藥科二 --- scifinder & innovation 報告 b303098200 潘姿瑜

Scifinder

主題:Prozac

Task Began December 12, 2011 08:01 PM

Explore references by research topic: prozac

Candidates Selected (ID 3)

715 references were found containing "prozac" as entered.

Answer Type: *Answers*

Result Count: *715*

Detailed display

From ID: 3

Type: Pharmaceuticals as neuroendocrine disruptors: lessons learned from fish on Prozac

1. Pharmaceuticals as neuroendocrine disruptors: lessons learned from fish on Prozac

By: Mennigen, Jan A.; Stroud, Pamela; Zamora, Jake M.; Moon, Thomas W.; Trudeau, Vance L.

Source: Journal of Toxicology and Environmental Health, Part B: Critical Reviews, Volume: 14, Issue: 5-7, Pages: 387-412, Journal; General Review; Online Computer File, 2011, CODEN: JTECFR, ISSN: 1093-7404, DOI: 10.1080/10937404.2011.578559

Company/Organization: Centre for Advanced Research in Environmental Genomics and Department of Biology, University of Ottawa, Ottawa, ON, Can.

Accession Number: 2011:1378276, CAN 155:633530, CAPLUS

Publisher: Taylor & Francis, Inc.

Language: English

Abstract

A review. Pharmaceuticals are increasingly detected in a variety of aquatic systems. One of the most prevalent environmental pharmaceuticals in North America and Europe is the antidepressant fluoxetine, a selective serotonin reuptake inhibitor (SSRI) and the active ingredient of Prozac. Usually detected in the range below 1 μg/L, fluoxetine and its active metabolite norfluoxetine are found to bioaccumulate in wild-caught fish, particularly in the brain. This has raised concerns over potential disruptive effects of neuroendocrine function in teleost fish, because of the known role of serotonin (5-HT) in the modulation of diverse physiol. processes such as reprodn., food intake and growth, stress and multiple behaviors. This review describes the evolutionary conservation of the 5-HT transporter (the therapeutic target of SSRIs) and reviews the disruptive effects of fluoxetine on several physiol. endpoints, including involvement of neuroendocrine mechanisms. Studies on the goldfish, Carassius auratus, whose neuroendocrine regulation of reprodn. and food intake are well characterized, are described and represent a reliable model to study neuroendocrine disruption. In addn., fish studies investigating the effects of fluoxetine, not only on reprodn. and food intake, but also on stress and behavior, are discussed to complement the emerging picture of neuroendocrine disruption of physiol. systems in fish exposed to fluoxetine. Environmental relevance and key lessons learned from the effects of the antidepressant fluoxetine on fish are highlighted and may be helpful in designing targeted approaches for future risk assessments of pharmaceuticals disrupting the neuroendocrine system in general.

Indexing

Toxicology (Section 4-0)

Section cross-reference(s): 61

Concepts

Drugs

Fish

Neuroendocrine system

Water pollution

pharmaceuticals as neuroendocrine disruptors in fish

Endocrine disrupting chemicals

pharmaceuticals as neuroendocrine disruptors in fishAdverse effect, including toxicity; Pollutant; Biological study; Occurrence

Supplementary Terms

review; pharmaceutical; endocrine; disruptor; neuroendocrine; system; fish; water; pollution;

5. Pharmacokinetics of Fluoxetine in Rhesus Macaques following Multiple Routes of Administration

By: Sawyer, E. K.; Howell, L. L.

Source: Pharmacology, Volume: 88, Issue: 1-2, Pages: 44-49, Journal, 2011, CODEN: PHMGBN, ISSN: 0031-7012, DOI: 10.1159/000329417

Company/Organization: Neuroscience Program, Emory University, Atlanta, GA, USA

Accession Number: 2011:1160760, CAPLUS

Publisher: S. Karger AG

Language: English

Abstract

Background/Aims: Fluoxetine (Prozac) is a selective serotonin reuptake inhibitor currently used to treat depression and mood disorders. It has been widely studied clin. and preclinically, yet there is limited knowledge of its pharmacokinetics in nonhuman primates. Methods: The present study characterized the pharmacokinetics of fluoxetine and its active metabolite norfluoxetine in rhesus macaques following both acute (1, 3, 5.6 and 10 mg/kg) and chronic doses (5.6 and 10 mg/kg/day) via different routes of administration (i.v., s.c., i.m., and oral). Blood samples were collected at multiple time points following administration and analyzed using mass spectrometry. Results: Fluoxetine had a half-life of 11-16 h and norfluoxetine had a half-life of 21-29 h. Potentially functionally significant serum concns. of norfluoxetine were present at 24 h even after a single administration of fluoxetine. Similar to observations in humans under steady state conditions, norfluoxetine accounted for the greater percentage of active drug in the blood stream. Conclusion: A daily dose of 10 mg/kg administered orally maintained serum concns. in the human clin. range over the course of 6 wk. Given the long half-lives of fluoxetine and norfluoxetine obsd. in this study, precautions should be taken when designing preclin. studies to prevent accumulation of drug serum concns.

Indexing

Pharmacology (Section 1)

22. Selective serotonin reuptake inhibitors for the treatment of depression

By: Childers, Wayne E., Jr.; Rotella, David P.

Source: Analogue-Based Drug Discovery II, Pages: 269-295, Conference; General Review, 2010, CODEN: 69NXYP, ISBN: 978-3-527-32549-8

Company/Organization: Wyeth Research, Chemical Sciences, Monmouth Junction, NJ, USA, 08852

Accession Number: 2011:307883, CAN 155:579526, CAPLUS

Publisher: Wiley-VCH Verlag GmbH & Co. KGaA

Language: English

Abstract

A review. Selective serotonin reuptake inhibitors (SSRI) are most widely used for the treatment of depression. Approved agents in this class include fluoxetine (Prozac), sertraline (Zoloft), paroxetine (Paxil), escitalopram (Lexapro), the active isomer of racemic citalopram that was approved initially, and fluvoxamine (Luvox, approved in the EU only). These compds. act by elevating levels of the neurotransmitter serotonin in regions of the brain that influence mood and represent a potentially useful symptomatic approach for the treatment of depression. Even though all these compds. share a common mechanism of action, there are features about specific members of the group that allow researchers and clinicians distinguish between them. The potency and secondary receptor selectivity profiles of these agents are also different and can play a role in efficacy and adverse event profiles. The array of different serotonin receptors, their role in the expression of SSRI activity, and the selectivity profile of each SSRI at these receptors differ. The opportunity for wide structural variation, coupled with the unmet medical need in the treatment of depression, has stimulated a substantial medicinal chem. effort to discover compds. with this activity, as well as novel org. chem. approaches to these important mols. This chapter will summarize the published structure-activity relationships for each of the com. available SSRIs, mechanism of action studies, preclin. and clin. pharmacol., and a survey of other potential uses for SSRIs.

26. Fluoxetine exerts age-dependent effects on behavior and amygdala neuroplasticity in the rat

By: Homberg, Judith R.; Olivier, Jocelien D. A.; Blom, Tom; Arentsen, Tim; van Brunschot, Chantal; Schipper, Pieter; Korte-Bouws, Gerdien; van Luijtelaar, Gilles; Reneman, Liesbeth

Source: PLoS One, Volume: 6, Issue: 1, Pages: e16646, Journal; Online Computer File, 2011, CODEN: POLNCL, ISSN: 1932-6203, DOI: 10.1371/journal.pone.0016646

Company/Organization: Department of Cognitive Neuroscience, Centre for Neuroscience, Donders Institute for Brain, Cognition, and Behaviour, Radboud University Nijmegen Medical Centre, Nijmegen, Neth.

Accession Number: 2011:192200, CAN 155:320922, CAPLUS

Publisher: Public Library of Science

Language: English

Abstract

The selective serotonin reuptake inhibitor (SSRI) Prozac (fluoxetine) is the only registered antidepressant to treat depression in children and adolescents. Yet, while the safety of SSRIs has been well established in adults, serotonin exerts neurotrophic actions in the developing brain and thereby may have harmful effects in adolescents. Here we treated adolescent and adult rats chronically with fluoxetine (12 mg/kg) at postnatal day (PND) 25 to 46 and from PND 67 to 88, resp., and tested the animals 7-14 days after the last injection when (nor)fluoxetine in blood plasma had been washed out, as detd. by HPLC. Plasma (nor)fluoxetine levels were also measured 5 h after the last fluoxetine injection, and matched clin. levels. Adolescent rats displayed increased behavioral despair in the forced swim test, which was not seen in adult fluoxetine treated rats. In addn., beneficial effects of fluoxetine on wakefulness as measured by electroencephalog. in adults was not seen in adolescent rats, and age-dependent effects on the acoustic startle response and prepulse inhibition were obsd. On the other hand, adolescent rats showed resilience to the anorexic effects of fluoxetine. Exploratory behavior in the open field test was not affected by fluoxetine treatment, but anxiety levels in the elevated plus maze test were increased in both adolescent and adult fluoxetine treated rats. Finally, in the amygdala, but not the dorsal raphe nucleus and medial prefrontal cortex, the no. of PSA-NCAM (marker for synaptic remodeling) immunoreactive neurons was increased in adolescent rats, and decreased in adult rats, as a consequence of chronic fluoxetine treatment. No fluoxetine-induced changes in 5-HT1A receptor immunoreactivity were obsd. In conclusion, we show that fluoxetine exerts both harmful and beneficial age-dependent effects on depressive behavior, body wt. and wakefulness, which may relate, in part, to differential fluoxetine-induced neuroplasticity in the amygdala.

聽完 Scifinder 檢索平台的介紹後，覺得 Scifinder 是一個可以提供全面即時且具有權威性的平台，利用 Scifinder，除了可以找到分子的結構式和物化性質的基本介紹外，也可以找到可行及適當合成的方法，而在藥物方面，除了藥物的作用分類和基本性質外，Scifinder 也提供了藥物在許多臨床上不同試驗中的資料，我想這樣全面且方便的平台，不論對於一個是在開發中的新藥，亦或是企圖改良成人體可用率更高的的新劑型，都提供了一個相當快速且具有權威性的資料檢索方式。

THOMSON Innovation

主題:**Prozac**

Bibliography

DWPI Title

New tetralone based amine derivatives useful for treating a central nervous system disorders e.g. as depression, fibromyalgia, pain and attention deficit hyperactivity disorder

Original Title

Tetralone-based monoamine reuptake inhibitors

Assignee/Applicant

Standardized: SUNOVION PHARMACEUTICALS INC

Original: Sunovion Pharmaceuticals Inc., Marlborough, MA, US

Inventor

Shao Liming, Lincoln, MA, US Wang Fengjiang, Northborough, MA, US Malcolm Scott Christopher, Southborough, MA, US Hewitt Michael Charles, Somerville, MA, US Bush Larry R., Worcester, MA, US Varney Mark A., Laguna Niguel, CA, US Campbell Una, Marlborough, MA, US Engel Sharon Rae, Hudson, MA, US Hardy Larry Wendell, Sturbridge, MA, US Koch Patrick, Marlborough, MA, US Ma Jianguo, Natick, MA, US

Publication Date (Kind Code)

2011-11-08 (B2)

Application Number / Date

US2006643190A / 2006-12-21

Priority Number / Date / Country

US2006756555P / 2006-01-06 / US

US2006643190A / 2006-12-21 / US

Abstract

Abstract

The invention relates to novel tetralone based amines and their use in the treatment of central nervous system (CNS) disorders, such as depression, attention deficit hyperactivity disorder (ADHD) and Parkinson's disease. The invention further relates to pharmaceutical compositions containing the compounds and compositions of the invention as well as methods of inhibiting reuptake of one or more monoamine, such as such as dopamine and norepinephrine, from the synaptic cleft, and methods of modulating one or more monoamine transporter.

Classes/Indexing

IPC

Current IPC	Invention	Version	Additional	Version
Full	C07C 211/42 A61K 31/133 A61K 31/135	20060101 20060101 20060101	-	-
Main Group	-	-	-	-
Subclass	-	-	-	-

Original IPC	Invention	Version	Additional	Version
Advanced/Full	C07C 211/42 A61K 31/133 A61K 31/135	20060101 20060101 20060101	-	-
Core/Main Group	-	-	-	-
Subclass	-	-	-	-

ECLA

C07C 211/42 C07C 17/16+22/04 C07C 17/16+25/22 C07C 17/35+25/22 C07C 45/38+47/453 C07C 45/52+49/67 C07C 45/63+49/697 C07C 45/67+49/755 C07C 45/67+49/255 C07C 45/68+49/67 C07C 45/68+49/697 C07C 45/74+49/683 C07C 45/74+49/755 C07C 45/74+49/697 C07C 211/29 C07C 215/44 C07C 217/74 M07C 102/10

US Class

Current:

564/308; 564/428; 564/454; 564/456; 560/028; 514/510; 514/647; 514/657

Original:

564/308; 564/428; 564/454; 564/456; 560/028; 514/510; 514/647; 514/657

Field Of Search: -

Locarno Class

-

Legal Status

INPADOC Legal Status

Gazette Date	Code	Description
2011-01-26	AS	ASSIGNMENT SUNOVION PHARMACEUTICALS INC., MASSACHUSETTS CHANGE OF NAME ASSIGNOR:SEPRACOR INC. REEL/FRAME:025699/0042 2010-10-12
2007-04-23	AS	ASSIGNMENT SEPRACOR INC., MASSACHUSETTS ASSIGNMENT OF ASSIGNORS INTEREST ASSIGNORS:SHAO, LIMING WANG, FENGJIANG MALCOLM, SCOTT CHRISTOPHER AND OTHERS SIGNING DATES FROM 20070417 TO 20070420 REEL/FRAME:019196/0084
2007-04-23	AS	ASSIGNMENT SEPRACOR INC., MASSACHUSETTS ASSIGNMENT OF ASSIGNORS INTEREST ASSIGNORS:SHAO, LIMING WANG, FENGJIANG MALCOLM, SCOTT CHRISTOPHER AND OTHERS REEL/FRAME:019196/0084 SIGNING DATES FROM 20070417 TO 20070420

Claims

Claims

1. A compound having a structure, which is selected from Formula (II), Formula (III), and Formula (IV), or a pharmaceutically acceptable salt thereof:

wherein

n is an integer selected from 0 to 2;

D is CX—Ar1;

m is an integer selected from 0 to 6;

each X is independently selected from H, halogen, CN, OR5, SR5, S(O)2R5, NR6R7, NR6S(O)2R5, NR6C(O)R5, acyl, ═X1, substituted or unsubstituted alkyl except CF3, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, and substituted or unsubstituted heterocycloalkyl,

wherein

X1 is selected from O, S, and NOR5′ wherein R5′ is selected from H, substituted or unsubstituted alkyl, and substituted or unsubstituted heteroalkyl;

each R5, R6 and R7 is independently selected from H, acyl, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or

unsubstituted aryl, and substituted or unsubstituted heteroaryl,
wherein two of R 5, R6 and R7, together with the atoms to which they are attached, are optionally joined to form a 3- to 7-membered ring;
Ar1 is

wherein
Y and Z are each independently Cl, CF3, or CN;
V and W are independently selected from H, halogen, CF3, CN, OR9, SR9, S(O)2R9, NR10R11, NR10S(O)2R9, NR10C(O)R9, acyl, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, and substituted or unsubstituted heterocycloalkyl, or
V and W, together with the atoms to which they are attached, are joined to form a 5- to 7-membered ring;
wherein each R9, R10, and R11 is independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, and substituted or unsubstituted heterocycloalkyl;
wherein any two of R9, R10, and R11, together with the atoms to which they are attached, are optionally joined to form a 3- to 7-membered ring;
each R1 and R2 is independently selected from H, halogen, CN, CF3, OR12, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, and substituted or unsubstituted heterocycloalkyl,
wherein
R12 is selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, and substituted or unsubstituted heterocycloalkyl;
R3 and R4 are independently selected from H, OR13, acyl, S(O)2R14, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, and substituted or unsubstituted heterocycloalkyl,
wherein
R13 is selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, and substituted or unsubstituted heterocycloalkyl;
R14 is selected from substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl, substituted or unsubstituted

heteroaryl, and substituted or unsubstituted heterocycloalkyl; and
wherein at least two of R1, R2, R3 and R4, together with the atoms to which they are attached, are optionally joined to form a 3- to 7-membered ring,

and any enantiomer, diastereoisomer, racemic mixture, enantiomerically enriched mixture, and enantiomerically pure form thereof

Claims (English)
What is claimed is:
1. A compound having a structure, which is selected from Formula (II), Formula (III), and Formula (IV), or a pharmaceutically acceptable salt thereof:
wherein
n is an integer selected from 0 to 2;
D is CX—Ar1;
m is an integer selected from 0 to 6;
each X is independently selected from H, halogen, CN, OR5, SR5, S(O)2R5, NR6R7, NR6S(O)2R5, NR6C(O)R5, acyl, ═X1, substituted or unsubstituted alkyl except CF3, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, and substituted or unsubstituted heterocycloalkyl,
wherein
X1 is selected from O, S, and NOR5′ wherein R5′ is selected from H, substituted or unsubstituted alkyl, and substituted or unsubstituted heteroalkyl;
each R5, R6 and R7 is independently selected from H, acyl, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl,
wherein two of R 5, R6 and R7, together with the atoms to which they are attached, are optionally joined to form a 3- to 7-membered ring;
Ar1 is

wherein
Y and Z are each independently Cl, CF3, or CN;
V and W are independently selected from H, halogen, CF3, CN, OR9, SR9, S(O)2R9, NR10R11, NR10S(O)2R9, NR10C(O)R9, acyl, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, and substituted or unsubstituted heterocycloalkyl, or
V and W, together with the atoms to which they are attached, are joined to form a 5- to 7-membered ring;

wherein each R9, R10, and R11 is independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, and substituted or unsubstituted heterocycloalkyl;
wherein any two of R9, R10, and R11, together with the atoms to which they are attached, are optionally joined to form a 3- to 7-membered ring;
each R1 and R2 is independently selected from H, halogen, CN, CF3, OR12, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, and substituted or unsubstituted heterocycloalkyl,
wherein
R12 is selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, and substituted or unsubstituted heterocycloalkyl;
R3 and R4 are independently selected from H, OR13, acyl, S(O)2R14, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, and substituted or unsubstituted heterocycloalkyl,
wherein
R13 is selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, and substituted or unsubstituted heterocycloalkyl;
R14 is selected from substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, and substituted or unsubstituted heterocycloalkyl; and
wherein at least two of R1, R2, R3 and R4, together with the atoms to which they are attached, are optionally joined to form a 3- to 7-membered ring,

and any enantiomer, diastereoisomer, racemic mixture, enantiomerically enriched mixture, and enantiomerically pure form thereof

2. The compound of claim 1, wherein said compound is chiral.

3. The compound of claim 1, having a structure, which is selected from:

4. A composition comprising a first stereoisomer and at least one additional stereoisomer of a compound of claim 1, wherein said first stereoisomer is present in a diastereomeric excess of at least 80% relative to said at least one additional stereoisomer.

5. A pharmaceutical composition comprising a compound of claim 1, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable

carrier, vehicle or diluent.

6. A method for treating a central nervous system disorder, said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound of claim 1, or a pharmaceutically acceptable salt thereof.

7. The method of claim 6, wherein said central nervous system disorder is selected from depression, fibromyalgia, pain, sleep apnea, attention deficit disorder (ADD), attention deficit hyperactivity disorder (ADHD), restless leg syndrome, schizophrenia, anxiety, obsessive compulsive disorder, post-traumatic stress disorder, seasonal affective disorder (SAD), premenstrual dysphoria, and a neurodegenerative disease.

8. The method of claim 6, wherein said central nervous system disorder is Parkinson's disease.

9. The method of claim 6, wherein said central nervous system disorder is neuropathic pain.

10. A method of inhibiting reuptake of one or more monoamines from the synaptic cleft, said method comprising administering to a mammalian subject a compound of claim 1, or a pharmaceutically acceptable salt thereof.

11. The method of claim 10, wherein said monoamine is selected from serotonin, dopamine, and norepinephrine, or any combination thereof.

12. A method of modulating one or more monoamine transporters, said method comprising administering to a mammalian subject a compound of claim 1, or a pharmaceutically acceptable salt thereof

13. The method of claim 12, wherein said monoamine transporter is selected from serotonin transporter (SERT), dopamine transporter (DAT), and norepinephrine transporter (NET), or any combination thereof

14. The compound of claim 1, wherein Y and Z are both Cl.

15. The compound of claim 14, wherein R3 and R4 are independently H or substituted or unsubstituted C1-C4 alkyl.

16. The compound of claim 14, wherein m is 1, and X is H or OR5.

17. The compound of claim 14, wherein m is 1, X is H or OR5, and R3 and R4 are independently H or substituted or unsubstituted C1-C4 alkyl.

18. The compound of claim 17, wherein R5 is H.

19. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is:

and any enantiomer, diastereoisomer, racemic mixture, enantiomerically enriched mixture, and enantiomerically pure form thereof.

20. A pharmaceutical composition comprising a compound of claim 19, or a

pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, vehicle or diluent.

21. The compound of claim 3, wherein Y and Z are both Cl.

22. The compound of claim 21, wherein m is 1, X is H or OR5, and R3 and R4 are independently H or substituted or unsubstituted C1-C4 alkyl.

23. The compound of claim 22, wherein R5 is H.

Other

Examiner

Davis, Brian J

Related Applications

Parent/Child	Application Number	Filed Date	Publication Number	Publication Date	Type of Relationship	Status
P	US2006756555P	2006-01-06	-	-	Provisional	-
P	US200664319 0A	2006-12-21	US20070197588A1	2007-08-23	Related publication	-

Parent Case

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