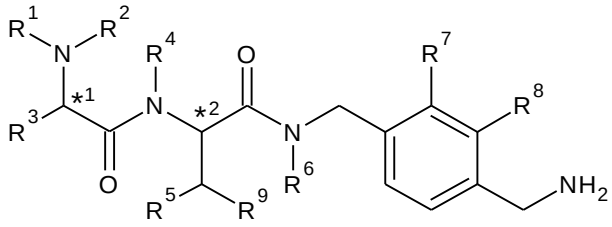
CLAIMS

1. A pharmaceutical composition in the form of an aqueous solution for parenteral administration comprising at least one non-ionic tonicity agent, at least one buffer and an active ingredient, wherein said active ingredient is a compound of formula I



(I)

wherein:

R^1 is selected from H, alkyl, -COalkyl, -COaryl, -COheteroaryl, $-CO_2$alkyl, $-(CH_2)_aOH$, $-(CH_2)_bCOOR^{10}$, $-(CH_2)_cCONH_2$, $-SO_2$alkyl and $-SO_2$aryl;

R^2 is selected from H and alkyl;

R^3 is selected from H, alkyl, $-(CH_2)_d$aryl, $-(CH_2)_e$heteroaryl, $-(CH_2)_f$cycloalkyl, $-(CH_2)_g$heterocycloalkyl, $-CH(cycloalkyl)_2$ and $-CH(heterocycloalkyl)_2$;

R^4 and R^6 are independently selected from H and alkyl;

R^5 is selected from H, alkyl, alkoxy and OH;

or R^4 and R^5, together with the atoms to which they are attached, may join to form a 5- or 6-membered azacycloalkyl structure;

R^7 and R^8 are independently selected from H, alkyl, alkoxy, CN and halo;

R^9 is aryl or heteroaryl;

R^{10} is H or alkyl;

a, b, c, d, e, f and g are independently 1, 2 or 3;

*1 and *2 denote chiral centres;

alkyl is a linear saturated hydrocarbon having up to 10 carbon atoms (C_1-C_{10}) or a branched saturated hydrocarbon of between 3 and 10 carbon atoms (C_3-C_{10}); alkyl may optionally be substituted with 1 or 2 substituents independently selected from (C_3-C_{10})cycloalkyl, (C_1-C_6)alkoxy, OH, CN, CF_3, $COOR^{11}$, fluoro and $NR^{11}R^{12}$;

cycloalkyl is a mono- or bi-cyclic saturated hydrocarbon of between 3 and 10 carbon atoms; cycloalkyl may optionally be fused to an aryl group;

heterocycloalkyl is a C-linked or N-linked 3 to 10 membered saturated, mono- or bi-cyclic ring, wherein said heterocycloalkyl ring contains, where possible, 1, 2 or 3 heteroatoms independently selected from N, NR^{11} and O;

alkoxy is a linear O-linked hydrocarbon of between 1 and 6 carbon atoms (C_1-C_6) or a branched O-linked hydrocarbon of between 3 and 6 carbon atoms (C_3-C_6); alkoxy may optionally be substituted with 1 or 2 substituents independently selected from (C_3-C_{10})cycloalkyl, OH, CN, CF_3, $COOR^{11}$, fluoro and $NR^{11}R^{12}$;

aryl is phenyl, biphenyl or naphthyl; aryl may be optionally substituted with up to 5 substituents independently selected from alkyl, alkoxy, OH, halo, CN, $COOR^{11}$, CF_3 and $NR^{11}R^{12}$;

heteroaryl is a 5, 6, 9 or 10 membered mono- or bi-cyclic aromatic ring, containing, where possible, 1, 2 or 3 ring members independently selected from N, NR^{11}, S and O; heteroaryl may be optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, halo, CN, $COOR^{11}$, CF_3 and $NR^{11}R^{12}$;

R^{11} and R^{12} are independently selected from H and alkyl;

and tautomers, isomers, stereoisomers (including enantiomers, diastereoisomers and racemic and scalemic mixtures thereof), and pharmaceutically acceptable salts thereof.

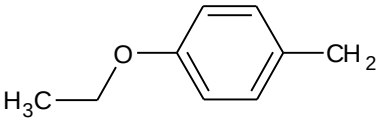
2. The composition of claim 1, wherein R^9 is selected from phenyl and naphthyl, wherein phenyl may be optionally substituted with up to 3 substituents independently selected from alkyl, alkoxy, OH, halo, CN, $COOR^{11}$, CF_3 and $NR^{11}R^{12}$.

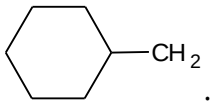
3. The composition of claim 1 or claim 2, wherein R^9 is selected from phenyl, 1-naphthalene, 2,4-dichlorophenyl, 3,4-dichlorophenyl, 3,4-difluorophenyl, 4-chlorophenyl, 4-trifluoromethylphenyl and 4-ethoxyphenyl.

4. The composition as claimed in any one of claims 1 to 3, wherein R^1 is selected from H, -COaryl, -COalkyl, $-CH_2COOH$, $-SO_2Ph$ and $-SO_2CH_3$.

5. The composition as claimed in any one of claims 1 to 4, wherein R^1 is selected from -COalkyl and –COaryl.

6. The composition as claimed in any one of claims 1 to 5, wherein R^3 is selected from:



and 

.

7. The composition as claimed in any one of claims 1 to 6, wherein R^4 and R^6 are selected from H and CH_3.

8. The composition as claimed in any one of claims 1 to 7, wherein the stereochemical configuration about chiral centre *1 is *R*.

9. The composition as claimed in any one of claims 1 to 8, wherein the stereochemical configuration about chiral centre *2 is *S*.

10. The composition as claimed in any one of claims 1 to 9, wherein a is 2 and b, c, d, e, f, g, h, j, l and m are 1.

11. The composition of claim 1, wherein the compound of formula I is selected from:

(S)-N-(4-Aminomethyl-benzyl)-2-[(R)-3-(4-ethoxy-phenyl)-2-propionylamino-propionylamino]-3-phenyl-propionamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-benzamide;

{(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-cyclohexyl-ethylamino}-acetic acid;

(S)-N-(4-Aminomethyl-3-fluoro-benzyl)-2-[(R)-3-(4-ethoxy-phenyl)-2-propionylamino-propionylamino]-3-phenyl-propionamide;

(S)-N-(4-Aminomethyl-2-chloro-benzyl)-2-[(R)-3-(4-ethoxy-phenyl)-2-propionylamino-propionylamino]-3-phenyl-propionamide;

(S)-N-(4-Aminomethyl-benzyl)-3-(3,4-dichloro-phenyl)-2-[(R)-3-(4-ethoxy-phenyl)-2-propionylamino-propionylamino]-propionamide;

(S)-N-(4-Aminomethyl-3-chloro-benzyl)-2-[(R)-3-(4-ethoxy-phenyl)-2-propionylamino-propionylamino]-3-phenyl-propionamide;

(S)-N-(4-Aminomethyl-benzyl)-2-{[(R)-3-(4-ethoxy-phenyl)-2-propionylamino-propionyl]-methyl-amino}-3-phenyl-propionamide;

({(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-cyclohexyl-ethyl}-methyl-amino)-acetic acid;

(S)-N-(4-Aminomethyl-3-fluoro-benzyl)-2-{[(R)-3-(4-ethoxy-phenyl)-2-propionylamino-propionyl]-methyl-amino}-3-phenyl-propionamide;

N-[(R)-1-{[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-phenyl-ethyl]-methyl-carbamoyl}-2-(4-ethoxy-phenyl)-ethyl]-benzamide;

N-[(R)-1-{[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-phenyl-ethyl]-methyl-carbamoyl}-2-(4-ethoxy-phenyl)-ethyl]-isobutyramide;

Naphthalene-1-carboxylic acid [(R)-1-[(S)-1-(4-aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-amide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-4-chloro-benzamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-2,4-dichloro-benzamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-3,4-difluoro-benzamide;

(R)-2-Amino-N-[(1S,2S)-1-(4-aminomethyl-benzylcarbamoyl)-2-hydroxy-2-phenyl-ethyl]-3-(4-ethoxy-phenyl)-propionamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2- (4-ethoxy-phenyl)-ethyl]-nicotinamide;

(2S,3S)-N-(4-Aminomethyl-benzyl)-2-[(R)-3-(4-ethoxy-phenyl)-2-propionylamino-propionylamino]-3-hydroxy-3-phenyl-propionamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2- (4-ethoxy-phenyl)-ethyl]-isonicotinamide;

Thiophene-3-carboxylic acid-[(R)-1-[(S)-1-(4-aminomethyl-benzylcarbamoyl)- 2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-amide;

Thiophene-2-carboxylic acid [(R)-1-[(S)-1-(4-aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-amide;

Cyclohexanecarboxylic acid [(R)-1-[(S)-1-(4-aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-amide;

Isoxazole-5-carboxylic acid [(R)-1-[(S)-1-(4-aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-amide;

Pyridine-2-carboxylic acid [(R)-1-[(S)-1-(4-aminomethyl-benzylcarbamoyl)-2- phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-amide;

Benzo[b]thiophene-2-carboxylic acid[(R)-1-[(S)-1-(4-aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl] -2-(4-ethoxy-phenyl)-ethyl]-amide;

(R)-N-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-phenyl-ethyl]-2-(4-chloro-benzenesulfonylamino)-3-(4-ethoxy-phenyl)-propionamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-3-chloro-benzamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-2-chloro-benzamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-3-trifluoromethyl-benzamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-4-methyl-benzamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-3,4-dichloro-benzamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-4-methoxy-benzamide;

(S)-N-(4-Aminomethyl-benzyl)-2-[(R)-3-(4-ethoxy-phenyl)-2-(2-phenylacetylamino-acetylamino)-propionylamino]-3-phenyl-propionamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-4-fluoro-benzamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-6-methyl-nicotinamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-2-methyl-nicotinamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-2,6-dichloro-nicotinamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-5,6-dichloro-nicotinamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-2,3,6-trifluoro-isonicotinamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-3,3,3-trifluoro-propionamide;

2,4-Dimethyl-thiazole-5-carboxylic acid [(R)-1-[(S)-1-(4-aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-amide;

2-Methyl-thiazole-5-carboxylic acid [(R)-1-[(S)-1-(4-aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-amide;

3-Chloro-thiophene-2-carboxylic acid [(R)-1-[(S)-1-(4-aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-amide;

4-Methyl-thiazole-5-carboxylic acid[(R)-1-[(S)-1-(4-aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-amide;

Furan-2-carboxylic acid [(R)-1-[(S)-1-(4-aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-amide;

3-Methyl-thiophene-2-carboxylic acid [(R)-1-[(S)-1-(4-aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-amide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-2-methoxy-isonicotinamide;

3-Methyl-1H-pyrrole-2-carboxylic acid [(R)-1-[(S)-1-(4-aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-amide;

3-Amino-thiophene-2-carboxylic acid [(R)-1-[(S)-1-(4-aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-amide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-propoxy-phenyl)-ethyl]-benzamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-pyridin-2-yl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-benzamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-(3,4-dichloro-phenyl)-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-benzamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-(4-chloro-phenyl)-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-benzamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-(4-fluoro-phenyl)-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-benzamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-pyridin-3-yl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-benzamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-(4-methoxy-phenyl)-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-benzamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-pyridin-4-yl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-benzamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-(3-fluoro-phenyl)-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-benzamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-thiophen-2-yl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-benzamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-thiophen-3-yl-ethylcarbamoyl-2-(4-ethoxy-phenyl)-ethyl]-benzamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-thiazol-4-yl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-benzamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-benzo[b]thiophen-3-yl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-benzamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-3-fluoro-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-benzamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-3-chloro-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-benzamide;

Pyridine-2-carboxylic acid [(R)-1-[(S)-1-(4-aminomethyl-benzylcarbamoyl)-2-thiophen-2-yl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-amide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-pyridin-2-yl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-4-methoxy-benzamide;

Pyridine-2-carboxylic acid [(R)-1-[(S)-1-(4-aminomethyl-3-chloro-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-amide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-pyridin-3-yl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-4-methoxy-benzamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-(3,4-difluoro-phenyl)-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-isonicotinamide;

Thiophene-2-carboxylic acid [(R)-1-[(S)-1-(4-aminomethyl-benzylcarbamoyl)-2-pyridin-3-yl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-amide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-pyridin-2-yl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-4-chloro-benzamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-pyridin-2-yl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-4-methyl-benzamide;

Pyridine-2-carboxylic acid [(R)-1-[(S)-1-(4-aminomethyl-benzylcarbamoyl)-2-(3,4-dichloro-phenyl)-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-amide;

(R)-N-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-pyridin-2-yl-ethyl]-3-(4-ethoxy-phenyl)-2-propionylamino-propionamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-3-fluoro-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-isonicotinamide;

Pyridine-2-carboxylic acid [(R)-1-[(S)-1-(4-aminomethyl-3-fluoro-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-amide;

Thiophene-2-carboxylic acid [(R)-1-[(S)-1-(4-aminomethyl-benzylcarbamoyl)-2-(3,4-dichloro-phenyl)-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-amide;

(R)-N-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-pyridin-3-yl-ethyl]-3-(4-ethoxy-phenyl)-2-propionylamino-propionamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-(3,4-dichloro-phenyl)-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-isonicotinamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-(3,4-dichloro-phenyl)-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-3,3,3-trifluoro-propionamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-pyridin-3-yl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-4-chloro-benzamide;

Isoxazole-5-carboxylic acid [(R)-1-[(S)-1-(4-aminomethyl-benzylcarbamoyl)-2-pyridin-3-yl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-amide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-pyridin-3-yl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-4-methyl-benzamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-(3,4-difluoro-phenyl)-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-benzamide;

3-Chloro-thiophene-2-carboxylic acid [(R)-1-[(S)-1-(4-aminomethyl-benzylcarbamoyl)-2-pyridin-3-yl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-amide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-(1H-indol-3-yl)-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-benzamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-benzo[b]thiophen-3-yl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-isonicotinamide;

3-Acetylamino-thiophene-2-carboxylic acid-[(R)-1-[(S)-1-(4-aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-amide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-(2-fluoro-phenyl)-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-benzamide;

3-Methyl-thiophene-2-carboxylic acid [(R)-1-[(S)-1-(4-aminomethyl-benzylcarbamoyl)-2-pyridin-3-yl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-amide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-3-methyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-benzamide;

3-Amino-thiophene-2-carboxylic acid [(R)-1-[(S)-1-(4-aminomethyl-benzylcarbamoyl)-2-thiazol-4-yl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-amide;

3-Chloro-thiophene-2-carboxylic acid [(R)-1-[(S)-1-(4-aminomethyl-benzylcarbamoyl)-2-thiazol-4-yl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-amide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-thiazol-4-yl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-4-methyl-benzamide;

3-Methyl-1H-pyrrole-2-carboxylic acid [(R)-1-[(S)-1-(4-aminomethyl-benzylcarbamoyl)-2-benzo[b]thiophen-3-yl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-amide;

3-Amino-thiophene-2-carboxylic acid [(R)-1-[(S)-1-(4-aminomethyl-benzylcarbamoyl)-2-thiazol-4-yl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-amide;

3-Acetylamino-thiophene-2-carboxylic acid [(R)-1-[(S)-1-(4-aminomethyl-benzylcarbamoyl)-2-benzo[b]thiophen-3-yl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-amide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-pyridin-3-yl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-3-methyl-benzamide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-pyridin-3-yl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-2-methyl-benzamide;

3,5-Dimethyl-1H-pyrrole-2-carboxylic acid [(R)-1-[(S)-1-(4-aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-amide;

N-[(R)-1-[(S)-1-(4-Aminomethyl-3-methyl-benzylcarbamoyl)-2-pyridin-3-yl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-benzamide;

3-Acetylamino-thiophene-2-carboxylic acid [(R)-1-[(S)-1-(4-aminomethyl-benzylcarbamoyl)-2-thiophen-3-yl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-amide;

3-Amino-thiophene-2-carboxylic acid [(R)-1-[(S)-1-(4-aminomethyl-benzylcarbamoyl)-2-benzo[b]thiophen-3-yl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-amide;

3-Acetylamino-thiophene-2-carboxylic acid [(R)-1-[(S)-1-(4-aminomethyl-benzylcarbamoyl)-2-benzo[b]thiophen-3-yl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-amide;

3-Chloro-thiophene-2-carboxylic acid [(R)-1-{[(S)-1-(4-aminomethyl-benzylcarbamoyl)-2-phenyl-ethyl]-methyl-carbamoyl}-2-(4-ethoxy-phenyl)-ethyl]-amide;

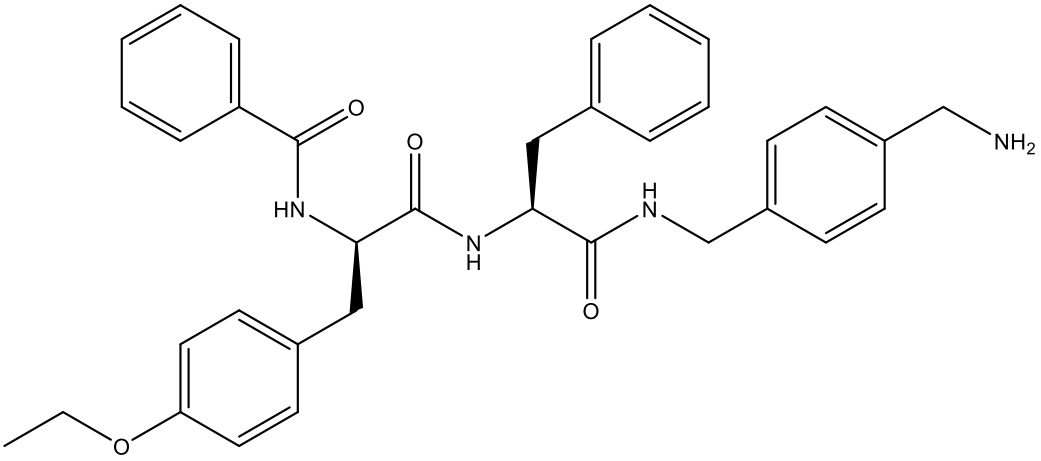
N-[(R)-1-[(1S,2R)-1-(4-Aminomethyl-benzylcarbamoyl)-2-hydroxy-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-benzamide;

3-Chloro-thiophene-2-carboxylic acid [(R)-1-[(1S,2R)-1-(4-aminomethyl-benzylcarbamoyl)-2-hydroxy-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-amide; and

N-{(R,S)-1-[(S)-1-(4-Aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-[4-(2,2,2-trifluoro-ethoxy)-phenyl]-ethyl}-benzamide;

and pharmaceutically acceptable salts thereof.

12. The composition of claim 1, wherein the compound of formula I is N-[(R)-1-[(S)-1-(4-aminomethyl-benzylcarbamoyl)-2-phenyl-ethylcarbamoyl]-2-(4-ethoxy-phenyl)-ethyl]-benzamide



,

or a pharmaceutically acceptable salt thereof.

13. The composition of any one of claims 1-12, wherein the compound of formula I is present in an amount from about 5 µg/mL to about 300 µg/mL based on the concentration of the free base of the compound of formula I in the composition.

14. The composition of any one of claims 1-13, wherein the at least one non-ionic tonicity agent is selected from the group comprising glycerine; sugars, e.g. glucose, mannitol, sorbitol, trehalose,

dextrose, lactose, maltose, fructose, sucrose, and inositol; hydroxyethyl starch, e.g. hetastarch and pentastarch.

15. The composition of any one of claims 1-13, wherein the at least one non-ionic tonicity agent is dextrose or trehalose, preferably trehalose.

16. The composition of any one of claims 1-15, wherein the at least one non-ionic tonicity agent is present in an amount from about 0.1% to about 30% by weight of the compositions.

17. The composition of any one of claims 1-16, wherein the composition has a pH of from about 2 to about 10, preferably from about 5 to about 7.5.

18. The composition of any one of claims 1-17, wherein the composition has an osmolality of from about 250 to about 350 mOsmol/kg.

19. The composition of any one of claims 1-18, wherein the at least one buffer is selected from the group comprising histidine, acetate, citrate, cacodylate, bis-tris, maleate, piperazine, MES (2-(N-morpholino)ethanesulfonic acid), tartrate, lactate; succinate; sulfate; phosphate; alanine; imidazole; arginine and asparagine.

20. The composition of any one of claims 1-19, wherein the at least one buffer is histidine.

21. The composition of any one of claims 1-20, wherein the composition is substantially free of saline.

22. The composition of any one of claims 1-21, wherein the composition contains histidine as the buffer and dextrose or trehalose as the non-ionic tonicity agent.

23. The composition of any one of claims 1-22, wherein the composition is substantially free of phosphate buffered saline.

24. The composition of any one of claims 1-23 further comprising a non-ionic surfactant, wherein the non-ionic surfactant is a polyoxyethylenesorbitan fatty acid ester, preferably wherein the non-ionic surfactant is polysorbate 20.

25. The composition of any one of claims 1-23, wherein the composition is substantially free of non-ionic surfactants, such as carboxylic esters, polyethylene glycol esters, glycol esters of fatty acids, ethoxylated aliphatic alcohols, polyoxyethelene surfactants, sorbitol esters, ethoxylated

derivatives of sorbitol esters, glycol esters of fatty acids, and poloxamers. Polyoxyethelene surfactants include polyoxyethylenesorbitan fatty acid esters, which are also referred to as polysorbates, *e.g.* polysorbate 80 (polyoxyethylene sorbitan monooleate, Tween® 80), polysorbate 40 (polyoxyethylene sorbitan monopalmitate, Tween® 40) and polysorbate 20 (polyoxyethylene sorbitan monolaurate, Tween® 20).

26. The composition of any one of claims 1-25, for injection into the eye, preferably intravitreal injection.

27. The composition of any one of claims 1 to 26, wherein the active ingredient is an HCl salt.

28. The composition of any one of claims 1 to 27, wherein the active ingredient has a half-life, $t_{1/2}$, in vitreous humor of at least about 1 day, e.g. at least about 3 days or at least about 5 days, or preferably about 7 days or more, following intravitreal injection.

29. The composition of any one of claims 1 to 28, wherein the active ingredient has a $t_{1/2}$ in vitreous humor of less than about 40 days, e.g. less than about 30 days, less than about 20 days, following intravitreal injection.

30. The composition of any one of claims 1 to 27, wherein the active ingredient has a $t_{1/2}$ in vitreous humor of between about 1 day and about 40 days, e.g. between about 3 days and about 30 days, or about 5 days and about 20 days, following intravitreal injection.

31. The composition of any one of claims 1 to 30, wherein the active ingredient has a half-life, $t_{1/2}$, in the retina of at least about 1 day, e.g. at least about 3 days or at least about 5 days, or preferably about 7 days or more, following intravitreal injection.

32. The composition of any one of claims 1 to 31, wherein the active ingredient has a $t_{1/2}$ in the retina of less than about 40 days, e.g. less than about 30 days, less than about 20 days, following intravitreal injection.

33. The composition of any one of claims 1 to 30, wherein the active ingredient has a $t_{1/2}$ in the retina of between about 1 day and about 40 days, e.g. between about 3 days and about 30 days, or about 5 days and about 20 days, following intravitreal injection.

34. The composition of any one of claims 1 to 30, wherein the active ingredient has a half-life, $t_{1/2}$, in the retina-choroid complex of at least about 1 day, e.g. at least about 3 days or at least about 5 days, or preferably about 7 days or more, following intravitreal injection.

35. The composition of any one of claims 1 to 30 or 34, wherein the active ingredient has a $t_{1/2}$ in the retina-choroid complex of less than about 40 days, e.g. less than about 30 days, less than about 20 days, following intravitreal injection.

36. The composition of any one of claims 1 to 30, wherein the active ingredient has a $t_{1/2}$ in the retina-choroid complex of between about 1 day and about 40 days, e.g. between about 3 days and about 30 days, or about 5 days and about 20 days, following intravitreal injection.

37. A method for treating a disease or condition mediated by plasma kallikrein comprising parenteral administration of a pharmaceutical composition of any one of claims 1 to 36 to a mammal.

38. The method of claim 37, wherein the disease or condition mediated by plasma kallikrein is selected from impaired visual acuity, diabetic retinopathy, retinal vascular permeability associated with diabetic retinopathy, diabetic macular edema, retinal vascular occlusion, hereditary angioedema, diabetes, pancreatitis, cerebral haemorrhage, cerebral haemorrhage in hyperglycemic patients, nephropathy, cardiomyopathy, neuropathy, inflammatory bowel disease, arthritis, inflammation, septic shock, hypotension, cancer, adult respiratory distress syndrome, disseminated intravascular coagulation, blood coagulation during cardiopulmonary bypass surgery and bleeding from post-operative surgery.

39. The method of claim 37, wherein the disease or condition mediated by plasma kallikrein is selected from impaired visual acuity, diabetic retinopathy, retinal vascular permeability associated with diabetic retinopathy, diabetic macular edema, and retinal vascular occlusion.

40. The method of claim 37, wherein the disease or condition mediated by plasma kallikrein is retinal vascular permeability associated with diabetic retinopathy or diabetic macular edema.

41. The method of any one of claims 37 to 40, for treating microvascular complications of a disease state.

42. The method of any one of claims 37 to 41, wherein the parenteral administration is intraarterial, intraperitoneal, intrathecal, intraventricular, intraurethral, intrasternal, intracranial, intramuscular, intrasynovial, subcutaneous, intravenous, injection into the eye, intravitreal, intravitreal injection or intravitreous.

43. The method of claim 42, wherein the parenteral administration is intravitreal injection.

44. The method of any one of claims 37 to 43, wherein the composition is administered from about once every two weeks to about once every 6 months, e.g. about once a month, or about once every two months, three months, four months, or five months.

45. The method of any one of claims 37 to 44, wherein the method involves combination therapy.

46. The method of claim 45, wherein the method involves laser treatment of the retina.

47. A method for preparing the composition of any one of claims 1 to 36, comprising the steps of

(a) preparing a solution of at least one non-ionic tonicity agent and at least one buffer in water;

(b) dissolving a compound of formula I, or a pharmaceutically acceptable salt thereof, in the solution prepared in step (a);

wherein the at least one non-ionic tonicity agent, the at least one buffer, and the compound of formula I are as defined in claim 1.

48. The method of claim 47, wherein the water used in step (a) is sterile water for injection.

49. The method of claim 47 or claim 48, further comprising the step of:

(c) adding an aqueous solution of at least one non-ionic tonicity agent and at least one buffer to the solution prepared in step (b).

50. The method of any one of claims 47 to 49, further comprising the step of:

(d) sterilising the solution.

51. The method of claim 50, wherein the sterilisation in step (d) is performed by sterile filtration.

52. A method for preparing the composition of any one of claims 1 to 36, comprising adding water to a non-aqueous formulation comprising at least one non-ionic tonicity agent, at least one buffer and an active ingredient, wherein said active ingredient is a compound of formula I or a pharmaceutically acceptable salt thereof; and

wherein the at least one non-ionic tonicity agent, the at least one buffer, and the compound of formula I are as defined in claim 1.