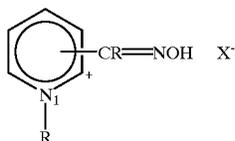


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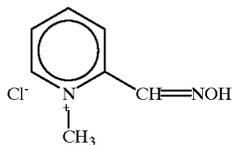
chloride, 1-[(2'-N,N-dimethylaminium)-1'-ethyl]2-(hydroxyimino)methyl-3- methylimidazolium chloride, 1-[2'-(hydroxyimino)methyl-3'-methyl-1'-imidazo]3-(4"-carbamoyl-1"-pyridino)propane dichloride, 1-(3'-bromopropyl-1'-oxy)methyl-2-(hydroxyimino)methyl-3- methylimidazolium chloride, 2-(hydroxyimino)methyl-3- methyl-1-(2'-pyrrolidinium-1'-)ethylimidazolium chloride hydrochloride, 1-(3'-butynyl-1'-thio)methyl-2-(hydroxyimino)methyl-3-methylimidazolium chloride, and 1-[(2'-N-ethyl-N-trifluoromethane sulfonyl) amino-1'-] ethyl-2-hydroxyimino)methyl-3-methylimidazolium chloride.

A preferred class of oximes suitable for use in the present invention may be depicted by the formula:



wherein R is hydrogen, C₁₋₅ alkyl, or NH₂; R¹ is C₁₋₅ alkyl (particularly methyl or ethyl), and X is an anion portion of the salt R¹X. Suitable acid addition salts include the chloride salt, the iodide salt and the methanesulfonate salt.

A specific oxime which is preferred for use in the present invention is 2-PAM chloride which is depicted by the following formula:



It is also advantageous to administer prodrug derivatives of oximes as disclosed in U.S. Pat. Nos. 3,929,813 and 3,962,447. Such prodrug derivatives exhibit an enhanced ability to pass the blood/brain barrier.

Oximes (such as 2-PAM and HI-6) have been used to provide in vivo protection against nerve gas agents and other organophosphate poisons. See, for example, U.S. Pat. Nos. 3,063,901; 4,713,391; 4,865,837; and 4,925,856. Also, one class of oximes (aminoacetamidoximes) is stated in U.S. Pat. No. 2,947,782 to be an effective sequestering agent for iron. However, the oximes of the present invention have not previously been employed to treat heavy metal toxicity in mammals such as humans. The amounts of the respective components required to provide the benefits of the present invention are orders of magnitude less than the amounts normally administered to provide protection against nerve gas agents or toxic organophosphate poisoning.

It is also within the scope of the present invention to combine administration of the oxime active ingredients with more conventional therapies such as antioxidant treatment, vitamin treatment, and other types of heavy metal antagonists. The identity of such compounds is well known to those skilled in the art as described in Goodman & Gilman's *The Pharmacological Basis of Therapeutics*, 9th edition, 1996.

It is within the scope of the present invention to employ both pharmaceutically acceptable analogs as well as tautomers, isomers and salts of the above listed compounds. Analogs differ from the above compounds by means of added alkyl or aryl substituents, added or deleted halogen moieties, presence of differing linkages such as ether linkage, saturation or unsaturation. As to possible salts, the

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present invention includes within its scope salts of alkali metals, alkaline earth metals, as well as acid addition salts of hydrochloric, hydrobromic, sulfuric, sulfamic, phosphoric, acetic, propionic, succinic, glycollic, stearic, lactic, malic, tartaric, citric, ascorbic, pantoic, maleic, hydroxymaleic, phenylacetic, glutamic, benzoic, salicylic, sulfanilic, fumaric, etc.

The compounds of the present invention may be administered by any pharmaceutically acceptable means and in any pharmaceutically acceptable form. For instance, the compounds may be administered orally in the form of pills, tablets, solutions, syrups, lozenges, etc. in which the compound is the sole or co-ingredient as the active agent. The compounds may also be administered parenterally (e.g., intravenously, intramuscularly or subcutaneously) in association with a pharmaceutically acceptable carrier. Topical administration such as by transdermal patch is also acceptable. The active components may also be administered by inhalers or intemasally.

Tablets or pills may contain the active ingredient(s) in admixture with conventional pharmaceutically acceptable excipients (i.e., inert diluents). Such tablets or pills may be uncoated or coated by conventional techniques to delay disintegration and absorption in the gastrointestinal tract. More specifically, such tablets or pills may include an enteric coating to ensure disintegration and absorption in the intestine. Such coatings are generally comprised of a cellulose lower fatty acid phthalate such as cellulose acetate phthalate.

The oxime chelating agent is employed or administered in an amount effective to inhibit or decrease heavy metal toxicity. With the above in mind, the various compounds of the present invention may be administered within a wide range of dosage levels while still enabling the benefits of the present invention to be achieved. For example, the oxime chelating agent is generally administered at a dosage level of from about 1 mg to 10 mg. Such dosage levels are based on a standard adult body weight of 70 kg. Such dosage administrations are repeated as required to provide the desired results, with administrations being repeated every 12 to 36 hours depending upon the extent of heavy metal poisoning observed.

From the above description, one of ordinary skill in the art can readily ascertain the essential characteristics of the present invention. Without departing from the scope of the invention, various changes and/or modifications can be made which are still within the scope and range of equivalence of the attached claims.

What is claimed is:

1. A method is provided for the treatment of heavy metal poisoning in a mammal comprising administering to a mammal suffering from heavy metal poisoning a therapeutically effective amount of an active agent selected from the group consisting of:

(a) a compound defined by the formula (R¹—CR=NOH)⁺ X⁻ where R is hydrogen, C₁₋₅ alkyl or NH₂, R¹ is C₁₋₅ alkyl and X⁻ is a pharmaceutically acceptable anion derived from a salt of an inorganic acid or a salt of an organic acid;

(b) a compound defined by the formula (R¹—CR=NOH)⁺ X⁻ where R is hydrogen, C₁₋₅ alkyl or NH₂, R¹ is aryl and X⁻ is a pharmaceutically acceptable anion derived from a salt of an inorganic acid or a salt of an organic acid;

(c) a compound defined by the formula (R¹—CR=NOH)⁺ X⁻ where R is hydrogen, C₁₋₅ alkyl or NH₂ and R¹ is a 5 or 6 membered heterocyclic moiety