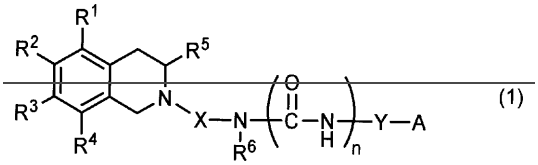
CLAIMS

[Claim 1]

Use of (+)-4-[[2-[6-fluoro-3-(4-fluorobenzyl)-3,4-dihydroisoquinolin-2(1H)-yl]ethylamino]methyl]-N-isopropylaniline monofumarate or (+)-N-[3-(methanesulfonylamino)benzyl]-2-[6-fluoro-3-(4-fluorobenzyl)-3,4-dihydroisoquinolin-2(1H)-yl]ethanamine monocitrate in the manufacture of a non-cellular root canal filler for dental tissue regeneration in an individual. ~~A non-cellular root canal filler comprising a tetrahydroisoquinoline compound represented by the following formula (1):~~

~~[Formula 1]~~



(1)

~~wherein~~

~~R^1, R^2, R^3 and R^4 are each independently -H, -halogen, substituted or unsubstituted C_{1-6} alkyl, -OH, -O-C_{1-6} alkyl, -SH, -S-C_{1-6} alkyl, -COOH, -CO-C_{1-6} alkyl, -CO-O-C_{1-6} alkyl, -CO-NH-C_{1-6} alkyl, $-NO_2$, $-NH_2$, -NH-C_{1-6} alkyl, -N(C_{1-6} alkyl)$_2$, or -NH-CO-C_{1-6} alkyl,~~

~~R^5 is substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{3-10} cycloalkyl, substituted or unsubstituted C_{6-14} aryl, -C_{1-6} alkylene-substituted or unsubstituted C_{3-10} cycloalkyl, or -C_{1-6} alkylene-substituted or unsubstituted C_{6-14} aryl,~~

~~R^6 is -H, substituted or unsubstituted -C_{1-6} alkyl, or -Y'-A',~~

~~X is C_{1-6} alkylene,~~

~~Y and Y' are each independently a single bond or C_{1-6} alkylene,~~

~~A and A' are each independently substituted or unsubstituted C_{6-14} aryl or a substituted or unsubstituted 3- to 15-membered heterocyclic group, and~~

~~n is 0 or 1;~~

~~or a pharmaceutically acceptable salt thereof or a solvate thereof.~~

~~[Claim 2]~~

~~The non-cellular root canal filler according to claim 1, comprising (+)-4-[[2-[6-fluoro-3-(4-fluorobenzyl)-3,4-dihydroisoquinolin-2(1H)-yl]ethylamino]methyl]-N-isopropylaniline monofumarate or (+)-N-[3-(methanesulfonylamino)benzyl]-2-[6-fluoro-3-(4-fluorobenzyl)-3,4-dihydroisoquinolin-2(1H)-yl]ethanamine monocitrate.~~

[Claim 2~~3~~]

The ~~non-cellular root canal filler~~use according to claim 1~~ or 2~~, wherein the non-cellular root canal filler further comprises~~ing~~ extracellular matrix.

[Claim 3~~4~~]

The ~~non-cellular root canal filler~~use according to any one of claims 1 or~~to~~ 2~~3~~, wherein the non-cellular root canal filler further comprises~~ing~~ an anti-CCL11 neutralizing antibody and/or an ALK5 inhibitor.

[Claim 4~~5~~]

The ~~non-cellular root canal filler~~use according to any one of claims 1 to 3~~4~~, wherein the non-cellular root canal filler further comprises~~ing~~ at least one chemotactic factor selected from the group consisting of G-CSF, bFGF and SDF-1.

[Claim 5~~6~~]

The ~~non-cellular root canal filler~~use according to any one of claims 1 to ~~5~~4, ~~for use in the dental tissue regeneration in a young~~ wherein the individual is a human 1 year of age or older and 29 years of age or younger, a rat at 1 week or more and 29 weeks or less after birth, or a dog at 1 week or more and 1 year or less after birth.

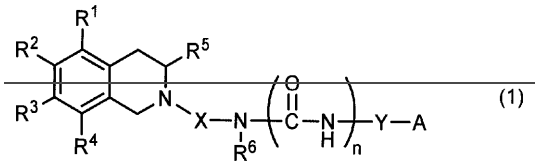
[Claim 6~~7~~]

Use of ~~A dental tissue regeneration promotion kit comprising:~~

~~a~~ a pretreatment agent comprising a serine protease; and

a non-cellular root canal filler comprising (+)-4-[[2-[6-fluoro-3-(4-fluorobenzyl)-3,4-dihydroisoquinolin-2(1H)-yl]ethylamino]methyl]-N-isopropylaniline monofumarate or (+)-N-[3-(methanesulfonylamino)benzyl]-2-[6-fluoro-3-(4-fluorobenzyl)-3,4-dihydroisoquinolin-2(1H)-yl]ethanamine monocitrate in the manufacture of a non-cellular dental tissue regeneration promotion kit for dental tissue regeneration in an individual.~~a tetrahydroisoquinoline compound represented by the following formula (1):~~

~~[Formula 2]~~



~~wherein~~

~~R^1, R^2, R^3 and R^4 are each independently -H, -halogen, substituted or unsubstituted C_{1-6} alkyl, -OH, -O-C_{1-6} alkyl, -SH, -S-C_{1-6} alkyl, -COOH, -CO-C_{1-6} alkyl, -CO-O-C_{1-6} alkyl, -CO-NH-C_{1-6} alkyl, $-NO_2$, $-NH_2$, -NH-C_{1-6} alkyl, -N(C_{1-6} alkyl)$_2$, or -NH-CO-C_{1-6} alkyl,~~

~~R^5 is substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{3-10} cycloalkyl, substituted or unsubstituted C_{6-14} aryl, -C_{1-6} alkylene-substituted or unsubstituted C_{3-10} cycloalkyl, or -C_{1-6} alkylene-substituted or unsubstituted C_{6-14} aryl,~~

~~R^6 is -H, substituted or unsubstituted -C_{1-6} alkyl, or -Y'-A',~~

~~X is C_{1-6} alkylene,~~

~~Y and Y' are each independently a single bond or C_{1-6} alkylene,~~

~~A and A' are each independently substituted or unsubstituted C_{6-14} aryl or a substituted or unsubstituted 3- to 15-membered heterocyclic group, and~~

~~n is 0 or 1,~~

~~or a pharmaceutically acceptable salt thereof, or a solvate of the compound or the salt.~~

~~[Claim 8]~~

~~The dental tissue regeneration promotion kit according to claim 7, comprising (+)-4-[[2-[6-fluoro-3-(4-fluorobenzyl)-3,4-dihydroisoquinolin-2(1H)-yl]ethylamino]methyl]-N-isopropylaniline monofumarate or (+)-N-[3-(methanesulfonylamino)benzyl]-2-[6-fluoro-3-(4-fluorobenzyl)-3,4-dihydroisoquinolin-2(1H)-yl]ethanamine monocitrate.~~

[Claim 7~~9~~]

The use ~~dental tissue regeneration promotion kit~~ according to claim 6~~7 or 8~~, wherein the non-cellular root canal filler further comprises extracellular matrix.

[Claim 8~~10~~]

The use~~dental tissue regeneration promotion kit~~ according to claim 6 or 7, ~~any one of claims 7 to 9,~~ wherein the non-cellular root canal filler further comprises an anti-CCL11 neutralizing antibody and/or an ALK5 inhibitor.

[Claim 9~~11~~]

The use ~~dental tissue regeneration promotion kit~~ according to any one of claims 6~~7~~ to 8~~10~~, wherein the non-cellular root canal filler further comprises at least one chemotactic factor selected from the group consisting of G-CSF, bFGF and SDF-1.

[Claim 10~~12~~]

The use ~~dental tissue regeneration promotion kit~~ according to any one of claims 6~~7~~ to 9~~11~~, wherein the serine protease is a chymotrypsin-like serine protease.

[Claim 11~~13~~]

The use ~~dental tissue regeneration promotion kit~~ according to any one of claims 6~~7~~ to 10~~12~~, wherein the chymotrypsin-like serine protease is trypsin.

[Claim 12~~14~~]

The use~~dental tissue regeneration promotion kit~~ according to any one of claims 6~~7~~ to 11, wherein the individual is ~~13 for use in the dental tissue regeneration in~~ a middle-aged and/or an~~and~~ elderly individual~~s~~.