about 5 hours, about 4 hours to about 6 hours, or about 5 hours to about 6 hours following administration of the thiosulfate salt).

In some examples, the subject is administered a platinum-based antineoplastic agent within about 1 hour to about 6 hours after administration of the thiosulfate salt (e.g., within about 1 hour to about 5 hours, about 1 hour to about 4 hours, about 1 hour to about 3 hours, about 1 hour to about 2 hours, about 2 hours to about 3 hours, about 2 hours to about 4 hours, about 2 hours to about 5 hours, about 2 hours to about 6 hours, about 3 hours to about 4 hours, about 3 hours to about 5 hours, about 3 hours to about 6 hours, about 4 hours to about 5 hours, about 4 hours to about 6 hours, or about 5 hours to about 6 hours after administration of the thiosulfate salt).

In some examples, the subject is administered a platinum-based antineoplastic agent within about 1 hour to about 6 hours before administration of the thiosulfate salt (e.g., within about 1 hour to about 5 hours, about 1 hour to about 4 hours, about 1 hour to about 3 hours, about 1 hour to about 2 hours, about 2 hours to about 3 hours, about 2 hours to about 4 hours, about 2 hours to about 5 hours, about 2 hours to about 6 hours, about 3 hours to about 4 hours, about 3 hours to about 5 hours, about 3 hours to about 6 hours, about 4 hours to about 5 hours, about 4 hours to about 6 hours, or about 5 hours to about 6 hours before administration of the thiosulfate salt).

In one aspect, the present disclosure refers to use of a thiosulfate salt in the manufacture of a medicament for mitigating platinum-induced hearing loss in a subject in need thereof, wherein the thiosulfate salt is to be administered as a hypertonic pharmaceutical composition comprising a concentration of 0.5M-1.5M of the thiosulfate salt, and wherein the subject is scheduled to be administered a platinum-based antineoplastic agent 1 to 3 hours after intratympanic or transtympanic injection of the thiosulfate salt. In another aspect, the present disclosure refers to use of a thiosulfate salt in the manufacture of a medicament for mitigating platinum-induced hearing loss in a subject in need thereof wherein the thiosulfate salt is to be administered as a hypertonic pharmaceutical composition comprising a concentration of 0.5M-1.5M of the thiosulfate salt, and wherein an effective amount of the thiosulfate salt is to be intratympanically or transtympanically administered to said subject to produce (i) a plasma thiosulfate C_{max} that is 30 μM or less at the time of administration of a platinum-based antineoplastic agent and (ii) a cochlear thiosulfate C_{max} that is at least 30 times greater than a cochlear C_{max} of the platinum-based antineoplastic agent, wherein the cochlear platinum concentrations and the cochlear C_{max} are modeled by a pharmacokinetic simulation of intravenous infusion in a two compartment model.

In yet further examples, the disclosure is described by the following enumerated items.

1. A method of mitigating platinum-induced ototoxicity in a subject in need thereof, the method comprising administering to the subject an effective amount of a thiosulfate salt, wherein the subject was administered a platinum-based neoplastic agent not more than 7 hours prior to administering the thiosulfate salt or is scheduled to be administered a platinum-based antineoplastic agent within 4 hours.

2. The method of item 1, wherein the effective amount is an amount that produces a plasma thiosulfate concentration that is 30 μM or less at the time the platinum-based antineoplastic agent is administered.

3. A method of mitigating platinum-induced ototoxicity in a subject in need thereof, the method comprising administering to the subject an effective amount of a thiosulfate salt to produce (i) a plasma thiosulfate C_{max} that is 30 μM or less at the time of administration a platinum-based antineoplastic agent and (ii) a cochlear thiosulfate C_{max} is at least 30 times greater than a cochlear C_{max} of the platinum-based antineoplastic agent, wherein the cochlear platinum concentrations and the cochlear C_{max} are modeled by a pharmacokinetic simulation of intravenous infusion in a two compartment model.

4. The method of item 2, wherein the subject was administered a platinum-based neoplastic agent not more than 7 hours prior administering the thiosulfate salt or is scheduled to be administered a platinum-based antineoplastic agent within 4 hours.

CLAIMS

1. Use of a thiosulfate salt in the manufacture of a medicament for mitigating platinum-induced hearing loss in a subject in need thereof, wherein the thiosulfate salt is to be administered as a hypertonic pharmaceutical composition comprising a concentration of 0.5M-1.5M of the thiosulfate salt, and wherein the subject is scheduled to be administered a platinum-based antineoplastic agent 1 to 3 hours after intratympanic or transtympanic injection of the thiosulfate salt.

2. The use of claim 1, further comprising that the platinum-based antineoplastic agent is to be administered.

3. The use of claim 1, wherein the thiosulfate salt is an alkaline thiosulfate salt, ammonium thiosulfate salt, or a solvate thereof.

4. The use of claim 1, wherein 200-1,000 µL of the hypertonic pharmaceutical composition are to be administered to the round window of the subject.

5. The use of claim 1, wherein the calculated osmolarity of the hypertonic pharmaceutical composition is 1,500-5,000 mOsm/L.

6. The use of claim 1, wherein the thiosulfate salt is to be administered in an amount that produces a plasma thiosulfate concentration that is 30 µM or less at the time the platinum-based antineoplastic agent is to be administered.

7. The use of claim 1, wherein the amount is 0.1-2.5 mmol of the thiosulfate salt.

8. The use of claim 1, wherein the thiosulfate salt is to be administered in an amount that produces a maximum thiosulfate concentration of 0.6-10 mmol/L by 1h post administration.

9. The use of claim 1, wherein the thiosulfate salt is to be administered in an amount that produces a thiosulfate concentration of 0.1-2 mmol/L by 7 h post administration in the subject's cochlea.

10. Use of a thiosulfate salt in the manufacture of a medicament for mitigating platinum-induced hearing loss in a subject in need thereof, wherein the thiosulfate salt is to be administered as a hypertonic pharmaceutical composition comprising a concentration of 0.5M-1.5M of the thiosulfate salt, and wherein an effective amount of the thiosulfate salt is to be intratympanically or transtympanically administered to said subject to produce (i) a plasma thiosulfate C_{max} that is 30 µM or less at the time of administration of a platinum-based antineoplastic agent and (ii) a cochlear thiosulfate C_{max} that is at least 30 times greater than a cochlear C_{max} of the platinum-based antineoplastic agent, wherein the cochlear platinum concentrations and the cochlear C_{max} are modeled by a pharmacokinetic simulation of intravenous infusion in a two compartment model.

11. The use of claim 10, wherein the effective amount of a thiosulfate salt is to be administered within 3 hours before a platinum-based antineoplastic agent is to be administered.