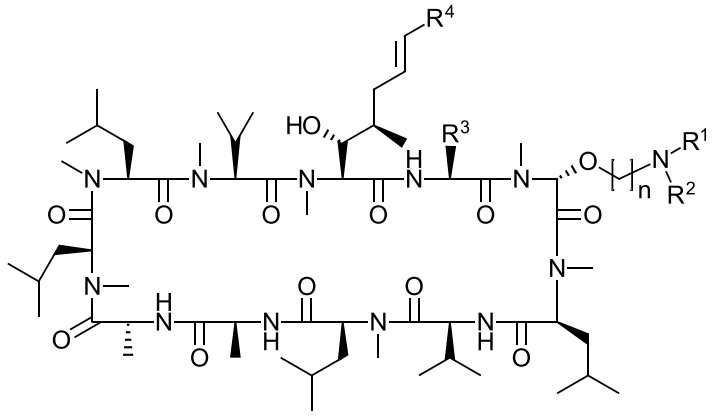
Claims

1. A compound of Formula 1, or a pharmaceutically acceptable salt thereof,



(Formula 1)

wherein:

n is selected from an integer between 2 and 5;

R^1 and R^2 are independently selected from H, C_1 to C_6 alkyl or wherein R^1 and R^2 may be joined together to form a C_3 to C_6 cycloalkyl or heterocycloalkyl ring;

R^3 is ethyl, 1-hydroxyethyl, isopropyl, or n-propyl; and

wherein R^4 is aryl, substituted aryl, heteroaryl and substituted heteroaryl, and wherein the substitution is optionally one or more substituents independently selected from C_1 to C_6 alkyl, halogen, haloalkyl, hydroxyl, C_1 to C_6 alkoxyl, amino, monoalkylamino, dialkylamino, thioalkyl, nitro, cyano, carboxyl, alkoxycarbonyl, aryl and heteroaryl.

2. The compound according to claim 1, wherein at least one of R^1 or R^2 is C_1 to C_6 alkyl.

3. The compound according to claim 2 wherein R^1 and R^2 are both $-CH_3$.

4. The compound according to claim 1, wherein R^1 and R^2 are joined together to form a C_3 to C_6 cycloalkyl or heterocycloalkyl ring.

5. The compound according to claim 4 wherein R^1 and R^2 are joined together to form a morpholinyl residue.

6. The compound according to any one of the preceding claims, wherein n is 2.

7. The compound according to any one of the preceding claims, wherein R^3 is ethyl.

8. The compound according to any one of the preceding claims, wherein R^3 is isopropyl, n-propyl, or 1-hydroxyethyl.

9. The compound according to any one of the preceding claims, wherein R^4 is aryl or substituted aryl.

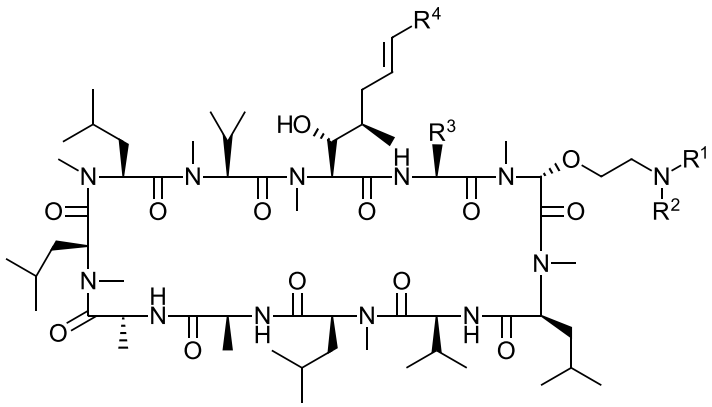
10. The compound according to any one of the preceding claims, wherein R^4 is phenyl, or substituted phenyl, wherein the substitution is optionally one or more substituents independently selected from C_1 to C_6 alkyl (e.g. methyl, or *t*-butyl), halogen (e.g. chloro, fluoro, bromo, or iodo), haloalkyl (e.g. trifluoromethyl), hydroxyl, C_1 to C_6 alkoxyl (e.g. methoxy, phenoxy, or t-butoxy), amino, monoalkylamino, dialkylamino (e.g. dimethylamino), thioalkyl, nitro, cyano, carboxyl ((e.g. -$COOCH_3$), alkoxycarbonyl (e.g. acetoxy), aryl (e.g. phenyl) and heteroaryl.

11. The compound according to any one of claims 1 to 9, wherein R^4 is naphthalene, or substituted naphthalene.

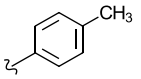
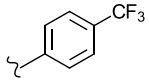
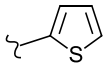
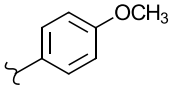
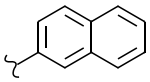
12. The compound according to any one of claims 1 to 8, wherein R^4 is heteroaryl or substituted heteroaryl.

13. The compound according to claim 12, wherein the R^4 is selected from the group consisting of pyridine, pyrrole, pyrazine, pyrimidine, thiophene, thiazole, oxazole, isoxazole, furan, quinoline, pyrazole, and imidazole, optionally substituted with one or more substituents independently selected from C_1 to C_6 alkyl, halogen, haloalkyl, hydroxyl, C_1 to C_6 alkoxyl, amino, monoalkylamino, dialkylamino, thioalkyl, nitro, cyano, carboxyl, alkoxycarbonyl, aryl and heteroaryl.

14. The compound according to claim 1, wherein the compound, or pharmaceutically acceptable salt thereof is of Formula 2, and selected from:



(Formula 2)

Compound	R^1	R^2	R^3	R^4
2	$-CH_3$	$-CH_3$	$-CH_2CH_3$	
3	$-CH_3$	$-CH_3$	$-CH_2CH_3$	
4	$-CH_3$	$-CH_3$	$-CH_2CH_3$	
5	$-CH_3$	$-CH_3$	$-CH_2CH_3$	
6	$-CH_3$	$-CH_3$	$-CH_2CH_3$	

15. A~~Use of a~~ compound or a pharmaceutical acceptable salt thereof as defined in any one of claims 1-14 for use in the prevention and/or treatment of a disease or a condition~~in the manufacture of a medicament~~.

16. Use of a compound or a pharmaceutical acceptable salt thereof as defined in any one of claims 1 to 14, in the manufacture of a medicament for: a) the prevention and/or treatment of a cyclophilin-mediated disease or condition and/or b) the prevention and/or treatment of a renal disease or condition.

17. Use of a compound or a pharmaceutically acceptable salt thereof as defined in any one of claims 1 to 14, in the manufacture of a medicament for the prevention and/or treatment of a disease or condition associated with cell injury or cell death; or for the prevention and/or treatment of organ failure or organ injury, optionally wherein the organ is selected from the group consisting of kidney, liver, heart, lung, pancreas, intestine, cornea, skin, brain and nerve tissue; or for the prevention and/or treatment of kidney failure or kidney injury.

~~18. The use according to claim 17, wherein the disease or condition associated with cell injury or cell death is organ failure or organ injury.~~

~~19. The use according to claim 18 wherein the organ is selected from the group consisting of kidney, liver, heart, lung, pancreas, intestine, cornea, skin, brain and nerve tissue; preferably wherein the organ is selected from the kidney.~~

18~~20~~. The use according to any one of claims 15 to 17~~19~~, wherein the medicament is for the prevention and/or treatment of a disease or condition selected from ~~is~~ ischemia-reperfusion injury, or renal ischemia-reperfusion injury, acute kidney injury, acute kidney injury associated with, or as a consequence of kidney transplantation.

~~21. The use according to claim 20, wherein the ischemia-reperfusion injury is renal ischemia-reperfusion injury.~~

~~22. The use according to any one of claims 15 to 19, wherein the disease or condition is acute kidney injury.~~

~~23. The use according to claim 22, wherein the acute kidney injury is associated with, or a consequence of kidney transplantation.~~

~~24. The use according to any one of claims 15 to 23, wherein medicament is administered to an organ transplant recipient.~~

19~~25~~. The use according to any one of claims 15 to 18~~24~~, wherein the medicament is to be adapted for oral administration, or is to be adapted for administration by intravenous injection or infusion.

20~~26~~. The use according to any one of claims 15-19~~25~~ wherein the medicament is to be administered to an organ donor and/or to an organ recipient prior to, during, and/or after transplantation of an organ from said organ donor to said organ recipient.

~~27. Use of a compound or a pharmaceutically acceptable salt thereof as defined in any one of claims 1-14 in the manufacture of a medicament for preserving an organ and/or protecting an organ from organ injury, the use comprising administering the compound to an organ donor prior to the removal of said organ from said donor and/or to an organ recipient prior to, during or after the transplantation of said organ.~~

~~28. Use of a compound or a pharmaceutically acceptable salt thereof as defined in any one of claims 1-14 for preserving an organ and/or protecting an organ from organ injury, the use comprising administering the compound to an organ donor prior to removal of said organ from said donor, and/or to an organ.~~

~~29. A method of preserving or protecting an organ from organ injury, wherein the method comprises a step of administering a compound or a pharmaceutically acceptable salt thereof as defined in any one of claims 1-14 to an organ donor prior to the removal of said organ from said donor, and/or to an organ.~~

~~30. The use or method according to any one of claims 27-29, wherein the organ is selected from the group consisting of kidney, liver, heart, lung, pancreas, intestine, cornea, skin, brain and nerve tissue.~~

~~31. The use or method according to any one of claims 27-30, wherein the donor is a live donor, or wherein the donor is a clinically dead donor.~~

~~32. The use or method according to any one of claims 27-31, wherein the compound is administered to the donor and/or recipient by intravenous injection or infusion.~~