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZM, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM,
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK,
TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, ML, MR, NE, SN, TD, TG).

Published:

— without international search report and to be republished
upon receipt of that report

*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

(54) Title: COMPOSITION, SYNTHESIS AND THERAPEUTIC APPLICATIONS OF POLYAMINES

(57) **Abstract:** This invention relates to a process of synthesis and composition of open chain (ring), closed ring, linear branched and or substituted polyamines, polyamine derived tyrosine phosphatase inhibitors and PPAR partial agonists/partial antagonists via a series of substitution reactions and optimizing the bioavailability and biological activities of the compounds. Polyamines prevent the toxicity of neurotoxins and diabetogenic toxins including paraquat, methyphenyl pyridine radical, rotenone, diazoxide, streptozotocin and alloxan. These polyamines can be to treat neurological, cardiovascular, endocrine acquired and inherited mitochondrial DNA damage diseases and other disorders in mammalian subjects, and more specifically to the therapy of Parkinson's disease, Alzheimer's disease, Lou Gehrig's disease, Binswanger's disease, Olivopontine Cerebellar Degeneration, Lewy Body disease, Diabetes, Stroke, Atherosclerosis, Myocardial Ischemia, Cardiomyopathy, Nephropathy, Ischemia, Glaucoma, Presbycusis, Cancer, Osteoporosis, Rheumatoid Arthritis, Inflammatory Bowel Disease, Multiple Sclerosis and as Antidotes to Toxin Exposure.



WO 03/051348 A2