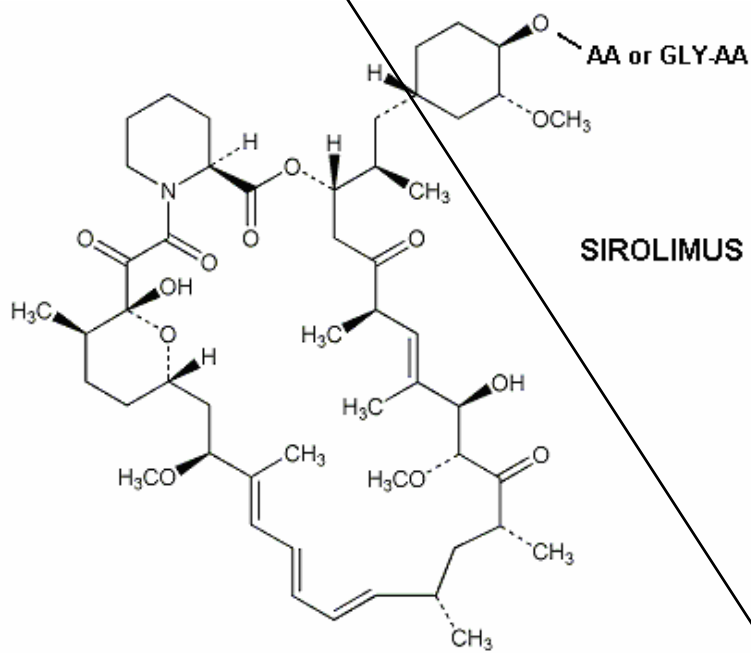
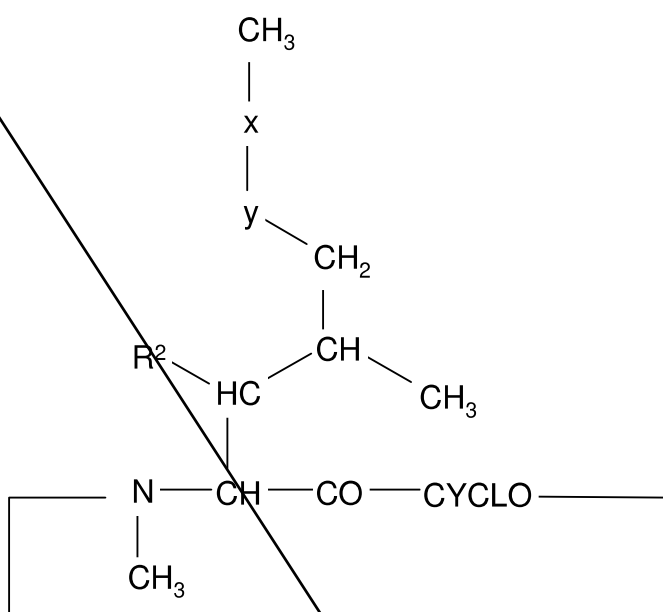


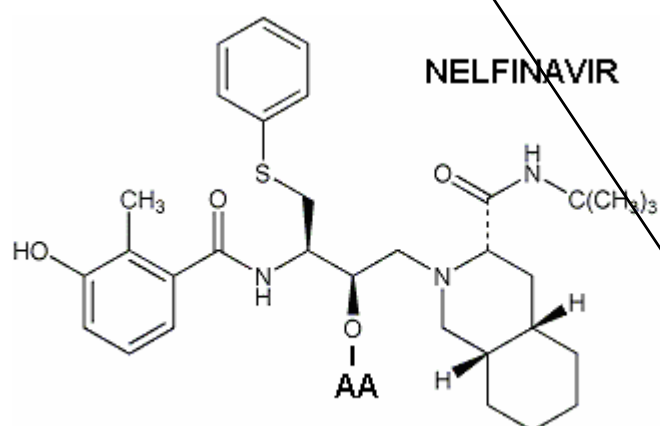
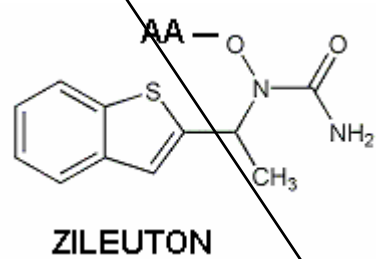
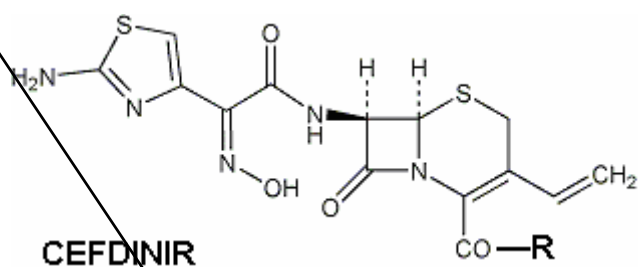
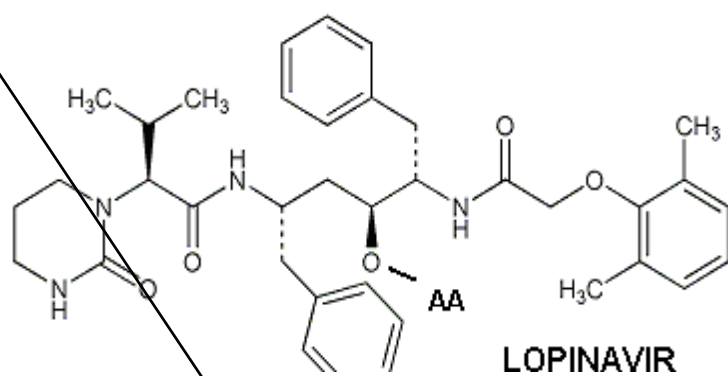
IN THE CLAIMS:

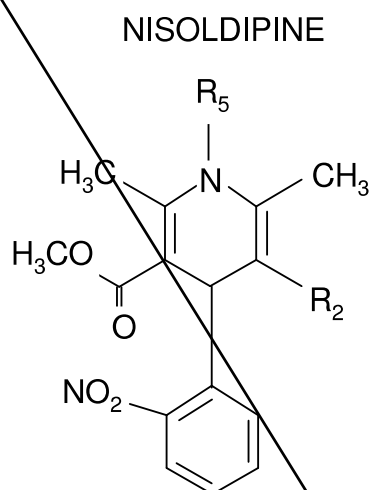
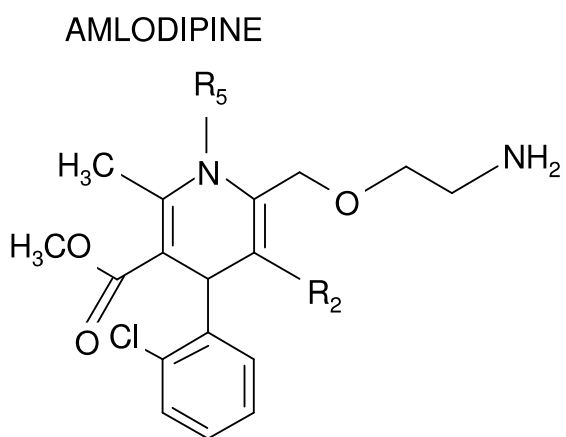
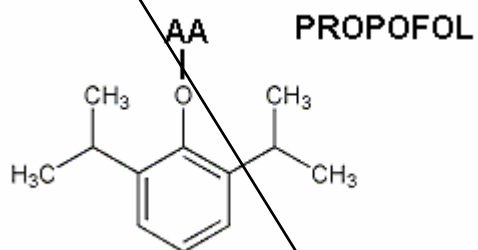
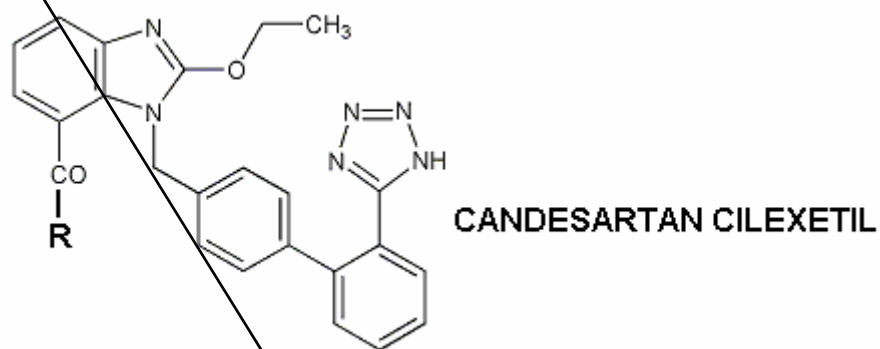
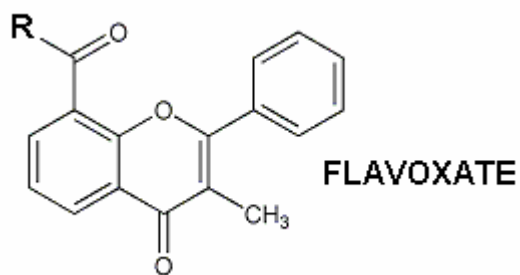
1. A method for enhancing at least two of the therapeutic qualities of a drug having a functionality group selected from the group consisting of hydroxy, amino, carboxy or acylating derivatives of said carboxy group, said improved therapeutic quality being
- 5 selected from the group consisting of:
- (a) improved taste or smell
 - (b) desired octanol/water partition coefficient
 - (c) improved stability
 - (d) enhanced penetration of blood-brain barrier
 - 10 (e) elimination of first pass effect in the liver
 - (f) reduction of entero-hepatic recirculation
 - (g) painless injection with parental formulation
 - (h) improved bioavailability
 - (i) improved changes in the rate of absorption
 - 15 (j) reduced side effects
 - (k) dose proportionality
 - (l) selective hydrolysis of the prodrug at site of action
 - (m) controlled release properties
 - (n) targeted drug delivery
 - 20 (o) reduction in toxicity
 - (p) reduced dose
 - (q) alteration of metabolic pathway to deliver more drug at site of action
 - (r) increased solubility in aqueous solution and
 - (s) enhanced efficacy,
- 25 the method comprising (a) reacting the drug with an amino acid under conditions effective to form a covalent bond between the drug and the amino acid and (b) administering the product of (a) to a patient in need thereof, wherein said amino acid is a naturally occurring α -L-amino acid.

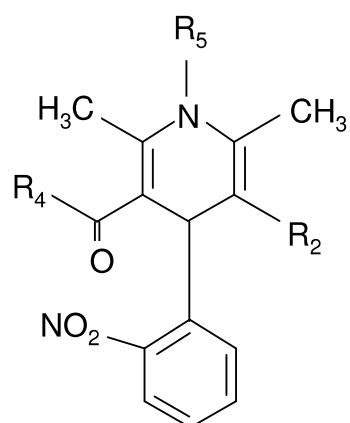
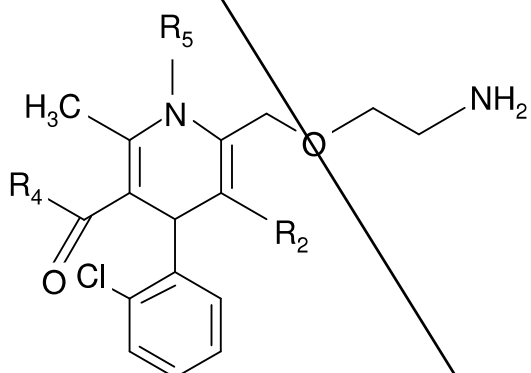
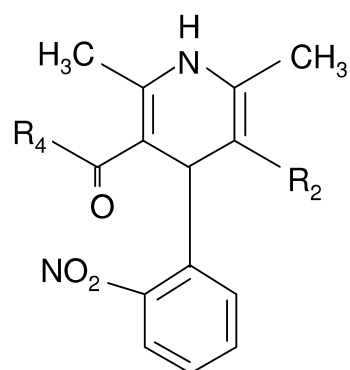
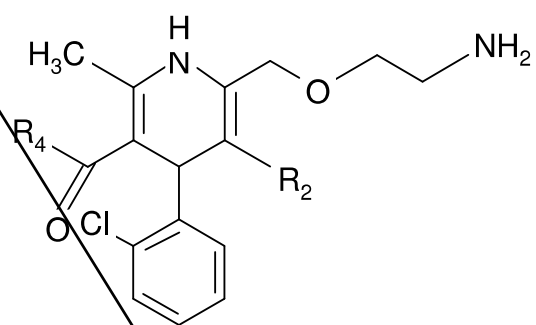
2. The method according to Claim 1 wherein the amino acid is Thr, Hyp, Ser, Tyr, Lys, Leu, Ile, Gly, Asp, Glu, Met, Ala, Val, Pro, His, Nor, Arg, Phe, Trp, Hsr, Car, Ort, Cav, Asn, Gln, Can, Tau, Djk, GABA, Cys, Dcy and Sar.
- 5 3. The method according to Claim 1 or 2 wherein the amino acid is Thr, Hyp, Ser, Tyr, Lys, Leu, Ile, Gly, Asp, Glu, Met, Ala, Val, Pro, His, Arg, Phe, Trp, Gln, Asn, or Cys.
4. The method according to any one of Claims 1 – 3 wherein the the drug is Cyclosporin, Lopinavir, Ritonavir, Cefdinir, Zileuton, Nelfinavir, Flavoxate, Candesarten, Propofol, Nisoldipine, Amlodipine, Ciprofloxacin, Ofloxacin, Fosinopril, Enalapril, Ramipril, Benazepril, Perinodopril, Moexipril, Trandolapril, Cromolyn, Amoxicillin, Cefuroxime, Ceftazidime, Cefpodoxime, Atovaquone, Gancyclovir, Penciclovir, Famciclovir, Acyclovir, Niacin, Bexarotene, Propoxyphene, Salsalate, Acetaminophen, Ibuprofen, Lovastatin, Simvastatin, Atorvastatin, Pravastatin, Fluvastatin, Nadolol, Valsartan, 15 Methylphenidate, Sulfa Drugs, Trovafloxacin, 5-amino-Salicyclic acid, Sulfasalazine, Methylprednisolone, Medroxyprogesterone, Estramustine, Miglitol, Mefloquine, Capacitabine, Danazol, Eprosartan, Valproic Acid, Gabapentin, Omeprazole, Lansoprazole, Megestrol, Metformin, Tazarotene, Sumatriptan, Naratriptan, Zolmitriptan, Aspirin, Olmesartan, Sirolimus, Tacrolimus, Pimecrolimus, Clopidogrel, 20 Amphotericin, Tenofovir, Unoprostone, Fulvestrant, Cefditoren, Efavirenz, Eplerenone, Treprostinil, Adefovir, Salicyclic Acid, Diflunisal, Fenoprofen, Carprofen, Flurbiprofen, Ketoprofen, Naproxen, Etodolac, Sulindac, Indomethacin, Tolmetin, Ketorolac, Ciprofric Acid, Clofibric Acid, Fenofibric Acid, Salazine, or Gemfibrozil or a pharmaceutically acceptable salt of any of said drug.
- 25 5. The method according to any one of Claims 1-4 wherein AA is Threonine, hydroxyproline or Serine.
6. The method according to any one of Claims 1-5 wherein the amino acid is Threonine.
- 30

7. The product from a reaction between a drug having a functionality selected from the group consisting of hydroxy, amino, carboxy or acylating derivative of said carboxy group and a L- α -amino acid under conditions sufficient to form a covalent bond from the reaction of said functional group and said amino acid, or the pharmaceutically acceptable salt thereof, wherein the drug is selected from the group consisting of cyclosporin, lopinavir, Cefdinir, Zileuton, Nelfinavir, Flavoxate, Candesartan, Propofol, nisolidipine, amlodipine, Ciprofloxacin, Ofloxacin, Enlarpril, Ramipril, Fosinopril, Benazepril, Perindopril, Moexipril, Trandolapril, Cromolyn, Amoxicillin, Cephalosporin, Cefuroxime, Cefazidime, Cefpodoxime, Atovaquone, Penciclovir, Famciclovir, Niacin, Bexarotene, Propoxyphene, Salsalate, Acetaminophen, Ibuprofen, Lovastatin, Simvastatin, Atorvastatin, Pravastatin, Fluvastatin, Nadolol, Valsartan, methylphenidate, Sulfa drug, Sulfasalazine, Trivafloxacin, methyl prednisolone, Medroxyprogesterone, Estramustine, Miglitol, Mefloquine, Capacitabine, Danazol, Eprosartan, Valproic acid, Gabapentin, Omeprazole, Lansoprazole, Megestrol, Metformin, Tazarotene, Sumatriptan, Naratriptan, Zolmitriptan, Olmesartan, Aspirin, Sirolimus, Tacrolimus, Pimecrolimus, Clopidogrel, Amphotericin, Tenofovir, Unoprostone, Fulvestrant, Cefditoren, Efavirenz, Eplerenone, salicylic acid, 5-amino salicylic acid, diflunisol, fenoprofen, carprofen, Flurbiprofen, Ketoprofen, naproxen, etodolac, sulindac, indomethacin, tolmetin, ketorolac, ciprofibrilic acid, clofibrilic acid, gemfibrozil, Fenofibrilic acid, or Salazine or a pharmaceutically acceptable salt of any of said drug and wherein the amino acid is Thr, Hyp, Ser, Tyr, Lys, Leu, Ile, Gly, Asp, Glu, Met, Ala, Val, Pro, His, Nor, Arg, Phe, Trp, Hsr, Car, Ort, Cav, Asn, Gln, Can, Tau, Djk, GABA, Cys, Sar or Dcy.
8. The product according to Claim 7 wherein the product is:

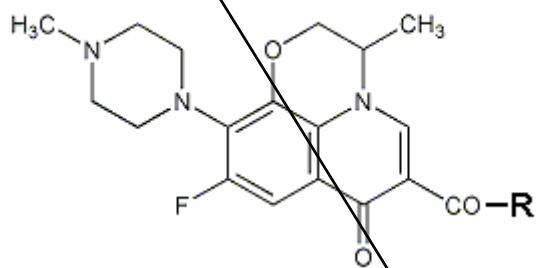




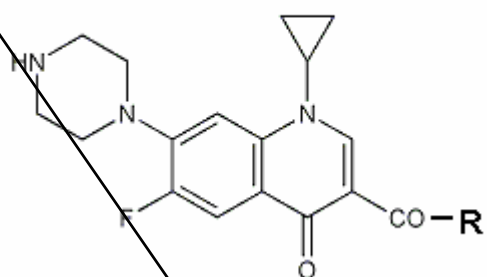




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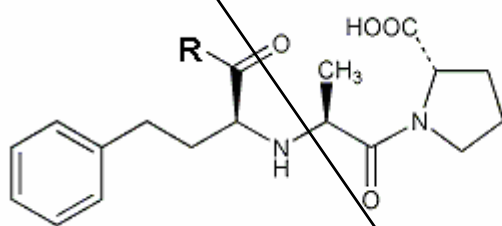


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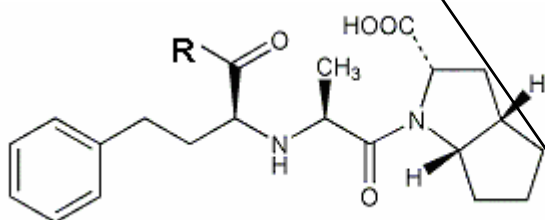
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ENALAPRIL

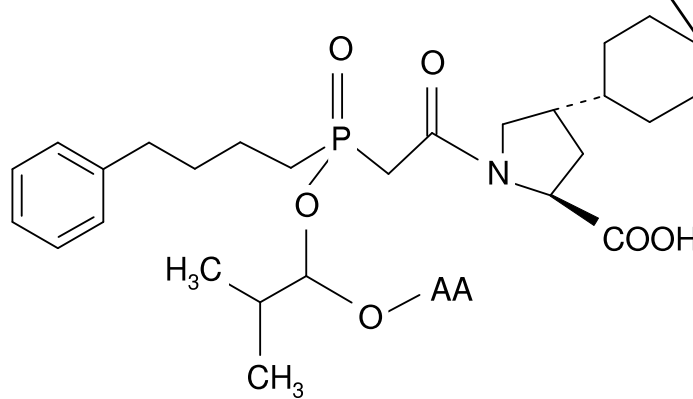


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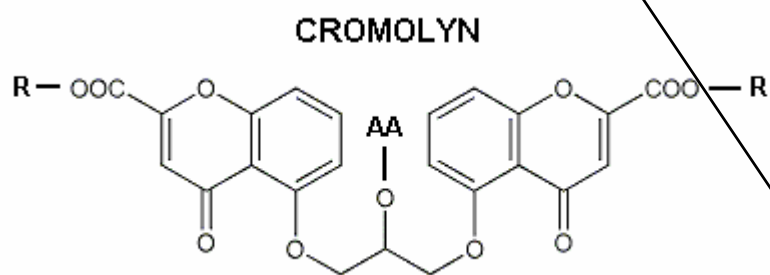
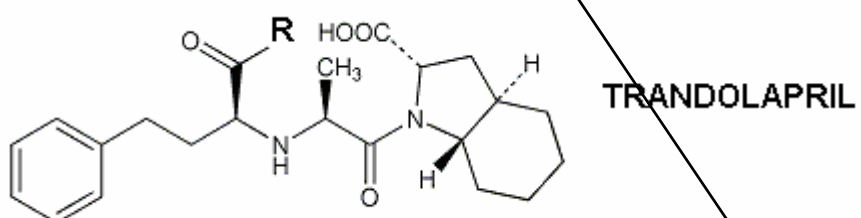
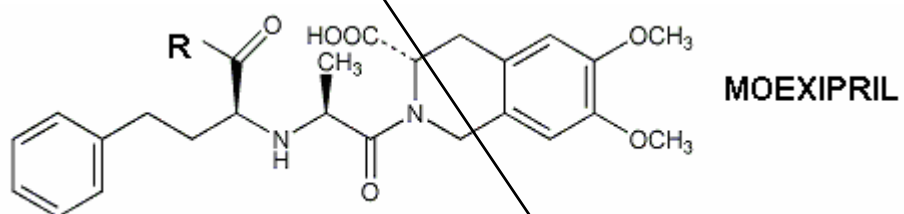
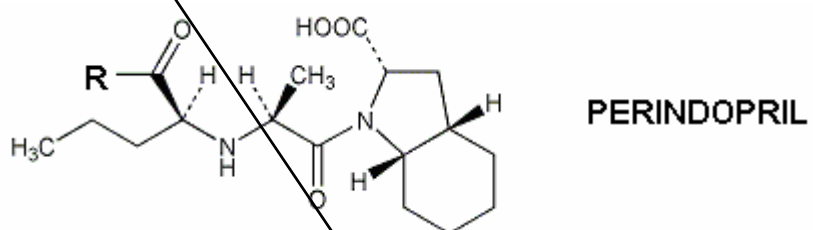
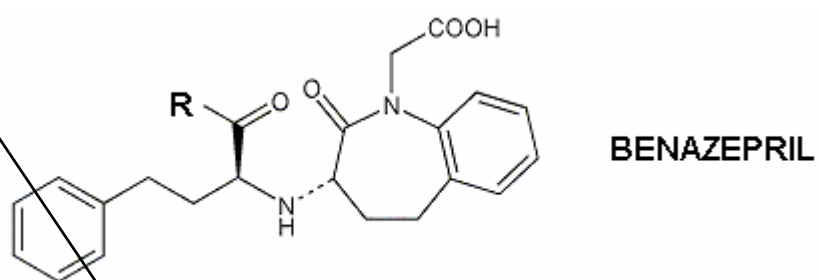
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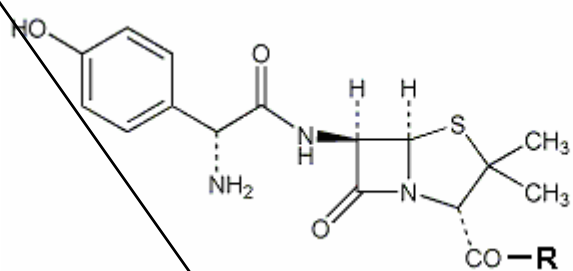


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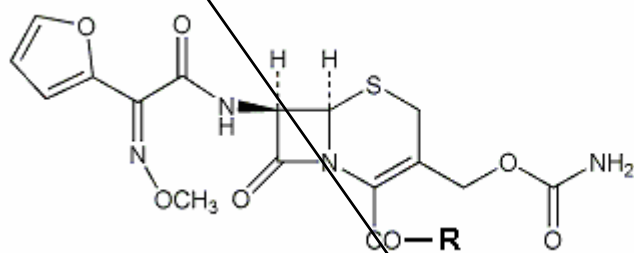


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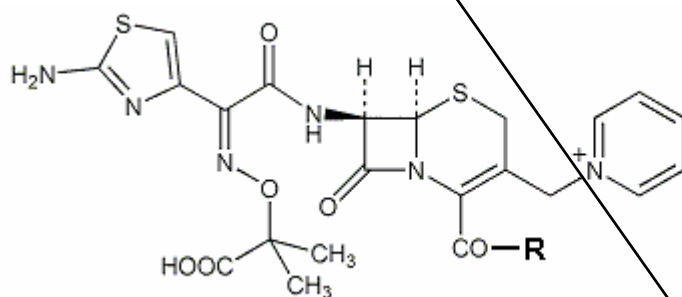




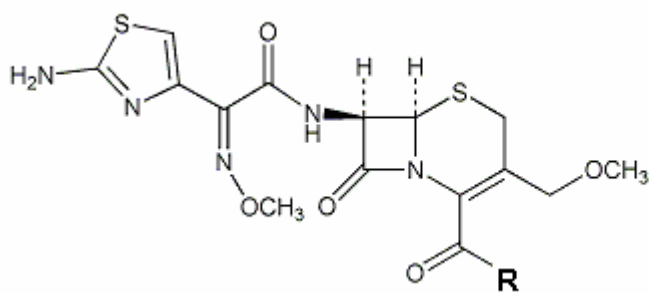
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CEFUROXIME

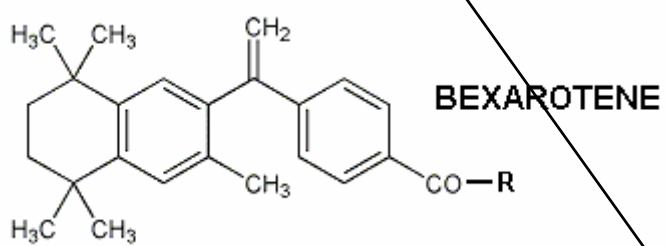
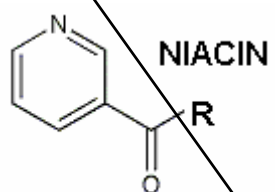
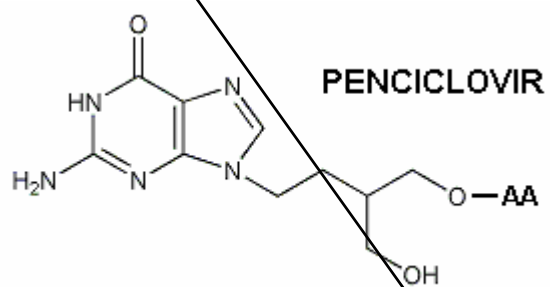
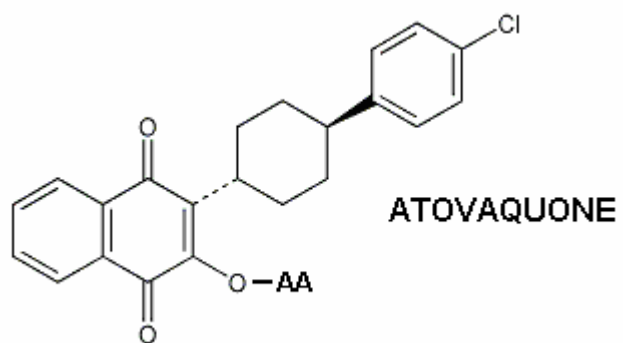


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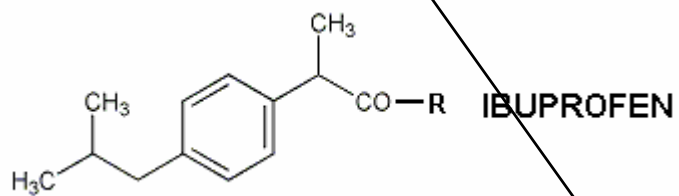
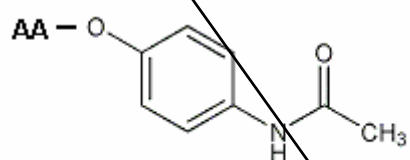
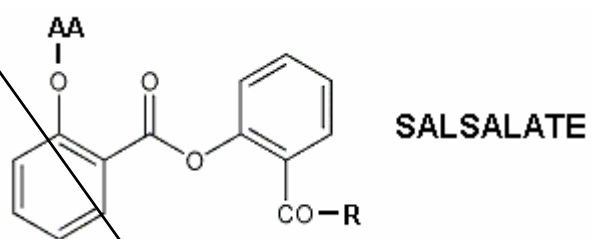
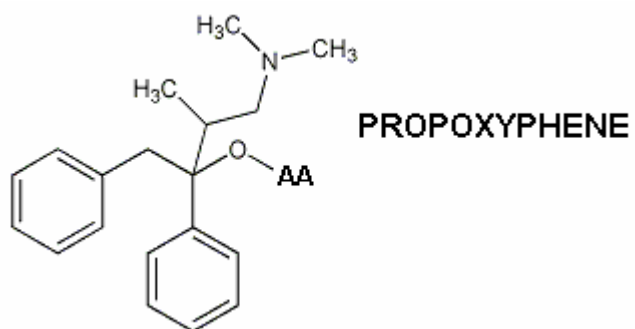


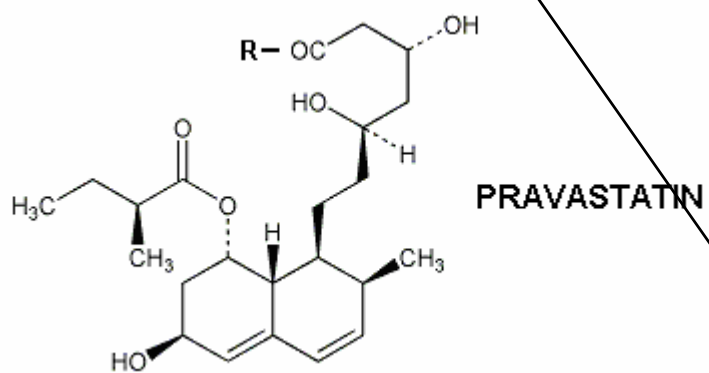
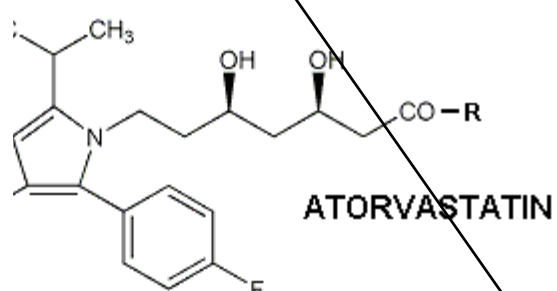
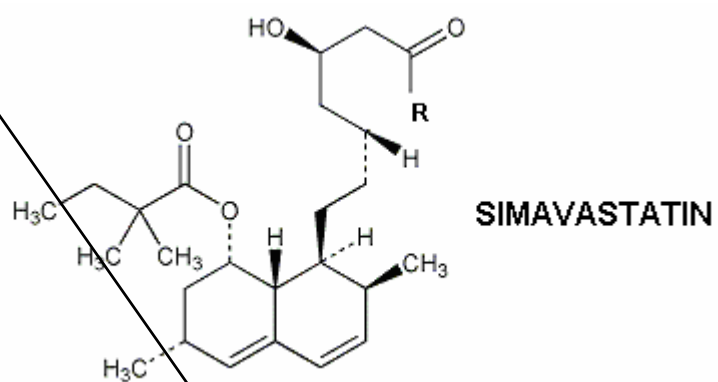
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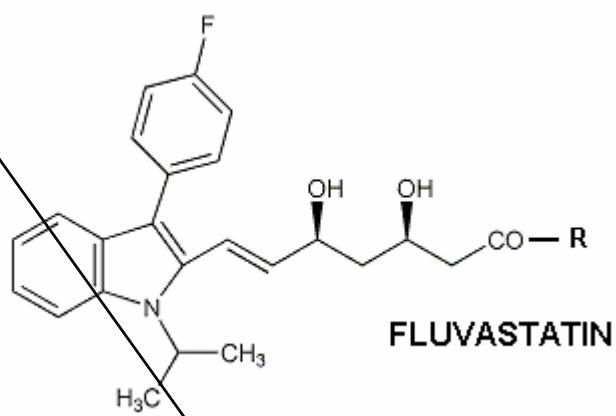
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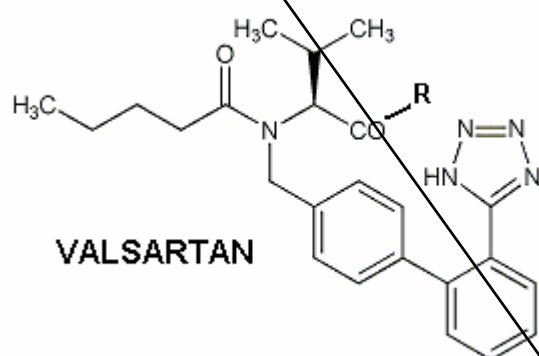
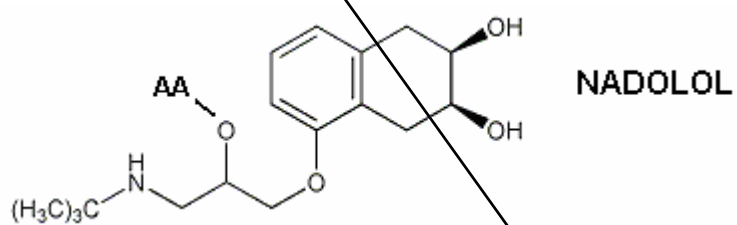
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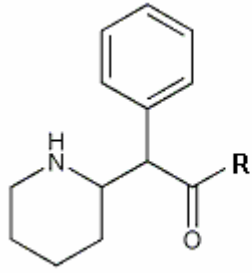




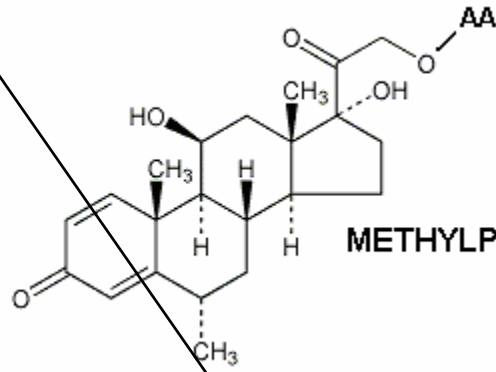


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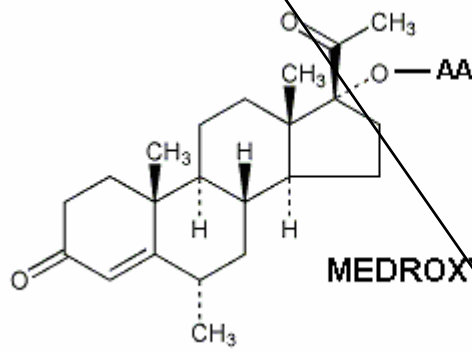




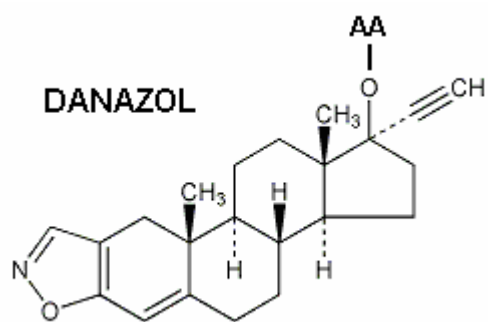
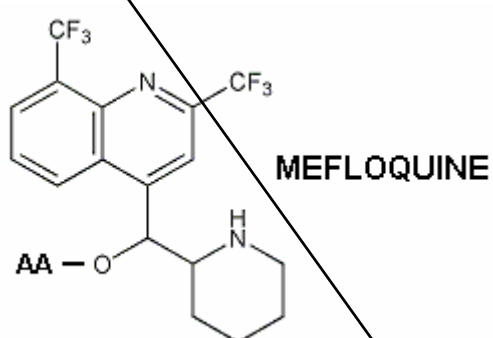
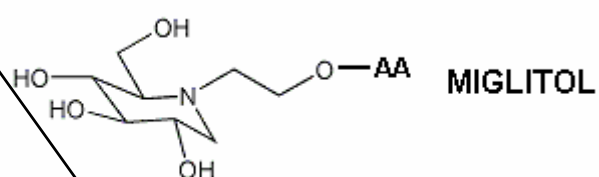
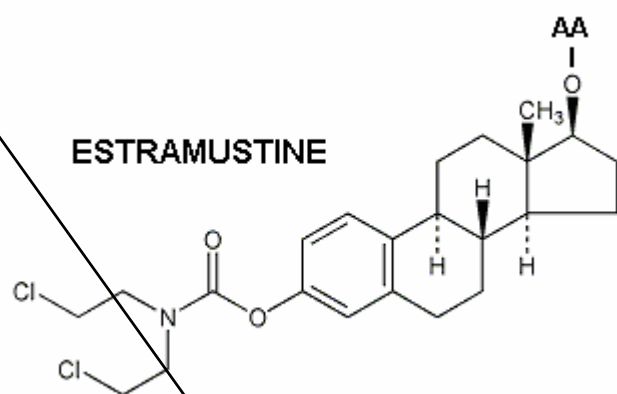
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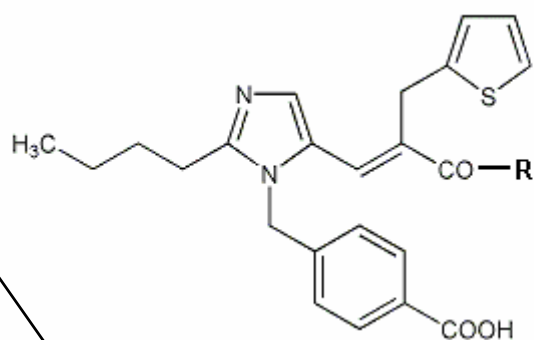


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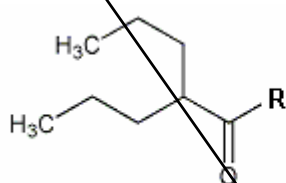


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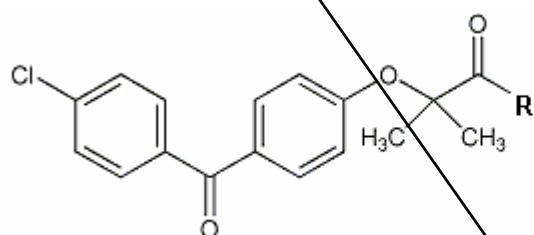




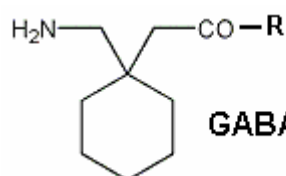
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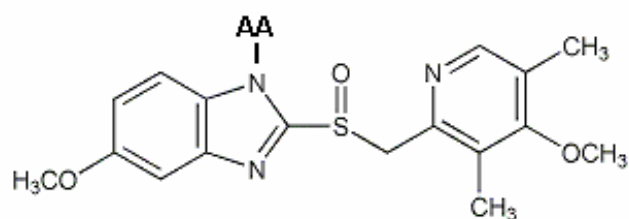
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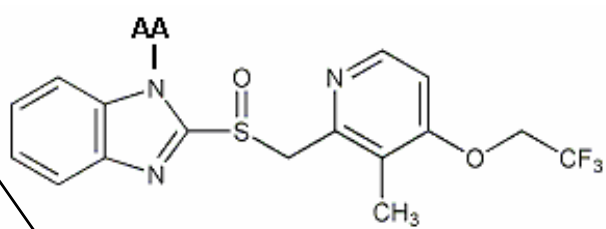
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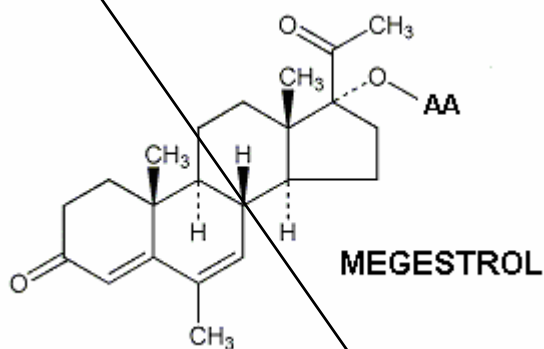
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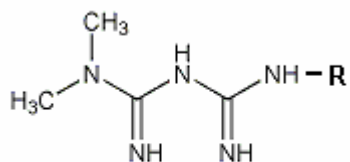
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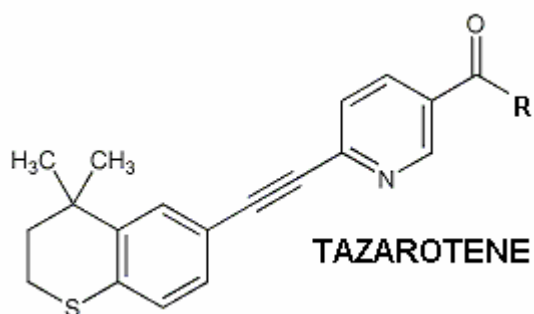
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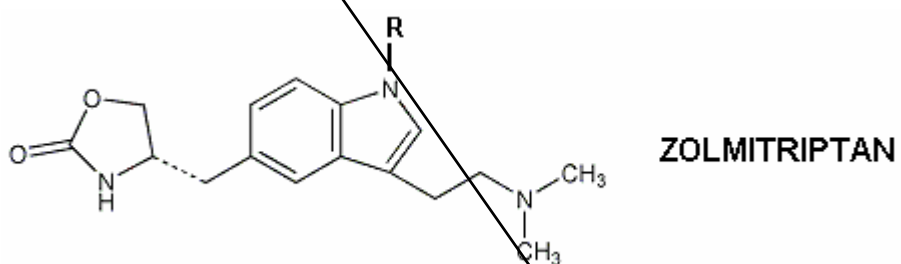
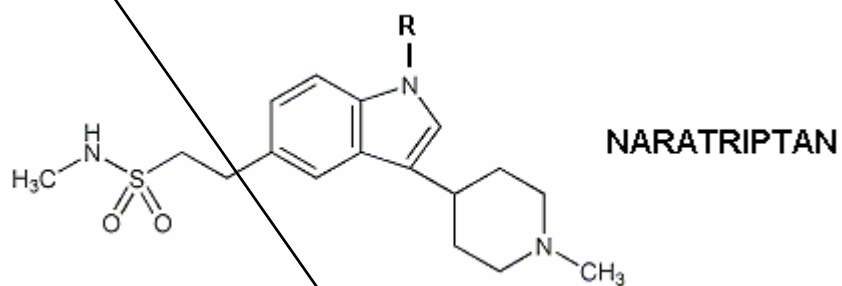
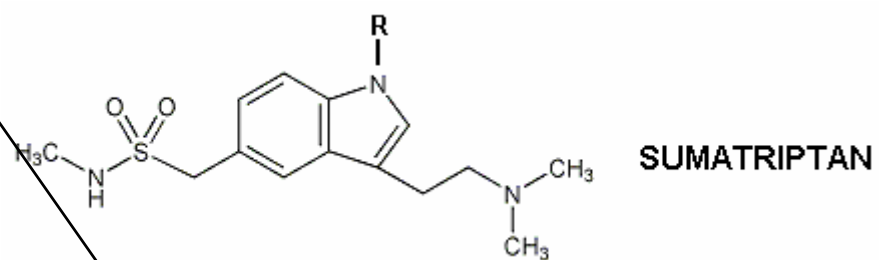
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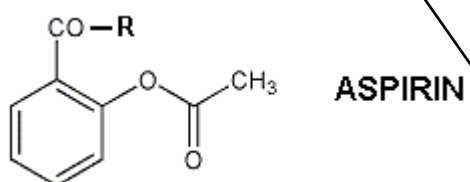
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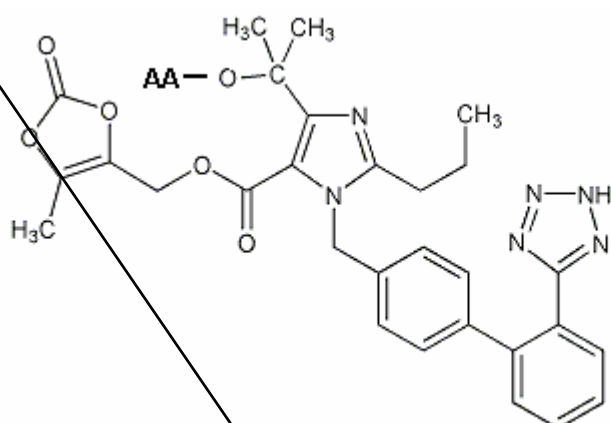
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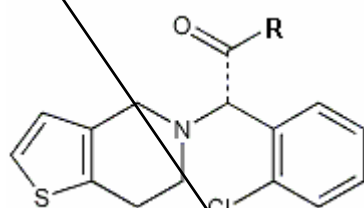


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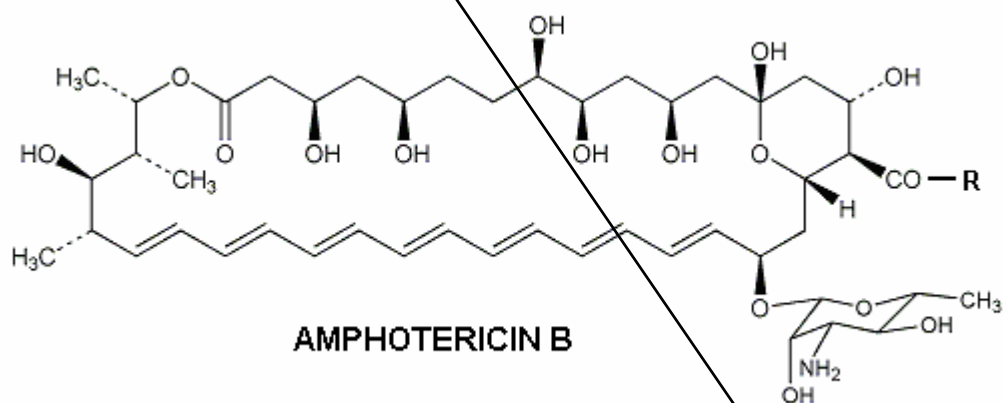




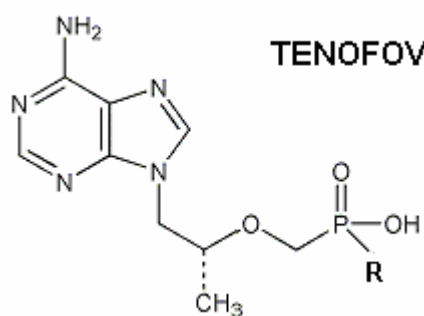
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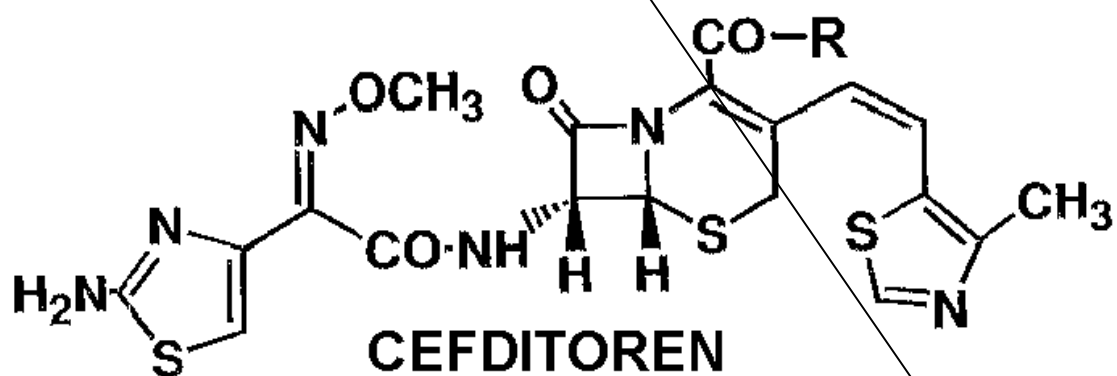
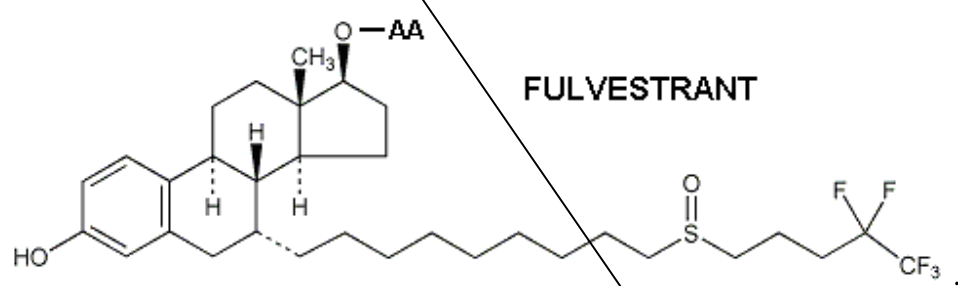
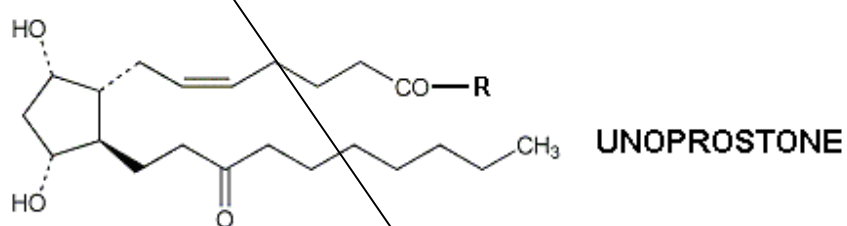
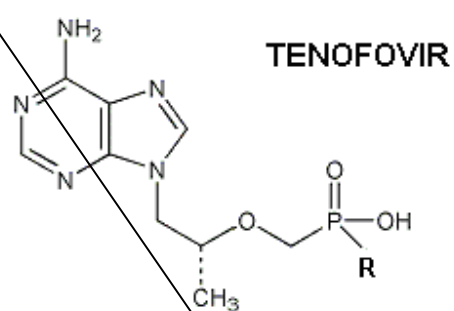
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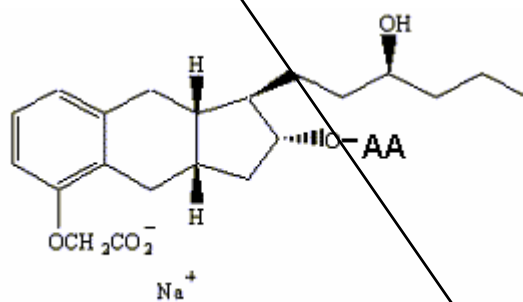
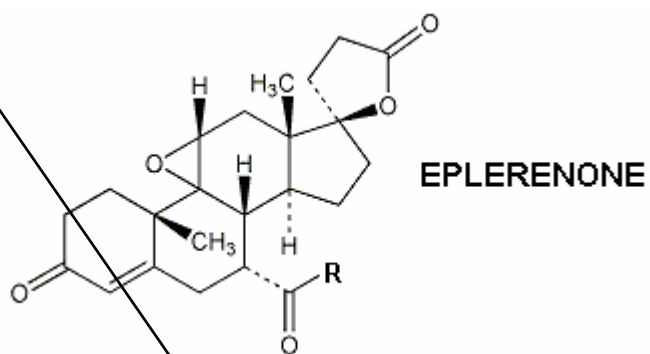


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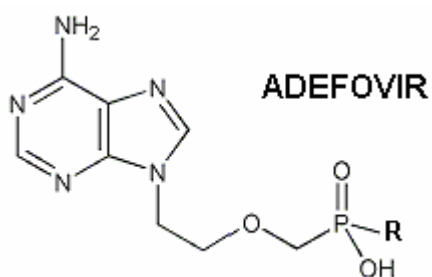


TENOFOVIR





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$R_8N=N-AA_5-COOH$,

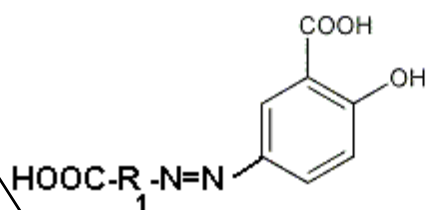
SULFO DRUG AZO DERIVATIVE ,

10 $R_8NH\ CO-AA_5NH_2$

SULFA DRUG AMIDE DERIVATIVE

15

or



GLUTAMIC ACID AZO
SALICYLIC ACID DERIVATIVE

- 5 or a pharmaceutically acceptable salt thereof,
wherein

AA is an amino acid without the hydroxyl group on the carboxy group, and is attached via the acyl group

R is AA₃ or OAA₆,

- 10 CYCLO represents the residues at positions 2 – 11 of a cyclosporin molecule;

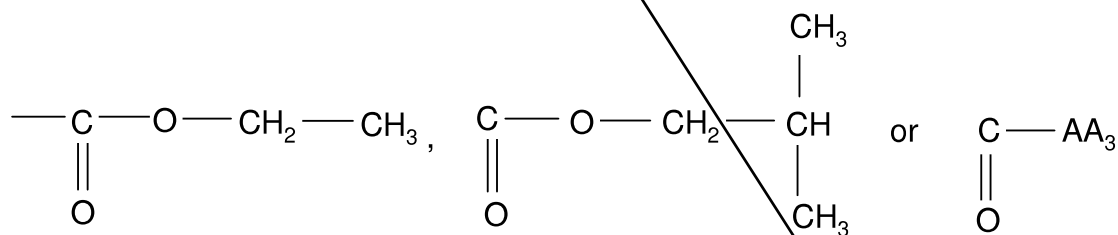
x-y is CH=CH or CH₂=CH₂;

R² is OAA or OGlyAA;

AA₁ is an amino acid without the hydroxy group on the carboxy group and is attached via the acyl group;

- 15 AA₆ is an amino acid residue having a hydroxy group on the side chain less said hydroxyl group, and wherein AA₆ is attached via an ester bond through its side chain hydroxy group;

R₂ is

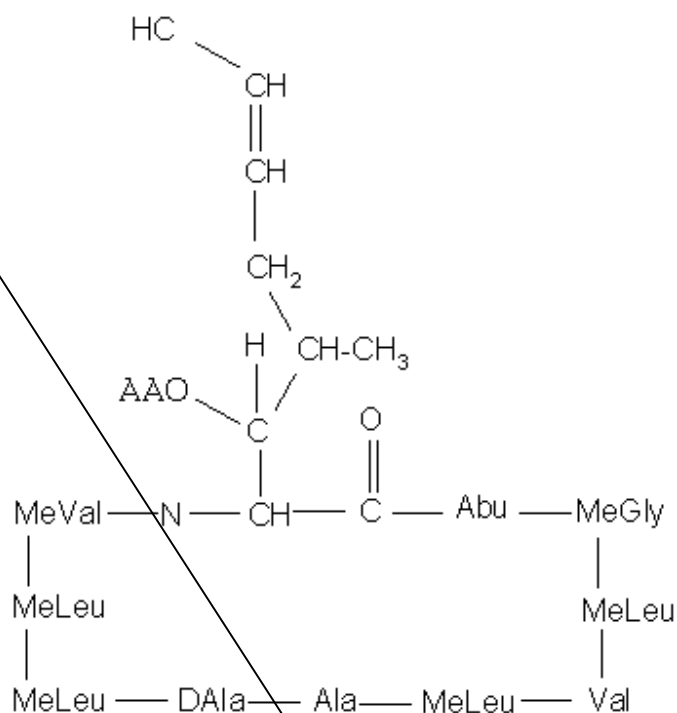


- 20 R₄ is AA₃ or OAA₆;

R₅ is AA₂;

AA₂ is an amino acid residue less the hydroxy group on the carboxy group, and is attached via the acyl group;

- AA₃ is an amino acid less the hydrogen atom on the amino group, and it is attached via the amino group;
- R₃ is ethyl;
- R₁ is an amino acid without the carboxy and amino groups;
- 5 R₆ is AA₁;
- R₇ is O-AA₁;
- AA₅ is an amino acid without the amino and carboxy groups;
- R₈ is a sulfanilamide moiety of the general class of sulfa drugs; and
- R₉ is AA₃ or OAA₆, and
- 10 AA, AA₁, AA₂, AA₃, and AA₅ are independently L-amino acids and are Thr, Hyp, Ser, Tyr, Lys, Leu, Ile, Gly, Asp, Glu, Met, Val, Pro, His, Nor, Arg, Phe, Trp, Hsr, Car, Ort, Cys, Cav, Asn, Gln, Can, Tau, Djk, GABA, Dcy or Sar, and AA₆ is an L-amino acid selected from Thr, Hyp, Ser or Tyr.
- 15 9. The product according to Claim 8 wherein AA₁, AA₂, AA₃, AA₄, and AA₅ are independently Thr, Ser, Tyr, Lys, Leu, Ile, Gly, Asp, Glu, Met, Ala, Val, Pro, His, Arg, Phe, Trp, Gln, Asn, Cys or Ser.
- 20 10. The method according to Claim 9 wherein AA₁, AA₂, AA₃, AA₄, AA₅ and AA₆ are independently Threonine, hydroxyproline or serine.
11. The compound according to Claim 10 wherein AA₁, AA₂, AA₃, AA₄, AA₅ and AA₆ are Thr.
- 25 12. The compound according to Claim 8 wherein the compound has the formula



- 5 13. A pharmaceutical composition comprising a therapeutically effective amount of a compound according to any one of Claims 8 – 12 and a pharmaceutically acceptable salt thereof.
- 10 14. A method of enhancing the bioavailability of a drug having a functionally selected from the group consisting of hydroxy, amino, carboxy or acylating derivative of said carboxy group, said drug being selected from the group consisting of Cyclosporin, Lopinavir, Cefdinir, Zileuton, Nelfinavir, Flavoxate, Candesarten, Propofol, Nisoldipine, Amlodipine, Ciprofloxacin, Ofloxacin, Fosinopril, Enalapril, Ramipril, Benazepril, Moexipril, Trandolapril, Cromolyn, Amoxicillin, Cefuroxime, Ceftazidime,
- 15 Cefpodoxime, Atovaquone, Gancyclovir, Penciclovir, Famciclovir, Acyclovir, Niacin, Bexarotene, Propoxyphene, Salsalate, Acetaminophen, Ibuprofen, Lovastatin, Simavastatin, Atorvastatin, Pravastatin, Fluvastatin, Nadolol, Valsartan,

Methylphenidate, Methyl Prednisolone, Sulfa Drugs, Sulfasalazine, Medroxyprogesterone, Estramustine, 5-aminosalicylic acid, Miglitol, Mefloquine, Danazol, Eprosartan, Divalproex, Fenofibrate, Gabapentin, Omeprazole, Lansoprazole, Megestrol, Metformin, Tazarotene, Sumatriptan, Naratriptan, Zolmitriptan, Aspirin, 5 Olmesartan, Sirolimus, Tacrolimus, Pimecrolimus, Clopidogrel, Amphotericin, Tenofovir, Unoprostone, Fulvestrant, Cefditoren, Efavirenz, Eplerenone, Treprostinil, and Adefovir, said method comprising reacting the drug with an amino acid under conditions effective to form a covalent bond between the drug and the amino acid and administering the product thereof to a patient in need thereof, wherein said amino acid is 10 a L-amino acid selected from the groups consisting of Thr, Hyp, Ser, Tyr, Lys, Leu, Ile, Gly, Asp, Glu, Met, Ala, Val, Pro, His, Nor, Ara, Phe, Trp, Hsr, Car, Ort, Cav, Asn, Gln, Can, Tau, Djk, GABA, Cys, Sar or Dcy.

15 15. A method of enhancing the solubility in an aqueous solution of a drug having a functionality selected from the group consisting of hydroxy, amino, carboxy or acylating derivative of said carboxy group, said drug being selected from the group consisting of lopinavir, cefdinir, amlodipine, nisoldipine, zileuton, nelfinavir, flavoxate, candesartan, cromolyn (sodium), atovaquone, niacin, bexarotene, propoxyphene, salsalate, acetaminophen, ibuprofen, valsartan, methyl phenidate, methyl prednisolone, medroxy 20 progesterone, cephalosporin antibiotic, estramustine, miglitol, mefloquine, danazol, eprosartan, divalproex, fenofibrate, gabapentin, megestrol, metformin, tazarotene, aspirin, olmesartan, clopidogrel, amphotericin, tenofovir, unoprostone, fulvestrant, cefditoren, efavirenz, eplerenone, treprostinil adefovir and salazine, said method comprising reacting the covalent bond with an amino acid under conditions effective to 25 form a drug between the drug and the amino acid and administering the product thereof to a patient in need thereof, wherein said amino acid is a L-amino acid selected from the group consisting of Thr, Hyp, Ser, Tyr, Lys, Leu, Ile, Gly, Asp, Glu, Met, Ala, Val, Pro, His, Nor, Ara, Phe, Trp, Hsr, Car, Ort, Cav, Asn, Gln, Can, Tau, Djk, GABA, Cys, Sar or Dcy.

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16. The method according to Claim 14 or 15 wherein the amino acid is Thr, Hyp, Ser, Tyr, Lys, Leu, Ile, Gly, Asp, Glu, Met, Ala, Val, Pro, His, Arg, Phe, Trp, Gln, Asn, or Cys.
- 5 17. The method according to Claim 14 or 15 wherein the amino AA is threonine, hydroxyproline or serine.
- 10 18. A method of enhancing the safety profile with longer anesthetic effect of propofol in an aqueous solution comprising reacting the hydroxy functionality of the propofol molecule with an amino acid or acylating derivative thereof under ester forming conditions and isolating the product thereof.
- 15 19. A method of enhancing the solubility of a quinolone antibiotic having a carboxy group or acylating group in an aqueous solution comprising reacting the carboxylic acid functionality of the quinolone antibiotic with an amino acid or acylating derivative thereof under either ester or amide forming conditions and isolating the product thereof.
- 20 20. A method of enhancing the bioavailability of a quinolone antibiotic having a carboxyl group or acylating group when administered to a patient which comprises reacting the carboxylic acid functionality of the quinolone antibiotic with an amino acid or acylating derivative under ester or amide forming conditions, isolating the product thereof and administering said product to the patient.
- 25 21. A method of enhancing the solubility of ace inhibitors having a carboxy or acylating group in an aqueous solution comprising reacting the carboxylic acid functionality of the ace inhibitor molecule with an amino acid or acylating derivative thereof under either ester or amide forming conditions and isolating the product thereof.

22. A method of enhancing the bioavailability of ace inhibitors having a carboxy or acylating group when administered to a patient which comprises reacting the carboxylic acid functionality of the ace inhibitors molecule with an amino acid or acylating derivative under ester or amide forming conditions, isolating the product thereof and
5 administering said product to the patient.

23. A method of reducing the gastric irritation of ibuprofen comprising reacting the carboxylic acid functionality of the ibuprofen molecule with an amino acid or acylating
10 derivative under either ester or amide forming conditions and administering the product to a patient in need thereof, said product resulting less gastric irritability then ibuprofen.

24. A method of enhancing the solubility of a proton pump inhibitor in an aqueous solution comprising reacting the amine functionality of the proton pump inhibitor with
15 the carboxylic acid moiety of the amino acid or acylating derivative thereof under amide forming conditions and isolating the product thereof.

25. A method of enhancing the bioavailability of a proton pump inhibitor when administered to a patient which comprises reacting the amine functionality of the proton
20 pump inhibitor with the carboxylic acid moiety of an amino acid or acylating derivative thereof under amide forming conditions, isolating the product thereof and administering said product to the patient.

26. A method of enhancing the solubility of Selective 5-HT receptor agonists in an aqueous solution comprising reacting the amine functionality of the Selective 5-HT
25 receptor agonists molecule with the carboxylic acid moiety of an amino acid or acylating derivative thereof under amide forming conditions and isolating the product thereof.

27. A method of enhancing the bioavailability of Selective 5-HT receptor agonists when
30 administered to a patient which comprises reacting the amine functionality of the

Selective 5-HT receptor agonists with the carboxylic acid moiety of an amino acid under amide forming conditions, isolating the product thereof and administering said product to the patient.

5 28. A method of reducing the gastric irritability in the stomach resulting from aspirin administration to a mammal which method comprises reacting the carboxylic acid functionality of the aspirin molecule with an amino acid or acylating derivative thereof under either amide or ester forming conditions, and administering the formed product to said mammal, wherein the gastric irritability is reduced relative to aspirin.

10

29. A method of enhancing the solubility of immunosuppressants in an aqueous solution comprising reacting the hydroxy functionality of the immunosuppressants with an amino acid or acylating derivative thereof under ester forming conditions and isolating the product thereof.

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30. A method of enhancing the bioavailability of immunosuppressants when administered to a patient which comprises reacting the hydroxy functionality of the immunosuppressants with an amino acid or acylating derivative under ester forming conditions, isolating the product thereof and administering said product to the patient.

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31. A method of enhancing the solubility of a sulfa drug in an aqueous solution comprising reacting the amine of the sulfa drug with an amino acid or acylating derivative thereof under either azo or amide forming conditions and isolating product thereof.

25

32. A method of enhancing the bioavailability of a sulfa drug when administered to a patient which comprises reacting the amine functionality of the sulfa drug with an amino acid or acylating derivative under azo or amide forming conditions, isolating the product thereof and administering said product to the patient.

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33. A method of providing a clear aqueous intravenous formulation comprising a Sulfa drug when administered to a patient which comprises reacting the amine of the Sulfa drug with an amino acid or acylating derivative under azo or amide forming conditions, isolating the product thereof and administering said product to the patient parenterally.

5

34. A method of enhancing the solubility in an aqueous solution of a nucleoside analog having an OH functionality comprising reacting the hydroxyl functionality of the nucleoside analog with an amino acid or acylating derivative thereof under ester forming conditions or isolating the product thereof.

10

35. A method for enhancing the bioavailability of a nucleoside analog having an OH group thereon which comprise reacting the hydroxyl functionality of the nucleoside analog with an amino acid or acylating derivative thereof under ester forming conditions and isolating the product thereof and administering the product to a patient.

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THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A method for enhancing at least two of the therapeutic qualities of a drug having a functionality group selected from the group consisting of hydroxy, amino, carboxy or acylating derivatives of said carboxy group, said improved therapeutic quality being selected from the group consisting of:

- (a) improved taste or smell
- (b) desired octanol/water partition coefficient
- (c) improved stability
- (d) enhanced penetration of blood-brain barrier
- (e) elimination of first pass effect in the liver
- (f) reduction of entero-hepatic recirculation
- (g) painless injection with parental formulation
- (h) improved bioavailability
- (i) improved changes in the rate of absorption
- (j) reduced side effects
- (k) dose proportionality
- (l) selective hydrolysis of the prodrug at site of action
- (m) controlled release properties
- (n) targeted drug delivery
- (o) reduction in toxicity
- (p) reduced dose
- (q) alteration of metabolic pathway to deliver more drug at site of action
- (r) increased solubility in aqueous solution and
- (s) enhanced efficacy,

the method comprising administering the product of the drug with an amino acid under conditions effective to form a covalent bond directly between the drug and the amino acid to a patient in need thereof, wherein said amino acid is a naturally occurring α -L-amino acid, wherein the drug is selected from the group consisting of 5-HETE, Abacavir, Acarbose, Acebutolol, Acetaminophen, Adefovir, Albuterol, Alfaprostol acid, Amlodipine, Amoxicillin, Amphotericin B, Amprenavir, Arachidonic Acid, Aspirin, Atenolol, Atorvastatin, Atropine,

Atovaquone, Baclofen, Benazeprilat, Beraprost, Betaxolol, Bexarotene, Bicalutamide, Biperiden,
Bisoprolol, Bitolterol, Brinzolamide, Bupivacaine, Buprenorphine, Bupropion, Butorphanol,
Candesartan, Capacitabine, Captopril, Carbidopa, Carboprost, Carnitine, Carteolol, Carvedilol,
Cefdinir, Cefditoren, Ceftazimide, Cefpodoxime, Cefuroxime, Cerivastatin, Chloramphenicol,
5 Cisapride, Clofibrate, Clopidogrel Acid, Cloprostenol, Clorazepic Acid, Cycloserine,
Cyclosporine, Cytarabine, Danazol, Dextroamphetamine, Diclofenac, Didanosine, Divalproex,
Docetaxel, Dorzolamide, Dyphylline, Dysopyramide, Efavirenz, Enalaprilat, Ephedrine,
Eplerenone, Eprosartan, Esmolol, Estramustine, Ethambutol, Ethchlorvynol, Ethosuximide,
Ethotoin, Etidocaine, Etoposide, Ezetimibe, Famciclovir, Fenofibrate, Fenoprofen, Fenprostalene
10 acid, Fexofenadine, Fibric acid derivatives, Finasteride, Flavoxate, Fluprostenol, Fluoxetine,
Flurbiprofen, Fluticasone, Fluvastatin, Fosinoprilat, Frovatriptan, Fulvestrant, Gemprost Acid,
Glimepiride, Goserelin, Hydroxychloroquine, Hydroxyzine, Hyoscyamine, Ibuprofen, Ibutilide,
Indapamide, Indinavir, Ipratropium, Irinotecan, Isosorbide, Isradipine, Ketoprofen, Ketorolac,
Labetalol, Lamivudine, Lansoprazole, Latanoprost Acid, Leukotrienes (LTA₄, LTB₄, LTC₄,
15 LTD₄ and LTE₄) Leuprolide, Levobunolol, Levodopa, Levorphanol, Limaprost, γ -Linolenic
Acid, Liothyronine, Lisinopril, Lopinavir, Lorazepam, Lovastatin, Medroxyprogesterone,
Mefloquine, Megestrol, Mephobarbital, Mepivacaine, Metaproterenol, Metformin,
Methamphetamine, Methohexital, Methotrexate, Methylphenidate, Methylprednisolone,
Metolazone, Metoprolol, Mexiletine, Miglitol, Moexiprilat, Mometasone, Montelukast,
20 Mycophenolate Acid, Nadolol, Nalbuphine, Naproxen, Naratriptan, Nateglinide, Nelfinavir,
Niacin, Nicotinic Acid, Nicotinamide, Nicardipine, Nimidipine, Nisoldipine, Norgestimate,
Octreotide, Ofloxacin, Olmesartan, Omeprazole, Ozagrel, Paclitaxel, Pantothenic Acid,
Paroxetine, Pemoline, Penbutolol, Penciclovir, Pentazocine, Pentobarbital, Perindoprilat,
Phenylephrine, Phenylpropanolamine, Pindolol, Pioglitazone, Pirbuterol, Pramipexole,
25 Pravastatin, Propafenone, Propofol, Propoxyphene, Propranolol, Prostacyclin, Prostaglandins
(E₁, E₂ and F_{2 α}), Prostanoic Acid, Pseudoephedrine, Quinacrine, Quinaprilat, Quinethazone,
Quinidine, Quinine, Ramiprilat, Reboxetine, Repaglinide, Repaglinide, Ribavirin, Ritonavir,
Ropivacaine, Rosaprostol, Rosiglitazone, Rosuvastatin, Salmeterol, Salsalate, Sertraline,
Simvastatin, Sotalol, Sulfa Drugs, Sulfasalazine, Sumatriptan, Tacrolimus, Tazorotene,
30 Telmisartan, Tenofovir, Terbutaline, Tiagabine, Timolol, Tirofiban, Tocainide, Tramadol,
Trandolaprilat, Tranlycypromine, Treprostinil, Triamcinolone, Trimoprostil, Troglitazone,

Unoprostone, Valproic Acid, Valsartan, Venlafaxine, Vidarabine, Warfarin, Zalcitabine, Zidovudine, Zileuton and Zolmitriptan or a pharmaceutically acceptable salt of any of said drug.

2. The method according to Claim 1 wherein the amino acid is Thr, Hyp, Ser, Tyr, Lys, Leu, Ile, Gly, Asp, Glu, Met, Ala, Val, Pro, His, Nor, Arg, Phe, Trp, Hsr, Car, Ort, Cav, Asn, Gln, Can, Tau, Djk, GABA, Cys, Dcy and Sar.

3. The method according to Claim 1 or 2 wherein the amino acid is Thr, Hyp, Ser, Tyr, Lys, Leu, Ile, Gly, Asp, Glu, Met, Ala, Val, Pro, His, Arg, Phe, Trp, Gln, Asn, or Cys.

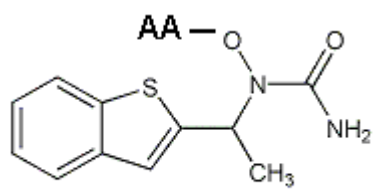
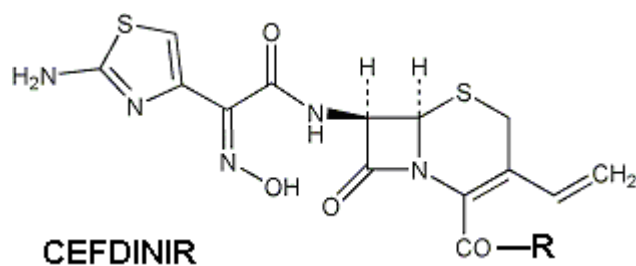
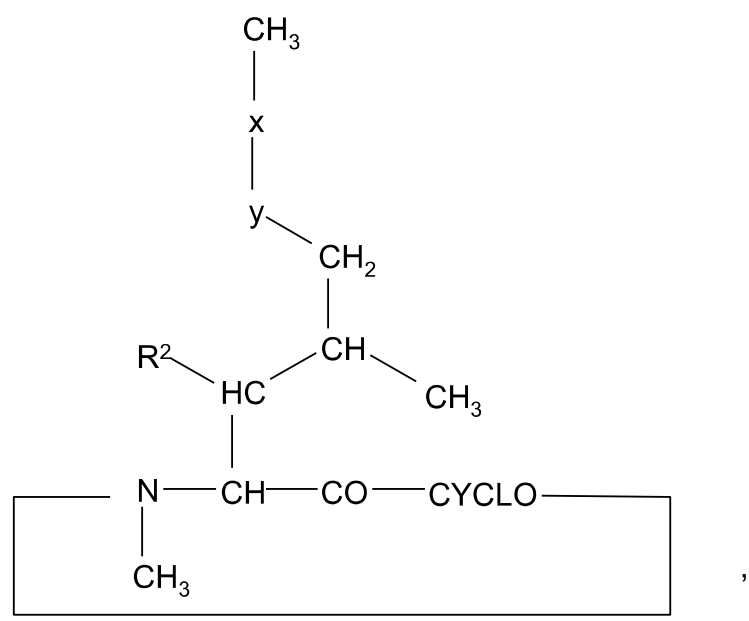
4. The method according to any one of Claims 1-3 wherein AA is Threonine, hydroxyproline or Serine.

5. The method according to any one of Claims 1-4 wherein the amino acid is Threonine.

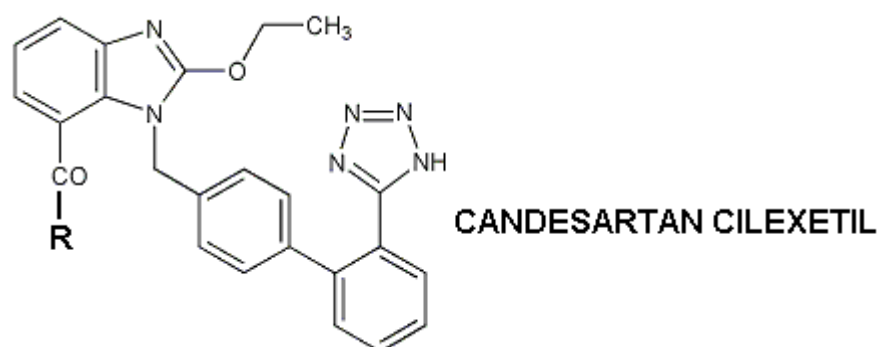
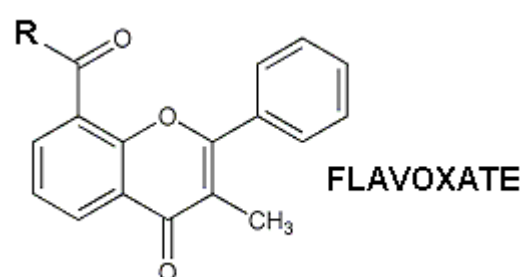
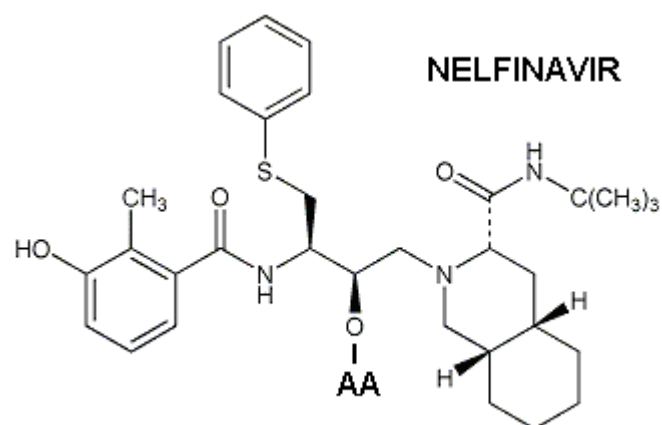
6. The product from the reaction between a drug having a functionality selected from the group consisting of hydroxy, amino, carboxy or acylating derivative of said carboxy group and a L- α -amino acid under conditions sufficient to form a covalent bond from the reaction of said functional group and said amino acid, or the pharmaceutically acceptable salt thereof, wherein the drug is selected from the group consisting of 5-HETE, Abacavir, Acarbose, Acebutolol, Acetaminophen, Adefovir, Albuterol, Alfaprostol acid, Amlodipine, Amoxicillin, Amphotericin B, Amprenavir, Arachidonic Acid, Aspirin, Atenolol, Atorvastatin, Atropine, Atovaquone, Baclofen, Benazeprilat, Beraprost, Betaxolol, Bexarotene, Bicalutamide, Biperiden, Bisoprolol, Bitolterol, Brinzolamide, Bupivacaine, Buprenorphine, Bupropion, Butorphanol, Candesartan, Capacitabine, Captopril, Carbidopa, Carboprost, Carnitine, Carteolol, Carvedilol, Cefdinir, Cefditoren, Ceftazimide, Cefpodoxime, Cefuroxime, Cerivastatin, Chloramphenicol, Cisapride, Clofibrate, Clopidogrel Acid, Cloprostenol, Clorazepic Acid, Cycloserine, Cyclosporine, Cytarabine, Danazol, Dextroamphetamine, Diclofenac, Didanosine, Divalproex, Docetaxel, Dorzolamide, Dyphylline, Dysopyramide, Efavirenz, Enalaprilat, Ephedrine, Eplerenone, Eprosartan, Esmolol, Estramustine, Ethambutol, Ethchlorvynol, Ethosuximide, Ethotoin, Etidocaine,

5 Etoposide, Ezetimibe, Famciclovir, Fenofibrate, Fenoprofen, Fenprostalene acid,
Fexofenadine, Fibric acid derivatives, Finasteride, Flavoxate, Fluprostenol, Fluoxetine,
Flurbiprofen, Fluticasone, Fluvastatin, Fosinoprilat, Frovatriptan, Fulvestrant, Gemprost
Acid, Glimepiride, Goserelin, Hydroxychloroquine, Hydroxyzine, Hyoscyamine, Ibuprofen,
Ibutilide, Indapamide, Indinavir, Ipratropium, Irinotecan, Isosorbide, Isradipine, Ketoprofen,
Ketorolac, Labetalol, Lamivudine, Lansoprazole, Latanoprost Acid, Leukotrienes (LTA₄,
LTB₄, LTC₄, LTD₄ and LTE₄) Leuprolide, Levobunolol, Levodopa, Levorphanol, Limaprost,
γ-Linolenic Acid, Liothyronine, Lisinopril, Lopinavir, Lorazepam, Lovastatin,
Medroxyprogesterone, Mefloquine, Megestrol, Mephobarbital, Mepivacaine,
 10 Metaproterenol, Metformin, Methamphetamine, Methohexital, Methotrexate,
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Pseudoephedrine, Quinacrine, Quinaprilat, Quinethazone, Quinidine, Quinine, Ramiprilat,
 20 Reboxetine, Repaglinide, Repaglinide, Ribavirin, Ritonavir, Ropivacaine, Rosaprostol,
Rosiglitazone, Rosuvastatin, Salmeterol, Salsalate, Sertraline, Simvastatin, Sotalol, Sulfa
Drugs, Sulfasalazine, Sumatriptan, Tacrolimus, Tazorotene, Telmesartan, Tenofovir,
Terbutaline, Tiagabine, Timolol, Tirofiban, Tocainide, Tramadol, Trandolaprilat,
Tranylcypromine, Treprostinil, Triamcinolone, Trimoprostil, Troglitazone, Unoprostone,
 25 Valproic Acid, Valsartan, Venlafaxine, Vidarabine, Warfarin, Zalcitabine, Zidovudine,
Zileuton and Zolmitriptan or a pharmaceutically acceptable salt of any of said drug.

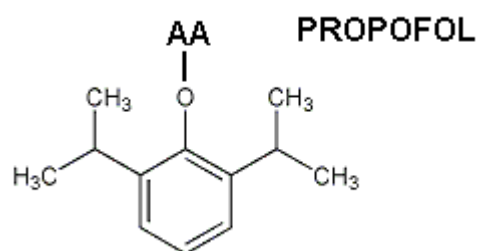
7. The product according to Claim 6 wherein the product is:



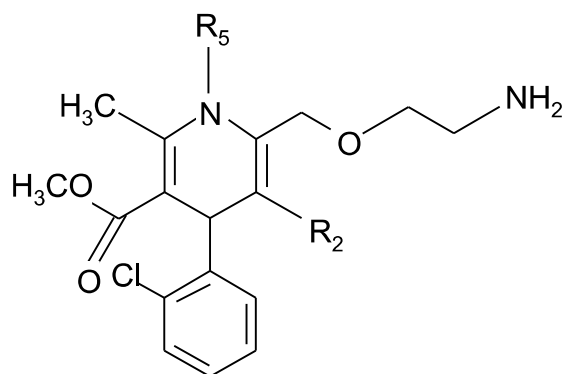
ZILEUTON



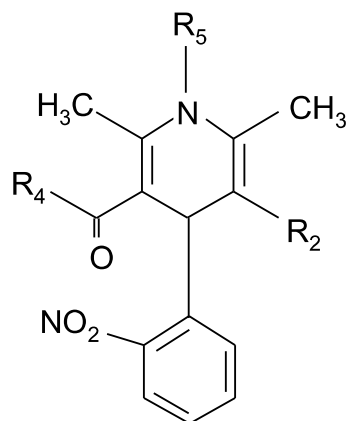
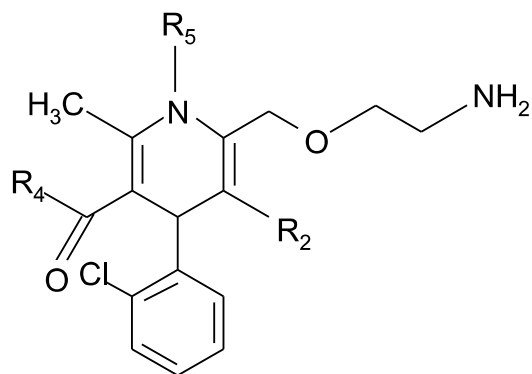
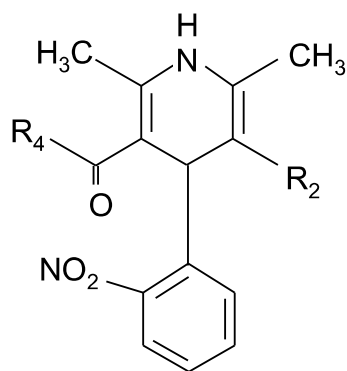
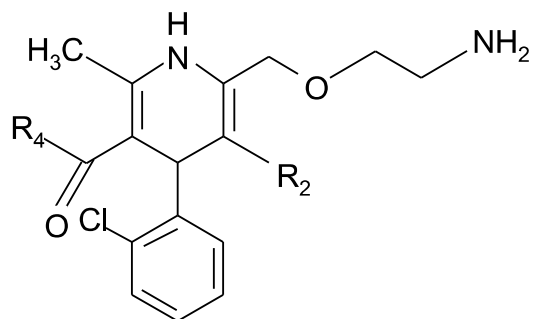
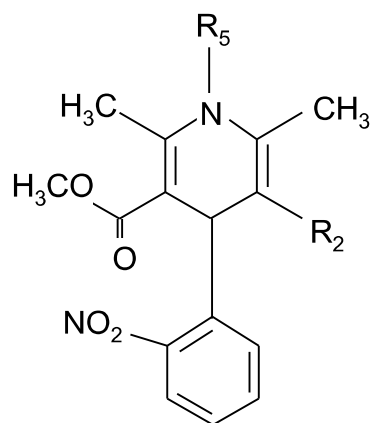
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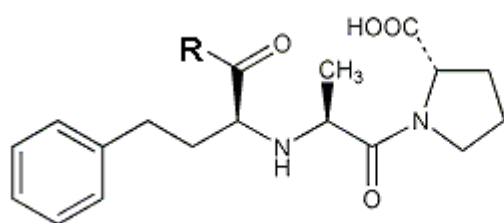
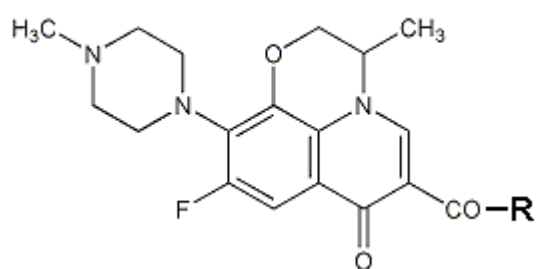
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NISOLDIPINE

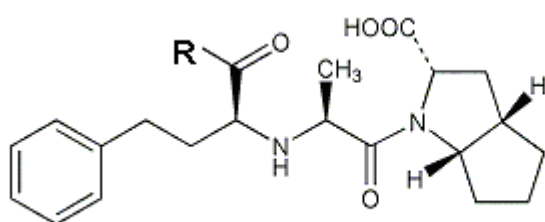


OFLOXACIN

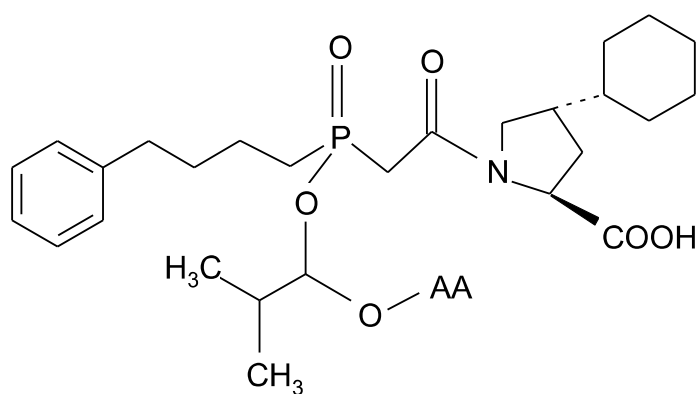


ENALAPRIL

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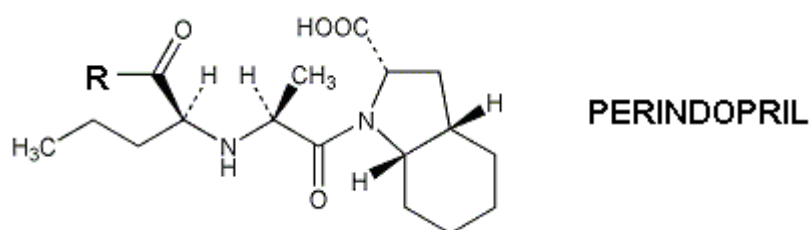
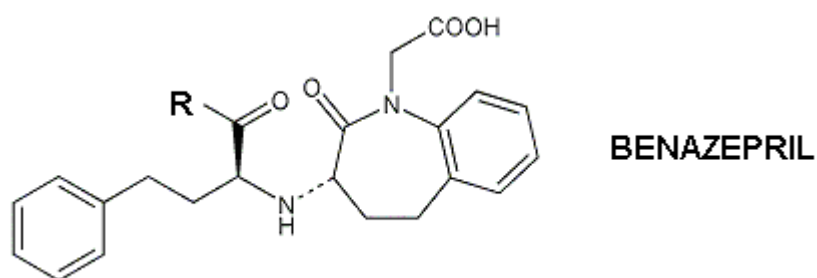


RAMIPRIL

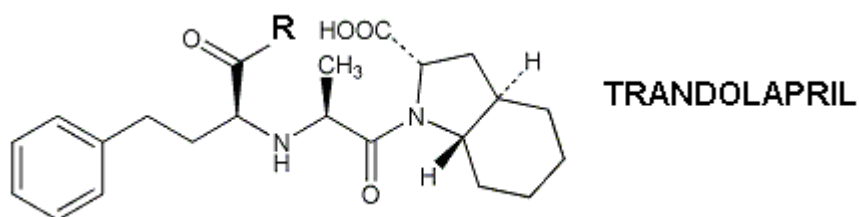
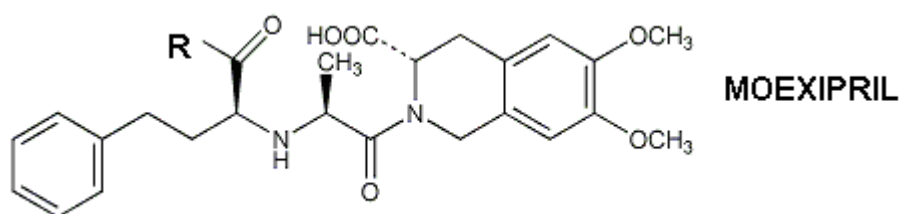


FOSINOPRIL Na

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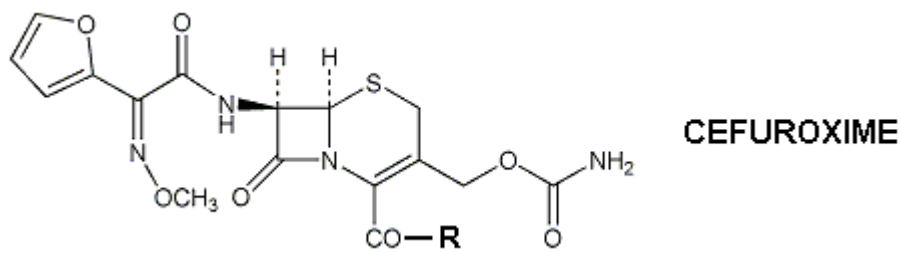
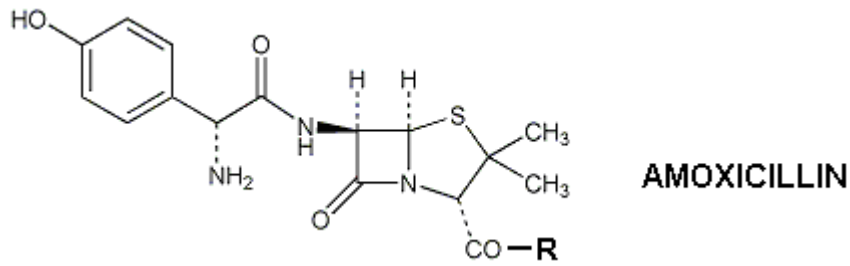
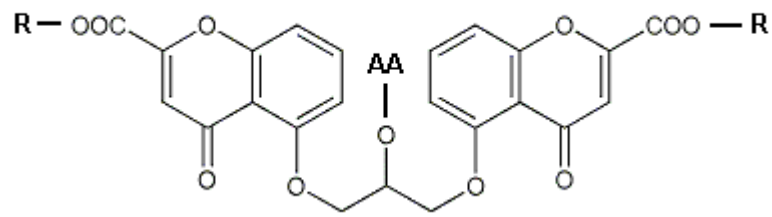


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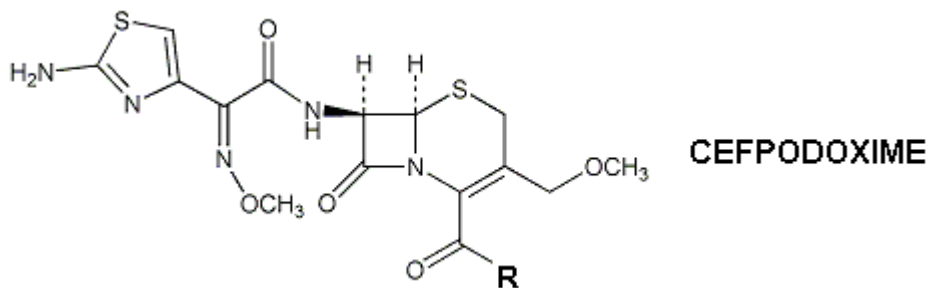
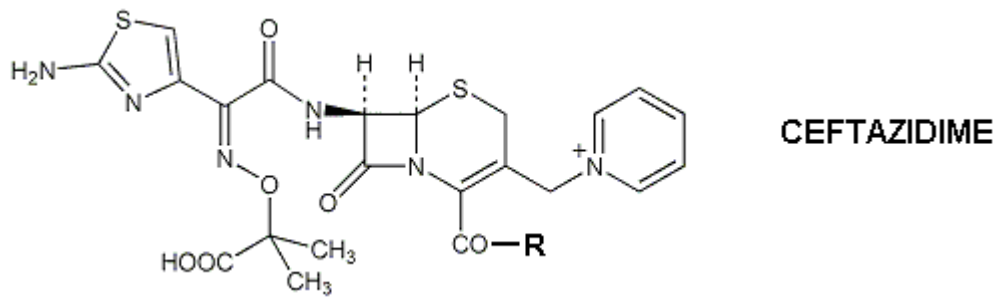


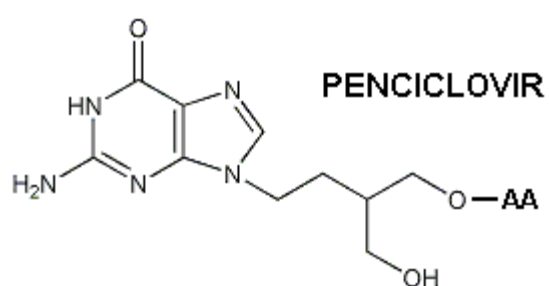
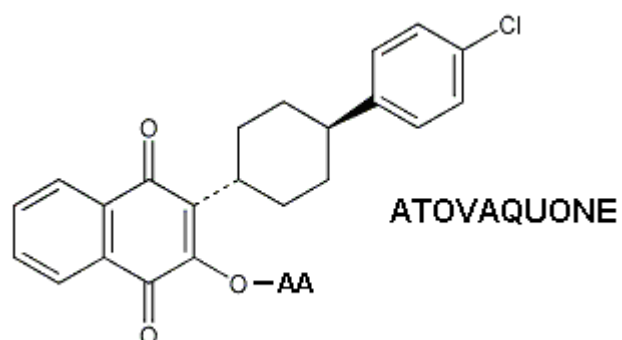
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CROMOLYN

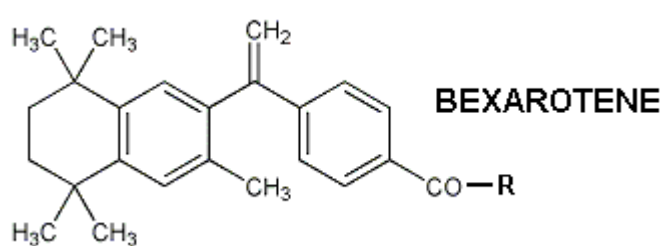


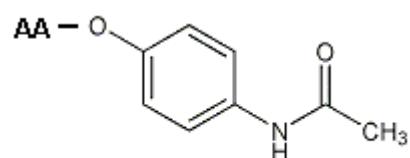
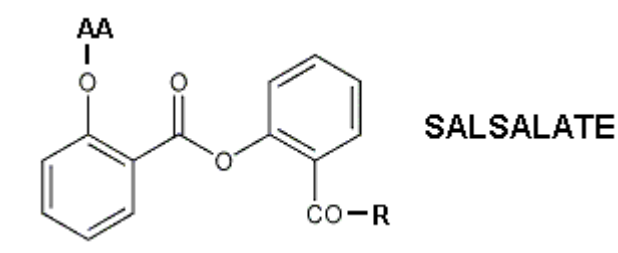
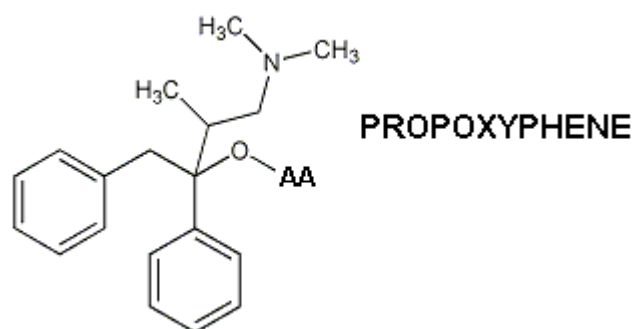
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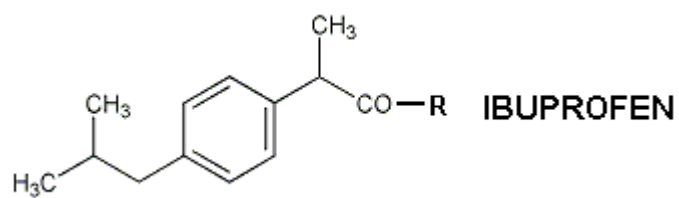


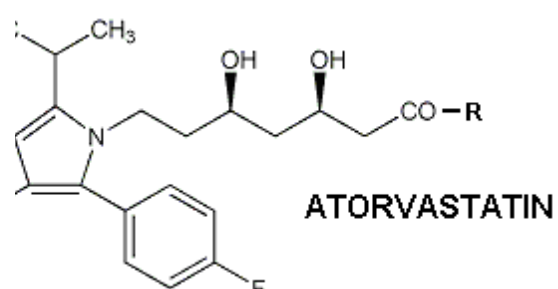
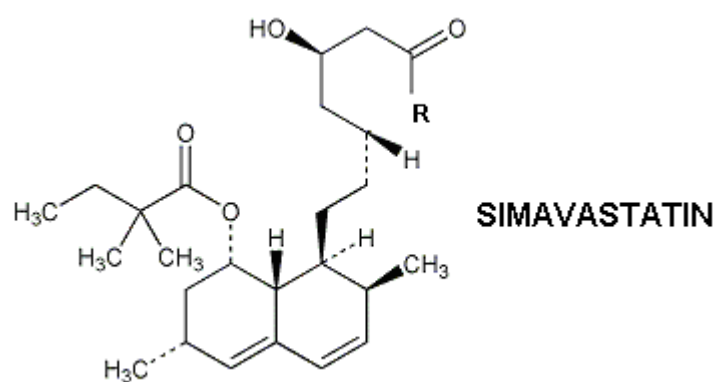
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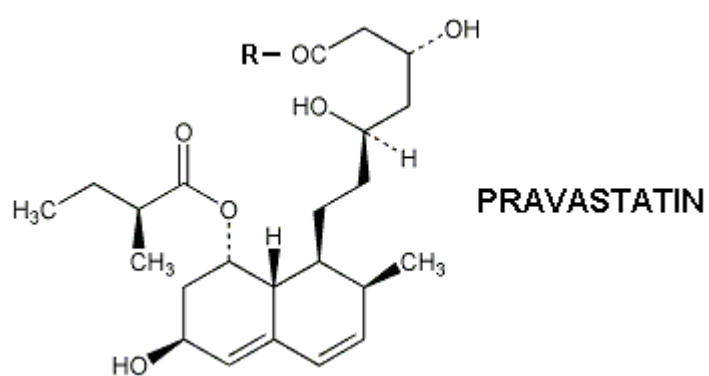


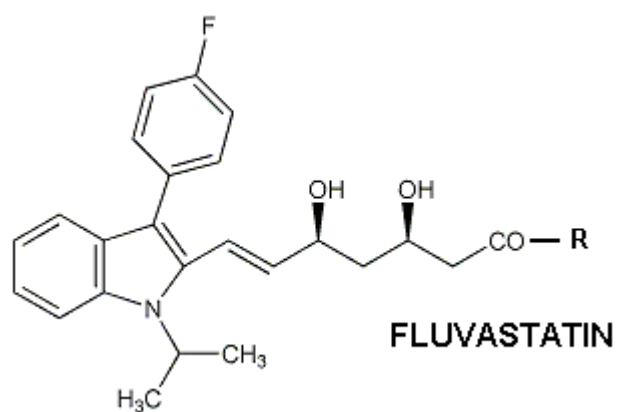
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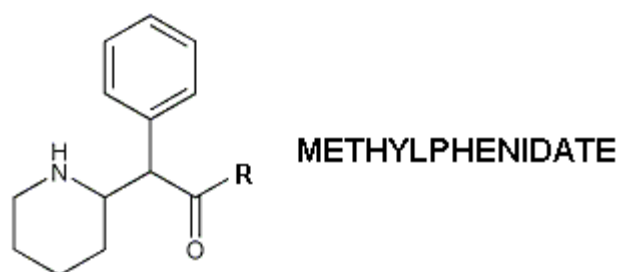
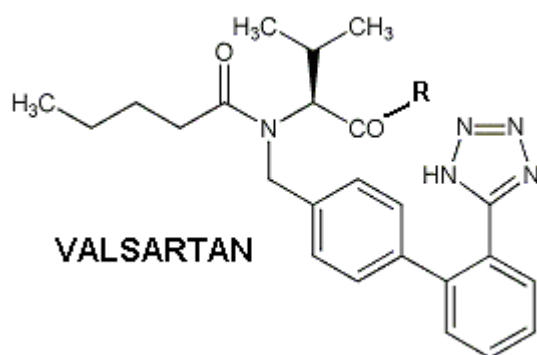
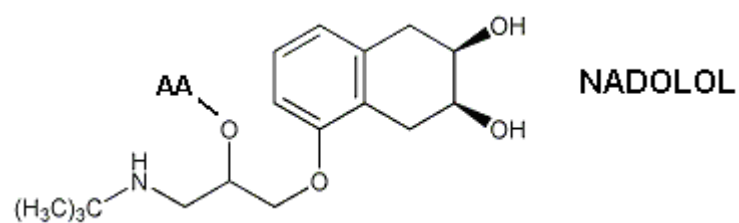


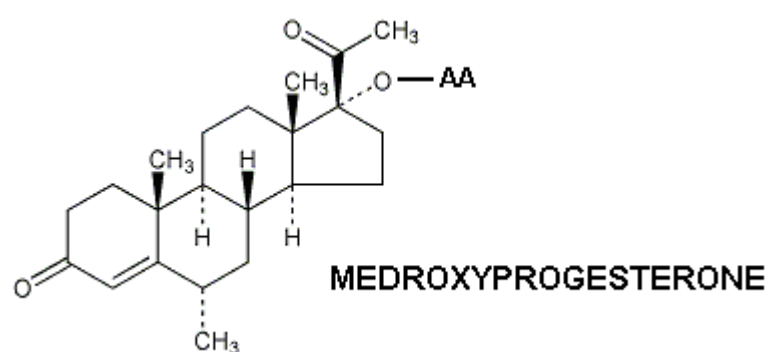
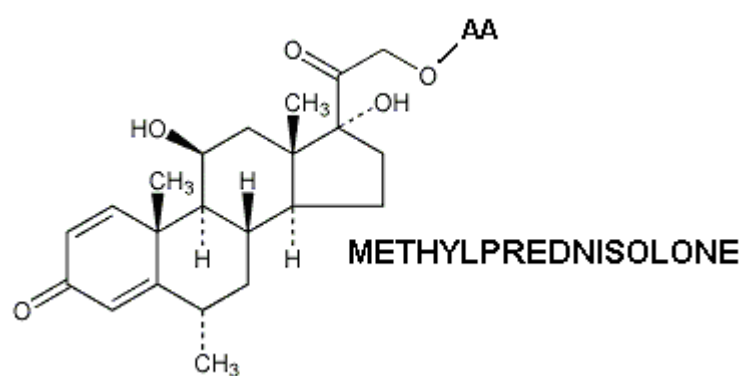
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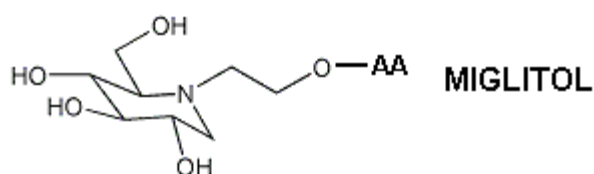
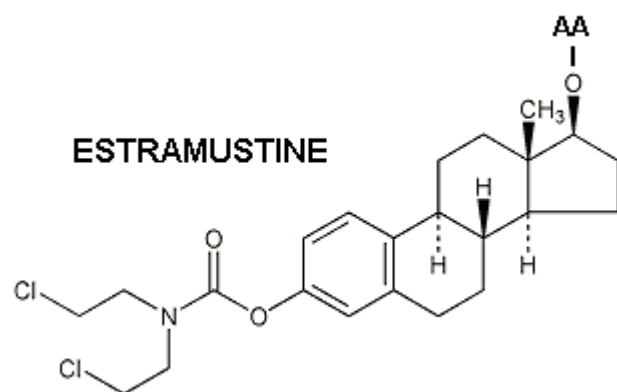


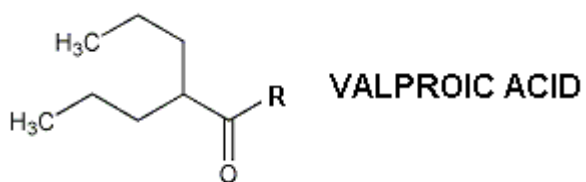
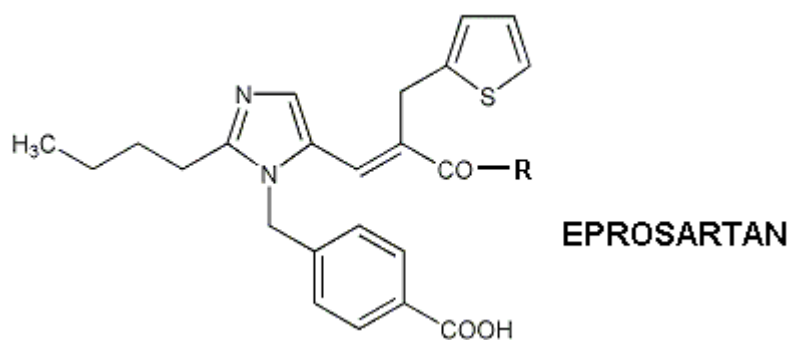
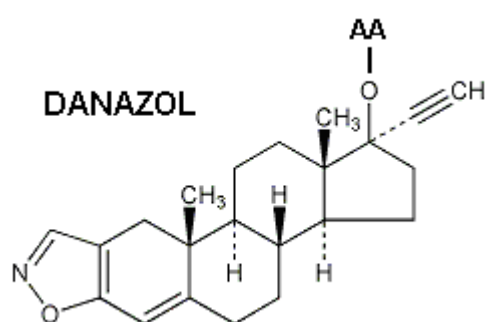
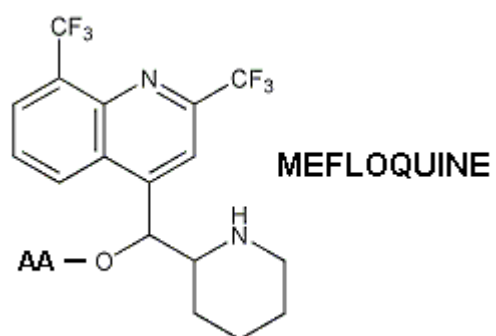
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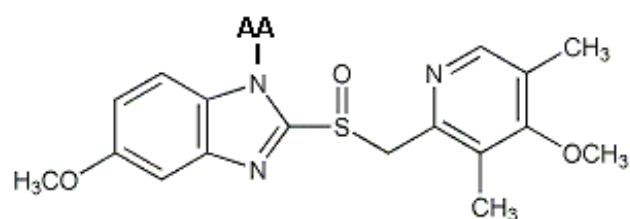
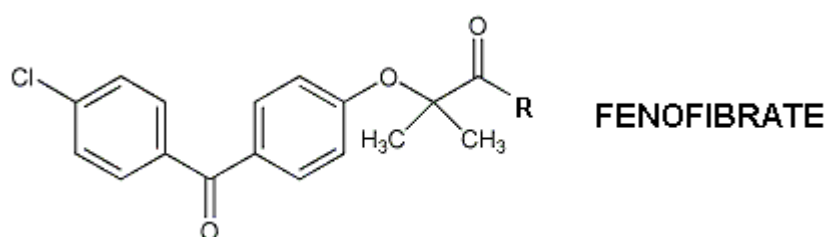




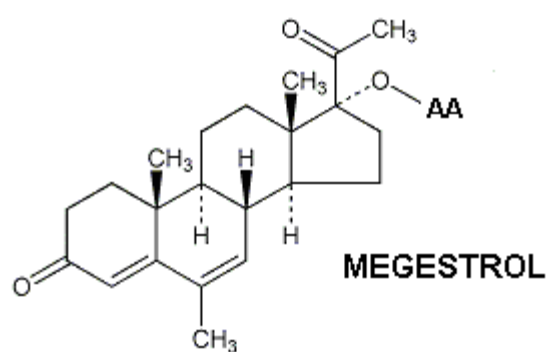
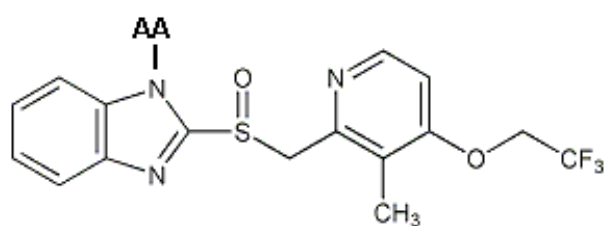
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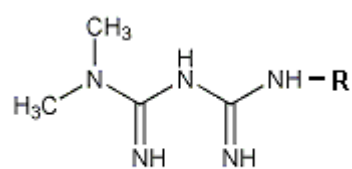




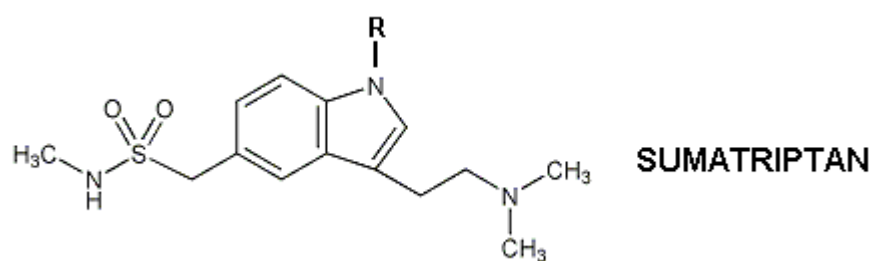
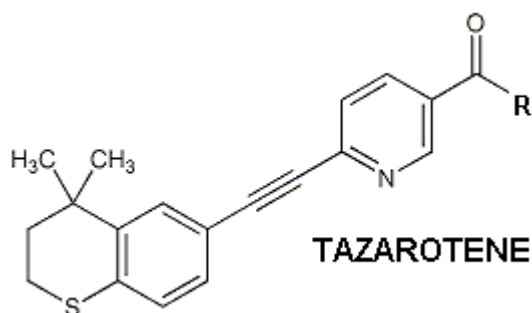
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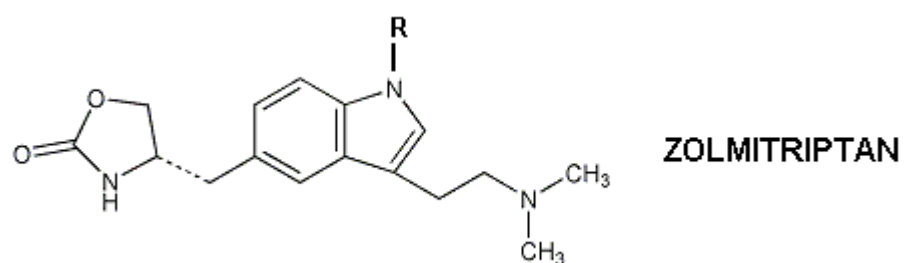
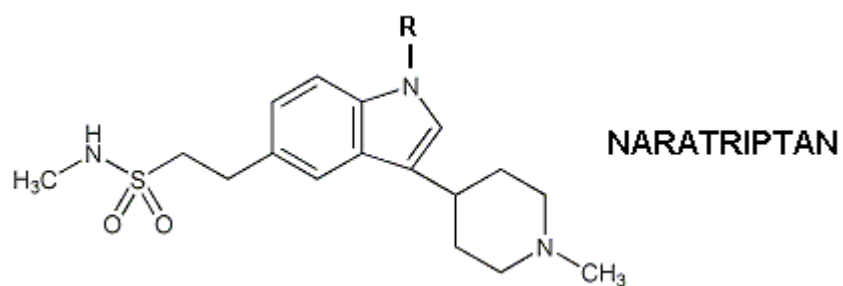
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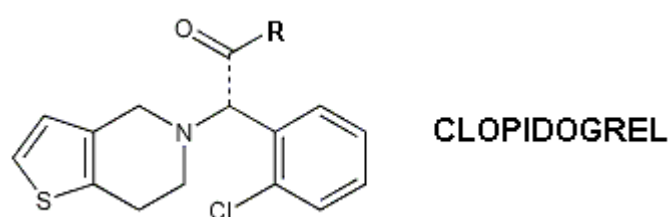
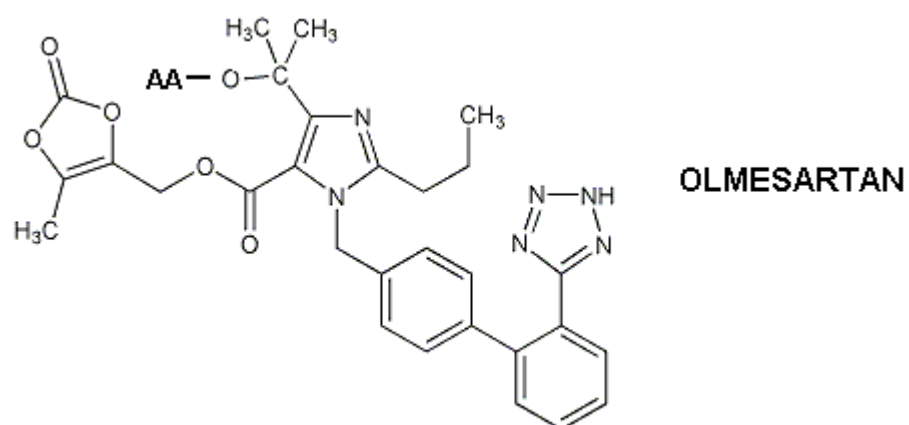
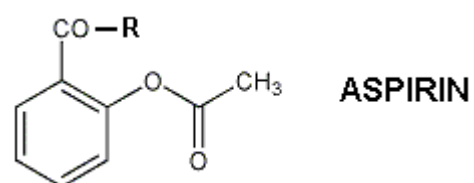


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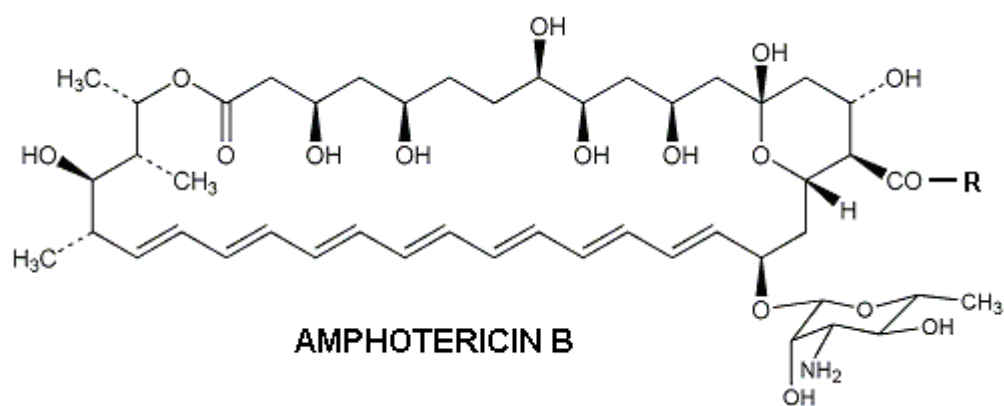


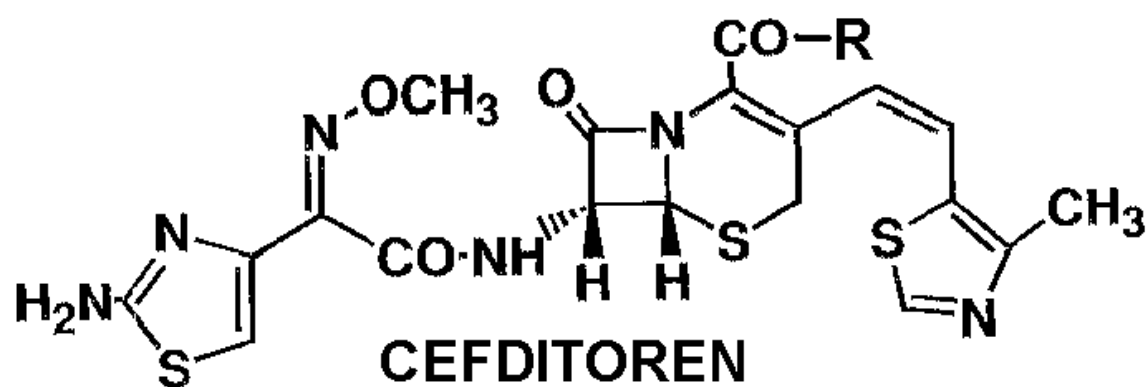
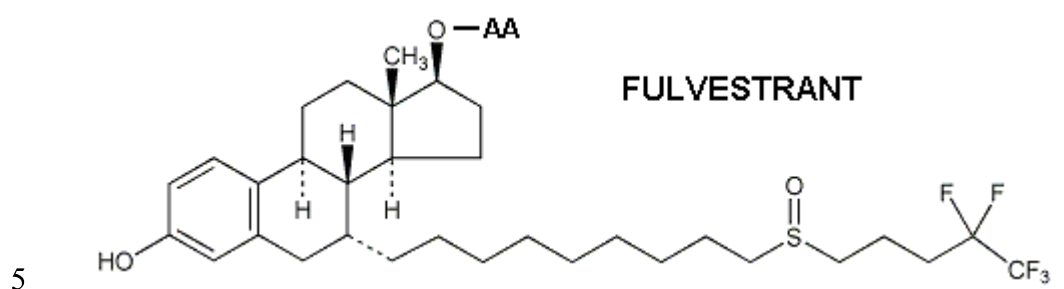
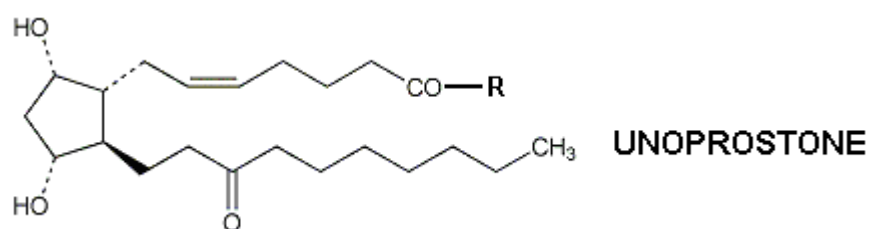
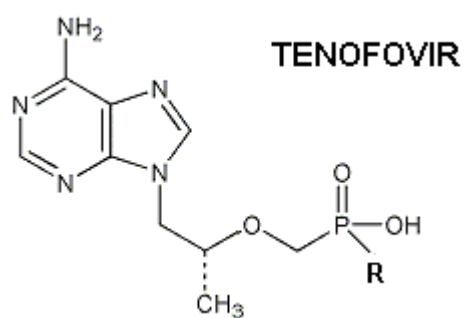
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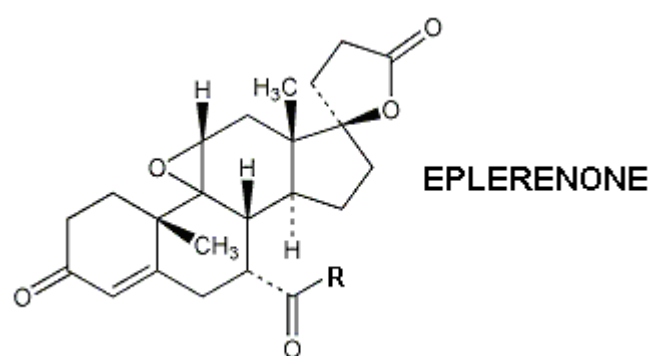
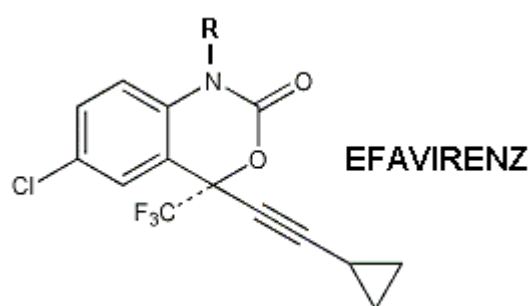


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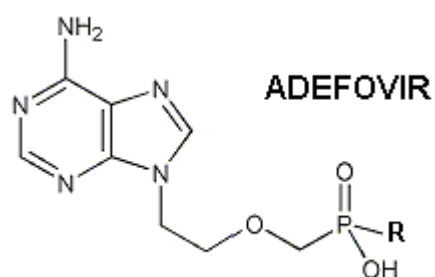
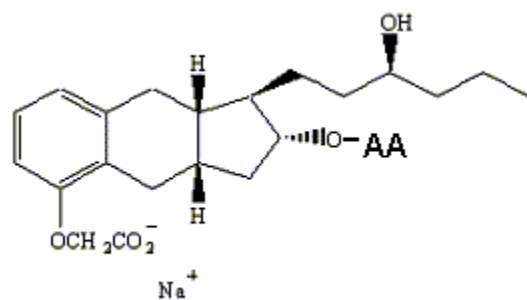




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$R_8N=N-AA_5-COOH$,

SULFO DRUG AZO DERIVATIVE , _____

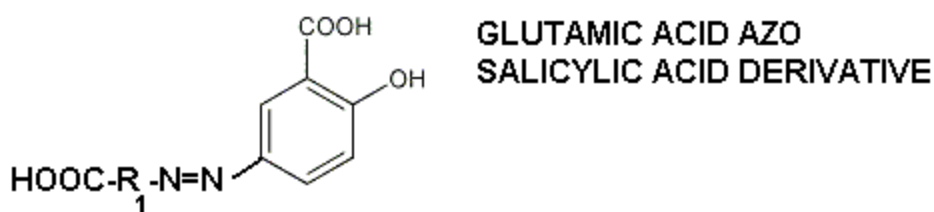
$R_8NH\ CO-AA_5NH_2$

SULFA DRUG AMIDE DERIVATIVE

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or

10



or a pharmaceutically acceptable salt thereof,

wherein

15 AA is an amino acid without the hydroxyl group on the carboxy group, and is attached via the acyl group

R is AA_3 or OAA_6 ,

CYCLO represents the residues at positions 2 – 11 of a cyclosporin molecule;

x-y is $CH=CH$ or $CH_2=CH_2$,

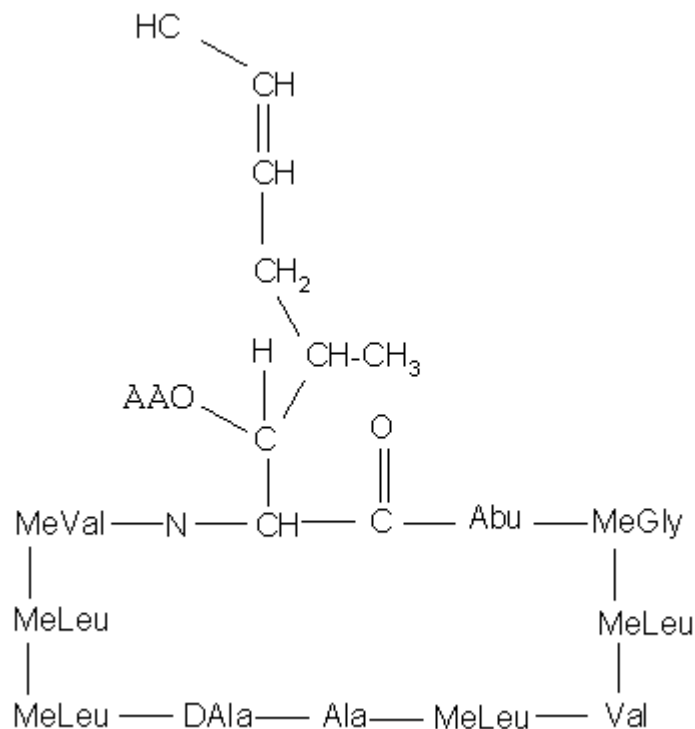
20 R^2 is OAA or OGlyAA;

AA_1 is an amino acid without the hydroxy group on the carboxy group and is attached via the acyl group;

AA_6 is an amino acid residue having a hydroxy group on the side chain less said hydroxyl group, and wherein AA_6 is attached via an ester bond through its side chain hydroxy group;

25 R_2 is

11. The product according to Claim 7 wherein the compound has the formula



- 5 12. A pharmaceutical composition comprising a therapeutically effective amount of the compound according to any one of Claims 7-11 and a pharmaceutically acceptable salt thereof.
- 10 13. A method of enhancing the bioavailability of a drug having a functionally selected from the group consisting of hydroxy, amino, carboxy or acylating derivative of said carboxy group, said drug being selected from the group consisting of Cyclosporin, Lopinavir, Cefdinir, Zileuton, Nelfinavir, Flavoxate, Candesarten, Propofol, Nisoldipine, Amlodipine, Ofloxacin, Fosinopril, Enalapril, Ramipril, Benazepril, Moexipril, Trandolapril, Cromolyn, Amoxicillin, Cefuroxime, Ceftazidime, Cefpodoxime, Atovaquone, Niacin, Bexarotene, Propoxyphene,
- 15 Salsalate, Acetaminophen, Ibuprofen, Lovastatin, Simvastatin, Atorvastatin, Pravastatin, Fluvastatin, Nadolol, Valsartan, Methylphenidate, Methyl Prednisolone, Sulfa Drugs, Sulfasalazine, Medroxyprogesterone, Estramustine, 5-aminosalicylic acid, Miglitol, Mefloquine, Danazol, Eprosartan, Divalproex, Fenofibrate, Omeprazole, Lansoprazole,

Megestrol, Metformin., Tazarotene, Sumatriptan, Naratriptan, Zolmitriptan, Aspirin, Olmesartan, Pimecrolimus, Clopidogrel, Amphotericin, Tenofovir, Unoprostone, Fulvestrant, Cefditoren, Efavirenz, Eplerenone, Treprostinil, and

Adefovir, , said method comprising reacting the drug with an amino acid under conditions effective to form a covalent bond between the drug and the amino acid and administering the product thereof to a patient in need thereof, wherein said amino acid is selected from the groups consisting of Thr, Hyp, Ser, Tyr, Lys, Leu, Ile, Gly, Asp, Glu, Met, Ala, Val, Pro, His, Nor, Ara, Phe, Trp, Hsr, Car, Ort, Cav, Asn, Gln, Can, Tau, Djk, GABA, Cys, Sar or Dcy.

14. A method of enhancing the solubility in an aqueous solution of a drug having a functionality selected from the group consisting of hydroxy, amino, carboxy or acylating derivative of said carboxy group, said drug being selected from the group consisting of lopinavir, cefdinir, amlodipine, nisoldipine, zileuton, nelfinavir, flavoxate, candesartan, cromolyn (sodium), atovaquone, niacin, bexarotene, propoxyphene, salsalate, acetaminophen, ibuprofen, valsartan, methyl phenidate, methyl prednisolone, medroxy progesterone, cephalosporin antibiotic, estramustine, miglitol, mefloquine, danazol, eprosartan, divalproex, fenofibrate, megestrol, metformin, tazarotene, aspirin, olmesarten, clopidogrel, amphotericin, tenofovir, unoprostone, fulvestrant, cefditoren, efavirenz, eplerenone, treprostinil adefovir and salazine, said method comprising reacting the drug with an amino acid under conditions effective to form a covalent bond between the drug and the amino acid, wherein said amino acid is selected from the group consisting of Thr, Hyp, Ser, Tyr, Lys, Leu, Ile, Gly, Asp, Glu, Met, Ala, Val, Pro, His, Nor, Ara, Phe, Trp, Hsr, Car, Ort, Cav, Asn, Gln, Can, Tau, Djk, GABA, Cys, Sar or Dcy.

15. The method according to Claim 13 or 14 wherein the amino acid is Thr, Hyp, Ser, Tyr, Lys, Leu, Ile, Gly, Asp, Glu, Met, Ala, Val, Pro, His, Arg, Phe, Trp, Gln, Asn, or Cys.

16. The method according to Claim 15 or 16 wherein the amino acid is threonine, hydroxyproline or serine.

17. A method of enhancing the safety profile with longer anesthetic effect of propofol in an aqueous solution comprising reacting the hydroxy functionality of the propofol molecule with an amino acid or acylating derivative thereof under ester forming conditions and isolating the product thereof.

18. A method of enhancing the solubility of a quinolone antibiotic having a carboxy group or acylating group in an aqueous solution comprising reacting the carboxylic acid functionality of the quinolone antibiotic with an amino acid or acylating derivative thereof under either ester or amide forming conditions and isolating the product thereof.

19. A method of enhancing the bioavailability of a quinolone antibiotic having a carboxyl group or acylating group when administered to a patient which comprises reacting the carboxylic acid functionality of the quinolone antibiotic with an amino acid or acylating derivative under ester or amide forming conditions, isolating the product thereof and administering said product to the patient, said antibiotic being other than ciprofloxacin.

20. A method of enhancing the solubility of ace inhibitors having a carboxy or acylating group in an aqueous solution comprising reacting the carboxylic acid functionality of the ace inhibitor molecule with an amino acid or acylating derivative thereof under either ester or amide forming conditions and isolating the product thereof, said antibiotic being other than ciprofloxacin.

21. A method of enhancing the bioavailability of ace inhibitors having a carboxy or acylating group when administered to a patient which comprises reacting the carboxylic acid functionality of the ace inhibitors molecule with an amino acid or acylating derivative under ester or amide forming conditions, isolating the product thereof and administering said product to the patient.

22. A method of reducing the gastric irritation of ibuprofen comprising reacting the carboxylic acid functionality of the ibuprofen molecule with an amino acid or acylating derivative under either ester or amide forming conditions and administering the product to a patient in need thereof, said product resulting less gastric irritability than ibuprofen.

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23. A method of enhancing the solubility of a proton pump inhibitor in an aqueous solution comprising reacting the amine functionality of the proton pump inhibitor with the carboxylic acid moiety of the amino acid or acylating derivative thereof under amide forming conditions and isolating the product thereof.

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24. A method of enhancing the bioavailability of a proton pump inhibitor when administered to a patient which comprises reacting the amine functionality of the proton pump inhibitor with the carboxylic acid moiety of an amino acid or acylating derivative thereof under amide forming conditions, isolating the product thereof and administering said product to the patient.

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25. A method of enhancing the solubility of Selective 5-HT receptor agonists in an aqueous solution comprising reacting the amine functionality of the Selective 5-HT receptor agonists molecule with the carboxylic acid moiety of an amino acid or acylating derivative thereof under amide forming conditions and isolating the product thereof.

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26. A method of enhancing the bioavailability of Selective 5-HT receptor agonists when administered to a patient which comprises reacting the amine functionality of the Selective 5-HT receptor agonists with the carboxylic acid moiety of an amino acid under amide forming conditions, isolating the product thereof and administering said product to the patient.

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27. A method of reducing the gastric irritability in the stomach resulting from aspirin administration to a mammal which method comprises reacting the carboxylic acid functionality of the aspirin molecule with an amino acid or acylating derivative thereof under either amide or ester forming conditions, and administering the formed product to said mammal, wherein the gastric irritability is reduced relative to aspirin.

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28. A method of enhancing the solubility of immunosuppressants in an aqueous solution comprising reacting the hydroxy functionality of the immunosuppressants with an amino acid or acylating derivative thereof under ester forming conditions and isolating the product thereof, said immunosuppressant being other than sirolimus.
29. A method of enhancing the bioavailability of immunosuppressants when administered to a patient which comprises reacting the hydroxy functionality of the immunosuppressants with an amino acid or acylating derivative under ester forming conditions, isolating the product thereof and administering said product to the patient, said immunosuppressant being other than sirolimus.
30. A method of enhancing the solubility of a sulfa drug in an aqueous solution comprising reacting the amine of the sulfa drug with an amino acid or acylating derivative thereof under either azo or amide forming conditions and isolating product thereof.
31. A method of enhancing the bioavailability of a sulfa drug when administered to a patient which comprises reacting the amine functionality of the sulfa drug with an amino acid or acylating derivative under azo or amide forming conditions, isolating the product thereof and administering said product to the patient.
32. A method of providing a clear aqueous intravenous formulation comprising a Sulfa drug when administered to a patient which comprises reacting the amine of the Sulfa drug with an amino acid or acylating derivative under azo or amide forming conditions, isolating the product thereof and administering said product to the patient parenterally.
33. A method of enhancing the solubility in an aqueous solution of a nucleoside analog having an OH functionality comprising reacting the hydroxyl functionality of the nucleoside analog with an amino acid or acylating derivative thereof under ester forming conditions or isolating the product thereof.

34. A method for enhancing the bioavailability of a nucleoside analog having an OH group thereon which comprise reacting the hydroxyl functionality of the nucleoside analog with an amino acid or acylating derivative thereof under ester forming conditions and isolating the product thereof and administering the product to a patient.

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35. The method according to any one of Claims 17-34, wherein the medicament is lopinavir, cefdinir, amlodipine, nisoldipine, zileuton, nelfinavir, flavoxate, candesartan, cromolyn (sodium), atovaquone, niacin, bexarotene, propoxyphene, salsalate, acetaminophen, ibuprofen, valsartan, methyl phenidate, methyl prednisolone, medroxy progesterone, cephalosporin antibiotic, estramustine, miglitol, mefloquine, danazol, eprosartan, divalproex, fenofibrate, megestrol, metformin, tazarotene, aspirin, olmesartan, clopidogrel, amphotericin, tenofovir, unoprostone, fulvestrant, cefditoren, efavirenz, eplerenone, treprostinil adefovir and salazine, said compound being the product of the reaction of said drug with an amino acid under conditions effective to form a covalent bond between the drug and the amino acid, wherein said amino acid is a L-amino acid selected from the group consisting of Thr, Hyp, Ser, Tyr, Lys, Leu, Ile, Gly, Asp, Glu, Met, Ala, Val, Pro, His, Nor, Ara, Phe, Trp, Hsr, Car, Ort, Cav, Asn, Gln, Can, Tau, Djk, GABA, Cys, Sar or Dcy.

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36. The method according to any one of Claims 17-35 wherein the amino acid is threonine, hydroxyproline or serine.

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37. The method according to Claim 36 wherein the amino acid is threonine.

38. The product from a reaction between a drug selected from thyroxine, folic acid and digoxin and an amino acid under conditions sufficient to form a covalent bond between said drug and the amino acid or the pharmaceutically acceptable salt of said product wherein the amino acid is L-Hyp, L-Ser, L-Lys, L-Leu, L-Ile, Gly, L-Asp, L-Glu, L-Met, L-Ala, L-Val, L-Pro, L-His, L-Nor, L-Arg, L-Phe, L-Trp, L-Hsr, L-Car, L-Ort, L-Cav, L-Asn, L-Gln, Can, Tau, Djk, GABA, L-Cys, Sar or L-Dcy.

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39. A product from a reaction between Gabapentin and an amino acid under conditions sufficient to form a covalent bond between the amino acid and Gabapentin, or the pharmaceutically acceptable salt of said product, wherein the amino acid is L-Hyp, L-Lys, L-Leu, L-Ile, Gly, L-Asp, L-Glu, L-Met, L-Ala, L-Val, L-Pro, L-His, L-Nor, L-Arg, L-Phe, L-Trp, L-Hsr, L-Car, L-Ort, L-Cav, L-Asn, L-Gln, Can, Tau, Djk, GABA, L-Cys or L-Dcy.
40. The product from the reaction between sirolimus and an amino acid under conditions sufficient to form a covalent bond between the amino acid and sirolimus, or the pharmaceutically acceptable salt of said product, wherein the amino acid is L-Hyp, L-Ser, L-Tyr, L-Lys, L-Leu, L-Ile, L-Asp, L-Glu, L-Met, L-Ala, L-Val, L-Pro, L-His, L-Nor, L-Arg, L-Phe, L-Trp, L-Hsr, L-Car, L-Ort, L-Cav, L-Asn, L-Gln, Can, Tau, Djk, GABA, L-Cys, Sar or L-Dcy.
41. The product from the reaction between nicotinic acid and an amino acid under conditions sufficient to form a covalent bond between the amino acid and nicotinic acid or the pharmaceutically acceptable salt thereof, wherein the amino acid is L-Hyp, L-Ser, L-Tyr, L-Lys, L-Leu, L-Ile, Gly, L-Asp, L-Glu, L-Met, L-Ala, L-Val, L-Pro, L-His, L-Nor, L-Arg, L-Trp, L-Hsr, L-Car, L-Ort, L-Cav, L-Asn, L-Gln, Can, Tau, Djk, GABA, L-Cys, Sar or L-Dcy.
42. A product from the reaction of an amino acid and penicillamine under conditions sufficient to form a covalent bond therebetween, wherein said amino acid is L-Hyp, L-Tyr, L-Leu, L-Ile, L-Asp, L-Met, L-Ala, L-Pro, L-His, L-Car, L-Ort, L-Cav, L-Asn, L-Gln, L-Can, Tau, Djk, GABA, L-Cys, Sar or L-Dcy.
43. A product from the reaction of biotin and an amino acid or a compound selected from L-Can, Djk and L-Dcy under conditions sufficient to form a covalent bond between biotin and the amino acid or the compound, wherein said amino acid is L-Hyp, L-Ser, L-Tyr, L-Lys, L-Leu, L-Ile, Gly, L-Asp, L-Glu, L-Met, L-Ala, L-Val, L-Pro, L-His, L-Nor, L-Phe, L-Trp, L-Hsr, L-Car, L-Ort, L-Cav, L-Asn, L-Gln, GABA, L-Cys, or Sar.