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METHOD FOR TREATMENT OF HEAVY METAL POISONING

BACKGROUND OF THE PRESENT INVENTION

The present invention is directed to a method for the treatment of heavy metal poisoning in a mammal.

Toxic contaminants such as heavy metals are widely present in the environment. Such contaminants come into contact with mammals such as humans on a regular basis. Such heavy metals include lead, cadmium, mercury, iron and the like. Exemplary sources of such metals includes contaminated water, contaminated wildlife (such as fish), plumbing, paints, auto emissions, and manufacturing processes. Recently, questions have even been raised regarding the safety of mercury amalgam fillings in teeth. Unfortunately, the presence of such contaminants in the body leads to a variety of health problems, including mental disfunction, coronary problems, circulation problems, nervous system disfunction, etc.

Exemplary heavy metal detoxification treatments are disclosed in U.S. Pat. Nos. 2,847,308 (calcium salt of calcium chelate); 2,875,129 (calcium chelate); 2,947,782 (aminoacetamidoximes); 3,072,529 (5-aminohexahydro pyrimidine); 4,043,998 (1-(p-benzenediazonium)-ethylenediamine tetraacetic acid); 5,217,998 (soluble polymer substrate having chelate attached thereto); and 5,443,847 (soluble manganese salt). Unfortunately, none of the above methods of treatment have been totally successful.

OBJECTS AND SUMMARY OF THE PRESENT INVENTION

It is accordingly an object of the present invention to provide a method for the treatment of or alleviation of symptoms of heavy metal contamination.

In accordance with the present invention, there is accordingly provided a method for the treatment of heavy metal contamination in a mammal comprising administering to a mammal including humans suffering from heavy metal contamination a therapeutically effective amount of an oxime chelating agent.

DETAILED DESCRIPTION OF THE PRESENT INVENTION

The present invention is directed to a method for treatment of heavy metal contamination in mammals.

The present invention involves the administration to a mammal suffering from heavy metal contamination a therapeutically effective amount of an oxime active agent, and preferably an oxime selected from the group consisting of bisquaternary and triquaternary oximes.

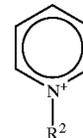
The oximes which may be employed in the present invention are well known to those skilled in the art and well-described in the literature. Such oximes found early use as nerve gas and toxic pesticide poisoning antidotes. Exemplary oximes include but are not limited to those compounds disclosed in U.S. Pat. Nos. 2,816,113; 2,996,510; 3,063,901; 3,077,476; 3,852,294; 3,928,594; 4,002,760; 4,352,810; 4,675,326; 4,865,837; 4,925,856; 4,988,710; 5,206,371 and U.K. application 2,016,920, each herein incorporated by reference in their entirety.

The oxime compounds which are be used in the present invention are defined by the formula $(R^1-CR=NOH)^+X^-$ where R is hydrogen, C_{1-5} alkyl or NH_2 and X^- is a pharmaceutically acceptable anion derived from a salt of an

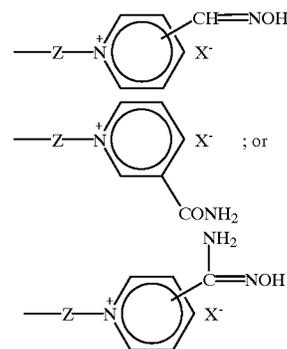
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inorganic or organic acid. R^1 may take many forms. For example R^1 may be C_{1-5} alkyl, aryl (e.g., phenyl), or a 5 or 6-membered heterocyclic moiety having from 1 to 3 nitrogen atoms in the heterocyclic ring.

The oxime may also be bicyclic in nature, as defined by the formula $R^1CR=NOH X^-$ where R is hydrogen, C_{1-5} alkyl or NH_2 and R^1 is



wherein R^2 is selected from the group consisting of:



where Z is, for example, a polyalkylene group having from 1 to 6 carbon atoms, optionally including at least one ether linkage, such as $-CH_2CH_2-$, $-CH_2OCH_2-$, $-CH_2CH_2OCH_2CH_2-$, $-CH_2OCH_2CH_2OCH_2-$; or $-(CH_2)_n$ -phenyl- $(CH_2)_n$ - where n ranges from 1 to 6 and the phenyl moiety may be substituted by C_{1-5} alkyl, and wherein X^- is a pharmaceutically acceptable anion derived from a salt of an inorganic or organic acid.

Exemplary oxime chelating agents include the following oximes: 2-pyridine aldoxime methiodide, 4-pyridine aldoxime methiodide, methyl-2-pyridyl ketoxime methiodide, 1-methyl-pyridinium-2-aldoxime (2-PAM); 2,3-butanedione-2-oxime (DAM), pyruvaldehyde aldoxime (MINA), 2-pyridine aldoxime methochloride (2-PAM-Cl) (marketed as Protopam chloride), pralidoxime methylsulphate (marketed as Contrathion), obidoxime chloride (marketed as Toxogonin), 1,1'-polymethylene bis (4-formylpyridinium) halide oximes; 1,1'-(2,5-dimethyl-p-phenylenedimethylene) bis (4-formylpyridinium) halide dioximes; 1,1'-polymethylene bis (3-formylpyridinium) halide dioximes; 1,1'-(p-phenylenedimethylene) bis (3-formylpyridinium) halide dioximes; bis quaternary 4-formylpyridinium halide monooximes; 1,1'-trimethylene bis (3-amidooximopyridinium) halides, quaternary pyridine aldoxime (TMB-4); HI-6; diacetyl monoxime; aldoxime-substituted triazolium compounds including 1,4-dimethyl-3-(hydroxyimino)methyl-1,2,4-triazolium chloride, 1-benzyl-3-(hydroxyimino)methyl-4-methyl-1,2,4-triazolium chloride, and 3-(hydroxyimino)methyl-1-methyl-4-(2'-methylsulfonyl-1'-ethyl)-1,2,4-triazolium chloride; and aldoxime-substituted imidazolium derivatives such as 1-[(1'-(2'-butyloxy)methyl]-2-(hydroxyimino)methyl-3-methylimidazolium chloride, 2-(hydroxyimino)methyl-3-methyl-1-[1'-2'-(methylsulfonyl)ethoxy)methyl]-imidazolium chloride, 2-(hydroxyimino)methyl-3-methyl-1-[(2'-methyl-2'-nitropropyloxy)methyl]-imidazolium