SUMMARY

[0008] The present disclosure is based in part on the inventors' recent research on apoaequorin, a calcium binding protein, and the unexpected finding that apoaequorin possesses novel neuroprotective abilities. In particular, apoaequorin has been found to be useful in preconditioning neurons in a subject to reduce subsequent neuronal inflammation. Accordingly, the present disclosure provides apoaquoring-containing compositions and methods of use which offer substantial advantageous in neuroprotective applications.

[0009] In a first aspect, there is provided apoaequorin for preconditioning neurons to reduce neuronal inflammation in a subject. In another aspect, there is provided use of apoaequorin for the manufacture of a composition for preconditioning neurons to reduce neuronal inflammation in a subject. The present disclosure is also directed to methods of preconditioning neurons to reduce neuronal inflammation in a subject. Such methods include the step of administering apoaequorin to a subject, wherein the subject's neurons are preconditioned to reduce neuronal inflammation.

[0010] In one embodiment, administering to the subject is by injection. In an alternative embodiment, administering to the subject is by oral delivery, for example, by apoaequorin formulated in a unit dosage form selected from a tablet or capsule. In certain embodiments, apoaequorin is administered to a subject in the form of a nutraceutical composition.

[0011] As can be appreciated, the present disclosure encompasses apoaequorin for preconditioning neurons to reduce neuronal inflammation in a subject, as well as the use of apoaequorin for the manufacture of a composition for preconditioning neurons to reduce neuronal inflammation in a subject.

[0012] In another aspect, there is provided apoaequorin for reducing Tumor Necrosis Factor α protein level in a subject. In yet another aspect, there is provided use of apoaequorin for the manufacture of a composition for reducing Tumor Necrosis Factor α (TNFα) protein level in a subject. The present disclosure is also directed to methods of reducing Tumor Necrosis Factor α (TNFα) protein level in a subject. Such methods include the step of administering apoaequorin to a subject, wherein the subject's level of TNFα protein is reduced.

[0013] In certain embodiments, administering to the subject is by injection. In alternative embodiments, administering to the subject is by oral delivery, for example, by apoaequorin formulated in a unit dosage form selected from a tablet or capsule. In certain embodiments, apoaequorin is administered to a subject in the form of a nutraceutical composition.

[0014] As can be appreciated, the present disclosure encompasses apoaequorin for reducing TNFα protein level in a subject, as well as the use of apoaequorin for the manufacture of a composition for reducing TNFα protein level in a subject.

[0015] The present disclosure provides various advantages over prior compositions and methods in that it provides for the general improvement of a subject's mental and physical health through its neuroprotective functions.

[0016] Other objects, features and advantages of the present disclosure will become apparent after review of the specification and claims.

BRIEF DESCRIPTION OF THE DRAWINGS

[0017] Fig. 1A-C depicts effects of oxygen-glucose deprivation on cell death in acute hippocampal brain slices. *A*) Diagram of experimental design. Coronal hippocampal slices were incubated for 1 hr in artificial cerebral spinal fluid (aCSF). Half of the slices were transferred to the ischemic condition for 5 min of oxygen-glucose deprivation (OGD) while the other half remained normoxic (no OGD). All of the slices were then transferred to aCSF for a 30 min reperfusion and trypan blue staining. The slices were then fixed in 10% neutral-buffered formalin. *B*) Representative images of trypan blue staining in area CA1 of the hippocampus in a slice that remained normoxic (no OGD) and in a slice subjected to 5 min OGD. Notice that there is less staining in the normoxic slice compared to the OGD slice. *C*) There was a significant increase in the number of trypan blue-stained neurons in area CA1 of the hippocampus from slices that underwent 5 min OGD compared to slices that remained normoxic (*, $p < .01$).

[0018] Fig. 2A-C depicts dose-dependent effects of apoaequorin on ischemic cell death. *A*) Diagram of experimental design. Rats that were cannulated bilaterally in the dorsal hippocampus were given an infusion of 0, 0.4, 1, or 4% apoaequorin (AQ) in one hemisphere and vehicle (0% AQ) in the other hemisphere. One day following the infusion, coronal hippocampal slices were cut and incubated in artificial cerebral spinal fluid (aCSF) for 1 hr. All slices were transferred to the ischemic condition for 5 min of oxygen-glucose deprivation (OGD). Slices were then transferred to aCSF for a 30 min reperfusion and trypan blue staining. The slices were then fixed in 10% neutral-buffered formalin. *B*) Representative images of trypan blue staining in area CA1 of the

CLAIMS

What is claimed is:

1. Apoaequorin for preconditioning neurons to reduce neuronal inflammation in a subject.

2. Use of apoaequorin for the manufacture of a composition for preconditioning neurons to reduce neuronal inflammation in a subject.

3. The use according to claim 2, wherein the composition is to be administered by injection.

4. The use according to claim 2, wherein the composition is to be administered by oral delivery.

5. The use according to claim 4, wherein said composition is in a unit dosage form selected from a tablet or capsule.

6. The use according to claim 4, wherein apoaequorin is to be administered to said subject in the form of a nutraceutical composition.

7. Apoaequorin for reducing Tumor Necrosis Factor α protein level in a subject.

8. Use of apoaequorin for the manufacture of a composition for reducing Tumor Necrosis Factor α (TNFα) protein level in a subject.

9. The use according to claim 8, wherein the composition is to be administered by injection.

10. The use according to claim 8, wherein the composition is to be administered by oral delivery.

11. The use according to claim 10, wherein said composition is in a unit dosage form selected from a tablet or capsule.

12. The use according to claim 10, wherein apoaequorin is to be administered to said subject in the form of a nutraceutical composition.