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(54) **TWO PHASE BIOACTIVE FORMULATIONS OF BIS-QUATERNARY PYRIDINIUM OXIME SULFONATE SALTS**

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CPC A61K 31/4425; A61K 47/06
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

2,305,947 A 12/1942 Armstrong
2,816,113 A 12/1957 Wilson
3,135,761 A * 6/1964 Hackley, Jr. et al. 546/264
3,137,702 A 6/1964 Luttringhaus
3,629,425 A 12/1971 Hussain
3,929,813 A 12/1975 Higuchi et al.
4,128,651 A 12/1978 Hagedorn
4,305,947 A 12/1981 Bartner
4,540,602 A 9/1985 Motoyama et al.
4,705,777 A 11/1987 Lehrer et al.
4,880,610 A 11/1989 Constantz
5,130,438 A 7/1992 Hsiao et al.
5,145,684 A 9/1992 Liversidge et al.
5,298,504 A 3/1994 Sommer et al.
5,589,167 A 12/1996 Cleland

(Continued)

FOREIGN PATENT DOCUMENTS

EP 1319400 6/2003
WO 9814587 4/1998

(Continued)

OTHER PUBLICATIONS

Garcia et al. (Walter Reed Army Institute of Research, Nov. 1, 2006, (8pgs.).*

(Continued)

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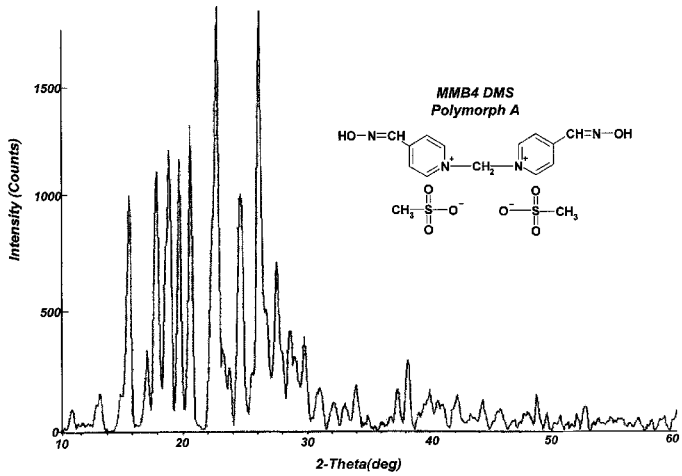
(57) **ABSTRACT**

The present invention relates to two phase systems of a bioactive ingredient in particle form that has limited or no solubility in a liquid medium, which provides stability to the bioactive ingredient that is similar to the bioactive ingredient when in the solid state. The bioactive ingredient may be capable of therapeutically treating for the presence of a cholinesterase inhibitor. The bio active ingredient comprises 1,1'-methlyenebis[4-[(hydroxyimino)methyl]-pyridinium] dimethanesulfonate.

5 Claims, 10 Drawing Sheets