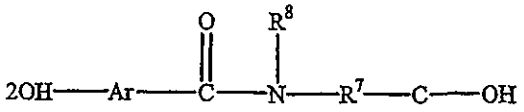
We claim:

1. A pharmaceutical composition comprising (a) acyclovir and (b) a delivery agent of the formula



or a salt thereof, wherein:

Ar is phenyl or naphthyl;

Ar is optionally substituted with one or more of -OH, halogen, C_1-C_4 alkyl, C_1-C_4 alkenyl, C_1-C_4 alkoxy or C_1-C_4 haloalkoxy;

R^7 is C_4-C_{20} alkyl, C_4-C_{20} alkenyl, phenyl, naphthyl, (C_1-C_{10} alkyl) phenyl, (C_1-C_{10} alkenyl)phenyl, (C_1-C_{10} alkyl) naphthyl, (C_1-C_{10} alkenyl) naphthyl, phenyl(C_1-C_{10} alkyl), phenyl(C_1-C_{10} alkenyl), naphthyl(C_1-C_{10} alkyl), or naphthyl(C_1-C_{10} alkenyl);

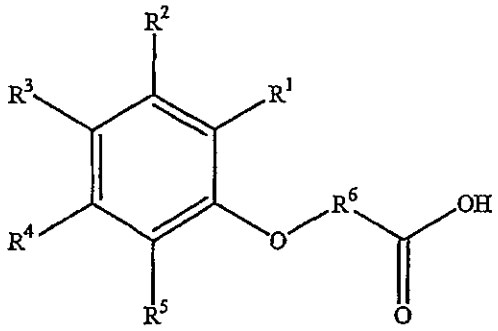
R^8 is hydrogen, C_1 to C_4 alkyl, C_2 to C_4 alkenyl, C_1 to C_4 alkoxy, or C_1-C_4 haloalkoxy;

R^7 is optionally substituted with C_1 to C_4 alkyl, C_2 to C_4 alkenyl, C_1 to C_4 alkoxy, C_1-C_4 haloalkoxy, -OH, -SH, $-CO_2R^9$, or any combination thereof;

R^9 is hydrogen, C_1 to C_4 alkyl, or C_2 to C_4 alkenyl; and

R^7 is optionally interrupted by oxygen, nitrogen, sulfur or any combination.

2. A pharmaceutical composition comprising (a) acyclovir and (b) a delivery agent of the formula



or a salt thereof, wherein

R^1, R^2, R^3, and R^4 are independently H, -OH, halogen, C_1-C_4 alkyl, C_2-C_4 alkenyl, C_1-C_4 alkoxy, $-C(O)R^8$, $-NO_2$, $-NR^9R^{10}$, or $-N^+R^9R^{10}R^{11}$ $(R^{12})^-$;

R^5 is H, -OH, $-NO_2$, halogen, $-CF_3$, $-NR^{14}R^{15}$, $-N^+R^{14}R^{15}R^{16}$ $(R^{13})^-$, amide, C_1-C_{12} alkoxy, C_1-C_{12} alkyl, C_2-C_{12} alkenyl, carbamate, carbonate, urea, or $-C(O)R^{18}$;

R^5 is optionally substituted with halogen, -OH, -SH, or -COOH;

R^5 is optionally interrupted by O, N, S, or -C(O)-;

R^6 is a C_1-C_{12} alkylene, C_2-C_{12} alkenylene, or arylene;

R^6 is optionally substituted with a C_1-C_4 alkyl, C_2-C_4 alkenyl, C_1-C_4 alkoxy, -OH, -SH, halogen, $-NH_2$, or $-CO_2R^8$;

R^6 is optionally interrupted by O or N;

R^7 is a bond or arylene;

R^7 is optionally substituted with -OH, halogen, $-C(O)CH_3$, $-NR^{10}R^{11}$, or - $N^+R^{10}R^{11}R^{12}$ $(R^{13})^-$;

each occurrence of R^8 is independently H, C_1-C_4 alkyl, C_2-C_4 alkenyl, or $-NH_2$;

R^9, R^{10}, R^{11}, and R^{12} are independently H or C_1-C_{10} alkyl;

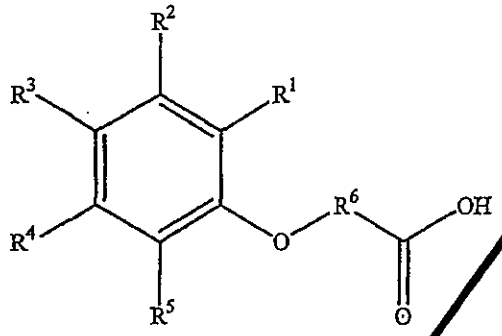
R^{13} is a halide, hydroxide, sulfate, tetrafluoroborate, or phosphate; and

R^{14}, R^{15} and R^{16} are independently H, C_1-C_{10} alkyl, C_1-C_{10} alkyl substituted with -COOH, C_2-C_{12} alkenyl, C_2-C_{12} alkenyl substituted with –COOH, or $-C(O)R^{17}$;

R^{17} is –OH, C_1-C_{10} alkyl, or C_2-C_{12} alkenyl; and

R^{18} is H, C_1-C_6 alkyl, -OH, $-NR^{14}R^{15}$, or $N^+R^{14}R^{15}R^{16}$ $(R^{13})^-$.

3. A pharmaceutical composition comprising (a) acyclovir and (b) a delivery agent of the formula



or a salt thereof, wherein

R^1, R^2, R^3, R^4 and R^5 are independently H, -CN, -OH, OCH_3, or halogen, at least one of R^1, R^2, R^3, R^4 and R^5 being -CN; and

R^6 is a C_1-C_{12} linear or branched alkylene, alkenylene, arylene, alkyl(arylene) or aryl(alkylene).

4. A pharmaceutical composition of any one of Claims 1, 2 or 3, wherein the delivery agent is selected from the group consisting of Delivery agents is SNAC or SNAD or a pharmaceutically acceptable salt thereof.

5. The pharmaceutical composition of Claim 1 wherein the delivery agent is N-(8-[2-hydroxybenzoyl]-amino)caprylic acid or a pharmaceutically acceptable salt thereof.

6. The pharmaceutical composition of Claim 1 wherein the delivery agent is wherein the delivery agent is N-(10-[2-hydroxybenzoyl]-amino)decanoic acid or a pharmaceutically acceptable salt thereof.

7. The pharmaceutical composition of any claims 1-6, wherein the pharmaceutical composition provides bioavailability (i.e., AUC) substantially equivalent to the acyclovir formulation marketed as Zovirax® under U.S. FDA NDA No. 18828, 19909, or 20089 when:

(1) 200, 400, or 800 mg of the acyclovir formulation is administered every 4

hours 5 times daily,

(2) 400 mg of the acyclovir formulation is administered 2 times daily,

(3) 200 mg of the acyclovir formulation is administered 3 times daily,

(4) 200 mg of the acyclovir formulation is administered 4 times daily, or

(5) 200 mg of the acyclovir formulation is administered 5 times daily.

8. A dosage unit form comprising:

(A) the pharmaceutical compositions of any one of the preceding claims; and

(B) (a) an excipient,

(b) a diluent,

(c) a disintegrant,

(d) a lubricant,

(e) a plasticizer,

(f) a colorant,

(g) a dosing vehicle, or

(h) any combination thereof.

9. The dosage unit form of Claim 8, wherein the dosage unit form is in the form of a tablet, a capsule, a particle, a powder, a sachet, or a liquid.

10. The dosage unit form of Claim 8, wherein the dosing vehicle is a liquid selected from the group consisting of water, aqueous propylene glycol, phosphate buffer, 1,2-propane diol, ethanol, and any combination thereof.

11. A method of treating a viral infection in a patient in need thereof, comprising the

step of administering to the patient an effective amount of the pharmaceutical composition of any one of claims 1-8.

12. A method of treating a condition or disorder caused by a virus in a patient in need thereof, comprising the step of administering an animal an effective amount of the pharmaceutical composition of any one of claims 1-8.

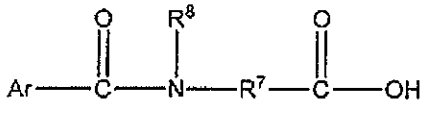
13. The method of Claim 12, wherein the condition or disorder is caused by a virus selected from the group consisting of herpes simplex 1, herpes simplex 2, varicella zoster virus, cytomegalovirus and Epstein-Barr virus.

14. A method of improving the bioavailability of acyclovir in an animal in need thereof, the method comprising the step of administering a formulation of any one of claims 1, 2 or 3.

15. A method of preparing a pharmaceutical composition comprising the step of mixing at least one delivery agent compound and acyclovir or a salt or prodrug thereof.

The claims defining the invention are as follows:

1. A pharmaceutical composition comprising (a) acyclovir and (b) a delivery agent of formula (A):



(A)

or a salt thereof, wherein:

Ar is 2-hydroxyphenyl or 2-hydroxynaphthyl;

Ar is optionally further substituted with one or more of -OH, halogen, C_1-C_4 alkyl, C_2-C_4 alkenyl, C_1-C_4 alkoxy or C_1-C_4 haloalkoxy;

R^7 is C_4-C_{20} alkyl, C_4-C_{20} alkenyl, phenyl, naphthyl, (C_1-C_{10} alkyl) phenyl, (C_2-C_{10} alkenyl)phenyl, (C_1-C_{10} alkyl) naphthyl, (C_2-C_{10} alkenyl) naphthyl, phenyl(C_1-C_{10} alkyl), phenyl(C_2-C_{10} alkenyl), naphthyl(C_1-C_{10} alkyl), or naphthyl(C_2-C_{10} alkenyl);

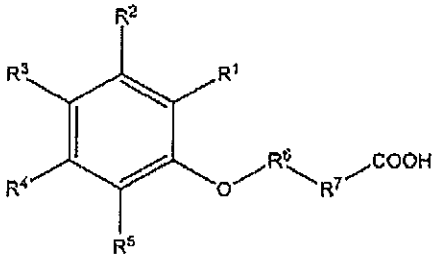
R^8 is hydrogen, C_1-C_4 alkyl, C_2-C_4 alkenyl, C_1-C_4 alkoxy, or C_1-C_4 haloalkoxy;

R^7 is optionally substituted with C_1-C_4 alkyl, C_2-C_4 alkenyl, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, -OH, -SH, $-CO_2R^9$, or any combination thereof;

R^9 is hydrogen, C_1-C_4 alkyl, or C_2-C_4 alkenyl; and

R^7 is optionally interrupted by oxygen, nitrogen, sulfur or any combination thereof.

2. A pharmaceutical composition comprising (a) acyclovir and (b) a delivery agent of formula (B):



(B)

or a salt thereof, wherein

R^1, R^2, R^3, and R^4 are independently H, -OH, halogen, C_1-C_4 alkyl, C_2-C_4 alkenyl, C_1-C_4 alkoxy, $-C(O)R^8$, $-NO_2$, $-NR^9R^{10}$, or $-N^+R^9R^{10}R^{11}$ $(R^{12})^-$;

R^5 is H, -OH, $-NO_2$, halogen, $-CF_3$, $-NR^{14}R^{15}$, $-N^+R^{14}R^{15}R^{16}$ $(R^{13})^-$, amide, C_1-C_{12} alkoxy, C_1-C_{12} alkyl, C_2-C_{12} alkenyl, carbamate, carbonate, urea, or $-C(O)R^{18}$;

R^5 is optionally substituted with halogen, -OH, -SH, or -COOH;

R^6 is optionally interrupted by O, N, S, or -C(O)-;

R^6 is a C_1-C_{12} alkylene, C_2-C_{12} alkenylene, or arylene;

R^6 is optionally substituted with a C_1-C_4 alkyl, C_2-C_4 alkenyl, C_1-C_4 alkoxy, -OH, -SH, halogen, $-NH_2$, or $-CO_2R^8$;

R^7 is a bond or arylene;

R^7 is optionally substituted with -OH, halogen, $-C(O)CH_3$, $-NR^{10}R^{11}$, or $-N^+R^{10}R^{11}R^{12}$ $(R^{13})^-$;

each occurrence of R^8 is independently H, C_1-C_4 alkyl, C_2-C_4 alkenyl, or $-NH_2$;

R^9, R^{10}, R^{11}, and R^{12} are independently H or C_1-C_{10} alkyl;

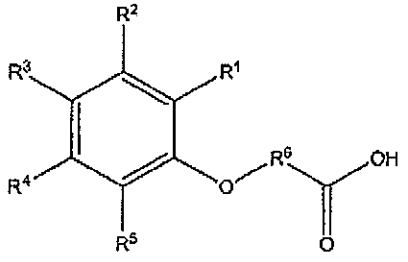
R^{13} is a halide, hydroxide, sulfate, tetrafluoroborate, or phosphate; and

R^{14}, R^{15} and R^{16} are independently H, C_1-C_{10} alkyl, C_1-C_{10} alkyl substituted with -COOH, C_2-C_{12} alkenyl, C_2-C_{12} alkenyl substituted with -COOH, or $-C(O)R^{17}$;

R^{17} is -OH, C_1-C_{10} alkyl, or C_2-C_{12} alkenyl; and

R^{18} is H, C_1-C_6 alkyl, -OH, $-NR^{14}R^{15}$, or $N^+R^{14}R^{15}R^{16}$ $(R^{13})^-$.

3. A pharmaceutical composition comprising (a) acyclovir and (b) a delivery agent of formula (C):



(C)

or a salt thereof, wherein

R^1, R^2, R^3, R^4 and R^5 are independently H, -CN, -OH, $-OCH_3$, or halogen, at least one of R^1, R^2, R^3, R^4 and R^5 being -CN; and

R^6 is a C_1-C_{12} linear or branched alkylene, alkenylene, arylene, alkyl(arylene) or aryl(alkylene).

4. A pharmaceutical composition of claim 1, wherein the delivery agent is N-(8-[2-hydroxybenzoyl]-amino)caprylic acid, N-(10-[2-hydroxybenzoyl]-amino)decanoic acid, or a pharmaceutically acceptable salt thereof.

5. The pharmaceutical composition of claim 1, wherein the delivery agent is N-(8-[2-hydroxybenzoyl]-amino)caprylic acid or a pharmaceutically acceptable salt thereof.

6. The pharmaceutical composition of claim 1, wherein the delivery agent is N-(10-[2-hydroxybenzoyl]-amino)decanoic acid or a pharmaceutically acceptable salt thereof.

7. The pharmaceutical composition of any one of claims 1-6, wherein the pharmaceutical composition provides bioavailability (i.e., AUC) substantially equivalent to the acyclovir formulation marketed as Zovirax® under U.S. FDA NDA No. 18828, 19909, or 20089 when:

(1) 200, 400, or 800 mg of the acyclovir formulation is administered every 4 hours 5 times daily,

(2) 400 mg of the acyclovir formulation is administered 2 times daily,

(3) 200 mg of the acyclovir formulation is administered 3 times daily,

(4) 200 mg of the acyclovir formulation is administered 4 times daily, or

(5) 200 mg of the acyclovir formulation is administered 5 times daily.

8. A dosage unit form comprising:

(A) a pharmaceutical composition of any one of the preceding claims; and

(B) (a) an excipient,

(b) a diluent,

(c) a disintegrant,

(d) a lubricant,

(e) a plasticizer,

(f) a colorant,

(g) a dosing vehicle, or

(h) any combination thereof.

9. The dosage unit form of claim 8, wherein the dosage unit form is in the form of a tablet, a capsule, a particle, a powder, a sachet, or a liquid.

10. The dosage unit form of claim 8, wherein the dosing vehicle is a liquid selected from the group consisting of water, aqueous propylene glycol, phosphate buffer, 1,2-propane diol, ethanol, and any combination thereof.

11. A method for administering an effective amount of acyclovir to a patient in need thereof, comprising the step of orally administering a pharmaceutical composition of any one of claims 1-7 or the dosage unit form of claim 8.

12. A method of improving the bioavailability of acyclovir in a patient in need thereof, the method comprising the step of administering to the patient a pharmaceutical composition of any one of claims 1-7 or the dosage unit form of claim 8.

13. A method of preparing a pharmaceutical composition comprising the step of mixing at least one delivery agent compound as defined in any one of claims 1 to 6 and acyclovir.

14. Use of acyclovir and a delivery agent as defined in any one of claims 1 to 6 in the manufacture of a medicament for treating a viral infection.

15. Use of acyclovir and a delivery agent as defined in any one of claims 1 to 6 in the manufacture of a medicament for treating a condition or disorder caused by a virus.

16. Use of acyclovir and a delivery agent as defined in any one of claims 1 to 6 in the manufacture of a medicament for improving the bioavailability of acyclovir.