ACS Medicinal Chemistry Letters

Patent Highlight

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Multifunctional Radical Quenchers for the Treatment of Mitochondrial Dysfunction

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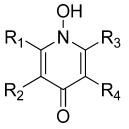
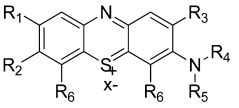
Title:	Multifunctional Radical Quenchers for the Treatment of Mitochondrial Dysfunction		
Patent/Patent Application Number:	WO 2012138713 A2	**Publication Date:**	October 11, 2012
Priority Application:	US 2011-471346P	**Priority Date:**	April, 4, 2011
Inventors:	Hecht, S.; Khdour, O.; Chowdhury, S. R.; Talukder, P.		
Assignee Company:	Arizona State University, United States		
Disease Area:	Mitochondrial disorders, neurodegenerative disease	**Mechanism of Action:**	Quench reactive oxygen species (ROS), augment ATP production

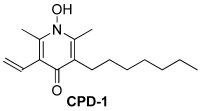
Summary: This invention provides a series of compounds as multifunctional radical quenchers. This class of compounds is useful for the treatment or suppression of diseases associated with decreased mitochondrial function resulting in ATP production and/or oxidative stress. In addition, such compounds may mitigate the effect of aging.

Important Compound Classes:

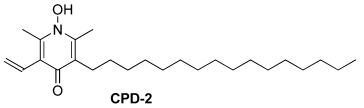




Key Structures:



CPD-1



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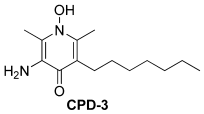

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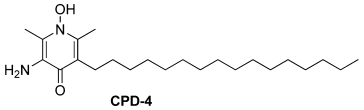

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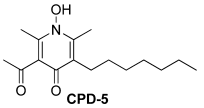

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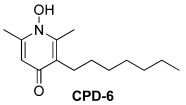

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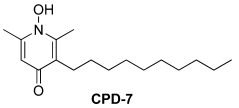

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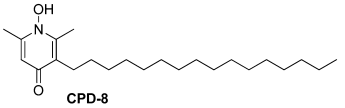

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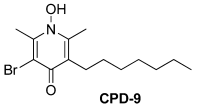

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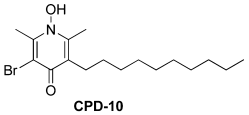

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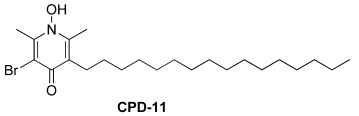

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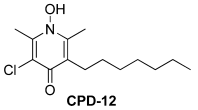

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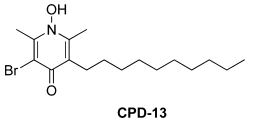

CPD-13

Recent Review Articles:

1. Davis, R. E.; Williams, M. Mitochondrial function and dysfunction: an update. *J. Pharm. Exp. Ther.* **2012**, *342* (3), 598−607.

2. Soustiel, J. F.; Zaaroor, M. Mitochondrial targeting for development of novel drug strategies in brain injury. *Cent. Nerv. Syst. Agents Med. Chem.* **2012**, *12* (2), 131−145.

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3. Mathew, B. B.; Tiwari, A.; Jatawa, S. K. Free radicals and antioxidants: a review. *J. Pharm. Res.* **2012**, *4* (12), 4340−4343.

Biological Assays (Description): Compounds have been evaluated in a series of in vitro assays:

- Lipid peroxidation assay
- Mitochondrial membrane potential assay
- Trypan Blue Cell viability assay ok
- Cell viability assay ok

Pharmacological Data: NADH oxidase inhibition assay

NADH oxidase inhibition assay

	NADH oxidase (complex I, III, IV) activity (%)	
	5 μM	**1 μM**
CPD-1	20.7 +/- 2.2	29.7 +/- 3.8
CPD-2	12 +/- 0.8	20.1 +/- 1.4
CPD-3	76.7 +/- 6.9	92.9 +/- 10.9
CPD-4	12.7 +/- 1.7	17.1 +/- 1
CPD-5	44.5 +/- 3.6	74.5 +/- 6.9

Lipid peroxidation suppression assay

	Scavenging activity (%)	
	5 μM	**1 μM**
Untreated control	100	100
Treated control	0	0
CPD-1	0	0
CPD-2	13 +/- 4.2	7 +/- 2.8
CPD-3	9.6 +/- 2.8	14 +/- 4.1
CPD-4	94 +/- 0.2	18 +/- 2.2
CPD-5	2.2 +/- 2.3	11 +/- 1.8
CPD-6	0	0
CPD-7	0	0
CPD-8	20 +/- 3.4	10 +/- 4.3
CPD-9	0	0
CPD-10	0	0
CPD-11	15 +/- 3.3	7 +/- 2.3
CPD-12	0	0
CPD-13	0	0

Claims: Claims 8, 12−16: Use of compounds for the treatment of Friedreich's ataxia, Kearns−Sayre syndrome, Huntingtons's disease, Alzheimer's disease, Parkinson's disease

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Notes

The author declares no competing financial interest.