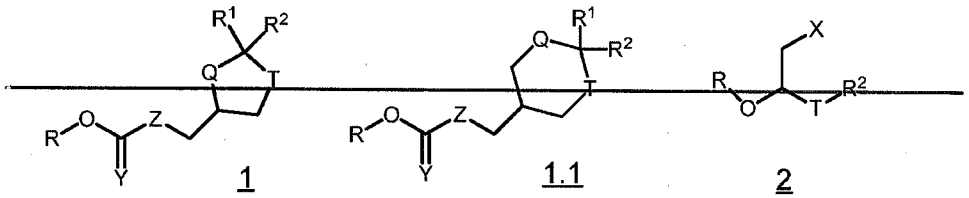
embodiment, there is provided compositions of acid labile, lipophilic molecular conjugates of cancer chemotherapeutic agents for use in treating cancer. In another embodiment, there is provided intermediate compounds for use in forming molecular conjugates, such as acid labile, lipophilic pro-drug conjugates, for use in treating cancer. In another embodiment, there is provided efficient methods for the preparation of acid labile, lipophilic drug conjugates. In another embodiment, there is provided methods for administering chemotherapeutic agents to patients that reduce or substantially eliminate side effects conventionally experienced by cancer patients. In another embodiment, there is provided methods for concentrating chemotherapeutic agents in cancer cells of a patient.

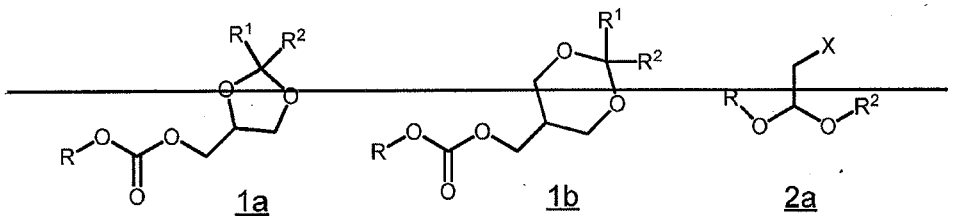
[0030] In one embodiment, there is provided an acid labile lipophilic molecular conjugate (ALLMC) of the formula **1**, **1.1** or formula **2**:



1 **1.1** **2**

wherein: R is a hydroxyl bearing cancer chemotherapeutic agent; for formula **1** or **1.1** R^1 is hydrogen, C_1-C_4 alkyl or C_5-C_{22} alkyl; R^2 is C_5-C_{22} alkyl; Y is selected from O, NR' or S wherein R' is hydrogen or C_1-C_6 alkyl; Z is O or S; Q is O or S; and T is O or S; for formula **2**: R^2 is a C_1-C_{22} alkyl; T is O or S; and X is hydrogen or a leaving group selected from the group consisting of mesylates, sulfonates and halogen (Cl, Br and I); and their isolated enantiomers, diastereoisomers or mixtures thereof, or a pharmaceutically acceptable salt thereof. The compound **1.1** includes the pure syn isomer, the pure anti isomer and mixtures of syn- and anti-isomers, and their diastereomers.

[0031] In another embodiment, there is provided the above acid labile lipophilic molecular conjugate of the formula **1** or **1.1** wherein: R is a hydroxyl bearing cancer chemotherapeutic agent; R^1 is hydrogen, C_1-C_4 alkyl or C_5-C_{22} alkyl; R^2 is C_5-C_{22} alkyl; Y is O or S; Z is O; Q is O; and T is O. In one aspect of the acid labile lipophilic molecular conjugate of the formula **2** wherein: R^2 is C_5-C_{22} alkyl; T is O; and X is hydrogen or selected from the group consisting of Cl, Br and I. In another variation, R^2 is C_9-C_{22}. In another aspect of the above acid labile lipophilic molecular conjugate comprising the formula **1a**, **1b** or formula **2a**:



1a 1b 2a

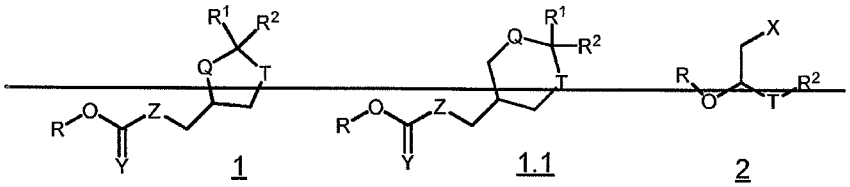
wherein: R is a hydroxyl bearing cancer chemotherapeutic agent (HBCCA);
for formula **1a** or **1b** R^1 is hydrogen, C_1-C_4 alkyl or C_5-C_{22} alkyl; and R^2 is C_5-C_{22} alkyl; and for formula **2a**: R^2 is C_1-C_{22} alkyl; and X is hydrogen or is selected from the group consisting of Cl, Br and I. In one variation of the compound that is the carbonate (i.e., -OC(O)O-) of the formula **1a** or **1b** the compound is the corresponding sulfonate (i.e., -OS(O)O-) of the formula **1a** wherein the carbonate group is replaced by a sulfonate group. The compound **1b** includes the pure syn isomer, the pure anti isomer and mixtures of syn and anti isomers, and their diastereomers.

[0032] In another variation of the compound of the formula **1**, **2**, **1a** and **2a**, R^1 is hydrogen or C_1-C_4 alkyl or C_5-C_{22} alkyl, and R^2 is the carbon residue of an unsaturated fatty acid, such as the carbon residue selected from the group consisting of the C_{19} residue of eicosenoic acid (including the cis isomer, trans isomer and mixtures of isomers), C_{17} residue of oleic acid and the C_{17} residue of elaidic acid. As used herein, the "carbon residue" (e.g., C_{17} residue, C_{19} residue etc ...) of the fatty acid means the carbon chain of the fatty acids excluding the carboxyl carbon.

[0033] In another aspect of the above acid labile lipophilic molecular conjugate, the hydroxyl bearing cancer chemotherapeutic agent is selected from the group consisting of taxanes, abeo-taxanes, camptothecins, epothilones, cucurbitacins, quassinoids, anthracyclines, and their analogs and derivatives. In another aspect of the above acid labile lipophilic molecular conjugate, the hydroxyl bearing cancer chemotherapeutic agent is selected from the group consisting of aclarubicin, camptothecin, masoprocol, paclitaxel, pentostatin, amrubicin, cladribine, cytarabine, docetaxel, gemcitabine, elliptinium acetate, epirubicin, etoposide, formestane, fulvestrant, idarubicin, pirarubicin, topotecan, valrubicin and vinblastine. In another aspect of the above acid labile lipophilic molecular conjugate, the conjugate is selected from the compounds in Figures 18, 19 and 20. In one variation, only one of the groups $-ALL^1$, $-ALL^2$, $-ALL^3$ ... to $-ALL^n$ is an -ALL group and the others are hydrogens. In another variation, two of the groups $-ALL^1$, $-ALL^2$, $-ALL^3$ ... to $-ALL^n$ are –ALL groups.

[0034] In another embodiment, there is provided a pharmaceutical composition comprising: a) a therapeutically effective amount of a compound of the above, in the form of a single diastereoisomer; and b) a pharmaceutically acceptable excipient. In another aspect, the pharmaceutical composition is adapted for oral administration; or as a liquid formulation adapted for parenteral administration. In another aspect, the composition is adapted for administration by a route selected from the group consisting of orally, parenterally, intraperitoneally, intravenously, intraarteriall, transdermally, intramuscularly, rectally, intranasally, liposomally, subcutaneously and intrathecally. In another embodiment, there is provided a method for the treatment of cancer in a patient comprising administering to the patient a therapeutically effective amount of a compound or composition of any of the above compound or composition, to a patient in need of such treatment. In one aspect of the method, the cancer is selected from the group consisting of leukemia, neuroblastoma, glioblastoma, cervical, colorectal, pancreatic, renal and melanoma. In another aspect of the method, the cancer is selected from the group consisting of lung, breast, prostate, ovarian and head and neck. In another aspect of the method, the method provides at least a 10%, 20%, 30%, 40%, or at least a 50% diminished degree of resistance expressed by the cancer cells when compared with the non-conjugated hydroxyl bearing cancer chemotherapeutic agent.

[0035] In another embodiment, there is provided a method for reducing or substantially eliminating the side effects of chemotherapy associated with the administration of a cancer chemotherapeutic agent to a patient, the method comprising administering to the patient a therapeutically effective amount of an acid labile lipophilic molecular conjugate of the formula **1**, **1.1** or formula **2**:

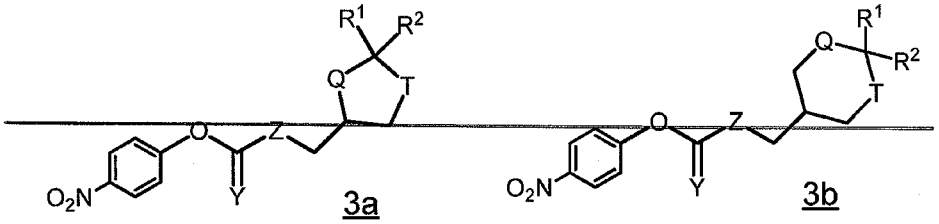


1 1.1 2

wherein: R is a hydroxyl bearing cancer chemotherapeutic agent; for formula **1** or **1.1**: R^1 is hydrogen, C_1-C_4 alkyl or C_5-C_{22} alkyl; R^2 is C_5-C_{22} alkyl; Y is selected from O, NR' or S wherein R' is hydrogen or C_1-C_6 alkyl; Z is O or S; Q is O or S; and T is O or S; for formula **2**: R^2 is C_1-C_{22} alkyl; T is O or S; and X is hydrogen or a leaving group selected from the group consisting of mesylates, sulfonates and halogen (Cl, Br and I); and their isolated enantiomers, diastereoisomers or mixtures thereof. The compound **1.1** includes the pure syn isomer, the pure anti isomer and

mixtures of syn and anti isomers, and their diastereomers. In one variation of the above, R^2 is C_9-C_{22} alkyl. In one aspect, the method provides a higher concentration of the cancer chemotherapeutic agent in a cancer cell of the patient. In another aspect, the method delivers a higher concentration of the cancer chemotherapeutic agent in the cancer cell, when compared to the administration of a non-conjugated cancer chemotherapeutic agent to the patient, by at least 5%, 10%, 20%, 30%, 40% or at least 50%.

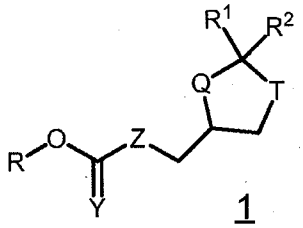
[0036] In another embodiment, there is provided a compound of the formula **3a** or **3b**:



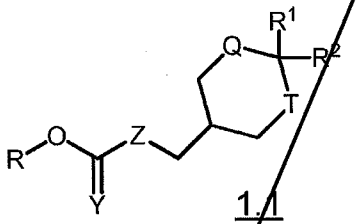
wherein: R^1 is hydrogen, C_1-C_4 alkyl or C_5-C_{22} alkyl; R^2 is C_5-C_{22} alkyl; Y is selected from O, NR' or S wherein R' is hydrogen or C_1-C_6 alkyl; Z is selected from O or S; Q is O or S; and T is O or S. In one aspect of the compound, R^1 is hydrogen or C_1-C_4 alkyl; R^2 is C_5-C_{22} alkyl; Y is O or S; Z is O; Q is O; and T is O. The activated compound of the formula **3a** or **3b** may be used to prepare the acid labile lipophilic conjugate when the activated compound is condensed with a hydroxyl bearing cancer chemotherapeutic agent (HBCCA). As defined herein, the HBCCA is represented generically with the residue or group "R" in the formulae **1**, **1a**, **1b**, **1.1**, **2** and **2a**, for example, and where the HBCCA is not coupled to form the acid labile, lipophilic molecular conjugates, then the HBCCA may also be generically represented as having the formula "R-OH" since the HBCCA may be functionalized by one or more hydroxyl (-OH) groups. Similarly, the acid labile lipophilic group (i.e., the "-ALL" group of the activated compound) that may be condensed with a HBCCA to form the acid labile, lipophilic molecular conjugate generically represented as "R-O-ALL." Accordingly, where more than one -ALL group is condensed or conjugated with a HBCCA group, then each –ALL group may be independently designated as $-ALL^1$, $-ALL^2$, $-ALL^3$ … to $-ALL^n$ where n is the number of available hydroxyl groups on the cancer chemotherapeutic agent that may be conjugated or couple with an –ALL group. As exemplified for the compound of formulae **1** and **2**, for example, the HBCCA and the –ALL groups as designated, are shown below.

What is claimed is:

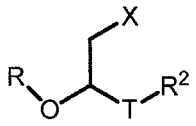
1. An acid labile lipophilic molecular conjugate (ALLMC) of the formula **1**, **1.1** or formula **2**:



1



1.1



2

wherein:

R is a hydroxyl bearing cancer chemotherapeutic agent;

for formula **1** or **1.1**:

R^1 is hydrogen, C_1-C_4 alkyl or C_5-C_{22} alkyl;

R^2 is C_5-C_{22} alkyl;

Y is selected from O, NR' or S wherein R' is hydrogen or C_1-C_6 alkyl;

Z is O or S;

Q is O or S; and T is O or S;

for formula **2**:

R^2 is a C_1-C_{22} alkyl;

T is O or S; and

X is a hydrogen or a leaving group selected from the group consisting of mesylates, sulfonates and halogen (Cl, Br and I);

and their isolated enantiomers, diastereoisomers or mixtures thereof;

or a pharmaceutically acceptable salt thereof.

2. The acid labile lipophilic molecular conjugate of Claim 1 of the formula **1** or **1.1**:

wherein:

R is a hydroxyl bearing cancer chemotherapeutic agent;

R^1 is hydrogen, C_1-C_4 alkyl or C_5-C_{22} alkyl;

R^2 is C_5-C_{22} alkyl;

Y is O or S;

Z is O; and

Q is O; and T is O.

3. The acid labile lipophilic molecular conjugate of Claim 1 of the formula **2**:

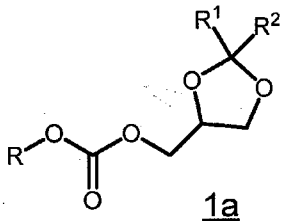
wherein:

R^2 is C_5-C_{22} alkyl;

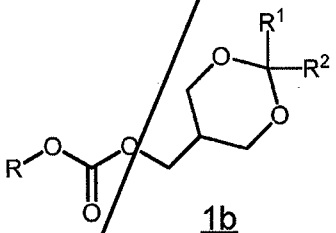
T is O; and

X is hydrogen or is selected from the group consisting of Cl, Br and I.

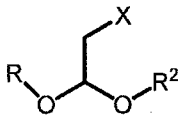
4. The acid labile lipophilic molecular conjugate of Claim 1 comprising the formula **1a**, **1b** or formula **2a**:



1a



1b



2a

wherein:

R is a hydroxyl bearing cancer chemotherapeutic agent (HBCCA);

for formula **1a** or **1b**:

R^1 is hydrogen, C_1-C_4 alkyl or C_5-C_{22} alkyl; and

R^2 is C_5-C_{22} alkyl;

for formula **2a**:

R^2 is C_1-C_{22} alkyl; and

X is hydrogen or is selected from the group consisting of Cl, Br and I.

5. The acid labile lipophilic molecular conjugate of any one of Claims 1 to 4, wherein the hydroxyl bearing cancer chemotherapeutic agent is selected from the group consisting of taxanes, abeo-taxanes, camptothecins, epothilones, cucurbitacins, quassinoids, anthracyclines, and their analogs and derivatives.

6. The acid labile lipophilic molecular conjugate of any one of Claims 1 to 5, wherein the hydroxyl bearing cancer chemotherapeutic agent is selected from the group consisting of aclarubicin, camptothecin, masoprocol, paclitaxel, pentostatin, amrubicin, cladribine, cytarabine,

docetaxel, elliptinium acetate, epirubicin, etoposide, formestane, fulvestrant, gemcitabine, idarubicin, pirarubicin, topotecan, valrubicin and vinblastine.

7. The acid labile lipophilic molecular conjugate of any one of Claims 1 to 4, wherein the conjugate is selected from the compounds in Figure 18, Figure 19 and Figure 20.

8. A pharmaceutical composition comprising: a) a therapeutically effective amount of a compound of any one of Claims 1 to 7, in the form of a single diastereoisomer; and b) a pharmaceutically acceptable excipient.

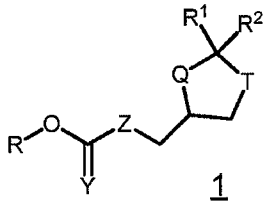
9. A method for the treatment of cancer in a patient comprising administering to the patient a therapeutically effective amount of a compound or composition of any one of Claims 1 to 7, to a patient in need of such treatment.

10. The method of Claim 9, wherein the cancer is selected from the group consisting of leukemia, neuroblastoma, glioblastoma, cervical, colorectal, pancreatic, renal and melanoma.

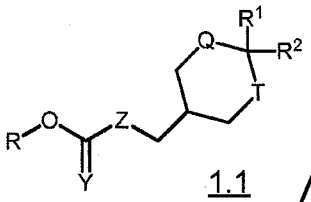
11. The method of Claim 9, wherein the cancer is selected from the group consisting of lung, breast, prostate, ovarian and head and neck.

12. The method of any one of Claims 9 to 11, wherein the method provides at least a 10% to 50% diminished degree of resistant expressed by the cancer cells when compared with the non-conjugated hydroxyl bearing cancer chemotherapeutic agent.

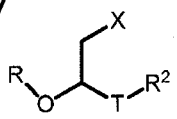
13. A method for reducing or substantially eliminating the side effects of chemotherapy associated with the administration of a cancer chemotherapeutic agent to a patient, the method comprising administering to the patient a therapeutically effective amount of an acid labile lipophilic molecular conjugate of the formula **1**, **1.1** or formula **2**:



1



1.1



2

wherein:

R is a hydroxyl bearing cancer chemotherapeutic agent;

for formula **1** or **1.1**:

R^1 is hydrogen, C_1-C_4 alkyl or C_5-C_{22} alkyl;

R^2 is C_5-C_{22} alkyl;

Y is selected from O, NR' or S wherein R' is hydrogen or C_1-C_6 alkyl;

Z is O or S; and

Q is O or S; and T is O or S;

for formula **2**:

R^2 is C_1-C_{22} alkyl;

T is O or S; and

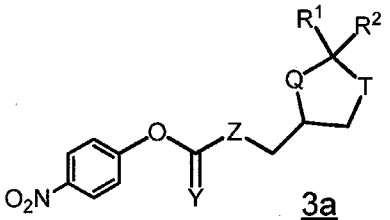
X is hydrogen or a leaving group selected from the group consisting of mesylates, sulfonates and halogen (Cl, Br and I);

and their isolated enantiomers, diastereoisomers or mixtures thereof.

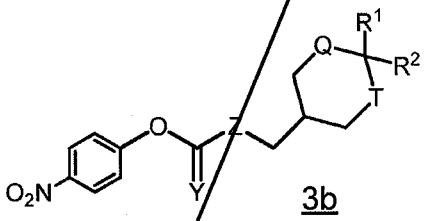
14. The method of Claim 13, wherein the method provides a higher concentration of the cancer chemotherapeutic agent in a cancer cell of the patient.

15. The method of Claim 14, wherein the method delivers a higher concentration of the cancer chemotherapeutic agent in the cancer cell, when compared to the administration of a non-conjugated cancer chemotherapeutic agent to the patient, by at least 5%, 10%, 20% or at least 50%.

16. A compound of the formula **3a** or **3b**:



3a



3b

wherein:

R^1 is hydrogen, C_1-C_4 alkyl or C_5-C_{22} alkyl;

R^2 is C_5-C_{22} alkyl;

Y is selected from O, NR' or S wherein R' is hydrogen or C_1-C_6 alkyl;

Z is selected from O or S; and

Q is O or S; and T is O or S.

17. The compound of Claim 16, wherein:

R^1 is hydrogen or C_1-C_4 alkyl;

R^2 is C_5-C_{22} alkyl;

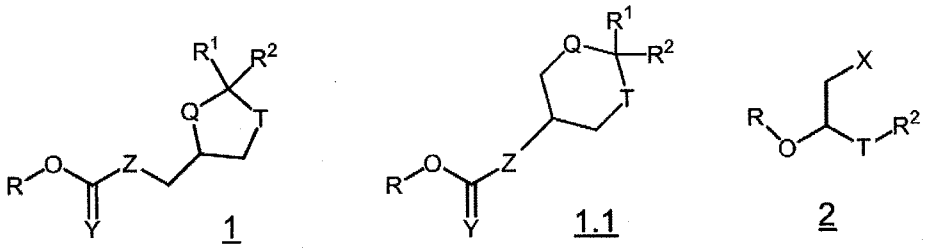
Y is O or S;

Z is O; and

Q is O; and T is O.

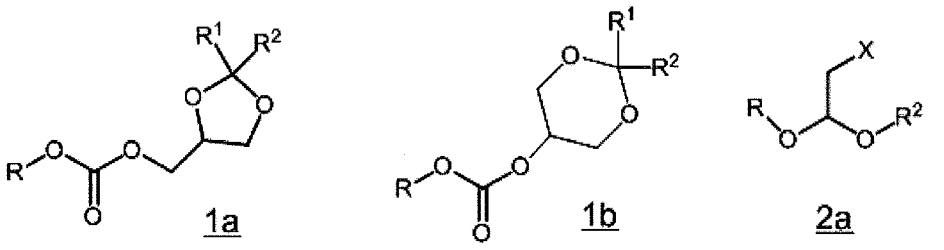
embodiment, there is provided compositions of acid labile, lipophilic molecular conjugates of cancer chemotherapeutic agents for use in treating cancer. In another embodiment, there is provided intermediate compounds for use in forming molecular conjugates, such as acid labile, lipophilic pro-drug conjugates, for use in treating cancer. In another embodiment, there is provided efficient methods for the preparation of acid labile, lipophilic drug conjugates. In another embodiment, there is provided methods for administering chemotherapeutic agents to patients that reduce or substantially eliminate side effects conventionally experienced by cancer patients. In another embodiment, there is provided methods for concentrating chemotherapeutic agents in cancer cells of a patient.

[0030] In one embodiment, there is provided an acid labile lipophilic molecular conjugate (ALLMC) of the formula **1**, **1.1** or formula **2**:



wherein: R is a hydroxyl bearing cancer chemotherapeutic agent; for formula **1** or **1.1** R^1 is hydrogen, C_1-C_4 alkyl or C_5-C_{22} alkyl; R^2 is C_5-C_{22} alkyl; Y is selected from O, NR' or S wherein R' is hydrogen or C_1-C_6 alkyl; Z is O or S; Q is O or S; and T is O or S; for formula **2**: R^2 is a C_1-C_{22} alkyl; T is O or S; and X is hydrogen or a leaving group selected from the group consisting of mesylates, sulfonates and halogen (Cl, Br and I); and their isolated enantiomers, diastereoisomers or mixtures thereof, or a pharmaceutically acceptable salt thereof. The compound **1.1** includes the pure syn isomer, the pure anti isomer and mixtures of syn- and anti-isomers, and their diastereomers.

[0031] In another embodiment, there is provided the above acid labile lipophilic molecular conjugate of the formula **1** or **1.1** wherein: R is a hydroxyl bearing cancer chemotherapeutic agent; R^1 is hydrogen, C_1-C_4 alkyl or C_5-C_{22} alkyl; R^2 is C_5-C_{22} alkyl; Y is O or S; Z is O; Q is O; and T is O. In one aspect of the acid labile lipophilic molecular conjugate of the formula **2** wherein: R^2 is C_5-C_{22} alkyl; T is O; and X is hydrogen or selected from the group consisting of Cl, Br and I. In another variation, R^2 is C_9-C_{22}. In another aspect of the above acid labile lipophilic molecular conjugate comprising the formula **1a**, **1b** or formula **2a**:



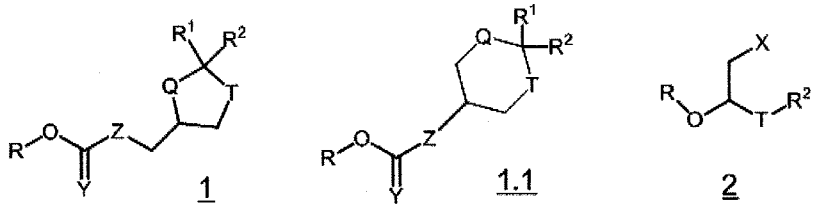
wherein: R is a hydroxyl bearing cancer chemotherapeutic agent (HBCCA);
for formula **1a** or **1b** R^1 is hydrogen, C_1-C_4 alkyl or C_5-C_{22} alkyl; and R^2 is C_5-C_{22} alkyl; and for formula **2a**: R^2 is C_1-C_{22} alkyl; and X is hydrogen or is selected from the group consisting of Cl, Br and I. In one variation of the compound that is the carbonate (i.e., -OC(O)O-) of the formula **1a** or **1b** the compound is the corresponding sulfonate (i.e., -OS(O)O-) of the formula **1a** wherein the carbonate group is replaced by a sulfonate group. The compound **1b** includes the pure syn isomer, the pure anti isomer and mixtures of syn and anti isomers, and their diastereomers.

[0032] In another variation of the compound of the formula **1**, **2**, **1a** and **2a**, R^1 is hydrogen or C_1-C_4 alkyl or C_5-C_{22} alkyl, and R^2 is the carbon residue of an unsaturated fatty acid, such as the carbon residue selected from the group consisting of the C_{19} residue of eicosenoic acid (including the cis isomer, trans isomer and mixtures of isomers), C_{17} residue of oleic acid and the C_{17} residue of elaidic acid. As used herein, the "carbon residue" (e.g., C_{17} residue, C_{19} residue etc ...) of the fatty acid means the carbon chain of the fatty acids excluding the carboxyl carbon.

[0033] In another aspect of the above acid labile lipophilic molecular conjugate, the hydroxyl bearing cancer chemotherapeutic agent is selected from the group consisting of taxanes, abeo-taxanes, camptothecins, epothilones, cucurbitacins, quassinoids, anthracyclines, and their analogs and derivatives. In another aspect of the above acid labile lipophilic molecular conjugate, the hydroxyl bearing cancer chemotherapeutic agent is selected from the group consisting of aclarubicin, camptothecin, masoprocol, paclitaxel, pentostatin, amrubicin, cladribine, cytarabine, docetaxel, gemcitabine, elliptinium acetate, epirubicin, etoposide, formestane, fulvestrant, idarubicin, pirarubicin, topotecan, valrubicin and vinblastine. In another aspect of the above acid labile lipophilic molecular conjugate, the conjugate is selected from the compounds in Figures 18, 19 and 20. In one variation, only one of the groups $-ALL^1$, $-ALL^2$, $-ALL^3$ ... to $-ALL^n$ is an -ALL group and the others are hydrogens. In another variation, two of the groups $-ALL^1$, $-ALL^2$, $-ALL^3$ ... to $-ALL^n$ are –ALL groups.

[0034] In another embodiment, there is provided a pharmaceutical composition comprising: a) a therapeutically effective amount of a compound of the above, in the form of a single diastereoisomer; and b) a pharmaceutically acceptable excipient. In another aspect, the pharmaceutical composition is adapted for oral administration; or as a liquid formulation adapted for parenteral administration. In another aspect, the composition is adapted for administration by a route selected from the group consisting of orally, parenterally, intraperitoneally, intravenously, intraarteriall, transdermally, intramuscularly, rectally, intranasally, liposomally, subcutaneously and intrathecally. In another embodiment, there is provided a method for the treatment of cancer in a patient comprising administering to the patient a therapeutically effective amount of a compound or composition of any of the above compound or composition, to a patient in need of such treatment. In one aspect of the method, the cancer is selected from the group consisting of leukemia, neuroblastoma, glioblastoma, cervical, colorectal, pancreatic, renal and melanoma. In another aspect of the method, the cancer is selected from the group consisting of lung, breast, prostate, ovarian and head and neck. In another aspect of the method, the method provides at least a 10%, 20%, 30%, 40%, or at least a 50% diminished degree of resistance expressed by the cancer cells when compared with the non-conjugated hydroxyl bearing cancer chemotherapeutic agent.

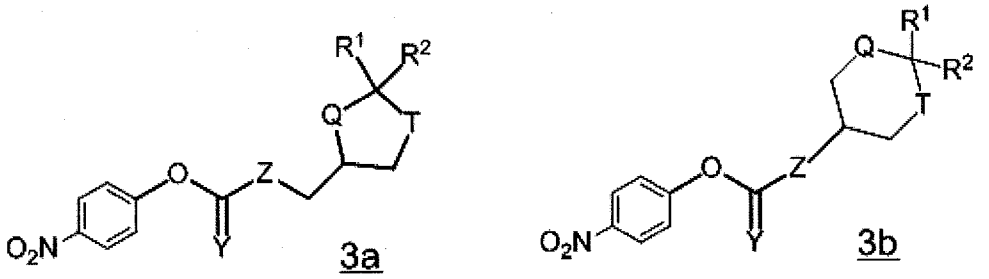
[0035] In another embodiment, there is provided a method for reducing or substantially eliminating the side effects of chemotherapy associated with the administration of a cancer chemotherapeutic agent to a patient, the method comprising administering to the patient a therapeutically effective amount of an acid labile lipophilic molecular conjugate of the formula **1**, **1.1** or formula **2**:



wherein: R is a hydroxyl bearing cancer chemotherapeutic agent; for formula **1** or **1.1**: R^1 is hydrogen, C_1-C_4 alkyl or C_5-C_{22} alkyl; R^2 is C_5-C_{22} alkyl; Y is selected from O, NR' or S wherein R' is hydrogen or C_1-C_6 alkyl; Z is O or S; Q is O or S; and T is O or S; for formula **2**: R^2 is C_1-C_{22} alkyl; T is O or S; and X is hydrogen or a leaving group selected from the group consisting of mesylates, sulfonates and halogen (Cl, Br and I); and their isolated enantiomers, diastereoisomers or mixtures thereof. The compound **1.1** includes the pure syn isomer, the pure anti isomer and

mixtures of syn and anti isomers, and their diastereomers. In one variation of the above, R^2 is C_9-C_{22} alkyl. In one aspect, the method provides a higher concentration of the cancer chemotherapeutic agent in a cancer cell of the patient. In another aspect, the method delivers a higher concentration of the cancer chemotherapeutic agent in the cancer cell, when compared to the administration of a non-conjugated cancer chemotherapeutic agent to the patient, by at least 5%, 10%, 20%, 30%, 40% or at least 50%.

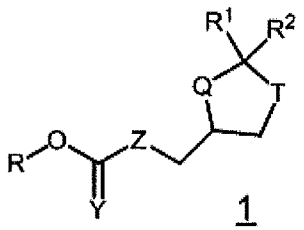
[0036] In another embodiment, there is provided a compound of the formula **3a** or **3b**:



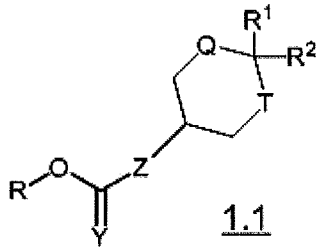
wherein: R^1 is hydrogen, C_1-C_4 alkyl or C_5-C_{22} alkyl; R^2 is C_5-C_{22} alkyl; Y is selected from O, NR' or S wherein R' is hydrogen or C_1-C_6 alkyl; Z is selected from O or S; Q is O or S; and T is O or S. In one aspect of the compound, R^1 is hydrogen or C_1-C_4 alkyl; R^2 is C_5-C_{22} alkyl; Y is O or S; Z is O; Q is O; and T is O. The activated compound of the formula **3a** or **3b** may be used to prepare the acid labile lipophilic conjugate when the activated compound is condensed with a hydroxyl bearing cancer chemotherapeutic agent (HBCCA). As defined herein, the HBCCA is represented generically with the residue or group "R" in the formulae **1**, **1a**, **1b**, **1.1**, **2** and **2a**, for example, and where the HBCCA is not coupled to form the acid labile, lipophilic molecular conjugates, then the HBCCA may also be generically represented as having the formula "R-OH" since the HBCCA may be functionalized by one or more hydroxyl (-OH) groups. Similarly, the acid labile lipophilic group (i.e., the "-ALL" group of the activated compound) that may be condensed with a HBCCA to form the acid labile, lipophilic molecular conjugate generically represented as "R-O-ALL." Accordingly, where more than one -ALL group is condensed or conjugated with a HBCCA group, then each –ALL group may be independently designated as –ALL^1, -ALL^2, -ALL^3 … to –ALL^n where n is the number of available hydroxyl groups on the cancer chemotherapeutic agent that may be conjugated or couple with an –ALL group. As exemplified for the compound of formulae **1** and **2**, for example, the HBCCA and the –ALL groups as designated, are shown below.

What is claimed is:

1. An acid labile lipophilic molecular conjugate (ALLMC) of the formula **1**, **1.1**:



1



1.1

wherein:

R is a hydroxyl bearing cancer chemotherapeutic agent;

R^1 is hydrogen, C_1-C_4 alkyl or C_5-C_{22} alkyl;

R^2 is C_5-C_{22} alkyl;

Y is selected from O;

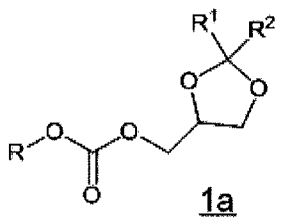
Z is O;

Q is O; and T is O;

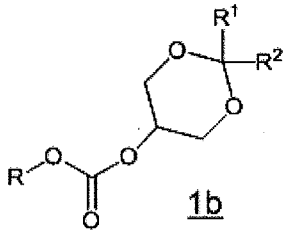
and their isolated enantiomers, diastereoisomers or mixtures thereof;

or a pharmaceutically acceptable salt thereof.

2. The acid labile lipophilic molecular conjugate of Claim 1 comprising the formula **1a**, or **1b**:



1a



1b

wherein:

R is a hydroxyl bearing cancer chemotherapeutic agent (HBCCA);

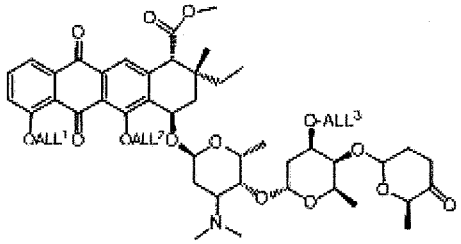
R^1 is hydrogen, C_1-C_4 alkyl or C_5-C_{22} alkyl; and

R^2 is C_5-C_{22} alkyl.

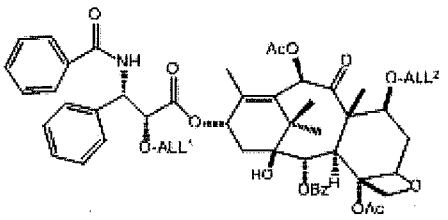
3. The acid labile lipophilic molecular conjugate of Claim 1, wherein the hydroxyl bearing cancer chemotherapeutic agent is selected from the group consisting of taxanes, abeo-taxanes, camptothecins, epothilones, cucurbitacins, quassinoids, anthracyclines, and their analogs and derivatives.

4. The acid labile lipophilic molecular conjugate of Claim 1, wherein the hydroxyl bearing cancer chemotherapeutic agent is selected from the group consisting of aclarubicin, camptothecin, masoprocol, paclitaxel, pentostatin, amrubicin, cladribine, cytarabine, docetaxel, elliptinium acetate, epirubicin, etoposide, formestane, fulvestrant, gemcitabine, idarubicin, pirarubicin, topotecan, valrubicin and vinblastine.

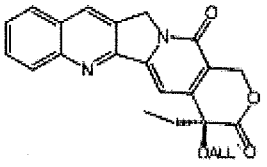
5. The acid labile lipophilic molecular conjugate of Claim 1, wherein the conjugate is selected from the following compounds:



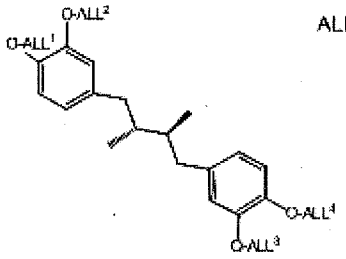
ALLMC of aclarubicin



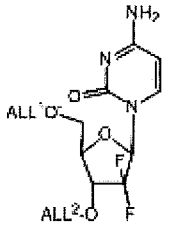
ALLMC of paclitaxel



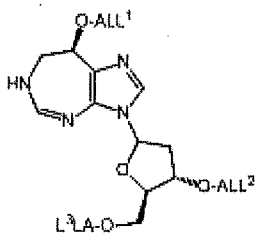
ALLMC of camptothecin



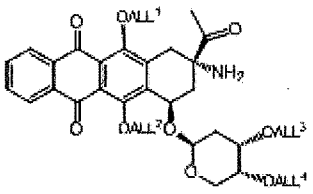
ALLMC of masoprocol



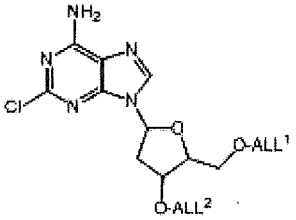
ALLMC of gemcitabine



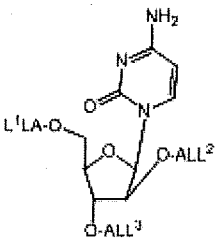
ALLMC of pentostatin



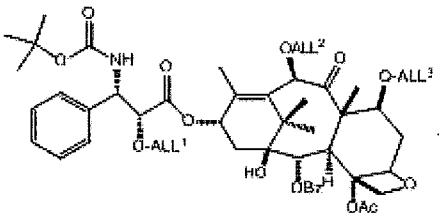
ALLMC of amrubicin



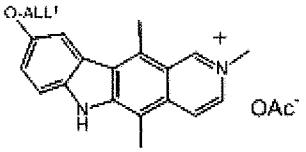
ALLMC of cladribine



ALLMC of cytarabine

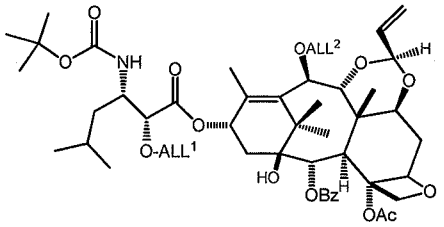


ALLMC of docetaxel

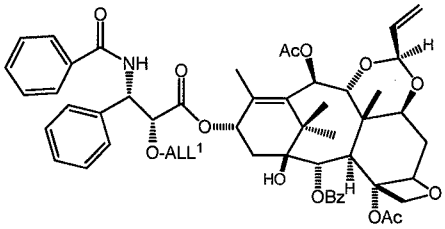


ALLMC of elliptinium acetate

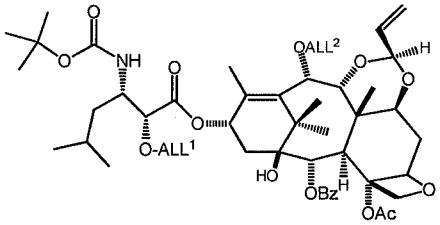
ART 489; ART 488; ART 467; ART 332



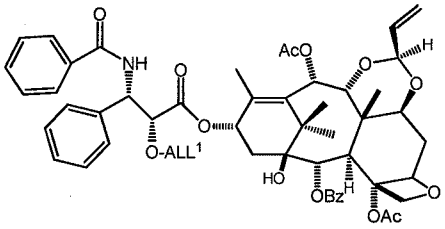
ALLMC of a 10-beta-taxane analog (19a)



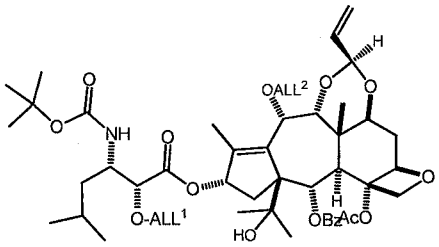
ALLMC of a 10-beta taxane analog (19b)



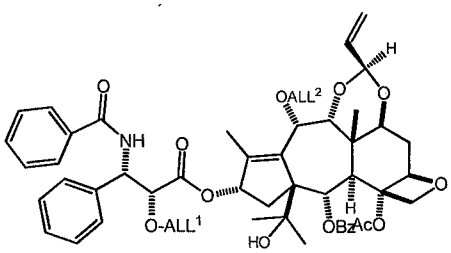
ALLMC of a 10-alpha taxane analog (19c)



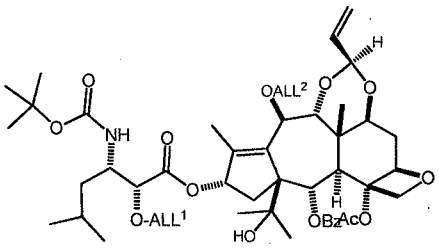
ALLMC of a 10-alpha analog (19d)



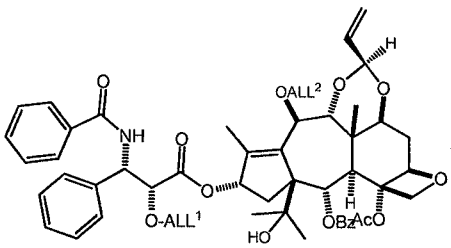
ALLMC of a 10-alpha abeo-taxane analog (19e)



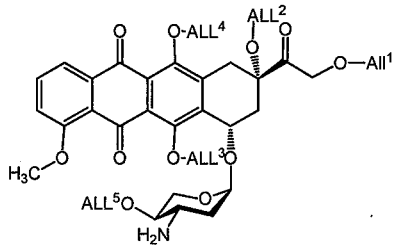
ALLMC of a 10-alpha abeo-taxane analog (19f)



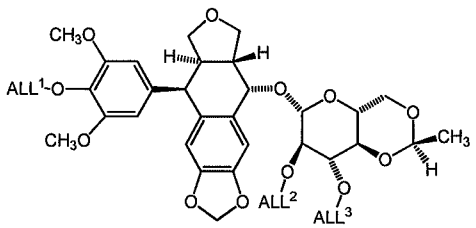
ALLMC of a 10-beta abeo-taxane analog (19g)



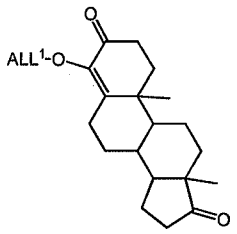
ALLMC of a 10-beta abeo-taxane analog (19h)



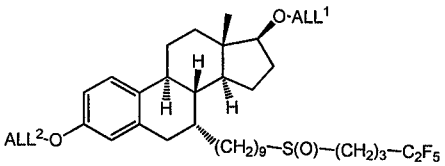
ALLMC of epirubicin



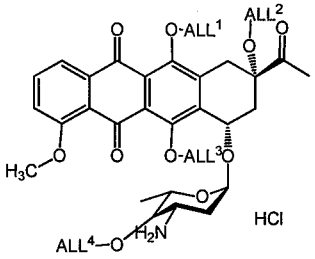
ALLMC of etoposide



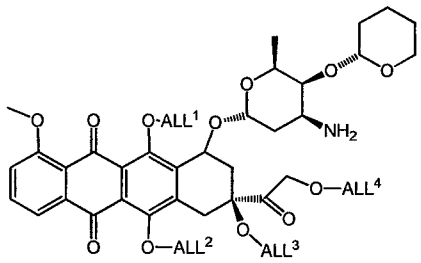
ALLMC of formestane



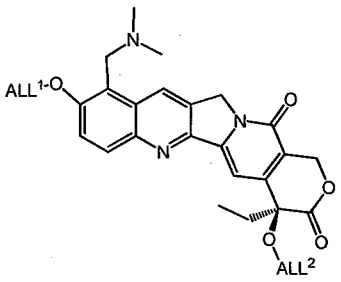
ALLMC of fulvestrant



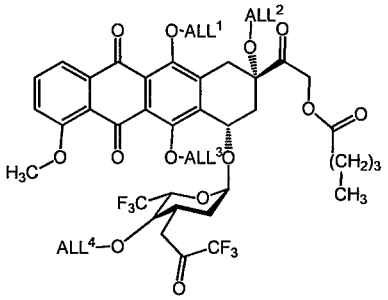
ALLMC of idarubicin



ALLMC of pirarubicin



ALLMC of topotecan



ALLMC of valrubicin

wherein –ALL^1, -ALL^2, -ALL^3 and –ALL^4 are each independently hydrogen or an acid labile lipophilic group, provided that at least one of –ALL^1, -ALL^2, -ALL^3 and –ALL^4 is an acid labile lipophilic group.

6. A pharmaceutical composition comprising: a) a therapeutically effective amount of a compound of Claims 1, in the form of a single diastereoisomer; and b) a pharmaceutically acceptable excipient.

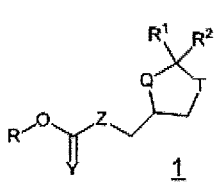
7. A pharmaceutical composition for the treatment of cancer in a patient in need of such treatment comprising a therapeutically effective amount of a compound of claim 1 and a pharmaceutically acceptable excipient.

8. The pharmaceutical composition of Claim 7, wherein the cancer is selected from the group consisting of leukemia, neuroblastoma, glioblastoma, cervical, colorectal, pancreatic, renal and melanoma.

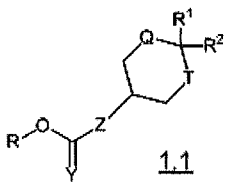
9. The pharmaceutical composition of Claim 7, wherein the cancer is selected from the group consisting of lung cancer, breast cancer, prostate cancer, ovarian cancer and head and neck cancer.

10. The pharmaceutical composition of Claim 7, wherein the pharmaceutical composition provides at least a 10% to 50% diminished degree of resistant expressed by the cancer cells when compared with the non-conjugated hydroxyl bearing cancer chemotherapeutic agent.

11. A pharmaceutical composition for reducing or eliminating the side effects of chemotherapy associated with the administration of a cancer chemotherapeutic agent to a patient, comprising a therapeutically effective amount of an acid labile lipophilic molecular conjugate of the formula **1**, or **1.1**:



1



1.1

wherein:

R is a hydroxyl bearing cancer chemotherapeutic agent;

R^1 is hydrogen, C_1-C_4 alkyl or C_5-C_{22} alkyl;

R^2 is C_5-C_{22} alkyl;

Y is O;

Z is O; and

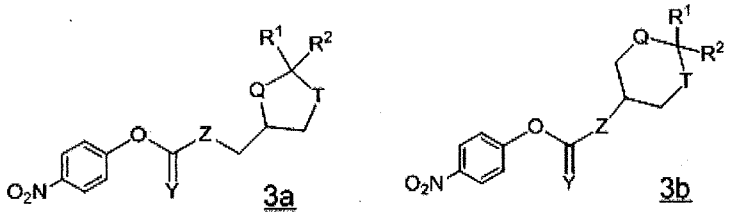
Q is O; and T is O;

and their isolated enantiomers, diastereoisomers or mixtures thereof.

12. The pharmaceutical composition of Claim 11, wherein the pharmaceutical composition provides a higher concentration of the cancer chemotherapeutic agent in a cancer cell of the patient.

13. The pharmaceutical composition of Claim 12, wherein the pharmaceutical composition delivers a higher concentration of the cancer chemotherapeutic agent in the cancer cell, when compared to the administration of a non-conjugated cancer chemotherapeutic agent to the patient, by at least 5%, 10%, 20% or at least 50%.

14. A compound of the formula **3a** or **3b**:



wherein:

R^1 is hydrogen, C_1-C_4 alkyl or C_5-C_{22} alkyl;

R^2 is C_5-C_{22} alkyl;

Y is selected from O, NR' or S wherein R' is hydrogen or C_1-C_6 alkyl;

Z is selected from O or S; and

Q is O or S; and T is O or S.

15. The compound of Claim 14, wherein:

R^1 is hydrogen or C_1-C_4 alkyl;

R^2 is C_5-C_{22} alkyl;

Y is O or S;

Z is O; and

Q is O; and T is O.