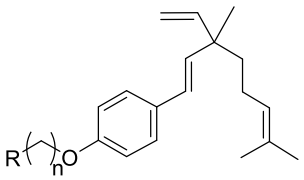
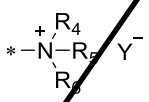
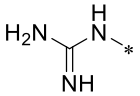
CLAIMS

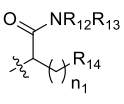
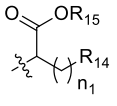
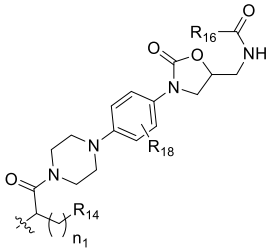
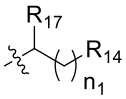
1. A bakuchiol derivative and a pharmaceutically acceptable salt thereof, the bakuchiol derivative having a structure shown in formula (I):

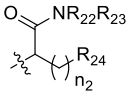
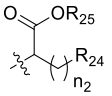
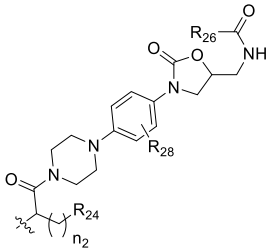
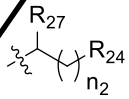


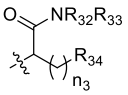
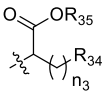
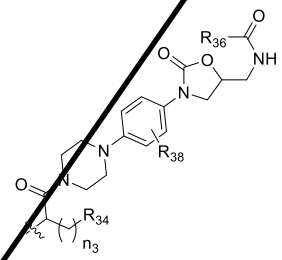
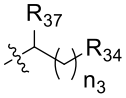
(I)

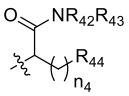
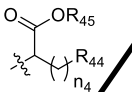
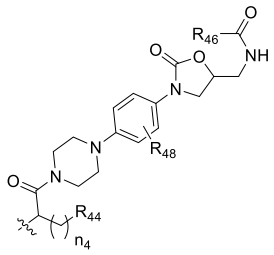
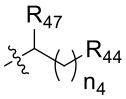
wherein n is an integer from 1 to 16;

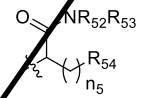
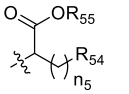
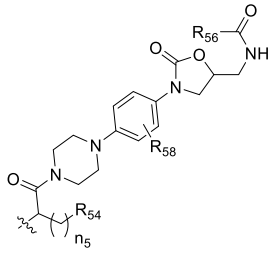
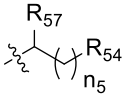
R is selected from halo, -$CONR_1R_2$, -$COOR_3$, -NR_4R_5,  or ;

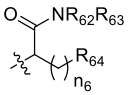
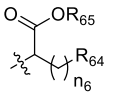
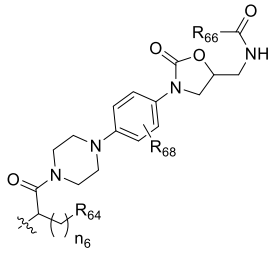
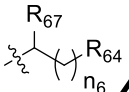
R_1 and R_2 are each independently selected from: -H, , ,  or ;

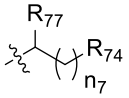
R_{12} and R_{13} are each independently selected from: -H, , ,  or ;

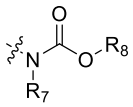
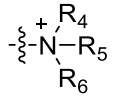
R_{22} and R_{23} are each independently selected from: -H, , ,  or ;

R_{32} and R_{33} are each independently selected from: -H, , ,  or ;

R_{42} and R_{43} are each independently selected from: -H, , ,  or ;

R_{52} and R_{53} are each independently selected from: -H, , ,  or ;

R_{62} and R_{63} are each independently selected from: -H or ;

wherein R_{14}, R_{24}, R_{34}, R_{44}, R_{54}, R_{64} and R_{74} are each independently selected from: -H, guanidyl, $-NR_4R_5$, $-SR_4$, 5- to 20-membered nitrogen-containing heteroaryl,  or ;

R_{15}-R_{17}, R_{25}-R_{27}, R_{35}-R_{37}, R_{45}-R_{47}, R_{55}-R_{57} and R_{65}-R_{67} are each independently selected from: -H or C_{1-6} alkyl;

R_{18}, R_{28}, R_{38}, R_{48}, R_{58} and R_{68} are each independently selected from: -H, C_{1-6} alkyl or halogen;

each of n_1, n_2, n_3, n_4, n_5, n_6 and n_7 is independently 0, 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10;

R_{77} is selected from: -H or C_{1-6} alkyl;

R_3 is selected from: -H or C_{1-4} alkyl;

R_4 and R_5 are each independently selected from: -H, C_{1-16} alkyl, $COOR_8$, -Fmoc or R_a-substituted C_{1-16} alkyl; or R_4 and R_5 together with N linked thereto are capable of forming a 5- to 20-membered heterocyclic ring, a 5- to 20-membered heteroaromatic ring, a 5- to 20-membered heterocyclic ring substituted by R_b or a 5- to 20-membered heteroaromatic ring substituted by R_b;

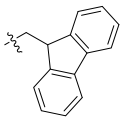
R_a is selected from: 5- to 10-membered aryl, 5- to 10-membered heteroaryl, $-NR_{a1}R_{a2}$ or $-SR_{a3}$;

R_b is selected from: C_{1-10} alkyl, $-(CH_2)_pNR_{b1}R_{b2}$ or $-SR_{b3}$, wherein p is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10;

each of R_{a1}, R_{a2}, R_{b1} and R_{b2} is independently -H, C_{1-10} alkyl or R_c-substituted C_{1-10} alkyl; or R_{a1} and R_{a2} together with a N atom linked thereto are capable of forming a 5- to 10-membered heterocyclic ring or a 5- to 10-membered heteroaromatic ring; or R_{b1} and R_{b2} together with a N atom linked thereto are capable of forming a 5- to 10-membered heterocyclic ring or a 5- to 10-membered heteroaromatic ring;

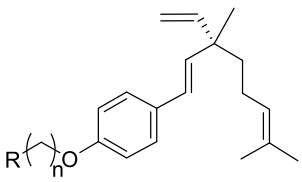
each of R_{a3} and R_{b3} is independently C_{1-10} alkyl;

R_c is selected from: $-NR_{c1}R_{c2}$, guanidyl or 5- to 6-membered nitrogen-containing heteroaryl, wherein each of R_{c1} and R_{c2} is independently: -H, C_{1-4} alkyl; or R_{c1} and R_{c2} together with a N atom linked thereto are capable of forming a 5- to 10-membered heterocyclic ring or a 5- to 10-membered heteroaromatic ring;

R_6 is C_{1-4} alkyl; R_7 is selected from: -H or C_{1-4} alkyl; R_8 is -H, C_{1-6} alkyl or  ; and

Y- is an anion.

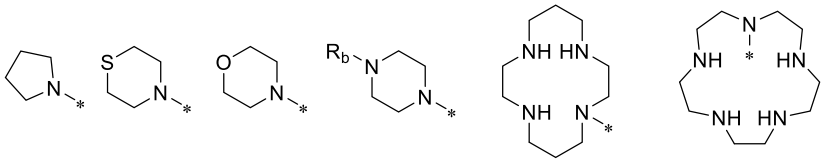
2. The bakuchiol derivative and a pharmaceutically acceptable salt thereof according to claim 1, having a structure shown in formula (I'):



(I').

3. The bakuchiol derivative and a pharmaceutically acceptable salt thereof according to

claim 1, wherein R_4 and R_5 are each independently selected from: H, C_{1-12} alkyl, $COOR_8$, -Fmoc or R_a-substituted C_{1-10} alkyl; or R_4 and R_5 together with N linked thereto are capable of forming the following heterocyclic rings:



,

wherein R_a is selected from pyridine, pyrimidine, triazine, $-NR_{a1}R_{a2}$ or $-SR_{a3}$;

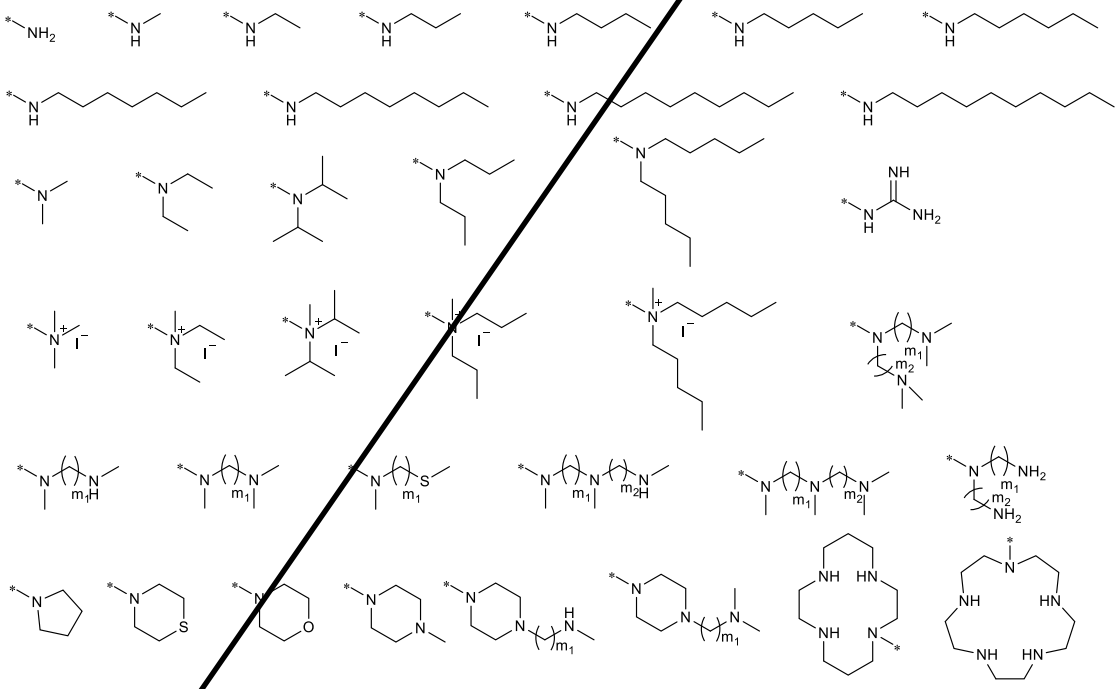
each of R_{a1} and R_{a2} is independently H, C_{1-4} alkyl or $NR_{c1}R_{c2}$-substituted C_{1-4} alkyl; R_{a3} is C_{1-4} alkyl;

each of R_{c1} and R_{c2} is independently H or C_{1-4} alkyl;

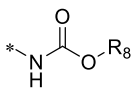
R_b is selected from H, C_{1-6} alkyl or $-(CH_2)_pNR_{b1}R_{b2}$, wherein p is 0, 1, 2, 3, 4, 5 or 6; and

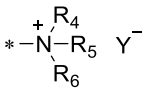
each of R_{b1} and R_{b2} is independently H or C_{1-4} alkyl.

4. The bakuchiol derivative and a pharmaceutically acceptable salt thereof according to claim 1, wherein R is selected from the following groups:



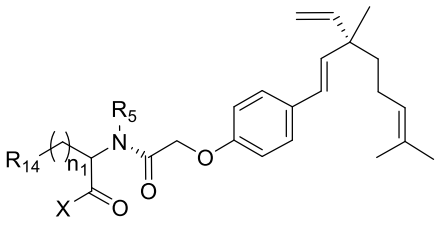
wherein each of m_1 and m_2 is independently 1, 2, 3, 4, 5, 6, 7 or 8.

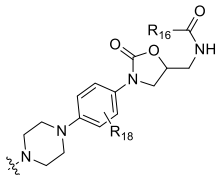
5. The bakuchiol derivative and a pharmaceutically acceptable salt thereof according to claim 1, wherein R_{14}, R_{24}, R_{34}, R_{44}, R_{54}, R_{64} and R_{74} are each independently selected from: -H, guanidyl, $-NR_4R_5$, $-SR_4$, 5-membered nitrogen-containing heteroaryl,  or

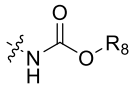

; and

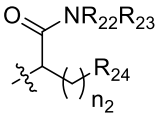
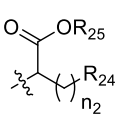
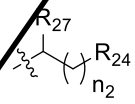
R_8 is C_{1-4} alkyl.

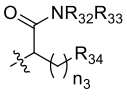
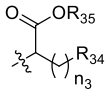
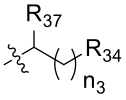
6. The bakuchiol derivative and a pharmaceutically acceptable salt thereof according to claim 1, selected from a compound of the following general formula:

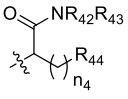
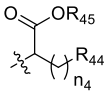
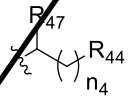

(II'),

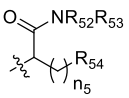
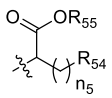
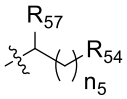
wherein X is $NR_{12}R_{13}$, OR_{15} or .

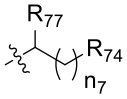
7. The bakuchiol derivative and a pharmaceutically acceptable salt thereof according to claim 6, wherein X is OR_{15}, and R_{14} is selected from: H, guanidyl, $-NH_2$, $-SCH_3$,  or .

8. The bakuchiol derivative and a pharmaceutically acceptable salt thereof according to claim 6, wherein X is $NR_{12}R_{13}$; one of R_{12} and R_{13} is H, and another one is selected from ,  or ;

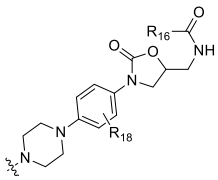
one of R_{22} and R_{23} is H, and another one is selected from ,  or ;

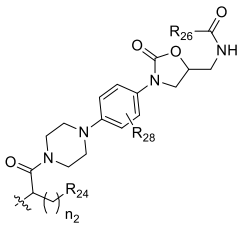
one of R_{32} and R_{33} is H, and another one is selected from ,  or ;

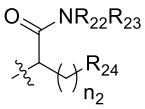
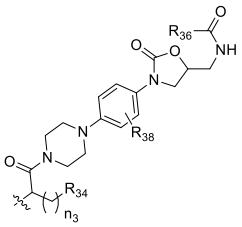
one of R_{42} and R_{43} is H, and another one is selected from ,  or  ; and

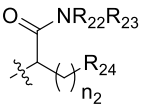
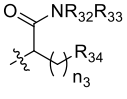
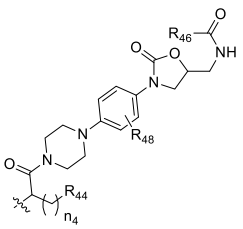
one of R_{62} and R_{63} is H, and another one is selected from  .

9. The bakuchiol derivative and a pharmaceutically acceptable salt thereof according to claim 6, wherein

X is  ; or

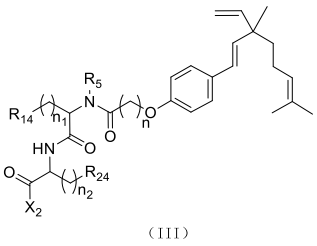
X is $NR_{12}R_{13}$; and one of R_{12} and R_{13} is H, and another one is selected from  ; or

X is $NR_{12}R_{13}$; one of R_{12} and R_{13} is H, and another one is selected from  ; and one of R_{22} and R_{23} is H, and another one is selected from  ; or

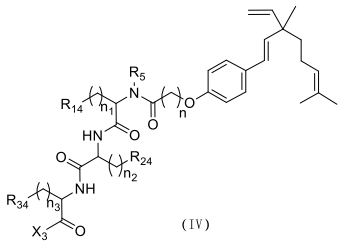
X is $NR_{12}R_{13}$; one of R_{12} and R_{13} is H, and another one is selected from  ; one of R_{22} and R_{23} is H, and another one is selected from  ; and one of R_{32} and R_{23} is H, and another one is selected from  .

10. The bakuchiol derivative and a pharmaceutically acceptable salt thereof according to

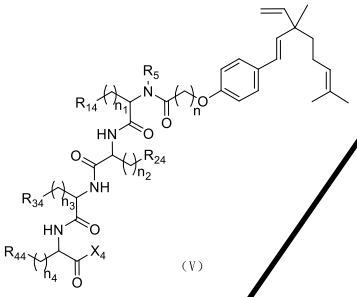
claim 1, selected from a compound of any of the following general formulae:



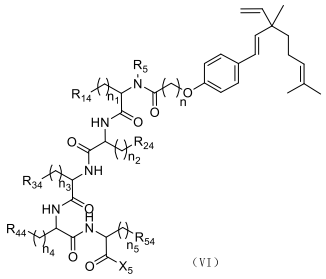
(III)



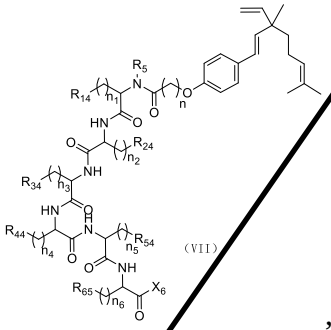
(IV)



(V)

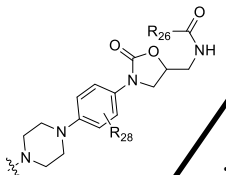
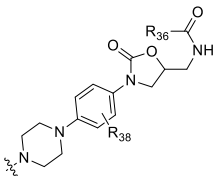


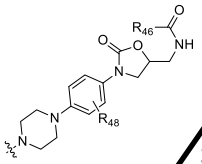
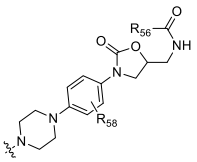
(VI)

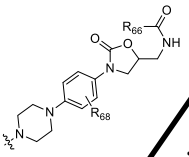


(VII)

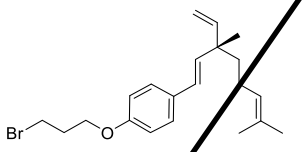
,

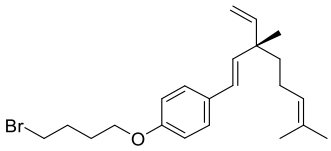
wherein X_2 is $NR_{22}R_{23}$, OR_{25} or  ; X_3 is $NR_{32}R_{33}$, OR_{35} or  ;

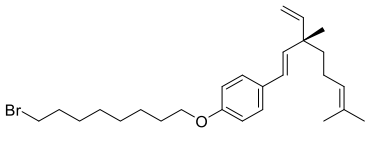
X_4 is $NR_{42}R_{43}$, OR_{45} or  ; X_5 is $NR_{52}R_{53}$, OR_{55} or  ; and X_6 is

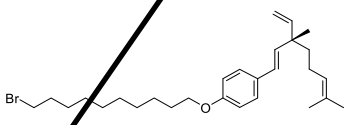
$NR_{62}R_{63}$, OR_{65} or  .

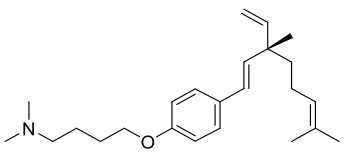
11. The bakuchiol derivative and a pharmaceutically acceptable salt thereof according to claim 1, selected from the following compounds:

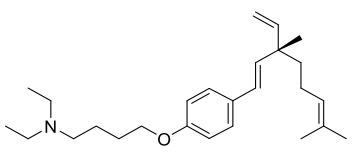


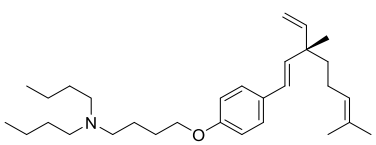
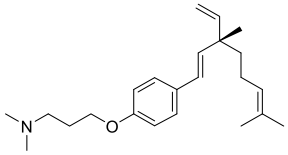
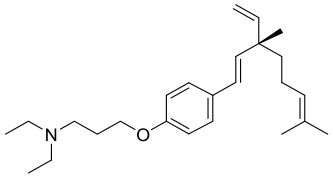
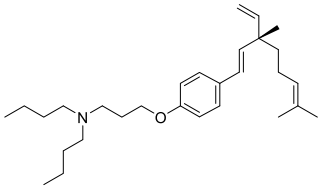
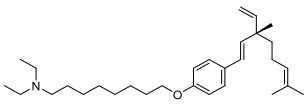
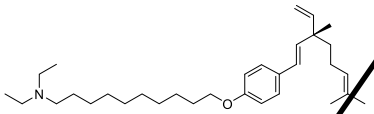
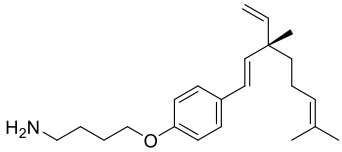
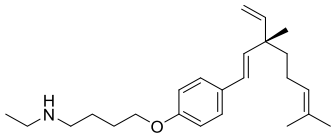
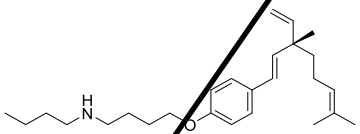
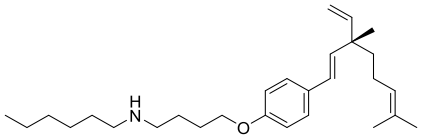
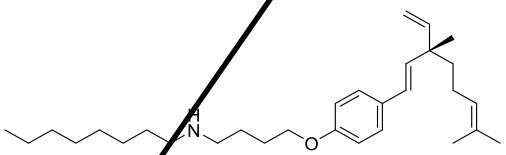
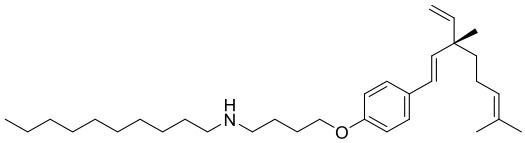
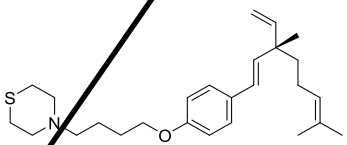
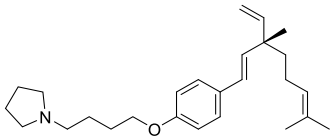
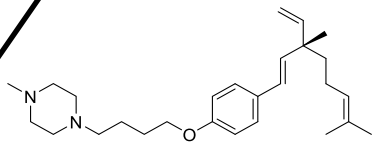
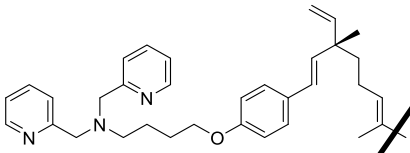
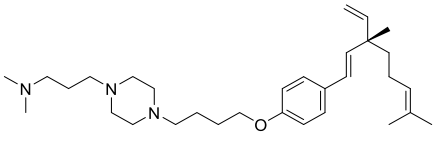
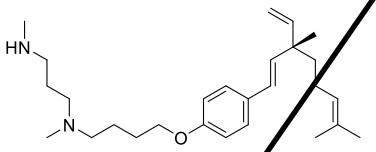
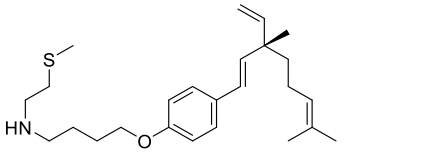
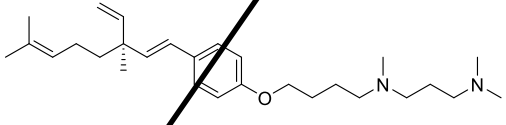
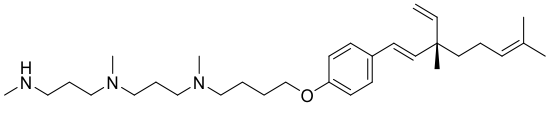
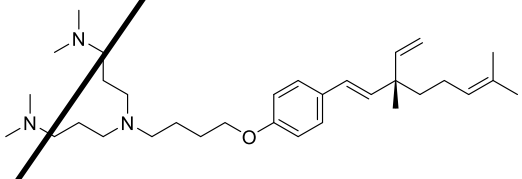
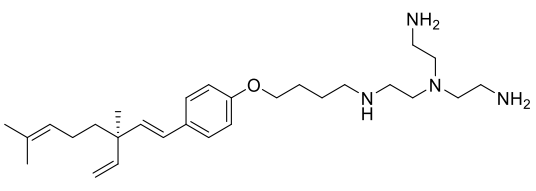


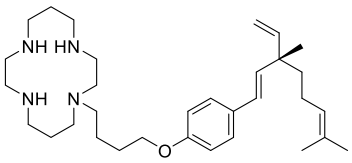
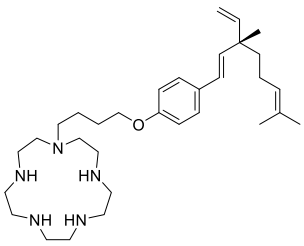
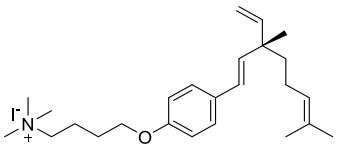
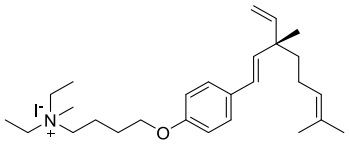
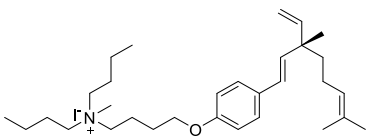
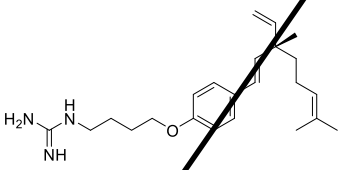
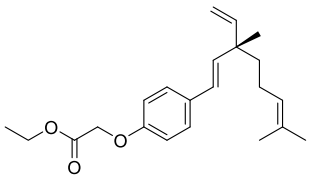
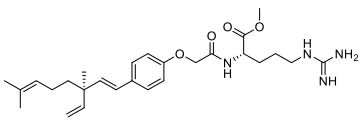
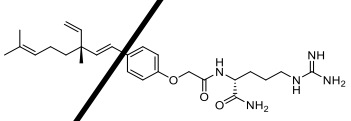
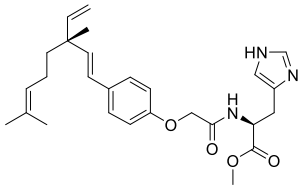
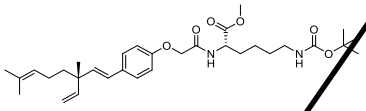
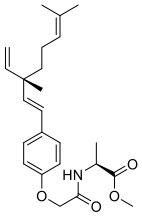
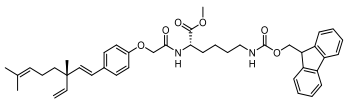
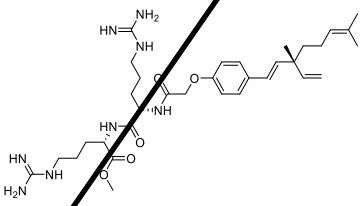
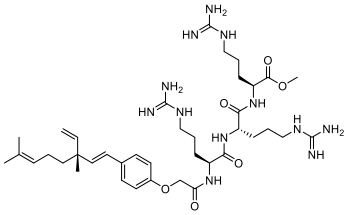


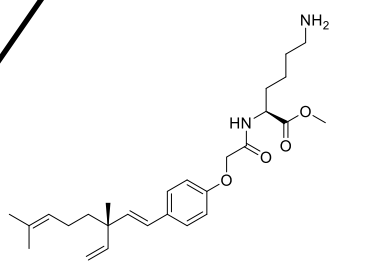
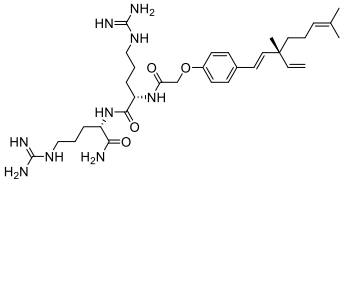


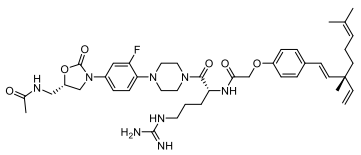
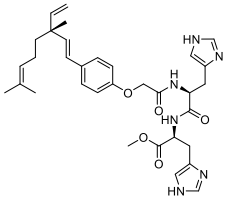
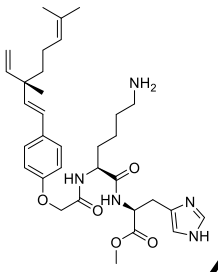
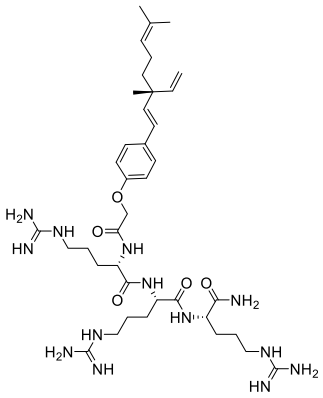
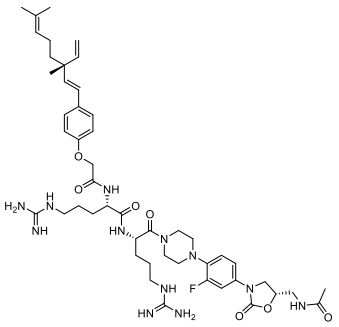
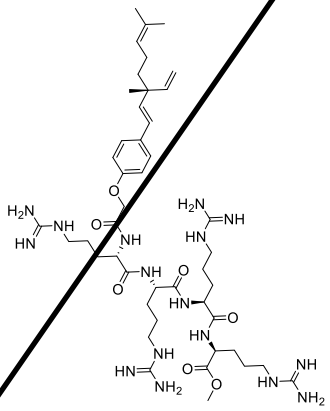
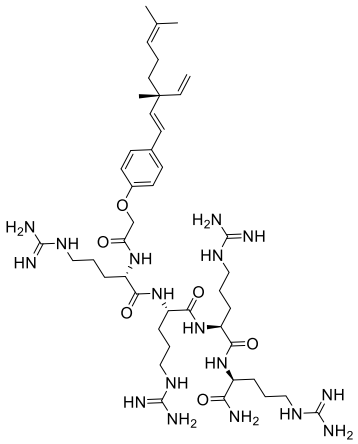
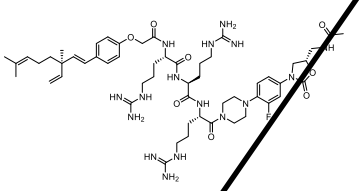
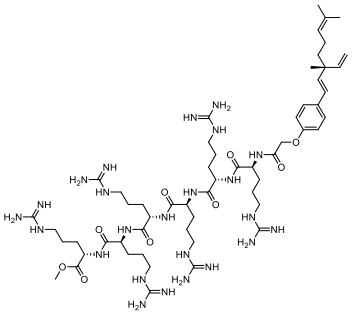
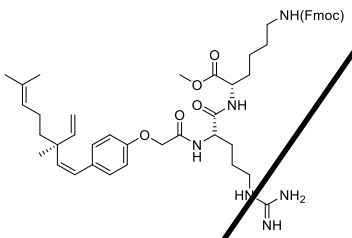
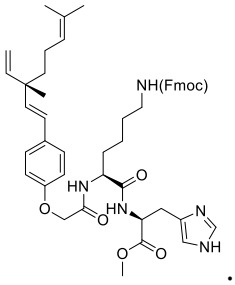




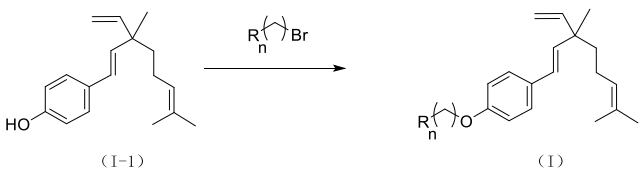
























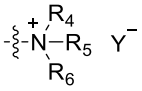
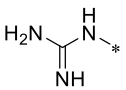
12. A preparation method of the bakuchiol derivative and a pharmaceutically acceptable salt thereof of any one of claims 1-11, wherein when R is a halogen, the preparation method comprises the following step:

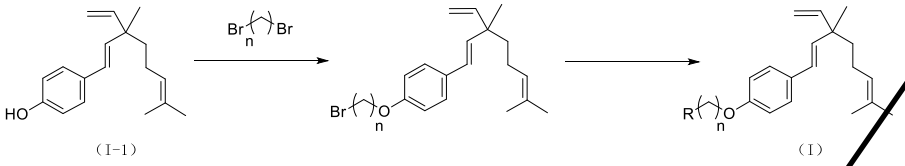


(I-1) (I)

reacting a compound shown in formula (I-1) with , to obtain a compound shown in

formula (I-1) with R being a halogen;

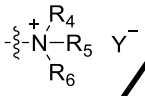
when R is NR_4R_5,  or , the preparation method comprises the following steps:

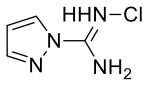
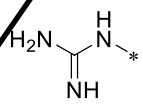


(I-1) (I)

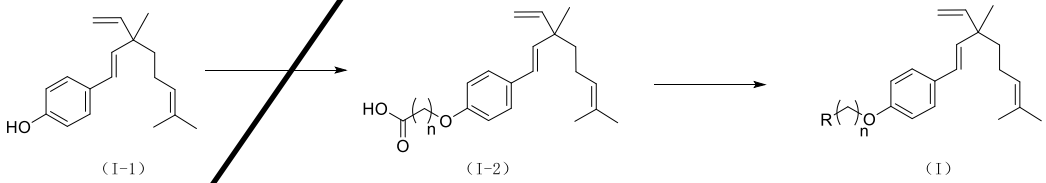
reacting a compound shown in formula (I-1) with , to obtain an intermediate with R being Br;

reacting the intermediate with R being Br with HNR_4R_5, to obtain a compound shown in formula (I) with R being NR_4R_5;

reacting the compound shown in formula (I) with R being NR_4R_5 with haloalkyl, to obtain a compound shown in formula (I) with R being ; and

reacting a compound shown in formula (I) with R being NH_2 with , to obtain a compound shown in formula (I) with R being ; and

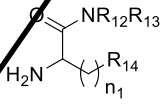
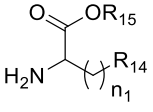
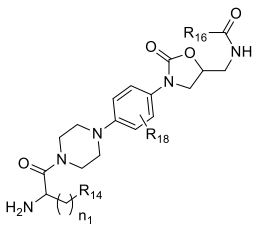
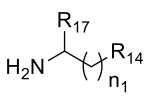
when R is selected from $CONR_1R_2$ and $-COOR_3$, the preparation method comprises the following steps:



(I-1) (I-2) (I)

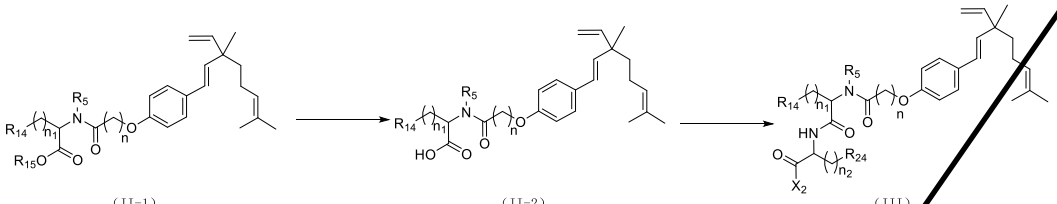
performing a condensation reaction on a compound shown in formula (I-1) and an alkyl bromoalkylate, to obtain a compound shown in formula (I) with R being $-COOR_3$;

hydrolyzing to obtain a compound shown in formula (I-2); and

performing a condensation reaction on the compound shown in formula (I-2) and , ,  or , to obtain a compound shown

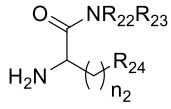
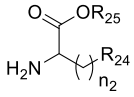
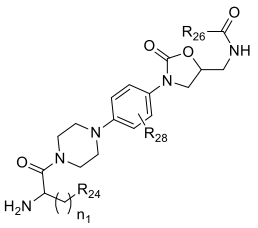
in formula (I) with R being $CONR_1R_2$.

13. The preparation method according to claim 12, wherein when R is selected from $CONR_1R_2$, the preparation method further comprises the following steps:



(II-1) (II-2) (III)

performing a hydrolysis reaction on a compound shown in formula (II-1), to obtain a compound shown in formula (II-2);

performing a condensation reaction on the compound shown in formula (II-2) and ,  or , to obtain a compound shown in formula (III); and

optionally, according to this cycle, hydrolyzing a compound containing an ester group, and then performing a condensation reaction with corresponding amine, to obtain a compound shown in formula (I) containing a target fragment;

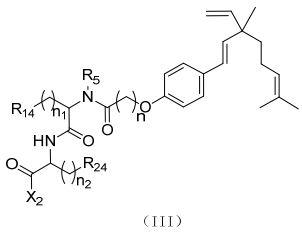
wherein X_2 is as defined in claim 10.

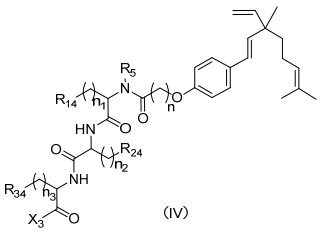
14. A pharmaceutical composition comprising at least one of the bakuchiol derivative and a pharmaceutically acceptable salt thereof of any one of claims 1-11, and a pharmaceutically acceptable excipient.

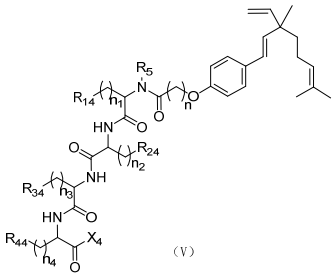
15. Use of the bakuchiol derivative and a pharmaceutically acceptable salt thereof of any one of claims 1-11 or the pharmaceutical composition of claim 14 in preparation of antibacterial agents.

CLAIMS

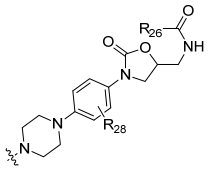
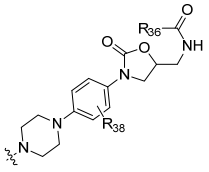
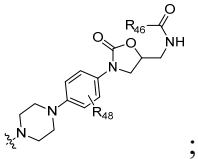
1. A bakuchiol derivative and a pharmaceutically acceptable salt thereof, selected from a compound of any of the following general formulae:


(III)


(IV)


(V)

,

wherein X_2 is $NR_{22}R_{23}$ or  ; X_3 is $NR_{32}R_{33}$, OR_{35} or  ; X_4 is OR_{45} or  ;

R_{22} and R_{23} are each independently selected from: -H;

R_{32} and R_{33} are each independently selected from: -H;

wherein R_{14}, R_{24}, R_{34} and R_{44} are each independently selected from: guanidyl, $-NR_4R_5$ or 5- to 20-membered nitrogen-containing heteroaryl;

R_4 and R_5 are each independently selected from: -H;

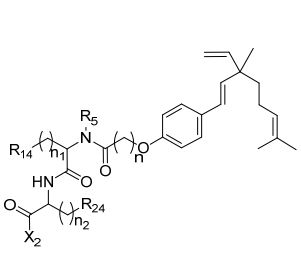
R_{26}, R_{35}, R_{36}, R_{45} and R_{46} are each independently selected from: C_{1-6} alkyl;

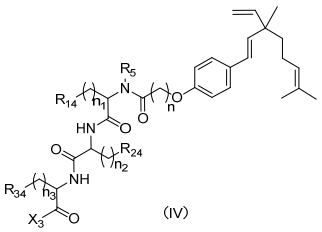
R_{28}, R_{38} and R_{48} are each independently selected from: -H or halogen;

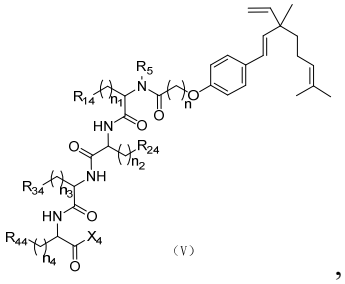
each of n_1, n_2, n_3 and n_4 is independently 0, 1, 2, 3 or 4;

n is an integer from 1 to 10.

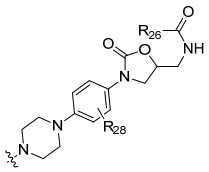
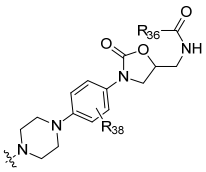
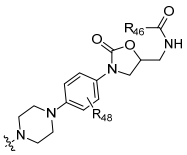
2. The bakuchiol derivative and a pharmaceutically acceptable salt thereof according to claim 1, selected from a compound of any of the following general formulae:


(III)


(IV)


(V)

,

X_2 is  ; X_3 is  ; X_4 is  ;

wherein R_{14}, R_{24}, R_{34} and R_{44} are each independently selected from: guanidyl, -NR_4R_5 or 5- to 20-membered nitrogen-containing heteroaryl;

R_4 and R_5 are each independently selected from: -H;

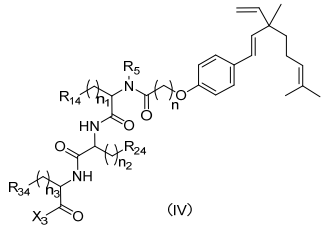
R_{26}, R_{36} and R_{46} are each independently selected from: C_{1-6} alkyl;

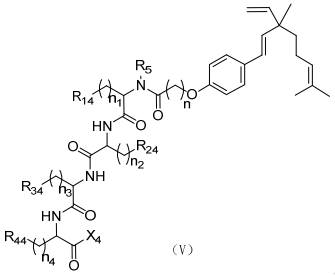
R_{28}, R_{38} and R_{48} are each independently selected from: -H or halogen;

each of n_1, n_2, n_3 and n_4 is independently 0, 1, 2, 3 or 4;

n is an integer from 1 to 10.

3. The bakuchiol derivative and a pharmaceutically acceptable salt thereof according to claim 1, selected from a compound of any of the following general formulae:


(IV)


(V)

,

X_3 is OR_{35}; X_4 is OR_{45};

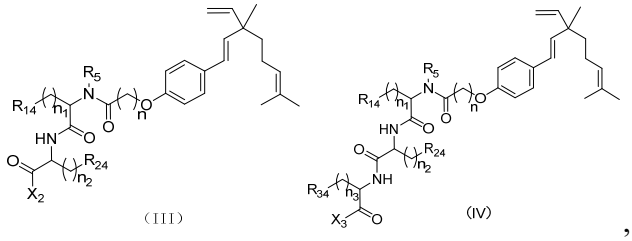
wherein R_{14}, R_{24}, R_{34} and R_{44} are each independently selected from: guanidyl, -NR_4R_5 or 5- to 20-membered nitrogen-containing heteroaryl;

R_{35} and R_{45} are each independently selected from: C_{1-6} alkyl;

each of n_1, n_2, n_3 and n_4 is independently 0, 1, 2, 3 or 4;

n is an integer from 1 to 10.

4. The bakuchiol derivative and a pharmaceutically acceptable salt thereof according to claim 1, selected from a compound of any of the following general formulae:



(III) (IV)

,

wherein X_2 is $NR_{22}R_{23}$; X_3 is $NR_{32}R_{33}$;

R_{22} and R_{23} are each independently selected from: -H;

R_{32} and R_{33} are each independently selected from: -H;

wherein R_{14}, R_{24} and R_{34} are each independently selected from: guanidyl, $-NR_4R_5$ or 5- to 20-membered nitrogen-containing heteroaryl;

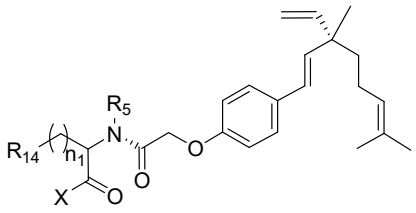
R_4 and R_5 are each independently selected from: -H;

each of n_1, n_2, n_3 and n_4 is independently 0, 1, 2, 3 or 4;

n is an integer from 1 to 10.

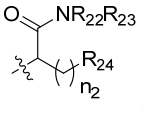
5. The bakuchiol derivative and a pharmaceutically acceptable salt thereof according to claim 1, wherein R_{14}, R_{24}, R_{34} and R_{44} are each independently selected from: guanidyl, $-NR_4R_5$, $-SR_4$, 5-membered nitrogen-containing heteroaryl.

6. The bakuchiol derivative and a pharmaceutically acceptable salt thereof according to claim 1, selected from a compound of the following general formula:

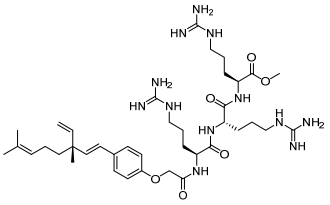


(II'),

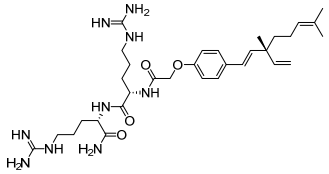
wherein X is $NR_{12}R_{13}$;

one of R_{12} and R_{13} is H, and another one is selected from  .

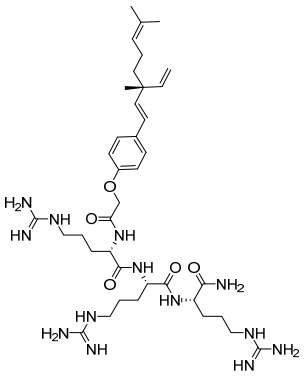
7. The bakuchiol derivative and a pharmaceutically acceptable salt thereof according to claim 1, selected from the following compounds:



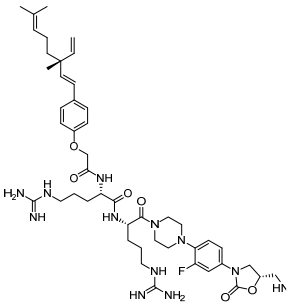
compound 45



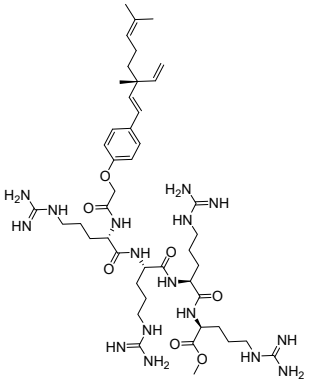
compound 49



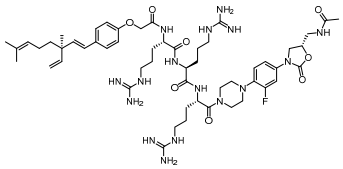
compound 58



compound 59



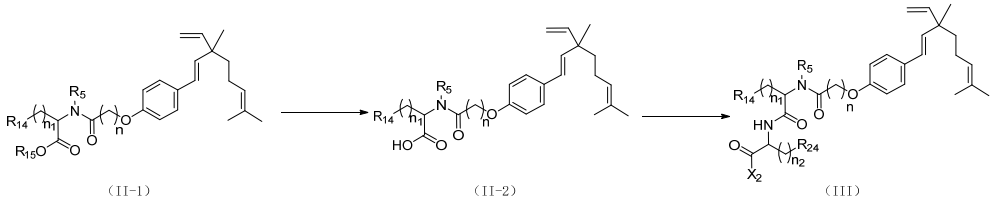
compound 60



compound 63

.

8. A preparation method of the bakuchiol derivative and a pharmaceutically acceptable salt thereof of any one of claims 1-7, wherein the preparation method comprises the following step:



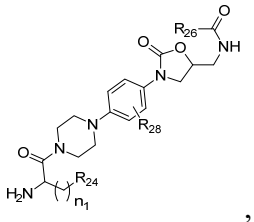
(II-1) (II-2) (III)

performing a hydrolysis reaction on a compound shown in formula (II-1), to obtain a compound shown in formula (II-2);

performing a condensation reaction on the compound shown in formula (II-2) and



or



, to obtain a compound shown in formula (III); and

R_{15} is defined as R_{35} in claim 1.

9. A pharmaceutical composition comprising at least one of the bakuchiol derivative and a pharmaceutically acceptable salt thereof of any one of claims 1-7, and a pharmaceutically acceptable excipient.

10. Use of the bakuchiol derivative and a pharmaceutically acceptable salt thereof of any one of claims 1-7 or the pharmaceutical composition of claim 9 in preparation of antibacterial agents.