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(54) **6-MERCAPTO-CYCLODEXTRIN DERIVATIVES:REVERSAL AGENTS FOR DRUG-INDUCED NEUROMUSCULAR BLOCK**

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A61K 31/452	(2006.01)
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USPC **514/58**; 514/231.5; 514/316; 514/547; 536/103

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

(56) **References Cited**

U.S. PATENT DOCUMENTS

3,929,813	A		12/1975	Higuchi et al.
4,599,327	A		7/1986	Nogradi
4,603,123	A		7/1986	Chiesi
4,727,064	A		2/1988	Pitha
4,816,462	A		3/1989	Nowicky
4,834,985	A		5/1989	Elger
4,869,904	A		9/1989	Uekama
4,983,586	A		1/1991	Bodor
4,983,636	A		1/1991	Takeuchi
5,002,935	A		3/1991	Bodor
5,008,386	A		4/1991	Szabo
5,017,566	A		5/1991	Bodor
5,180,716	A		1/1993	Yaksh et al.
5,250,520	A	*	10/1993	Kurita et al. 514/58
5,385,891	A		1/1995	Moriya et al.
5,767,112	A		6/1998	Poll et al.
5,834,446	A	*	11/1998	Dow et al. 514/58
5,840,881	A		11/1998	Uda et al.
5,935,941	A		8/1999	Pitha
6,670,340	B1		12/2003	Akzo
6,949,527	B2		9/2005	Akzo
7,026,304	B2		4/2006	Zhang et al.
7,265,099	B1		9/2007	Organon
2002/0111377	A1		8/2002	Stinchcomb
2002/0173550	A1		11/2002	Calignano
2004/0029833	A1		2/2004	Zhang

FOREIGN PATENT DOCUMENTS

AU	36628 95		9/1996
EP	0197571		4/1986
EP	0 447 171	A	9/1991
EP	0447 171	B1	2/1994
EP	0465535		3/1998
JP	11-246603		9/1999
WO	WO9200331		1/1992
WO	WO 97/17977	*	5/1997

(Continued)

OTHER PUBLICATIONS

Baer, H. et al "Heptakis[6-S-(2,3-dihydroxypropyl)-6-thio]cyclomaltoheptaose . . ." Carbohyd. Res. (1996) vol. 280, pp. 315-321.*

(Continued)

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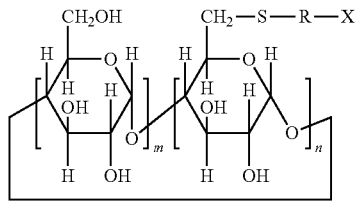
(57) **ABSTRACT**

Disclosed is a 6-mercapto-cyclodextrin derivative having general formula (I) wherein m is 0-7 and n is 1-8 and m+n=7 or 8; R is (C_{1-6})alkylene, optionally substituted with 1-3 OH groups, or $(CH_2)_o$-phenylene-$(CH_2)_p$—; o and p are independently 0-4; X is COOH, $CONHR_1$, $NHCOR_2$, SO_2OH, $PO(OH)_2$, $O(CH_2—CH_2—O)_q$—H, OH or tetrazol-5-yl; R_1 is H or (C_{1-3})alkyl; R_2 is carboxyphenyl; q is 1-3; or pharmaceutically acceptable salts thereof. The 6-mercaptocyclodextrin derivative is highly suitable for use in the reversal of drug-induced neuromuscular block.

(I)



21 Claims, No Drawings