AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

Claims 1-12 (Canceled)

Claim 13 (Previously Presented): A method for reduction of a substrate with thioredoxin reductase, comprising combining the thioredoxin reductase, the substrate and NADPH under conditions to reduce the substrate, the substrate comprising a substance selected from the group consisting of a compound represented by the following general formula (1) or (1') and a physiologically acceptable salt thereof, and a hydrate thereof and a solvate thereof:

![Chemical Structure 1](image1)

![Chemical Structure 1'](image2)
wherein $R^1$ and $R^2$ independently represent a hydrogen atom, a halogen atom, a trifluoromethyl group, a nitro group, a C$_1$-C$_6$ alkyl group, or a C$_1$-C$_6$ alkoxy group, or $R^1$ and $R^2$ may combine together to represent methylenedioxy group; $R^3$ represents an aryl group, an aromatic heterocyclic group, a 5- to 7-membered cycloalkyl group, or a 5- to 7-membered cycloalkenyl group, and the aryl group, the aromatic heterocyclic group, the cycloalkyl group, and the cycloalkenyl group may be substituted with one or more substituents; $R^4$ represents a hydrogen atom, a hydroxyl group, a -S-glutathione group, a -S-$\alpha$-amino acid group, or an aralkyl group whose aryl moiety may be substituted with one or more substituents; $R^5$ represents a hydrogen atom or a C$_1$-C$_6$ alkyl group, or $R^4$ and $R^5$ may combine together to represent single bond; $Y$ represents oxygen atom or sulfur atom; $n$ represents an integer of from 0 to 5; and the selenium atom may be oxidized.

Claim 14 (Previously Presented): The method according to claim 13 wherein the substrate comprises a substance selected from the group consisting of 2-phenyl-1,2-benziso-selenazol-3(2H)-one or a ring-opened form thereof and a physiologically acceptable salt thereof, and a hydrate thereof and a solvate thereof.

Claim 15 (Currently Amended): A method of enhancing peroxidase activity of thioredoxin reductase, comprising combining NAPDH, thioredoxin reductase, thioredoxin and a substrate under conditions to enhance peroxidase activity of thioredoxin reductase, the substrate comprising a substance selected from the group consisting of a compound represented by the following general formula (1) or (1') and a physiologically acceptable salt thereof, and a hydrate thereof and a solvate thereof:
wherein $R^1$ and $R^2$ independently represent a hydrogen atom, a halogen atom, a trifluoromethyl group, a nitro group, a C$_1$-C$_6$ alkyl group, or a C$_1$-C$_6$ alkoxy group, or $R^1$ and $R^2$ may combine together to represent methylenedioxy group; $R^3$ represents an aryl group, an aromatic heterocyclic group, a 5- to 7-membered cycloalkyl group, or a 5- to 7-membered cycloalkenyl group, and the aryl group, the aromatic heterocyclic group, the cycloalkyl group, and the cycloalkenyl group may be substituted with one or more substituents; $R^4$ represents a hydrogen atom, a hydroxyl group, a -S-glutathione group, a -S- $\alpha$-amino acid group, or an aralkyl group whose aryl moiety may be substituted with one or more substituents; $R^5$ represents a hydrogen atom or a C$_1$-C$_6$ alkyl group, or $R^4$ and $R^5$ may combine together to represent single bond; $Y$ represents oxygen atom or sulfur atom; $n$ represents an integer of from 0 to 5; and the selenium atom may be oxidized.
Claim 16 (Previously Presented): The method according to claim 17 wherein the substrate comprises a substance selected from the group consisting of 2-phenyl-1,2′benzisoselenazol-3(2H)-one or a ring-opened form thereof and a physiologically acceptable salt thereof, and a hydrate thereof and a solvate thereof.

Claim 17 (Currently Amended): A method of oxidizing reduced thioredoxin by a substrate, the method comprising combining reduced thioredoxin and a substrate under conditions to oxidize the reduced thioredoxin with the substrate, the substrate comprising a substance selected from the group consisting of a compound represented by the following general formula (1) or (1') and a physiologically acceptable salt thereof, and a hydrate thereof and a solvate thereof:

\[
\begin{align*}
Y & \quad \text{(1)} \\
\begin{array}{c}
\text{R}^1 \\
\text{R}^2 \\
\text{R}^4 \\
\text{R}^5
\end{array} & \quad \text{Se} & \quad \text{N} & \quad \begin{array}{c}
\text{C} \quad \text{(CH}_2\text{)}_n \quad \text{R}^3
\end{array}
\end{align*}
\]

\[
\begin{align*}
\begin{bmatrix}
\text{Y} \\
\text{R}^1 \\
\text{R}^2 \\
\text{R}^4 \\
\text{R}^5
\end{bmatrix} & \quad \text{Se} & \quad \text{N} & \quad \begin{array}{c}
\text{C} \quad \text{(CH}_2\text{)}_n \quad \text{R}^3
\end{array} \\
& \quad \text{(1')} \\
& \quad \text{2}
\end{align*}
\]

wherein \(R^1\) and \(R^2\) independently represent a hydrogen atom, a halogen atom, a trifluoromethyl group, a nitro group, a \(C_1\text{-}C_6\) alkyl group, or a \(C_1\text{-}C_6\) alkoxy group, or \(R^1\) and \(R^2\) may combine together to represent methylenedioxy group; \(R^3\) represents an aryl group, an aromatic heterocyclic
group, a 5- to 7-membered cycloalkyl group, or a 5- to 7-membered cycloalkenyl group, and the aryl
group, the aromatic heterocyclic group, the cycloalkyl group, and the cycloalkenyl group may be
substituted with one or more substituents; R^4 represents a hydrogen atom, a hydroxyl group, a -S-
glutathione group, a -S- α-amino acid group, or an aralkyl group whose aryl moiety may be
substituted with one or more substituents; R^5 represents a hydrogen atom or a C_1-C_6 alkyl group, or
R^4 and R^5 may combine together to represent single bond; Y represents oxygen atom or sulfur atom;
n represents an integer of from 0 to 5; and the selenium atom may be oxidized.

Claim 18 (Currently Amended): A method for reducing a peroxide comprising oxidizing
reduced thioredoxin in a peroxidase reaction wherein the thioredoxin has been reduced by
thioredoxin reductase and NADPH in the presence in a substrate combining thioredoxin, thioredoxin
reductase, NAPDH and a substrate under conditions to reduce the peroxide, the substrate comprising
a substance selected from the group consisting of a compound represented by the following general
formula (I) or (I’) and a physiologically acceptable salt thereof, and a hydrate thereof and a solvate
thereof:
wherein $R^1$ and $R^2$ independently represent a hydrogen atom, a halogen atom, a trifluoromethyl group, a nitro group, a $C_1$-$C_6$ alkyl group, or a $C_1$-$C_6$ alkoxy group, or $R^1$ and $R^2$ may combine together to represent methylenedioxy group; $R^3$ represents an aryl group, an aromatic heterocyclic group, a 5- to 7-membered cycloalkyl group, or a 5- to 7-membered cycloalkenyl group, and the aryl group, the aromatic heterocyclic group, the cycloalkyl group, and the cycloalkenyl group may be substituted with one or more substituents; $R^4$ represents a hydrogen atom, a hydroxyl group, a -S-glutathione group, a -S- $\alpha$-amino acid group, or an aralkyl group whose aryl moiety may be substituted with one or more substituents; $R^5$ represents a hydrogen atom or a $C_1$-$C_6$ alkyl group, or $R^4$ and $R^5$ may combine together to represent single bond; $Y$ represents oxygen atom or sulfur atom; $n$ represents an integer of from 0 to 5; and the selenium atom may be oxidized.
Claim 19 (Currently Amended): A method of preventing peroxidation of a substance comprising combining thioredoxin, thioredoxin reductase and NADPH with a substrate under conditions to prevent peroxidation of the substance, the substrate comprising a substance being selected from the group consisting of a compound represented by the following general formula (1) or (1') and a physiologically acceptable salt thereof, and a hydrate thereof and a solvate thereof:

\[
\begin{align*}
&\text{Y} \\
&\text{N} \left( \text{CH}_2\text{n} \right) \text{R}^3 \\
&\text{R}^1 \text{R}^2 \\
&\text{Se} \\
&\text{R}^4 \text{R}^5
\end{align*}
\]  

(1)

\[
\begin{align*}
&\text{Y} \\
&\text{N} \left( \text{CH}_2\text{n} \right) \text{R}^3 \\
&\text{R}^1 \text{R}^2 \\
&\text{Se} \\
&\text{R}^4 \text{R}^5
\end{align*}
\]

(1')

wherein \(R^1\) and \(R^2\) independently represent a hydrogen atom, a halogen atom, a trifluoromethyl group, a nitro group, a C\(_1\)-C\(_6\) alkyl group, or a C\(_1\)-C\(_6\) alkoxy group, or \(R^1\) and \(R^2\) may combine together to represent methylenedioxy group; \(R^3\) represents an aryl group, an aromatic heterocyclic group, a 5- to 7-membered cycloalkyl group, or a 5- to 7-membered cycloalkenyl group, and the aryl group, the aromatic heterocyclic group, the cycloalkyl group, and the cycloalkenyl group may be substituted with one or more substituents; \(R^4\) represents a hydrogen atom, a hydroxyl group, a \(-S\)-glutathione group, a \(-S\)-\(\alpha\)-amino acid group, or an aralkyl group whose aryl moiety may be
substituted with one or more substituents; \( R^3 \) represents a hydrogen atom or a C\(_1\)-C\(_6\) alkyl group, or \( R^4 \) and \( R^5 \) may combine together to represent single bond; \( Y \) represents oxygen atom or sulfur atom; \( n \) represents an integer of from 0 to 5; and the selenium atom may be oxidized.

Claim 20 (Previously Presented): A method for enhancing peroxidase activity of thioredoxin reductase in vivo which comprises administering a peroxidase activity enhancing effective amount of a substrate to a mammal, the substrate comprising a substance selected from the group consisting of a compound represented by the following general formula (1) or (1') and a physiologically acceptable salt thereof, and a hydrate thereof and a solvate thereof:

\[
\begin{align*}
\text{(1)} & \quad \begin{array}{c}
\text{R}^1 \\
\text{Y} \\
\text{R}^2 \\
\text{Se} \\
\text{R}^4 \\
\text{R}^5 \\
\text{N} \\
\text{(CH}_2\text{)}_n\text{R}^3
\end{array}
\end{align*}
\]

\[
\begin{align*}
\text{(1')} & \quad \begin{array}{c}
\text{R}^1 \\
\text{Y} \\
\text{R}^2 \\
\text{Se} \\
\text{R}^4 \\
\text{R}^5 \\
\text{N} \\
\text{(CH}_2\text{)}_n\text{R}^3
\end{array}
\end{align*}
\]
wherein R¹ and R² independently represent a hydrogen atom, a halogen atom, a trifluoromethyl group, a nitro group, a C₁-C₆ alkyl group, or a C₁-C₆ alkoxy group, or R¹ and R² may combine together to represent methylenedioxy group; R³ represents an aryl group, an aromatic heterocyclic group, a 5- to 7-membered cycloalkyl group, or a 5- to 7-membered cycloalkenyl group, and the aryl group, the aromatic heterocyclic group, the cycloalkyl group, and the cycloalkenyl group may be substituted with one or more substituents; R⁴ represents a hydrogen atom, a hydroxyl group, a -S-glutathione group, a -S- α-amino acid group, or an aralkyl group whose aryl moiety may be substituted with one or more substituents; R⁵ represents a hydrogen atom or a C₁-C₆ alkyl group, or R⁴ and R⁵ may combine together to represent single bond; Y represents oxygen atom or sulfur atom; n represents an integer of from 0 to 5; and the selenium atom may be oxidized.

Claim 21 (Previously Presented): The method according to claim 20 wherein the mammal is a human.

Claim 22 (Previously Presented): A method of reducing a peroxide in vivo which comprises administering an peroxide reducing effective amount of a substrate to a mammal, the substrate comprising a substance selected from the group consisting of a compound represented by the following general formula

(1) or (1') and a physiologically acceptable salt thereof, and a hydrate thereof and a solvate thereof:
wherein R<sup>1</sup> and R<sup>2</sup> independently represent a hydrogen atom, a halogen atom, a trifluoromethyl group, a nitro group, a C<sub>1</sub>-C<sub>6</sub> alkyl group, or a C<sub>1</sub>-C<sub>6</sub> alkoxy group, or R<sup>1</sup> and R<sup>2</sup> may combine together to represent methylenedioxy group; R<sup>3</sup> represents an aryl group, an aromatic heterocyclic group, a 5- to 7-membered cycloalkyl group, or a 5- to 7-membered cycloalkenyl group, and the aryl group, the aromatic heterocyclic group, the cycloalkyl group, and the cycloalkenyl group may be substituted with one or more substituents; R<sup>4</sup> represents a hydrogen atom, a hydroxyl group, a -S-glutathione group, a -S- α-amino acid group, or an aralkyl group whose aryl moiety may be substituted with one or more substituents; R<sup>5</sup> represents a hydrogen atom or a C<sub>1</sub>-C<sub>6</sub> alkyl group, or R<sup>4</sup> and R<sup>5</sup> may combine together to represent single bond; Y represents oxygen atom or sulfur atom; n represents an integer of from 0 to 5; and the selenium atom may be oxidized.

Claim 23 (Previously Presented): The method according to claim 22 wherein the mammal is a human.
Claim 24 (Currently Amended): A method of preventing peroxidation of a substance in vivo by oxidizing reduced thioredoxin in a peroxidase reaction proceeded by thioredoxin reductase comprising administering a peroxidation preventing effective amount of a substrate to a mammal, the substrate comprising a substance being selected from the group consisting of a compound represented by the following general formula (1) or (1') and a physiologically acceptable salt thereof, and a hydrate thereof and a solvate thereof:

\[
\begin{align*}
\text{R}^1 & \quad \text{Y} & \quad \text{N} & \quad (\text{CH}_2)_n & \quad \text{R}^3 \\
\text{R}^2 & \quad \text{Se} & \quad \text{R}^4 & & \text{R}^5
\end{align*}
\]

(1)

\[
\begin{align*}
\left[ \begin{array}{c}
\text{R}^1 \\
\text{R}^2 \\
\text{Se} & \quad \text{R}^4 & \quad \text{R}^5
\end{array} \right] & \quad \text{Y} & \quad \text{N} & \quad (\text{CH}_2)_n & \quad \text{R}^3 \\
2
\end{align*}
\]

(1')

wherein \( \text{R}^1 \) and \( \text{R}^2 \) independently represent a hydrogen atom, a halogen atom, a trifluoromethyl group, a nitro group, a \( \text{C}_1-\text{C}_6 \) alkyl group, or a \( \text{C}_1-\text{C}_6 \) alkoxy group, or \( \text{R}^1 \) and \( \text{R}^2 \) may combine together to represent methylenedioxy group; \( \text{R}^3 \) represents an aryl group, an aromatic heterocyclic group, a 5- to 7-membered cycloalkyl group, or a 5- to 7-membered cycloalkenyl group, and the aryl group, the aromatic heterocyclic group, the cycloalkyl group, and the cycloalkenyl group may be substituted with one or more substituents; \( \text{R}^4 \) represents a hydrogen atom, a hydroxyl group, a \(-\text{S-}
\)glutathione group, a \(-\text{S- \alpha-amino acid group, or an aralkyl group whose aryl moiety may be}

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substituted with one or more substituents; $R^5$ represents a hydrogen atom or a C$_1$-C$_6$ alkyl group, or $R^4$ and $R^5$ may combine together to represent single bond; $Y$ represents oxygen atom or sulfur atom; $n$ represents an integer of from 0 to 5; and the selenium atom may be oxidized.

Claim 25 (Previously Presented): The method according to claim 24 wherein the mammal is a human.