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Declarations under Rule 4.17:

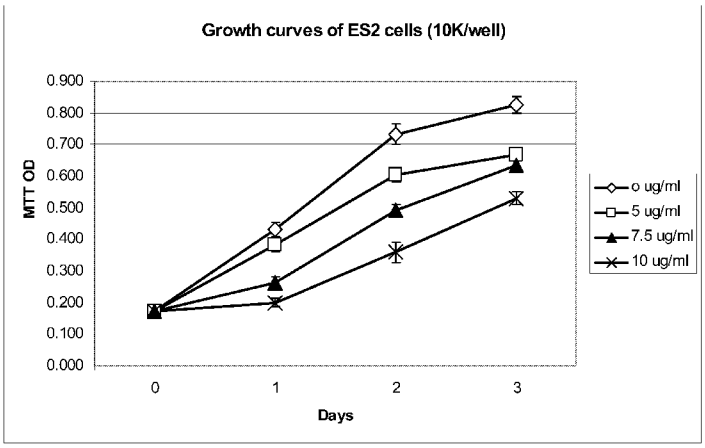
— *as to the identity of the inventor (Rule 4.17(i))*

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

[Continued on next page]

(54) Title: INHIBITING THE INVASION AND METASTASIS OF CANCER CELLS

Figure 1
Growth of ES2 (ovary) cells in presence of compound Y10



(57) Abstract: This invention provides compounds, compositions, extracts, and their methods and uses for inhibiting the cancer invasion, cells invasion, cancer cell invasion,and cancer metastasis, wherein the cells comprise cancer cells, wherein the cancers comprise breast cancer, leukocytic cancer, liver cancer, ovarian cancer, bladder cancer, prostatic cancer, skin cancer, bone cancer, brain cancer, leukemia cancer, lung cancer, colon cancer, CNS cancer, melanoma cancer, renal cancer, cervical cancer, esophageal cancer, testicular cancer, spleenic cancer, kidney cancer, lymphhatic cancer, pancreatic cancer, stomach cancer and thyroid cancer.

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— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

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INHIBITING THE INVASION AND METASTASIS OF CANCER CELLS

This application claims benefit of U.S. Serial No. 12/541,713, filed August 14, 2009 and claims benefit of U.S. Serial No. 61/226,043, filed July 16, 2009. This application claims benefit of International App'l No. PCT/US09/34115, filed February 13, 2009, This application claims benefit of U.S. Serial No. 61/038,277 filed March 20, 2008, U.S. Serial No. 61/054,308, filed May 19, 2008, International App'l No. PCT/US2008/002086, filed February 15, 2008, International App'l No. PCT/US2007/077273, filed August 30, 2007, U.S. Serial No. 60/890,380, filed on February 16, 2007, U.S. No. 60/947,705, filed on July 3, 2007, and U.S. Serial No.11/683,198, filed on March 7, 2007, which claims benefit of U.S. Serial Nos. 60/795,417, filed on April 27, 2006, 60/841,727, filed on September 1, 2006, 60/890,380, filed on February 16, 2007, and International Application No. PCT/US2006/016158, filed April 27, 2006, which claims the benefit of the priority of the following applications: (1) U.S. Serial Nos. 11/289142, filed November 28, 2005, and 11/267,523, filed November 4, 2005; (2) International Application No. PCT/US05/31900, filed September 7, 2005 (which claims the priority of U.S. Serial Nos. 60/617,379, filed October 8, 2004, 60/613,811, filed September 27, 2004, and 60/607,858, filed September 7, 2004); (3) U.S. Serial No. 11/131,551, filed May 17, 2005; and (4) U.S. Serial No. 11/117,760, filed April 27, 2005. This application also claims benefit of U.S. Serial No.11/412,659, filed April 27, 2006, U.S. Serial No. 10/906,303, filed February 14, 2005, and U.S. Serial No. 12/344,682, filed December 29, 2008. The contents of these preceding applications are hereby incorporated in their entireties by reference into this application.

FIELD OF THE INVENTION

This invention provides compounds, compositions, extracts and methods for inhibiting cancer invasion, cell invasion, or cancer cell invasion.

BACKGROUND OF THE INVENTION

Cancer is a group of diseases in which cells demonstrate three key characteristics – uncontrolled growth, division beyond normal limits; invasion, intrusion on and destruction of adjacent tissues; and metastasis, the spread of such cells to other organs in the body by vascular and lymphatic means. Cancer invasion is cancer cell invasion, where the cancer cell intrudes on adjacent tissues or crosses the membrane of another cell. This invention provides methods, compounds and compositions for inhibiting cancer invasion, cell invasion, or cancer cell invasion, wherein the cancers comprise

breast, leukocytic, liver, ovarian, bladder, prostatic, skin, bone, brain, leukemia, lung, colon, CNS, melanoma, renal, cervical, esophageal, testicular, spleenic, kidney, lymphatic, pancreatic, stomach and thyroid cancers.(Ref: http://en.wikipedia.org/wiki/cancer) From Wikipedia, the free encyclopedia **Cancer** (medical term: malignant neoplasm) is a class of diseases in which a group of cells display uncontrolled growth (division beyond the normal limits), invasion (intrusion on and destruction of adjacent tissues), and sometimes metastasis (spread to other locations in the body via lymph or blood). These three malignant properties of cancers differentiate them from benign tumors, which are self-limited, and do not invade or metastasize. Most cancers form a tumor but some, like leukemia, do not. The branch of medicine concerned with the study, diagnosis, treatment, and prevention of cancer is oncology.

http://www.cancer.gov/dictionary/?CdrID=45333
http://www.cancer.gov/dictionary/?CdrID=46710

SUMMARY OF THE INVENTION

This invention provides compounds, compositions, extracts and methods for inhibiting cancer invasion, cell invasion, cancer cell invasion, and metastasis. This invention provides a use of compounds, compositions, or extracts for manufacturing medicament for inhibiting cancer invasion, and metastasis. In an embodiment, this invention comprises inhibiting cancer cell invasion. The compounds comprise the structures selected from the formulae in the present application, wherein the compounds are synthesized or isolated, wherein the compounds comprise the saponins, triterpenes, pentacyclic triterpenes, and compounds selected from formulae in the present application, wherein the extract comprises the extracts of Maesa balansae and Barringtonia acutangula, Xanthoceras Sorbifolia, Harpullia, Aesculus hippocastanum, wherein the cancers comprise breast, leukocytic, liver, ovarian, bladder, prostatic, skin, bone, brain, leukemia, lung, colon, CNS, melanoma, renal, cervical, esophageal, testicular, spleenic, kidney, lymphatic, pancreatic, stomach and thyroid cancers.

DETAILED DESCRIPTION OF THE FIGURES

Figure 1 shows growth of ES2 cells in presence of different concentrations of compound Y10

Results: 1. After 24 hours, the growth of ES2 cells is inhibited in the presence of Y10. 2. The degree of inhibition increases with doses of Y10. 3. There are no dead cells

observed in concentrations lower than 10 ug/ml of Y10. 4. Accordingly, 10 ug/ml of Y10 or less is non-cytotoxic.

Figure 2 shows growth curves of ES2 (ovary) cells in the presence of drugs: compound X, Y0, Y1, Y3, and Y7

Figure 3 shows growth curves of ES2 (ovary) cells in the presence of drugs: compound ACH-(Y)Y3, AKOH-Y3, b-ES and M10

Figure 4 shows growth curves of TB9 cells (bladder) in the presence of drugs: compound X, Y0, Y1, and Y3

Figure 5 shows growth curves of TB9 cells (bladder) in the presence of drugs: compound Y7, ACH-(Y)Y3, AKOH-(Y)Y3, bES, and M10

Figure 6 shows growth curves of H460 cells (lung) in the presence of drugs: compound X, Y0, Y1, and Y3.

Figure 7 shows growth curves of H460 cells (lung) in the presence of drugs: compound Y7, ACH-(Y)Y3, AKOH-(Y)Y3, bES, and M10

Figure 8 shows growth curves of T98G cells (brain) in the presence of drugs: compound X, Y0, Y1, Y3, and Y7

Figure 9 shows growth curves of T98G cells (brain) in the presence of drugs: compound ACH-(Y)Y3, AKOH-(Y)Y3, bES, and M10

Figure 10 shows growth curves of U2OS cells (bone) in the presence of drugs: compound X, Y0, Y1, Y3, and Y7.

Figure 11 shows growth curves of U2OS cells (bone) in the presence of drugs: compound ACH-(Y)Y3, AKOH-(Y)Y3, bES, and M10.

Note: (Y)Y3, Y and Y3 represent the same compound

DETAILED DESCRIPTION OF THE INVENTION

Cancer is a group of diseases in which cells demonstrate three key characteristics – uncontrolled growth, division beyond normal limits; invasion, intrusion on and destruction of adjacent tissues; and metastasis, the spread of such cells to other organs in the body by vascular and lymphatic means to form a secondary tumour. Cancer invasion is cancer cell invasion, where the cancer cell intrudes on adjacent tissues, or cross the membrane of another cell. It degrades the surrounding extracellular matrix. Metastasis is the spread of a disease from one organ to another organ. Cancer/tumor cells can break away from a primary tumor through a media comprising lymphatic and blood vessels to other parts of the body and grow within other organ. The new tumor is called a secondary tumor. If an ovarian cancer metastasizes to the lung, the secondary tumor is made up of abnormal ovarian cells, not abnormal lung cells.

This invention provides compounds, compositions, extracts and methods for inhibiting cancer invasion, cells invasion, cancer cell invasion or for inhibiting cancer metastasis, wherein the compounds comprise the structures selected from the formulae of the present application, wherein the compounds can be synthesized or isolated, wherein the compounds comprise the triterpenes, pentacyclic triterpenes, saponins, and compounds selected from formulae in this application, wherein the extract comprises the extracts of Maesa balansae, Barringtonia acutangula, Xanthoceras Sorbifolia, Harpullia, Aesculus hippocastanum, and the plants are from the Sapindaceae family, wherein the cancers comprise breast cancer, leukocytic cancer, liver cancer, ovarian cancer, bladder cancer, prostatic cancer, skin cancer, bone cancer, brain cancer, leukemia cancer, lung cancer, colon cancer, CNS cancer, melanoma cancer, renal cancer, cervical cancer, esophageal cancer, testicular cancer, spleenic cancer, kidney cancer, lymphhatic cancer, pancreatic cancer, stomach cancer and thyroid cancer ;wherein the cells comprise breast cell, leukocytic cell, liver cell, ovarian cell, bladder cell, prostatic cell, skin cell, bone cell, brain cell, leukemia cell, lung cell, colon cell, CNS cell, melanoma cell, renal cell, cervical cell, esophageal cell, testicular cell, spleenic cell, kidney cell, lymphhatic cell, pancreatic cell, stomach cell and thyroid cell. The method of inhibiting cancer invasion, cell invasion or cancer cell invasion uses non-cytotoxic drug concentrations. The method of inhibiting metastasis uses non-cytotoxic drug concentrations. There is no noticeable change in cell morphology

This invention shows that the presence of angeloyl, tigloyl, senecioyl, acetyl, alkyl, dibenzoyl, benzoyl, alkanoyl, alkenoyl, benzoyl alkyl substituted alkanoyl, alkanoyl

substituted phenyl, alkenoyl substituted phenyl, aryl, acyl, heterocylic, heteroraryl, or sugar moiety substituted with diangeloyl groups, at a pentacyclic triterpene, triterpene, triterpeniod, triterpeniod saponin or compound selected from formulae of the present application, produces the inhibiting for cancer invasion, cells invasion or cancer cell invasion.

This invention shows that the presence of angeloyl, tigloyl, senecioyl, acetyl, alkyl, dibenzoyl, benzoyl, alkanoyl, alkenoyl, benzoyl alkyl substituted alkanoyl, alkanoyl substituted phenyl, alkenoyl substituted phenyl, aryl, acyl, heterocylic, heteroraryl, or sugar moiety substituted with diangeloyl groups, at carbon position 21, 22 and/or 28 of a pentacyclic triterpene, triterpene, triterpeniod, triterpeniod saponin or compound selected from formulae of the present application, produces the inhibiting for cancer invasion, cells invasion or cancer cell invasion. In an embodiment, the presence of angeloyl, tigloyl, senecioyl, acetyl groups at carbon position 21, 22 and/or 28 of a triterpene, triterpeniod, triterpeniod saponin or compound selected from formulae of the present application, produces the inhibiting for cancer invasion, cells invasion or cancer cell invasion. In an embodiment, the presence of angeloyl groups at carbon position 21, 22 and/or 28 of a triterpene, triterpeniod, triterpeniod saponin or compound selected from formulae of the present application, produces the inhibiting for cancer invasion, cells invasion or cancer cell invasion.

This invention shows that the ability for inhibiting cancer invasion, cells invasion or cancer cell invasion are lost by removing the angeloyl, tigloyl, senecioyl, acetyl, alkyl, dibenzoyl, benzoyl, alkanoyl, alkenoyl, benzoyl alkyl substituted alkanoyl, alkanoyl substituted phenyl, alkenoyl substituted phenyl, aryl, acyl, heterocylic, heteroraryl, or sugar moiety substituted with diangeloyl groups from carbon position 21, 22 and 28 of a triterpene, triterpeniod, triterpeniod saponin or compound selected from formulae of the present application. In an embodiment, the ability for inhibiting cancer invasion, cells invasion or cancer cell invasion are lost by removing the angeloyl, tigloyl, senecioyl, acetyl groups from carbon position 21, 22 and 28 of a triterpene, triterpeniod, triterpeniod saponin or compound selected from formulae of the present application. In an embodiment, the ability for inhibiting cancer invasion, cells invasion or cancer cell invasion are lost by removing the angeloyl groups from carbon position 21, 22 and 28 of a triterpene, triterpeniod, or a triterpeniod saponin or compound selected from formulae of the present application.

Experiments presented in this invention showed that the compound AKOH has no effect for inhibiting cancer invasion, cells invasion or cancer cell invasion. AKOH was obtained by removing the angeloyl groups from carbon positions 21 and 22 of the active Xanifolia Y(Y3). This invention shows that the ability for inhibiting cancer invasion, cells invasion or cancer cell invasion of Xanifolia Y(Y3) are lost by removing angeloyl groups from carbon positions 21 and 22.

This invention shows that the ability for inhibiting cancer invasion, cells invasion or cancer cell invasion are maintained when the sugar moieties are removed from carbon position 3 of an active compound, triterpene, triterpeniod, or triterpeniod saponin. Experiments presented in this invention showed that the compound ACH-Y3 has the ability to inhibit cancer invasion, cells invasion or cancer cell invasion. The compound ACH-Y3 was obtained by removing the sugar moieties from carbon position 3 of a active Xanifolia Y(Y3). This invention shows that the ability for inhibiting cancer invasion, cells invasion or cancer cell invasion are maintained when the sugar moieties are removed from the carbon position 3 of active Xanifolia Y(Y3).

This invention shows that the ability for inhibiting cancer invasion, cell invasion or cancer cell invasion are more potent when the sugar moieties are removed from the carbon position 3 of an active compound, triterpene, triterpeniod, or triterpeniod saponin. Experiments presented in this invention demonstrated that the compound ACH-Y3, in which the sugar moieties of the active Xanifolia Y(Y3) are removed from carbon position 3, is more potent for invasion inhibiting ability. This invention shows that the ability for inhibiting cancer invasion, cells invasion or cancer cell invasion are more potent in cancers of bladder, lung, brain, skin, prostate and pancreas cancer when the sugar moieties are removed from the carbon position 3 of active Xanifolia Y(Y3). A compound inhibiting cancer invasion, cells invasion or cancer cell invasion is called active compound.

This invention provides a use of compounds, compositions, extracts and methods for manufacturing medicament for inhibiting cancer invasion, cells invasion or cancer cell invasion or for inhibiting cancer metastasis, wherein the compounds comprise the structures selected from the formulae of the present application, wherein the compounds can be synthesized or isolated, wherein the compounds comprise the pentacyclic triterpenes, wherein the extract comprises the extracts of Maesa balansae and Barringtonia acutangula, Xanthoceras Sorbifolia, Harpullia, Aesculus hippocastanum,

wherein the cells comprise cancer cells, wherein the cancers comprise breast cancer, leukocytic cancer, liver cancer, ovarian cancer, bladder cancer, prostatic cancer, skin cancer, bone cancer, brain cancer, leukemia cancer, lung cancer, colon cancer, CNS cancer, melanoma cancer, renal cancer, cervical cancer, esophageal cancer, testicular cancer, spleenic cancer, kidney cancer, lymphhatic cancer, pancreatic cancer, stomach cancer and thyroid cancer.. The method of inhibiting cancer invasion, cells invasion or cancer cell invasion activities uses non-cytotoxic drug concentrations. The method of inhibiting metastasis uses non-cytotoxic drug concentrations. There is no noticeable change in cell morphology

This invention provides methods for inhibiting cancer invasion, cell invasion, cancer cell invasion, migration, metastasis or growth of cancers, wherein the methods comprise affecting gene expression, wherein the methods comprise stimulating gene expression, or wherein the methods comprise inhibiting the gene expression, or wherein the methods comprise administering to a subject an effective amount of compounds, compositions, or extracts in this application. In an embodiment, the method comprises contacting said cell with a compound selected from Xanifolia Y0, Y1, Y2, Y(Y3), Y5, Y7, Y8, Y9, Y10, Xanifolia (x), M10, Escin(bES), Aescin, ACH-Y(Y3), ACH-Y10, ACH-Y2, ACH-Y8, ACH-Y7, ACH-Y0, ACH-X, ACH-Z4, ACH-Z1, ACH-Escin(bES), ACH-M10 and a salt, ester, metabolite thereof, and the compounds selected from formulae 2A, 1A, 1B, 1E, 1F, 1G, 1H, and 1J.

(Our purification methods and biological assays include the MTT assay in International Application No. PCT/US05/31900, filed September 7, 2005, U.S. Serial No. 11/289142, filed November 28, 2005, and U.S. Serial No. 11/131551, filed May 17, 2005, and PCT/US2008/002086, 1188-ALA-PCT, filed February 15, 2008, the contents of which are incorporated herein by reference)

This invention provides a use of compounds or methods for inhibiting cancer invasion, cell invasion, cancer cell invasion, migration, metastasis or growth of cancers, wherein this invention comprises a process and method for administration of the composition, wherein administration is by intravenous injection, intravenous drip, intraperitoneal injection or oral administration; wherein administration is by intravenous drip: 0.003-0.03mg/kg body weight of compound dissolved in 250ml of 10% glucose solution or in 250ml of 0.9% NaCl solution, or by intravenous injection: 0.003-0.03mg/kg body weight per day of compound dissolved in 10-20ml of 10% glucose solution or of 0.9% NaCl

solution, or 0.01-0.03mg/kg body weight of compound dissolved in 250ml of 10% glucose solution or in 250ml of 0.9% NaCl solution, or by intravenous injection: 0.01-0.03mg/kg body weight per day of compound dissolved in 10-20ml of 10% glucose solution or of 0.9% NaCl solution, or 0.01-0.05mg/kg body weight of compound dissolved in 250ml of 10% glucose solution or in 250ml of 0.9% NaCl solution, or by intravenous injection: 0.01-0.05mg/kg body weight per day of compound dissolved in 10-20ml of 10% glucose solution or of 0.9% NaCl solution, or 0.05-0.2mg/kg body weight of compound dissolved in 250ml of 10% glucose solution or in 250ml of 0.9% NaCl solution, or by intravenous injection: 0.05-0.2mg/kg body weight per day of compound dissolved in 10-20ml of 10% glucose solution or of 0.9% NaCl solution, or by intravenous drip: 0.1-0.2mg/kg body weight per day of compound dissolved in 250ml of 10% glucose solution or in 250ml of 0.9% NaCl solution, or by intravenous injection: 0.1-0.2mg/kg body weight per day compound dissolved in 10-20ml of 10% glucose solution or of 0.9% NaCl solution, or by intraperitoneal injection(I.P.): 2.5mg/kg body weight per day compound dissolved in 10% glucose solution or of 0.9% NaCl solution, or by oral administration wherein the dosage of mammal is 1-10mg/kg, 10-30mg/kg, 30-60mg/kg, or 60-90mg/kg body weight of compound, or by intravenous injection or intravenous drip wherein the dosage of mammal is 0.01- 0.1mg/kg body weight , 0.1-0.2mg/kg, 0.2 - 0.4mg/kg body weight, or 0.4 – 0.6 mg/kg body weight of compound, or by intraperitoneal injection (I.P.) wherein the dosage of mammal is 1-3mg/kg, 3-5mg/kg, 4-6mg/kg, or 6-10mg/kg body weight of compound.

This invention provides a use of compounds or methods for inhibiting cancer invasion, cell invasion, cancer cell invasion, migration, metastasis or growth of cancers, wherein the invention comprises a pharmaceutical composition comprising the compound of this invention or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or diluent, wherein said compound is present in a concentration of 0.01 ug/ml to 65ug/ml, or wherein said compound is present in a concentration of 0.01 ug/ml to 40ug/ml, or wherein said compound is present in a concentration of 0.01 ug/ml to 30ug/ml, or wherein said compound is present in a concentration of 0.01ug/ml to 10ug/ml, or wherein said compound is present in a concentration of 0.01ug/ml to 5ug/ml, or wherein said compound is present in a concentration of 5ug/ml to 10ug/ml, or wherein said compound is present in a concentration of 0.1 ug/ml to 5ug/ml, or wherein said compound is present in a concentration of 0.1ug/ml to 7.5ug/ml, or wherein said compound is present in a concentration of 0.1ug/ml to 10ug/ml, or wherein said compound is present in a concentration of 0.1ug/ml to 15ug/ml, or wherein said

compound is present in a concentration of 0.1ug/ml to 20ug/ml, or wherein said compound is present in a concentration of 0.1ug/ml to 30ug/ml, or wherein said compound is present in a concentration of 1 ug/ml to 5ug/ml, or wherein said compound is present in a concentration of 1ug/ml to 7.5ug/ml, or wherein said compound is present in a concentration of 1ug/ml to 10ug/ml, or wherein said compound is present in a concentration of 1ug/ml to 15ug/ml, or wherein said compound is present in a concentration of 1ug/ml to 20ug/ml, or wherein said compound is present in a concentration of 1ug/ml to 30ug/ml, or wherein said compound is present in a concentration of 3ug/ml to 5ug/ml, or wherein said compound is present in a concentration of 3ug/ml to 7.5ug/ml, or wherein said compound is present in a concentration of 3ug/ml to 10ug/ml, or wherein said compound is present in a concentration of 3ug/ml to 15ug/ml, or wherein said compound is present in a concentration of 3ug/ml to 20ug/ml, or wherein said compound is present in a concentration of 3ug/ml to 30ug/ml, or wherein said compound is present in a concentration of 4ug/ml to 5ug/ml, or wherein said compound is present in a concentration of 4ug/ml to 7.5ug/ml, or wherein said compound is present in a concentration of 4ug/ml to 10ug/ml, or wherein said compound is present in a concentration of 4ug/ml to 15ug/ml, or wherein said compound is present in a concentration of 4ug/ml to 20ug/ml, or wherein said compound is present in a concentration of 4ug/ml to 30ug/ml, or wherein said compound is present in a concentration of 5ug/ml to 8ug/ml, or wherein said compound is present in a concentration of 5ug/ml to 9ug/ml, or wherein said compound is present in a concentration of 5ug/ml to 10ug/ml, or wherein said compound is present in a concentration of 5ug/ml to 15ug/ml, or wherein said compound is present in a concentration of 5ug/ml to 20ug/ml, or wherein said compound is present in a concentration of 5ug/ml to 30ug/ml, or wherein said compound is present in a concentration of 7ug/ml to 8ug/ml, or wherein said compound is present in a concentration of 7ug/ml to 9ug/ml, or wherein said compound is present in a concentration of 7ug/ml to 10ug/ml, or wherein said compound is present in a concentration of 7ug/ml to 15ug/ml, or wherein said compound is present in a concentration of 7ug/ml to 20ug/ml, or wherein said compound is present in a concentration of 7ug/ml to 30ug/ml.

This invention provides a use of compounds or methods for inhibiting cancer invasion, cell invasion, cancer cell invasion, migration, metastasis or growth of cancers, wherein the invention comprises a pharmaceutical composition comprising the compound of this

invention or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or diluent, wherein said compound is present in a concentration of 0.008uM to 80uM, or wherein said compound is present in a concentration of 0.01uM to 60uM, or wherein said compound is present in a concentration of 0.01uM to 50uM, or wherein said compound is present in a concentration of 0.01uM to 40uM, or wherein said compound is present in a concentration of 0.01uM to 30uM, or wherein said compound is present in a concentration of 0.01uM to 20uM, or wherein said compound is present in a concentration of 0.01uM to 10uM, or wherein said compound is present in a concentration of 5uM to 10uM, or wherein said compound is present in a concentration of 0.1uM to 5uM, or wherein said compound is present in a concentration of 0.1uM to 7.5uM, or wherein said compound is present in a concentration of 0.1uM to 10uM, or wherein said compound is present in a concentration of 0.1uM to 15uM, or wherein said compound is present in a concentration of 0.1uM to 20uM, or wherein said compound is present in a concentration of 0.1uM to 30uM or wherein said compound is present in a concentration of 0.1uM to 40uM, or wherein said compound is present in a concentration of 0.1uM to 50uM or wherein said compound is present in a concentration of 0.1uM to 60uM, or wherein said compound is present in a concentration of 0.1uM to 80uM, or wherein said compound is present in a concentration of 1uM to 5uM, or wherein said compound is present in a concentration of 1uM to 7.5uM, or wherein said compound is present in a concentration of 1uM to 10uM, or wherein said compound is present in a concentration of 1uM to 15uM, or wherein said compound is present in a concentration of 1uM to 20uM, or wherein said compound is present in a concentration of 1uM to 30uM or wherein said compound is present in a concentration of 1uM to 40uM, or wherein said compound is present in a concentration of 1uM to 50uM or wherein said compound is present in a concentration of 1uM to 60uM, or wherein said compound is present in a concentration of 1uM to 80uM, or wherein said compound is present in a concentration of 3uM to 5uM, or wherein said compound is present in a concentration of 3uM to 7.5uM, or wherein said compound is present in a concentration of 3uM to 10uM, or wherein said compound is present in a concentration of 3uM to 15uM, or wherein said compound is present in a concentration of 3uM to 20uM, or wherein said compound is present in a concentration of 3uM to 30uM or wherein said compound is present in a concentration of 3uM to 40uM, or wherein said compound is present in a concentration of 3 uM to 50uM or wherein said compound is present in a concentration of 3 uM to 60uM, or wherein said compound is present in a concentration of 3uM to 80uM, or wherein said compound is present in a concentration of 5uM to 8uM, or wherein said compound is present in a concentration of 5uM to 10uM, or wherein said

compound is present in a concentration of 5uM to 15uM, or wherein said compound is present in a concentration of 5uM to 20uM, or wherein said compound is present in a concentration of 5uM to 30uM or wherein said compound is present in a concentration of 5uM to 40uM, or wherein said compound is present in a concentration of 5uM to 50uM or wherein said compound is present in a concentration of 5uM to 60uM, or wherein said compound is present in a concentration of 5uM to 80uM. or wherein said compound is present in a concentration of 7uM to 8uM, or wherein said compound is present in a concentration of 7uM to 10uM, or wherein said compound is present in a concentration of 7uM to 15uM, or wherein said compound is present in a concentration of 7uM to 20uM, or wherein said compound is present in a concentration of 7uM to 30uM or wherein said compound is present in a concentration of 7uM to 40uM, or wherein said compound is present in a concentration of 7uM to 50uM or wherein said compound is present in a concentration of 7uM to 60uM, or wherein said compound is present in a concentration of 7uM to 80uM.

The invention will be better understood by reference to the Experimental Details which follow, but those skilled in the art will readily appreciate that the specific experiments detailed are only illustrative, and are not meant to limit the invention as described herein, which is defined by the claims which follow thereafter.

Throughout this application, various references or publications are cited. Disclosures of these references or publications in their entireties are hereby incorporated by reference into this application in order to more fully describe the state of the art to which this invention pertains.

It is to be noted that the transitional term "comprising", which is synonymous with "including", "containing" or "characterized by", is inclusive or open-ended and does not exclude additional, un-recited elements or method steps.

Example 1

Tablet for dose containing 10mg, 20mg 30mg of active compound

Active compound	1mg	5mg	10mg	20mg	30mg
Microcrystalline cellulose	20mg	20mg	19.75mg	60mg	100mg
Corn starch	29mg	24.5mg	19.75mg	19.25mg	18.5mg
Magnesium stearate	0mg	0.5mg	0.5mg	0.75mg	1.5mg

The active compound, cellulose, and a portion of the corn starch are mixed and granulated to 10% corn starch paste. The resulting granulation is sieved, dried and blended with the remainder of the corn starch and the magnesium stearate. The resulting granulation is then compressed into tablets containing 1, 5, 10, 20, 30mg, respectively of active ingredient per tablet.

Example 2

Intravenous solution preparation

An intravenous dosage form of the active compound is prepared as follows:

Active compound 1-10ug

Sodium citrate 5-50 mg

Citric acid 1-15 mg

Sodium chloride 1-8 mg

Water for injection (USP) q.s. to 1mL

Utilizing the above quantities, the active compound is dissolved at room temperature in a prepared solution of sodium chloride, citric acid, and sodium citrate in water for injection.

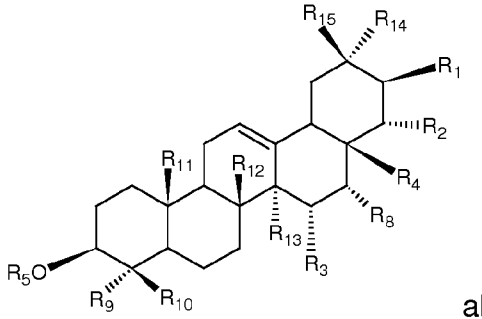
Example 3

Intravenous drip preparation

0.25-2.5mg compound dissolved in 250ml of 10% glucose solution or in 250ml of 0.9% NaCl solution.

Intravenous drip preparation: 1-2.mg compound dissolved in 250ml of 10% glucose solution or in 250ml of 0.9% NaCl solution

The methods and uses of an isolated, purified or synthesized compound or its salt, ester, metabolite or derivative thereof, for inhibiting cancer invasion, cells invasion, cancer cell invasion gene expression, or inhibiting cancer metastasis having the formula of :



also named (1A),

wherein R1 is selected from hydrogen, hydroxyl, O-angeloyl, O-tigloyl, O-senecioyl, O-alkyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-alkanoyl substituted phenyl, O-alkenoyl substituted phenyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, and derivatives thereof;

R2 is selected from hydrogen, hydroxyl, O-angeloyl, O-tigloyl, O-senecioyl, O-alkyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-alkanoyl substituted phenyl, O-alkenoyl substituted phenyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, and derivatives thereof;

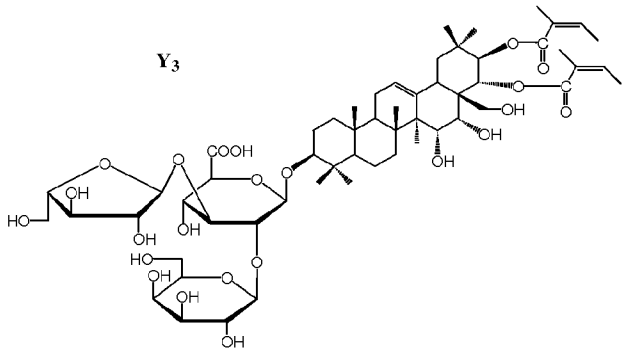
R4 represents CH_2R6 or COR6, wherein R6 is selected from a group consisting of hydroxyl, O-angeloyl, O-tigloyl, O-senecioyl, O-alkyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-alkanoyl substituted phenyl, O-alkenoyl substituted phenyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, and derivatives thereof; R3 is H or OH; R8 is H or OH;

R5 is a hydrogen, heterocyclic or sugar moiety(ies), wherein the sugar moiety(ies) is/are selected from a group consisting of glucose, galactose, rhamnose, arabinose, xylose, fucose, allose, altrose, gulose, idose, lyxose, mannose, psicose, ribose, sorbose, tagatose, talose, fructose, alduronic acid, glucuronic acid, galacturonic acid, and derivatives or combination thereof; wherein R9, R10, R11, R12, R13, R14, R15 are independently attached a group selecting from CH_3, CH_2OH, CHO, COOH, COO-alkyl, COO-aryl, COO-heterocyclic, COO-heteroaryl, CH_2Oaryl, CH_2O- heterocyclic, CH_2O-heteroaryl, alkyls group, hydroxyl, acetyl group, particularly CH_3; wherein at least two of R1, R2 and R6 are attached a group selected from O-angeloyl, O-tigloyl, O-senecioyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-alkanoyl substituted phenyl, O-alkenoyl substituted phenyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, and derivatives thereof; or at least one of R1, R2, and R4 is a sugar moiety substituted with at least two groups selected from a group consisting of angeloyl, acetyl, tigloyl, senecioyl, benzoyl, dibenzoyl, alkanoyl, alkenoyl, benzoyl alkyl substituted alkanoyl, O-alkanoyl substituted phenyl, O-alkenoyl substituted phenyl, aryl, acyl, heterocylic, heteroraryl, and a derivative thereof; or wherein R4 is CH_2R6; wherein R1 and R2 independently consists an O-angeloyl group, or at least two of R1, R2 and R6 are O-angeloyl or at least one of R1, R2 or R6 is a sugar moiety with two O-angeloyls; or wherein R5 is/are the sugar moiety(ies) selected from the following sugars and alduronic acids: glucose, galactose, rhamnose, arabinose, xylose, fucose, allose, altrose, gulose, idose, lyxose, mannose, psicose, ribose, sorbose, tagatose, talose, fructose, glucuronic acid, galacturonic acid; or their derivatives thereof, or the combination thereof; wherein the sugar preferably comprises glucuronic acid, arabinose

and galactose. In an embodiment, wherein R5 is/are sugar moiety(ies) selected from a group consisting of glucose, galactose, arabinose, alduronic acid, glucuronic acid, galacturonic acid, and a derivative or combination thereof; in embodiment, R5 is an acyl having 2 to 10 carbons; in embodiment, R4 is a CH3.

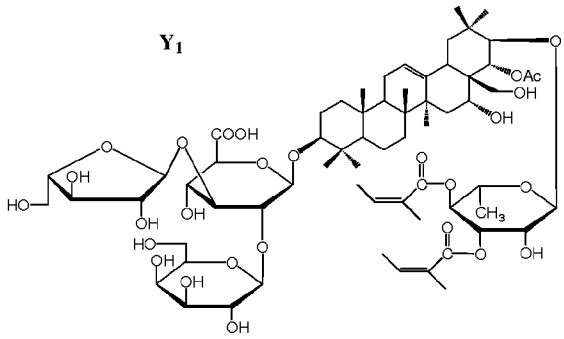
This invention provides uses of a compound for the manufacture of a medicament for inhibiting cancer invasion, cells invasion, cancer cell invasion, or metastasis, using the compounds selected from the following:

a) An isolated, purified or synthesized compound having structure Xanifolia(Y),



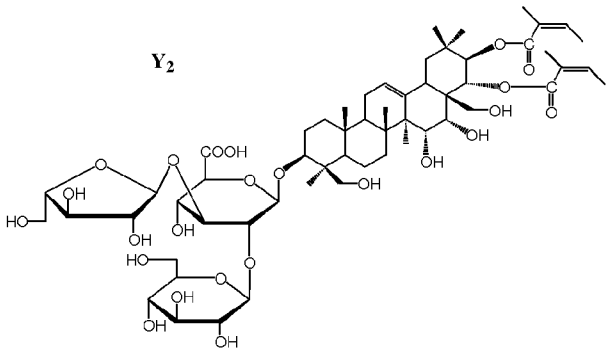
or chemical name: 3-O-[β-D-galactopyranosyl (1→2)]-α-L-arabinofuranosy (1→3)-β-D-glucuronopyranosyl-21,22-O-diangeloyl-3β, 15α, 16α, 21β, 22α, 28-hexahydroxyolean-12-ene;

b) An isolated, purified or synthesized compound having structure Xanifolia (Y1),



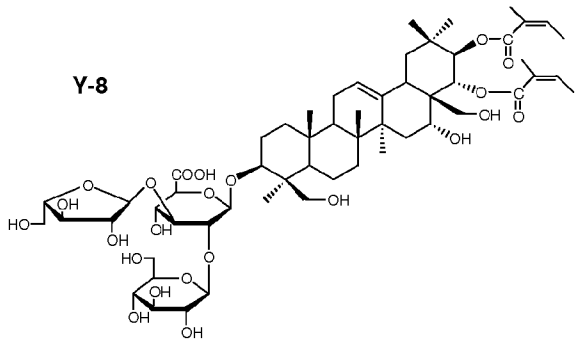
or chemical name: 3-O-[β-D-galactopyranosyl (1→2)]-α-L-arabinofuranosyl (1→3)-β-D-glucuronopyranosyl-21-O-(3,4-diangeloyl)-α-L-rhamnophyranosyl-22-O-acetyl-3β,16α, 21β, 22α, 28-pentahydroxyolean-12-ene;

c) An isolated, purified or synthesized compound having structure Xanifolia (Y2),



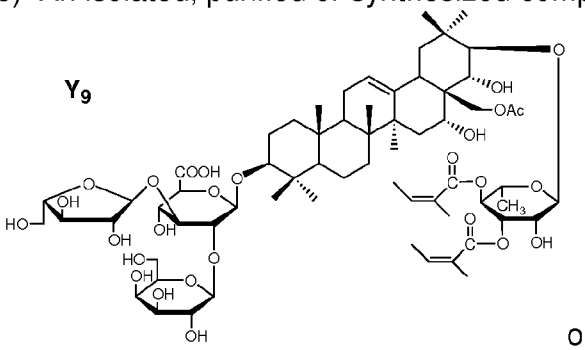
or chemical name: 3-O-[β-D-glucopyranosyl-(1→2)]-α-L-arabinofuranosy (1→3)-β-D-glucuronopyranosyl-21,22-O-diangeloyl-3β, 15α, 16α, 21β, 22α, 24β, 28-heptahydroxyolean-12-ene;

d) An isolated, purified or synthesized compound having structure Xanifolia (Y8),



or chemical name: 3-*O*-[*β*-glucopyranosyl (1→2)]-*α*-arabinofuranosyl (1→3)-*β*-glucuronopyranosyl-21, 22-*O*-diangeloyl-3*β*, 16*α*, 21*β*, 22*α*, 24*β*, 28-hexahydroxyolean-12-ene;

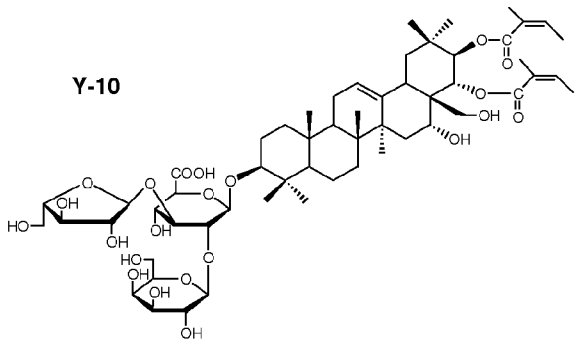
e) An isolated, purified or synthesized compound having structure Xanifolia (Y9),



or chemical name:3-*O*-[*β*-galactopyranosyl (1→2)]-*α*-arabinofuranosyl (1→3)-*β*-glucuronopyranosyl-21-*O*-(3,4-diangeloyl)-*α*-rhamnopyranosyl-28-*O*-acetyl-3*β*, 16*α*, 21*β*, 22*α*, 28-pentahydroxyolean-12-ene; and

f) An isolated, purified or synthesized compound having structure Xanifolia (Y10),

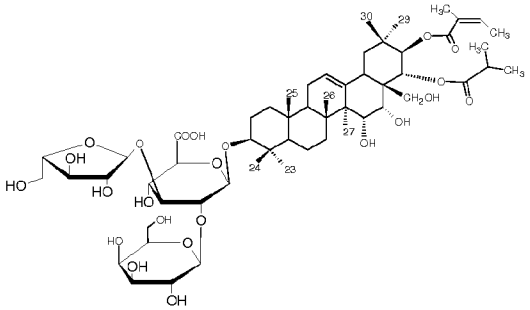
Y-10



or chemical name:

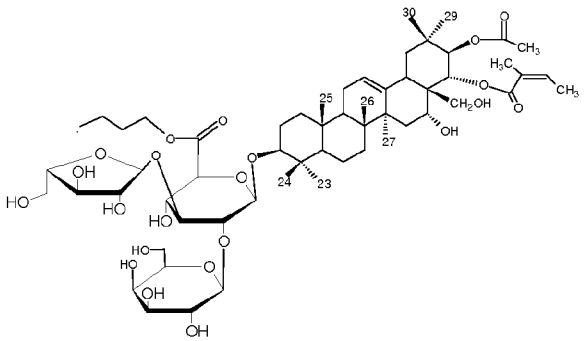
3-*O*-[*β*-galactopyranosyl (1→2)]-*α*-arabinofuranosyl (1→3)-*β*-glucuronopyranosyl-21, 22-*O*-diangeloyl-3*β*, 16*α*, 21*β*, 22*α*, 28-pentahydroxyolean-12-ene.

g) An isolated, purified or synthesized compound having structure Xanifolia (Y0),



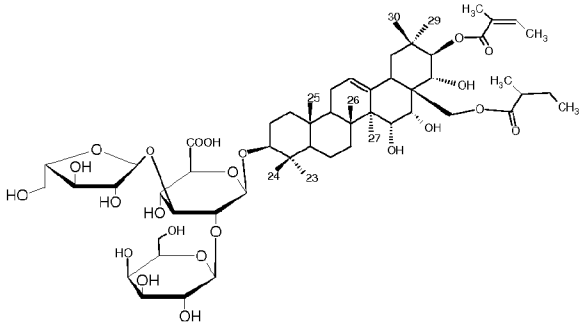
or chemical name: 3-O-[β-D-galactopyranosyl(1→2)]-α-L-arabinofuranosyl(1→3)-β-D-glucuronopyranosyl-21-O-angeloyl, 22-O-(2-methylpropanoyl)-3β, 15α, 16α, 21β, 22α, 28-hexahydroxyolean-12-ene,

h) An isolated, purified or synthesized compound having structure Xanifolia (X),



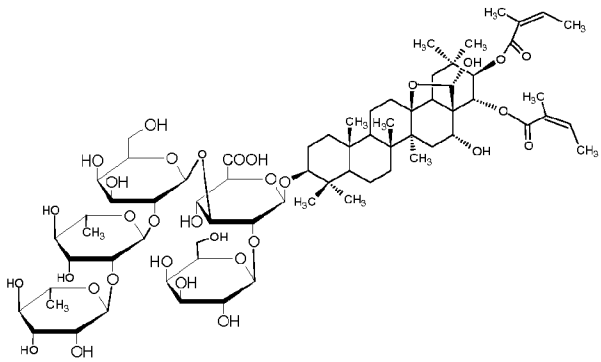
or chemical name: 3-*O*-{[*β*-D-galactopyranosyl (1→2)]-[*α*-L-arabinofuranosyl (1→3)]-*β*-D-glucuronopyranoside butyl ester}-21-*O*-acetyl-22-*O*-angeloyl- 3*β*,16*α*,21*β*,22*α*,28-pentahydroxyolean-12-ene.

i) An isolated, purified or synthesized compound having structure (Y7),

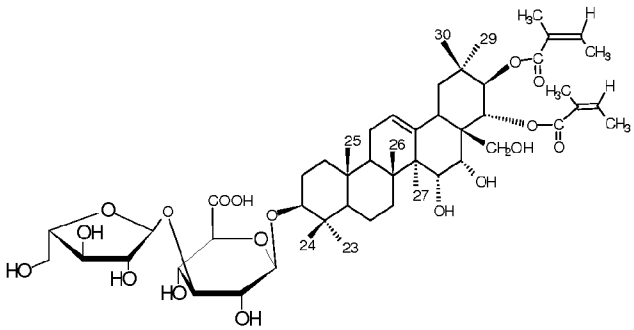


or chemical name: 3-*O*-[*β*-D-galactopyranosyl-(1→2)]-*α*-L-arabinofuranosyl-(1→3)-*β*-D--glucuronopyranosyl-21-*O*-angeloyl-28-*O*-2-methylbutanoyl-3*β*, 15 *α*, 16*α*, 21*β*, 22*α*, 28-hexahydroxyolean-12-ene

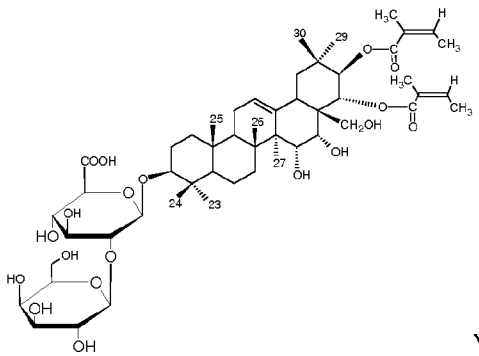
j) An isolated, purified or synthesized compound having structure (M10)



k) An isolated, purified or synthesized compound having structure:

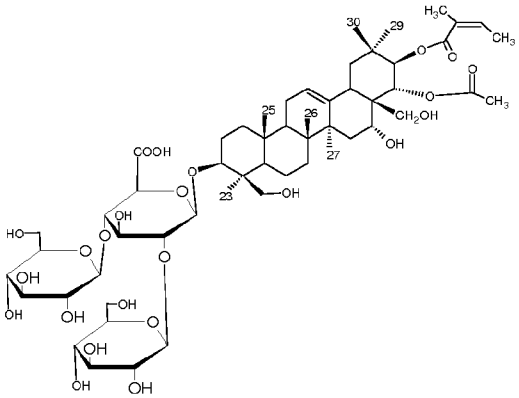


l) An isolated, purified or synthesized compound having a structure:

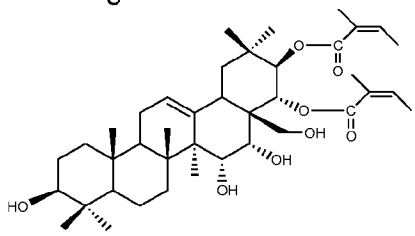


Y5

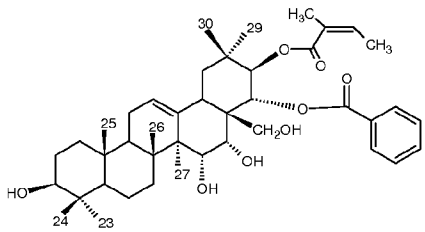
m) An isolated, purified or synthesized compound having structure (bES):



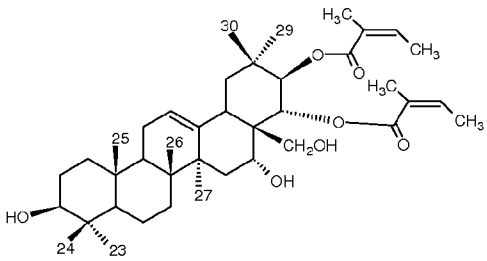
n) An isolated, purified or synthesized compound having structure (ACH) selected from following:



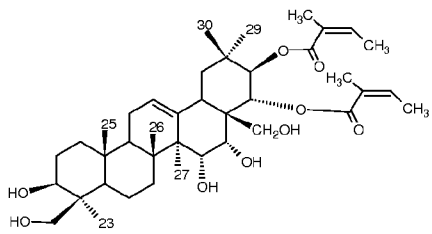
(ACH-Y);



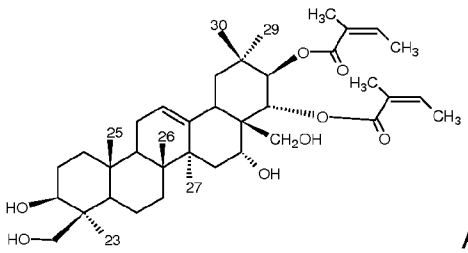
ACH-Z4



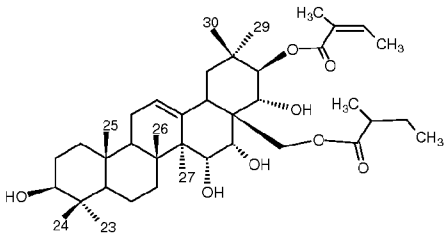
ACH-Y10;



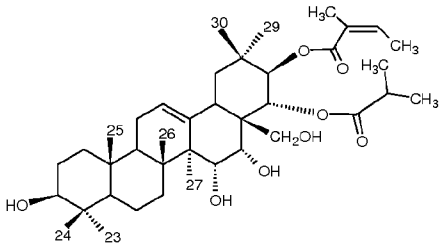
ACH-Y2;



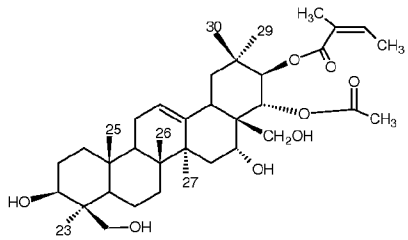
ACH-Y8;



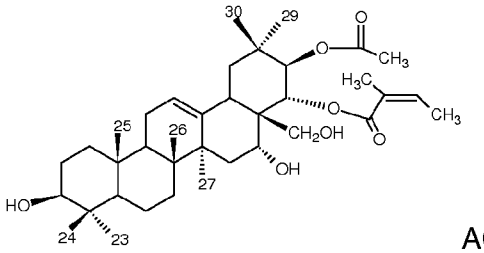
ACH-Y7;



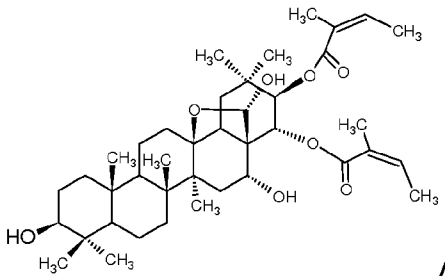
ACH-Y0;



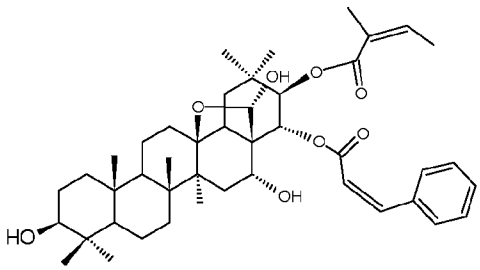
ACH-E;



ACH-X ;



ACH-M10



ACH-Z5

The composition comprises bioactive compounds from natural plants or synthesis. The majority of the plants are from the Sapindaceae family, which has 140-150 genera with 1400-2000 species. The program is based on our purification methods and biological assays including the MTT assay. See International Application No. PCT/US05/31900, filed September 7, 2005, U.S. Serial No. 11/289142, filed November 28, 2005, and U.S. Serial No. 11/131551, filed May 17, 2005, and PCT/US2008/002086, 1188-ALA-PCT, filed February 15, 2008, 12/344,682, 1020-B1-US, filed December 29, 2008, the contents of which are incorporated herein by reference. The details of Analysis of gene expression of ES2 cells after Y-treatment by Microarray, Data Analysis Methods and Western blot in PCT/US2008/002086, 1188-ALA-PCT, filed February 15, 2008, the contents of which are incorporated herein by reference.

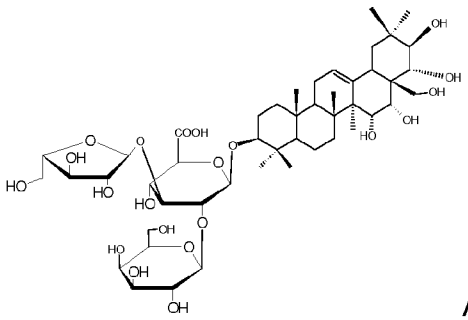
Acid Hydrolysis of Saponin

15mg Xanifolia-Y was dissolved in 1 ml of methanol. 1ml of 2N HCl was then added. The mixture was refluxed in 80C water bath for 5 hours. The solution was then neutralized by adding 2ml of 1N NaOH (to final pH 4-6). The aglycone was then extracted with ethylacetate 3ml x 2. The extracts were collected and pooled. Further isolation of aglycone (ACH-Y) was achieved by HPLC with isocratic elution of 80 -100% acetonitrile. Repeating the experiment with compounds Z4, Y10, Y2, Y8, Y7, Y0, X, M10 and ESCIN(bES) gives the following compounds respectively: ACH-Z4, ACH-Y10, ACH-Y2, ACH-Y8, ACH-Y7, ACH-Y0, ACH-X, ACH-E, ACH-Z5, ACH-M10 and ACH-bES.

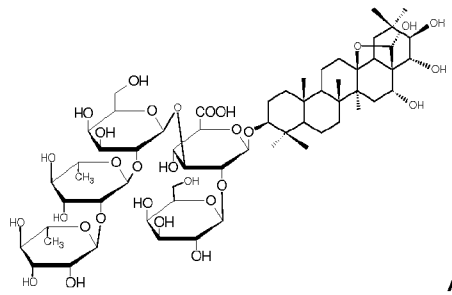
In mild conditions, the saponin will be partially hydrolysed to a mixture of products. These products can be separated by HPLC. Also, specific partial hydrolysis can be achieved with enzymes. The β-glucosidase enzyme is good for cleaving the β-glucose from saponin.

Removal of the acyl group by alkaline hydrolysis

20mg of Xanifolia-Y was dissolved in 0.5ml of 1N NaOH. The solution was incubated in 80C water bath for 4 hours. It was cooled to room temperature before being neutralized with 0.5ml 1N HCl (adjust pH to about 3). The mixture was extracted with 2ml 1-butanol 3 times. The butanol fractions were collected and lyophilized. The hydrolyzed saponin was further purified with HPLC in a C-18 column eluted with 25% acetonitrile.



AKOH-Y;

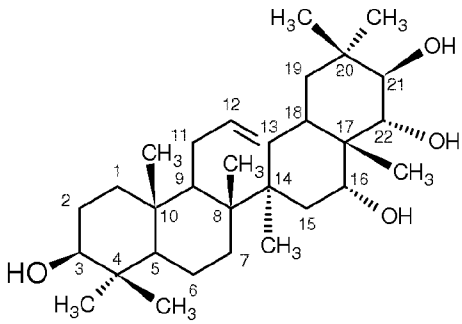


AKOH-M10

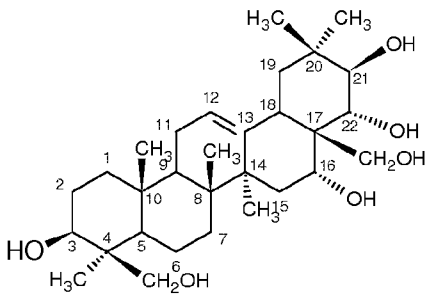
Compounds AKOH-Y and AKOH-M10 do not show the ability for inhibiting cancer invasion, cells invasion or cancer cell invasion.

A pentacyclic triterpene is obtained by acid and alkaline hydroysis of saponin from natural sources. A pentacyclic triterpene can also be obtained by synthetic methods.

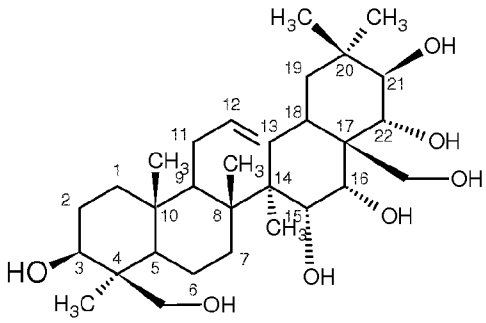
The structures of pentacyclic triterpene:



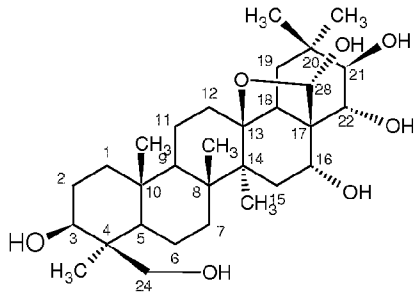
(A);



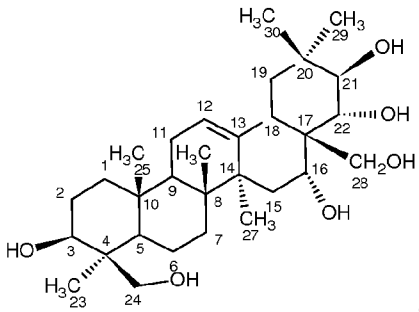
(B);



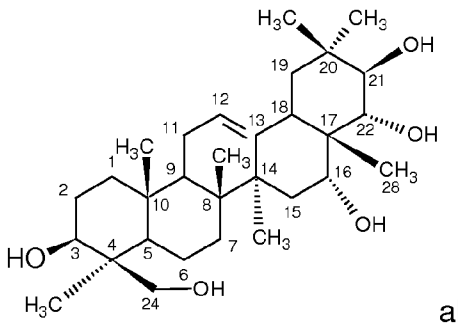
(C);



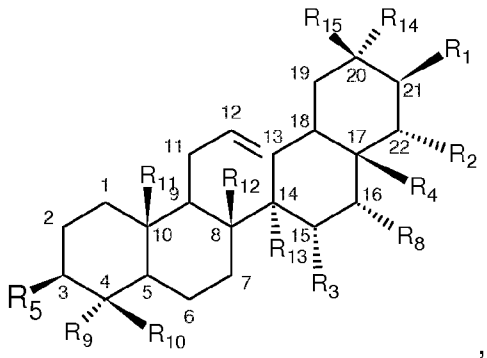
(D);



, also named as bES-core, or ES4A, or (E);

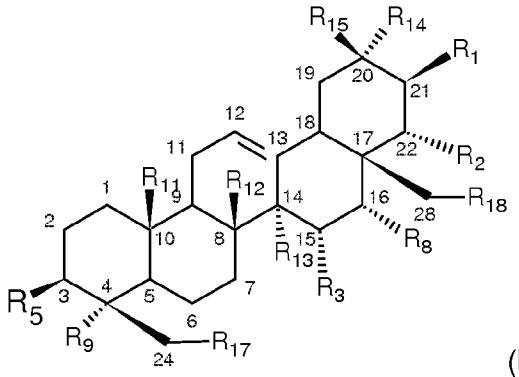


also named as ES V, or (F)



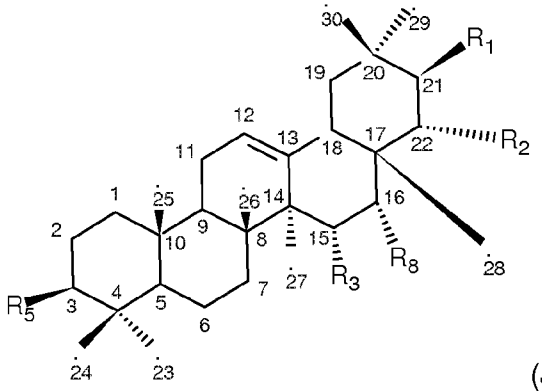
,(G),

wherein R1, R2, R5, R8 represent OH; R3 represents OH or H; R4, R10 represent CH3 or CH2OH; R9, R11, R12, R13, R14, R15 represent CH3;



(H),

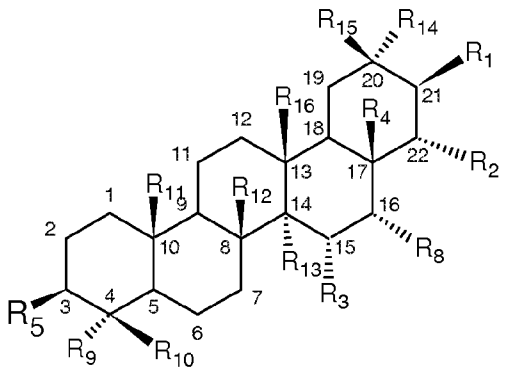
wherein R1, R2, R5, R8, R17, R18 represent OH; R3 represents OH or H; R9, R11, R12, R13, R14, R15 represent CH3.



(J)

A typical numbering 1 to 30 of carbon positions of a pentacyclic triterpene.

This invention provides methods, or uses of a compound for the manufacture of a medicament, or uses of a compound for medicament selected from formula (2A), for inhibiting cancer invasion, cell invasion, cancer cell invasion, or cancer metastasis, using the compounds selected from the following:



(2A)

R1, R2, R3, R4, R5, R8, R9, R10, R11, R12, R13, R14, R15 are independently selected from the group of hydrogen, hydroxyl, methyl, O-angeloyl, O-tigloyl, O-senecioyl, O-alkyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-alkanoyl substituted phenyl, O-alkenoyl substituted phenyl, O-aryl, O-acyl, O-

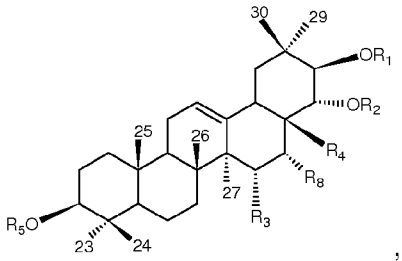
heterocylic, O-heteroraryl, O-alkenylcarbonyl, alkane, alkene and sugar moiety or derivatives thereof; wherein the structure (2A) comprises at least 2 groups selected from O-angeloyl, O-tigloyl, O-senecioyl, O-alkyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-alkanoyl substituted phenyl, O-alkenoyl substituted phenyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, O-alkenylcarbonyl; or wherein R1 and R2 are selected from O-angeloyl, O-tigloyl, O-senecioyl, O-alkyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-alkanoyl substituted phenyl, O-alkenoyl substituted phenyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, O-alkenylcarbonyl; In an embodiment, wherein the R1 and R2 are attached O-angeloyl. In an embodiment, wherein the R3 and R8 is hydrogen or hydroxyl, In an embodiment, wherein the R9, R10, R11, R12, R13, R14, R15 are independently attached with a methyl. In an embodiment, wherein R4 represents CH3, CHO, CH_2R6 or COR6, wherein R6 is selected from hydroxyl, O-angeloyl, O-tigloyl, O-senecioyl, O-alkyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-alkanoyl substituted phenyl, O-alkenoyl substituted phenyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, O-alkenylcarbonyl and derivatives thereof; In an embodiment, wherein R3 is H or OH; In an embodiment, wherein R8 is H or OH; In an embodiment, wherein R16 is H, CH3, OH ,or R4 and R16 may together form –CH2-X-, CH(OH)-X- or C(=O)-X-, wherein the –X- may be O or NH or S; wherein when the C12-13 of ring 3 of the triterpene has a double bond then R16 is absent. In an embodiment, wherein R10 represents CH3, CHO, CH_2R6 or COR6, wherein R6 is selected from hydroxyl, O-angeloyl, O-tigloyl, O-senecioyl, O-alkyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-alkanoyl substituted phenyl, O-alkenoyl substituted phenyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, O-alkenylcarbonyl and derivatives thereof;

In an embodiment, wherein R5 is a hydrogen, hydroxyl, heterocyclic or O-sugar moiety(ies), wherein the sugar moiety(ies) is/are selected from a group consisting of glucose, galactose, rhamnose, arabinose, xylose, fucose, allose, altrose, gulose, idose, lyxose, mannose, psicose, ribose, sorbose, tagatose, talose, fructose, alduronic acid, glucuronic acid, galacturonic acid, and derivatives or combinations thereof; wherein R9, R10, R11, R12, R13, R14, R15 are independently attached a group selecting from CH_3, CH_2OH, CHO, COOH, COO-alkyl, COO-aryl, COO-heterocyclic, COO-heteroaryl, CH_2Oaryl, CH_2O- heterocyclic, CH_2O- heteroaryl, alkyls group, hydroxyl, acetyl group; wherein R4 and R16 form a divalent radical of formula CH2O, CH(OR7)O, or COOR7, wherein R7 is hydrogen, alkyl, angeloyl, tigloyl, senecioyl, dibenzoyl, benzoyl, alkanoyl, alkenoyl, benzoyl alkyl substituted alkanoyl, aryl, acyl, heterocylic, heteroraryl, and

derivatives thereof; wherein at least two of R1, R2 and R6 are attached a group selected from O-angeloyl, O-tigloyl, O-senecioyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, and derivatives thereof; or at least one of R1, R2, and R4 is a sugar moiety substituted with at least two groups selected from a group consisting of angeloyl, acetyl, tigloyl, senecioyl, benzoyl, dibenzoyl, alkanoyl, alkenoyl, benzoyl alkyl substituted alkanoyl, aryl, acyl, heterocylic, heteroraryl, and their derivatives thereof; or wherein R4 is CH_2R6; wherein R1 and R2 independently consists an O-angeloyl group, or at least two of R1, R2 and R6 are O-angeloyl or at least one of R1, R2 or R6 is a sugar moiety with two O-angeloyls; wherein R5 is/are the sugar moiety(ies) selected from the following sugars and alduronic acids: glucose, galactose, rhamnose, arabinose, xylose, fucose, allose, altrose, gulose, idose, lyxose, mannose, psicose, ribose, sorbose, tagatose, talose, fructose, glucuronic acid, galacturonic acid; or their derivatives thereof, In an embodiment, wherein R5 is a hydroxyl, O-angeloyl, O-tigloyl, O-senecioyl, O-alkyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-alkanoyl substituted phenyl, O-alkenoyl substituted phenyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, O-alkenylcarbonyl and derivatives thereof. In an embodiment, R1, R2, R3, R4, R5, R8, R9, R10, R11, R12, R13, R14 or R15 comprise of one or more sugar moieties. In an embodiment, at least 1, or 2, or 3, or 4 of R1, R2, R3, R4, R5, R8, R9, R10, R11, R12, R13, R14 and R15 is hydroxyl. In an embodiment, at least 2, or 3, or 4, or 5, or 6, or 7 of R1, R2, R3, R4, R5, R8, R9, R10, R11, R12, R13, R14 and R15 are independently attached a group selected from the group of O-acetyl, O-angeloyl, O-tigloyl, O-senecioyl, O-alkyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-alkanoyl substituted phenyl, O-alkenoyl substituted phenyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, O-alkenylcarbonyl, alkane, alkene and derivatives thereof, wherein the group is attached to the triterpene directly or by connecting moiety(ies); In an embodiment, at least 2, or 3, or 4, or 5, or 6, or 7 of R1, R2, R3, R4, R5, R8 and R10 are independently attached a group selected from the group of O-acetyl, O-angeloyl, O-tigloyl, O-senecioyl, O-alkyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-alkanoyl substituted phenyl, O-alkenoyl substituted phenyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, O-alkenylcarbonyl, alkane, alkene and derivatives thereof, wherein the group is attached to the triterpene directly or by connecting moiety(ies). In an embodiment, the cancers comprise breast cancer, leukocytic cancer, liver cancer, ovarian cancer, bladder cancer, prostatic cancer, skin cancer, bone cancer, brain cancer, leukemia cancer, lung cancer, colon cancer, CNS cancer, melanoma cancer, renal cancer, cervical cancer,

esophageal cancer, testicular cancer, spleenic cancer, kidney cancer, lymphhatic cancer, pancreatic cancer, stomach cancer and thyroid cancer; wherein the cells comprise breast cell, leukocytic cell, liver cell, ovarian cell, bladder cell, prostatic cell, skin cell, bone cell, brain cell, leukemia cell, lung cell, colon cell, CNS cell, melanoma cell, renal cell, cervical cell, esophageal cell, testicular cell, spleenic cell, kidney cell, lymphhatic cell, pancreatic cell, stomach cell and thyroid cell.

This invention provides methods, or uses of a compound for the manufacture of a medicament, or uses of a compound for medicament, selected from formula (1B), for inhibiting cancer invasion, cell invasion, cancer cell invasion, or inhibiting cancer metastasis, using compounds selected from the following:



,also named as (1B),

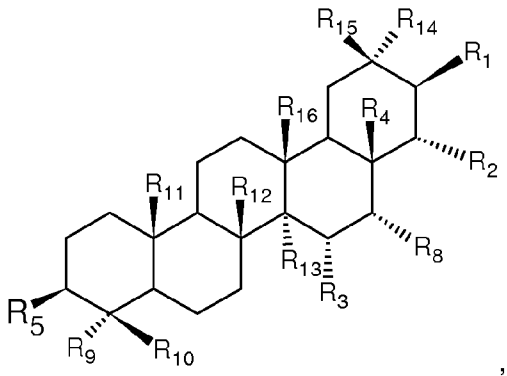
or a salt, ester, metabolite or derivative thereof, wherein R1 comprises a group selected from hydrogen, angeloyl, acetyl, tigloyl, senecioyl, alkyl, dibenzoyl, benzoyl, alkanoyl, alkenoyl, benzoyl alkyl substituted alkanoyl, acyl, aryl, heterocylic, heteroraryl, alkenylcarbonyl and derivatives thereof; R2 comprises a group selected from hydrogen, angeloyl, acetyl, tigloyl, senecioyl, alkyl, benzoyl, dibenzoyl, alkanoyl, alkenoyl, benzoyl alkyl substituted alkanoyl, aryl, acyl, heterocylic, heteroraryl, alkenylcarbonyl and derivatives thereof; R4 represents CH_2OR6 or COOR6, wherein R6 is selected from hydrogen, angeloyl, acetyl, tigloyl, senecioyl, alkyl, benzoyl, dibenzoyl, alkanoyl, alkenoyl, benzoyl alkyl substituted alkanoyl, aryl, acyl, heterocylic, heteroraryl and derivatives thereof; R3 is H or OH; wherein at least one of R1, R2,and R6 comprises a group selected from angeloyl, acetyl, tigloyl, senecioyl, benzoyl, dibenzoyl, alkanoyl, alkenoyl, benzoyl alkyl substituted alkanoyl, aryl, acyl, heterocylic, heteroraryl and derivatives thereof; R5 comprises a hydrogen or sugar moiety, wherein the sugar moiety comprises at least one sugar of, but is not limited to, D-glucose, D-galactose, L-rhamnose, L-arabinose, D-xylose, alduronic acid: D-glucuronic acid, D-galacturonic acid or derivatives thereof, or combinations thereof.

In an embodiment, R1 comprises a sugar moiety substituted with two groups selected from angeloyl, acetyl, tigloyl, senecioyl, benzoyl, dibenzoyl, alkanoyl, alkenoyl, benzoyl alkyl substituted alkanoyl, aryl, acyl, heterocylic heteroraryl and derivatives thereof. In

an embodiment, R1 comprises a sugar moiety substituted with at least one group selected from angeloyl, acetyl, tigloyl, senecioyl, benzoyl, dibenzoyl, alkanoyl, alkenoyl, benzoyl alkyl substituted alkanoyl, aryl, acyl, heterocylic, heteroraryl and a derivative thereof. In an embodiment, R2 comprises a sugar moiety wherein at least one group is selected from angeloyl, acetyl, tigloyl, senecioyl, alkyl, benzoyl, dibenzoyl, alkanoyl, alkenoyl, benzoyl alkyl substituted alkanoyl, aryl, acyl, heterocylic, heteroraryl and derivatives thereof. In an embodiment, R2 comprises a sugar moiety or a side chain wherein at least two groups are selected from angeloyl, acetyl, tigloyl, senecioyl, alkyl, benzoyl, dibenzoyl, alkanoyl, alkenoyl, benzoyl alkyl substituted alkanoyl, aryl, acyl, heterocylic, heteroraryl and derivatives thereof. In an embodiment, R4 comprises CH_2OR6 or COOR6 wherein R6 is a sugar moiety which comprises at least one group selected from angeloyl, acetyl, tigloyl, senecioyl, benzoyl, dibenzoyl, alkanoyl, alkenoyl, benzoyl alkyl substituted alkanoyl, aryl, acyl, heterocylic, heteroraryl and derivatives thereof. In an embodiment, R4 comprises CH_2OR6 or COOR6, wherein R6 is a sugar moiety which comprises at least two groups selected from angeloyl, acetyl, tigloyl, senecioyl, benzoyl, dibenzoyl, alkanoyl, alkenoyl, benzoyl alkyl substituted alkanoyl, aryl, acyl, heterocylic, heteroraryl and derivatives thereof. In an embodiment, R4 comprises CH_2OR6 or COOR6, wherein R6 is a sugar moiety which comprises at least two groups selected from angeloyl, acetyl, tigloyl and senecioyl. In an embodiment, R4 comprises CH_2OR6 or COOR6 of formula (1B), at least two of R1, R2 and R6 comprise the group selected from angeloyl, acetyl, tigloyl, senecioyl, benzoyl, dibenzoyl, alkanoyl, alkenoyl, benzoyl alkyl substituted alkanoyl, aryl, acyl, heterocylic, heteroraryl and derivatives thereof. In an embodiment, R4 comprises CH_2OR6 or COOR6 of formula (1B), wherein at least two of R1, R2 and R6 comprise of angeloyl, benzoyl, alkenoyl, or derivatives thereof. In an embodiment, R4 is a side chain comprising CH_2OCOCH_3, CH_2COO-alkyl, CH_2OH, COOH, angeloyl, acetyl, tigloyl, senecioyl, alkyl, benzoyl, dibenzoyl, alkanoyl, alkenoyl, benzoyl alkyl substituted alkanoyl, aryl, acyl, heterocylic or heteroraryl, alkanoyl substituted phenyl, alkenoyl substituted phenyl, or derivatives thereof. In a further embodiment, R5 comprises a sugar moiety, wherein the sugar moiety comprises one or more sugar of, but is not limited to, glucose, galactose, rhamnose, arabinose, xylose, fucose, allose, altrose, gulose, idose, lyxose, mannose, psicose, ribose, sorbose, tagatose, talose, fructose, or alduronic acid: glucuronic acid, galacturonic acid, or derivatives thereof, or combinations thereof. In an embodiment, R5 comprises a sugar moiety or a group capable of performing the function of the sugar moiety. In an embodiment, the R5 represents H. In an embodiment, R4 represents H, OH or CH_3. In an embodiment, positions C23, C24, C25, C26, C29 and C30 of the compound

independently comprise CH_3, CH_2OH, CHO, COOH, COO-alkyl, COO-aryl, COO-heterocyclic, COO-heteroaryl, CH_2Oaryl, CH_2O- heterocyclic, CH_2O- heteroaryl, alkyls group, acetyl group or derivatives thereof. In an embodiment, R1 and R2 independently comprise an angeloyl group. In an embodiment, R1 is a sugar moiety or a side chain which comprises of two angeloyl groups. In an embodiment, R1 and R2 independently comprise a benzoyl group. In an embodiment, R1 is a sugar moiety which is substituted with two benzoyl groups. In an embodiment, R_3 represents H or OH. In an embodiment, R8 may be OH. In an embodiment, the O at C21, 22 may be replaced by NH. In an embodiment, R3, R5, R8 of the compound independently comprise a group selected from hydrogen, angeloyl, acetyl, tigloyl, senecioyl, alkyl, benzoyl, dibenzoyl, alkanoyl, alkenoyl, benzoyl alkyl substituted alkanoyl, aryl, acyl, heterocylic, heteroraryl, alkenylcarbonyl and derivatives thereof; In an embodiment, the cancers comprise breast cancer, leukocytic cancer, liver cancer, ovarian cancer, bladder cancer, prostatic cancer, skin cancer, bone cancer, brain cancer, leukemia cancer, lung cancer, colon cancer, CNS cancer, melanoma cancer, renal cancer, cervical cancer, esophageal cancer, testicular cancer, spleenic cancer, kidney cancer, lymphhatic cancer, pancreatic cancer, stomach cancer and thyroid cancer. Substitution, deletion and/or addition of any group in the above-described compounds by other group(s) will be apparent to one of ordinary skill in the art based on the teachings of this application. In a further embodiment, the substitution, deletion and/or addition of the group(s) in the compound of the invention does not substantially affect the biological function of the compound.

This invention provides methods, or uses of a compound for the manufacture of a medicament, or uses of compounds for medicament selected from formula (1E), for inhibiting cancer invasion, cell invasion, cancer cell invasion, or inhibiting cancer metastasis, wherein the cancers comprise. breast cancer, leukocytic cancer, liver cancer, ovarian cancer, bladder cancer, prostatic cancer, skin cancer, bone cancer, brain cancer, leukemia cancer, lung cancer, colon cancer, CNS cancer, melanoma cancer, renal cancer, cervical cancer, esophageal cancer, testicular cancer, spleenic cancer, kidney cancer, lymphhatic cancer, pancreatic cancer, stomach cancer and thyroid cancer; wherein the cells comprise breast cell, leukocytic cell, liver cell, ovarian cell, bladder cell, prostatic cell, skin cell, bone cell, brain cell, leukemia cell, lung cell, colon cell, CNS cell, melanoma cell, renal cell, cervical cell, esophageal cell, testicular cell, spleenic cell, kidney cell, lymphhatic cell, pancreatic cell, stomach cell and thyroid cell. In an embodiment the method comprises administering the compounds to a subject, wherein the compound is selected from the formula (1E):



, also named (1E), wherein

R1 is selected from hydrogen, hydroxyl, O-angeloyl, O-tigloyl, O-senecioyl, O-alkyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-alkanoyl substituted phenyl, O-alkenoyl substituted phenyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, O-alkenylcarbonyl and derivatives thereof;

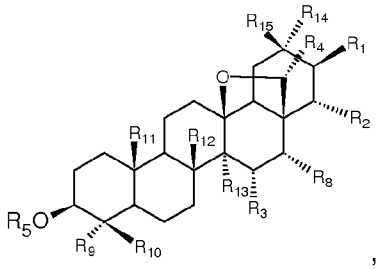
R2 is selected from hydrogen, hydroxyl, O-angeloyl, O-tigloyl, O-senecioyl, O-alkyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-alkanoyl substituted phenyl, O-alkenoyl substituted phenyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, O-alkenylcarbonyl and derivatives thereof;

R4 represents CH3, CHO, CH_2R6 or COR6, wherein R6 is selected from hydroxyl, O-angeloyl, O-tigloyl, O-senecioyl, O-alkyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-alkanoyl substituted phenyl, O-alkenoyl substituted phenyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, O-alkenylcarbonyl and derivatives thereof; R3 is H or OH; R8 is H or OH, R16 is H, CH3, OH ,or R4 and R16 may together form –CH2-X-, CH(OH)-X- or C(=O)-X-, wherein the –X- may be O or NH or S ; wherein when the C12-13 of ring 3 of the triterpene has a double bond then R16 is absent;

R5 is a hydrogen, hydroxyl, heterocyclic or O-sugar moiety(ies), wherein the sugar moiety(ies) is/are selected from a group consisting of glucose, galactose, rhamnose, arabinose, xylose, fucose, allose, altrose, gulose, idose, lyxose, mannose, psicose, ribose, sorbose, tagatose, talose, fructose, alduronic acid, glucuronic acid, galacturonic acid, and derivatives or combinations thereof; wherein at R9, R10, R11, R12, R13, R14, R15 are independently attached a group selected from CH_3, CH_2OH, CHO, COOH, COO-alkyl, COO-aryl, COO-heterocyclic, COO-heteroaryl, CH_2Oaryl, CH_2O-heterocyclic, CH_2O- heteroaryl, alkyls group, hydroxyl, acetyl group, particularly CH_3; wherein R4 and R16 form a divalent radical of formula CH2O, CH(OR7)O, or COOR7, wherein R7 is hydrogen, alkyl, angeloyl, tigloyl, senecioyl, dibenzoyl, benzoyl, alkanoyl, alkenoyl, benzoyl alkyl substituted alkanoyl, aryl, acyl, heterocylic, heteroraryl, and derivatives thereof; wherein at least two of R1, R2 and R6 are attached a group

selected from O-angeloyl, O-tigloyl, O-senecioyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, and derivatives thereof; or at least one of R1, R2, and R4 is a sugar moiety substituted with at least two groups selected from a group consisting of angeloyl, acetyl, tigloyl, senecioyl, benzoyl, dibenzoyl, alkanoyl, alkenoyl, benzoyl alkyl substituted alkanoyl, aryl, acyl, heterocylic, heteroraryl, and a derivative thereof; or wherein R4 is CH_2R6; wherein R1 and R2 are independently attached an O-angeloyl group, or at least two of R1, R2 and R6 are O-angeloyl or at least one of R1, R2 or R6 is a sugar moiety with two O-angeloyls; wherein R5 is/are the O-sugar moiety(ies) wherein the sugars moiety(ies) are selected from the following sugars and alduronic acids: glucose, galactose, rhamnose, arabinose, xylose, fucose, allose, altrose, gulose, idose, lyxose, mannose, psicose, ribose, sorbose, tagatose, talose, fructose, glucuronic acid, galacturonic acid; or their derivatives thereof, or combinations thereof; in an embodiment, wherein R5 is/are O-sugar moiety(ies) wherein the sugar moiety(ies) selected from a group consisting of glucose, galactose, arabinose, alduronic acid, glucuronic acid, galacturonic acid, and a derivative or combinations thereof. In an embodiment, wherein carbon ring 3 comprises a double bond when R16 is H; wherein the double bond in carbon ring 3 is reduced when R4 and R16 form a divalent radical. In an embodiment, the compound has no sugar moiety. In an embodiment, the number of sugar moiety(ies) at R5 is at least 1. In an embodiment, the number of sugar moieties at R5 is at least 2. In an embodiment, the number of sugar moieties at R5 is at least 3. In an embodiment, the number of sugar moieties at R5 is at least 4. In an embodiment, the number of sugar moieties at R5 is at least 5. In an embodiment, the number of sugar moiety(ies) at R5 is(are) 1, 2, 3, 4, or 5.

In an embodiment, the compound is selected from the formula (1F):



, also named (1F), wherein

R1 is selected from hydrogen, hydroxyl, O-angeloyl, O-tigloyl, O-senecioyl, O-alkyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-alkanoyl substituted phenyl, O-alkenoyl substituted phenyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, O-alkenylcarbonyl and derivatives thereof;

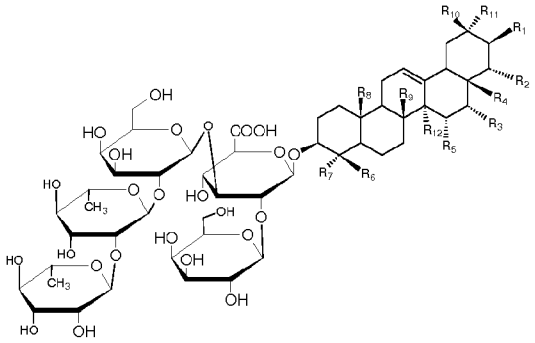
R2 is selected from hydrogen, hydroxyl, O-angeloyl, O-tigloyl, O-senecioyl, O-alkyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-alkanoyl substituted phenyl, O-alkenoyl substituted phenyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, O-alkenylcarbonyl and derivatives thereof;

R4 is selected from hydrogen, hydroxyl, O-angeloyl, O-tigloyl, O-senecioyl, O-alkyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-alkanoyl substituted phenyl, O-alkenoyl substituted phenyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, O-alkenylcarbonyl and derivatives thereof;

R3 is H or OH; R8 is H or OH;

R5 is a hydrogen or sugar moiety(ies), wherein the sugar moiety(ies) is/are selected from a group consisting of glucose, galactose, rhamnose, arabinose, xylose, fucose, allose, altrose, gulose, idose, lyxose, mannose, psicose, ribose, sorbose, tagatose, talose, fructose, alduronic acid, glucuronic acid, galacturonic acid, and derivatives or combinations thereof; wherein at R9, R10, R11, R12, R13, R14, R15 are independently attached a group selected from CH_3, CH_2OH, CHO, COOH, COO-alkyl, COO-aryl, COO-heterocyclic, COO-heteroaryl, CH_2Oaryl, CH_2O- heterocyclic, CH_2O- heteroaryl, alkyls group, hydroxyl, acetyl group, particularly CH_3; wherein at least two of R1, R2 and R4 are attached a group selected from O-angeloyl, O-tigloyl, O-senecioyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, and derivatives thereof; or at least one of R1, R2, and R4 is a sugar moiety substituted with at least two groups selected from a group consisting of angeloyl, acetyl, tigloyl, senecioyl, benzoyl, dibenzoyl, alkanoyl, alkenoyl, benzoyl alkyl substituted alkanoyl, aryl, acyl, heterocylic, heteroraryl, and derivatives thereof; or wherein R1, R2 and R4 independently consist an O-angeloyl group, or at least two of R1, R2 and R4 are O-angeloyl or at least one of R1, R2 or R4 is a sugar moiety with two O-angeloyls; wherein R5 is/are sugar moiety(ies) selected from the following sugars and alduronic acids: glucose, galactose, rhamnose, arabinose, xylose, fucose, allose, altrose, gulose, idose, lyxose, mannose, psicose, ribose, sorbose, tagatose, talose, fructose, glucuronic acid, galacturonic acid, or their derivatives thereof, or combinations thereof; wherein the sugar preferably comprises glucuronic acid, arabinose and galactose. In an embodiment, R5 is/are sugar moiety(ies) selected from a group consisting of glucose, galactose, arabinose, alduronic acid, glucuronic acid, galacturonic acid, and derivatives or combinations thereof; In an embodiment, R5 is 3-β-O-{[(α-L-rhamnopyranosyl-(1→2)]-α-L-rhamnopyranosyl--(1→2)-β-D- galactopyranosyl--(1→3)]-[β-D- galactopyranosyl--(1→2)]- β-D-glucuronopyranosyl}

In an embodiment, the compound is selected from the formula:



also named (1G), wherein

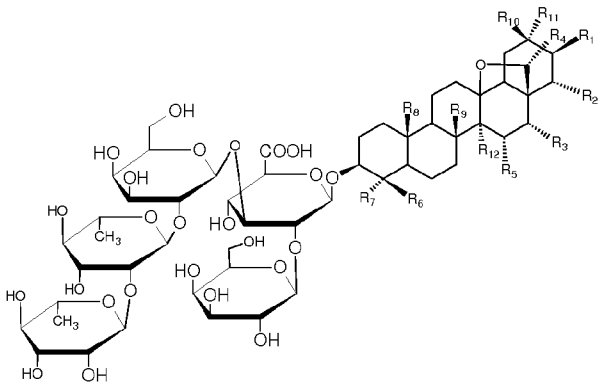
R1 is selected from hydrogen, hydroxyl, O-angeloyl, O-tigloyl, O-senecioyl, O-alkyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-alkanoyl substituted phenyl, O-alkenoyl substituted phenyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, O-alkenylcarbonyl and derivatives thereof;

R2 is selected from hydrogen, hydroxyl, O-angeloyl, O-tigloyl, O-senecioyl, O-alkyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-alkanoyl substituted phenyl, O-alkenoyl substituted phenyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, O-alkenylcarbonyl and derivatives thereof;

R4 represents CH3, CHO, CH_2R6 or COR6, wherein R6 is selected from hydroxyl, O-angeloyl, O-tigloyl, O-senecioyl, O-alkyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-alkanoyl substituted phenyl, O-alkenoyl substituted phenyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, O-alkenylcarbonyl and derivatives thereof; R3 is H or OH; R5 is H or OH;

wherein R6, R7, R8, R9, R10, R11, R12 are independently attached a group selected from CH_3, CH_2OH, CHO, COOH, COO-alkyl, COO-aryl, COO-heterocyclic, COO-heteroaryl, CH_2Oaryl, CH_2O- heterocyclic, CH_2O- heteroaryl, alkyls group, hydroxyl, acetyl group;

In an embodiment, the compound is selected from the formula:



also named (1H), wherein

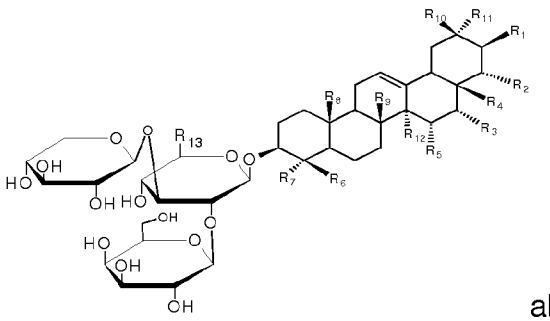
R1 is selected from hydrogen, hydroxyl, O-angeloyl, O-tigloyl, O-senecioyl, O-alkyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-alkanoyl substituted phenyl, O-alkenoyl substituted phenyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, O-alkenylcarbonyl and derivatives thereof;

R2 is selected from hydrogen, hydroxyl, O-angeloyl, O-tigloyl, O-senecioyl, O-alkyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-alkanoyl substituted phenyl, O-alkenoyl substituted phenyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, O-alkenylcarbonyl and derivatives thereof;

R4 is selected from hydroxyl, CH2OH, O-angeloyl, O-tigloyl, O-senecioyl, O-alkyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-alkanoyl substituted phenyl, O-alkenoyl substituted phenyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, O-alkenylcarbonyl and derivatives thereof;

R3 is H or OH; R5 is H or OH; wherein R6, R7, R8, R9, R10, R11, R12 are independently attached a group selected from CH_3, CH_2OH, CHO, COOH, COO-alkyl, COO-aryl, COO-heterocyclic, COO-heteroaryl, CH_2Oaryl, CH_2O- heterocyclic, CH_2O-heteroaryl, alkyls group, hydroxyl, acetyl group, particularly CH_3;

In an embodiment the use or method comprises contacting said cell with the following compounds:



also named (1J), wherein

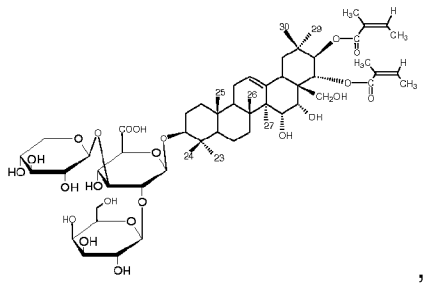
R1 is selected from hydrogen, hydroxyl, O-angeloyl, O-tigloyl, O-senecioyl, O-alkyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-alkanoyl substituted phenyl, O-alkenoyl substituted phenyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, O-alkenylcarbonyl and derivatives thereof;

R2 is selected from hydrogen, hydroxyl, O-angeloyl, O-tigloyl, O-senecioyl, O-alkyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-alkanoyl substituted phenyl, O-alkenoyl substituted phenyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, O-alkenylcarbonyl and derivatives thereof;

R4 represents CH3, CHO, CH_2R6 or COR6, wherein R6 is selected from hydroxyl, O-angeloyl, O-tigloyl, O-senecioyl, O-alkyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-alkanoyl substituted phenyl, O-alkenoyl substituted phenyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, O-alkenylcarbonyl and derivatives thereof;

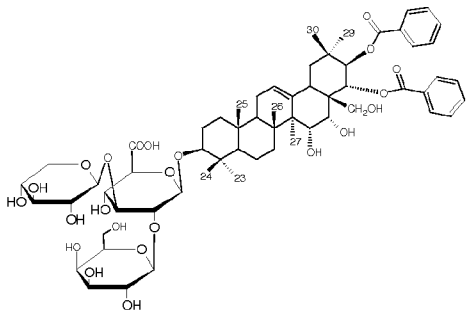
R3 is H or OH; R5 is H or OH, particularly OH; wherein R6, R7, R8, R9, R10, R11, R12 are independently attached a group selecting from CH_3, CH_2OH, CHO, COOH, COO-alkyl, COO-aryl, COO-heterocyclic, COO-heteroaryl, CH_2Oaryl, CH_2O- heterocyclic, CH_2O- heteroaryl, alkyls group, hydroxyl, acetyl group, particularly CH_3; R13 is COOH or COO-alkyl,

In an embodiment, the use or method comprises contacting said cell with the following compounds:



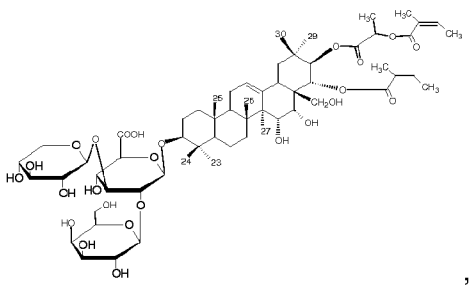
, or

3-O-[β-D-galactopyranosyl(1→2)] -β- D-xyopyranosyl (1→3)-β-D-glucuronopyranosyl-21-O-angeloyl, 22-O-angeloyl-3β, 15α, 16α, 21β, 22α, 28-hexahydroxyolean-12-ene;



,or

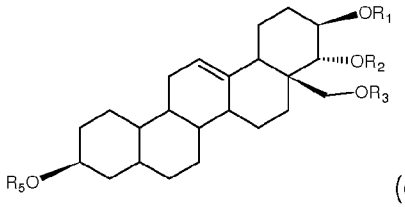
3-O-[β-D-galactopyranosyl(1→2)]-β- D-xyopyranosyl (1→3)-β-D-glucuronopyranosyl-21-O-benzoyl, 22-O-benzoyl-3β, 15α, 16α, 21β, 22α, 28-hexahydroxyolean-12-ene;



,or

3-O-[β-D-galactopyranosyl(1→2)]-β- D-xyopyranosyl (1→3)-β-D-glucuronopyranosyl-21-O-(2-methylpropanoyl)-O-angeloyl, 22-O-(2- methylbutanoyl) -3β, 15α, 16α, 21β, 22α, 28-hexahydroxyolean-12-ene.

In an embodiment, a triterpene comprising the following structure has activities including inhibiting cancer invasion, cell invasion, and cancer cell invasion or manufacturing an adjuvant composition.



(e)

wherein at least two of R1, R2 and R3 comprise compounds selected from angeloyl, acetyl, tigloyl, senecioyl, benzoyl, dibenzoyl, alkanoyl, alkenoyl, benzoyl alkyl substituted alkanoyl, aryl, heterocylic, heteroraryl, alkanoyl substituted phenyl, alkenoyl substituted phenyl, alkenylcarbonyl or substituted with an acid having 2 to 9 carbons or derivatives thereof. In an embodiment, at least one of R1, R2 and R3 comprise a sugar moiety comprising two compounds selected from angeloyl, acetyl, tigloyl, senecioyl, alkyl, benzoyl, dibenzoyl, alkanoyl, alkenoyl, benzoyl alkyl substituted alkanoyl, aryl, acyl, heterocylic, heteroraryl, alkanoyl substituted phenyl, alkenoyl substituted phenyl, alkenylcarbonyl or substituted with an acid having 2 to 9 carbons or derivatives thereof. In embodiment, R1, R2 or R3 comprise angeloyl groups, tigloyl groups, senecioyl groups or acetyl groups or their combinations, preferably wherein at least two of the R1, R2 and R3 comprise angeloyl groups. In an embodiment, R5 comprises a sugar moiety. In an embodiment, the sugar moiety comprises at least one sugar, or glucose, or galactose, or rhamnose, or arabinose, or xylose, or alduronic acid, or glucuronic acid, or galacturonic acid, or their derivative thereof, or combinations thereof. In an embodiment, the sugar moiety comprises one or more sugars selected from, but not limited to glucose, galactose, rhamnose, arabinose, xylose, fucose, allose, altrose, gulose, idose, lyxose, mannose, psicose, ribose, sorbose, tagatose, talose, fructose, alduronic acid, glucuronic acid, galacturonic acid, or derivatives thereof, or combinations thereof. In an embodiment, the sugar moiety comprises glucose, galactose or arabinose, or combinations thereof, or derivatives thereof. In an embodiment, the sugar moiety is comprised of alduronic acids, galactose, glucose and arabinose, wherein the alduronic acid comprises of glucuronic acid or galacturonic acid. In an embodiment, R5 is hydrogen. In an embodiment, R1, R2 and R3 may be attached at other positions of the structure.

In an embodiment, the compound having inhibiting cancer cell invasion, is a triterpenoid saponin comprising at least two angeloyl groups, tigloyl groups, senecioyl groups or acetyl group or their combinations, preferably wherein there is at least two angeloyl groups.

In an embodiment, a compound having at least two side bonds attaching a group selected from angeloyl, acetyl, tigloyl, senecioyl, benzoyl, dibenzoyl, alkanoyl, alkenoyl, benzoyl alkyl substituted alkanoyl, aryl, acyl, heterocylic, heteroraryl, alkanoyl substituted phenyl, alkenoyl substituted phenyl, alkenylcarbonyl or an acid having 2 to 9 carbons, or derivatives thereof, provides cancer cell invasion inhibition activity.

In an embodiment, a compound having at least one side bond comprising a sugar moiety substituted with two groups selected from angeloyl, acetyl, tigloyl, senecioyl, benzoyl, dibenzoyl, alkanoyl, alkenoyl, benzoyl alkyl substituted alkanoyl, aryl, acyl, heterocylic, heteroraryl, alkanoyl substituted phenyl, alkenoyl substituted phenyl, alkenylcarbonyl or an acid having 2 to 9 carbons or derivatives thereof, provides cancer cell invasion inhibition activity. In an embodiment, the compound comprises a sugar moiety. In a further embodiment, the sugar moiety comprises glucose, galactose or arabinose or combinations thereof. In an embodiment, the sugar moiety comprises at least one sugar, or glucose, or galactose, or rhamnose, or arabinose, or xylose, or alduronic acid, or glucuronic acid, or galacturonic acid, or their derivatives thereof, or combinations thereof. In an embodiment, the sugar moiety comprises one or more sugar selected from, but not limited to glucose, galactose, rhamnose, arabinose, xylose, fucose, allose, altrose, gulose, idose, lyxose, mannose, psicose, ribose, sorbose, tagatose, talose, fructose, alduronic acid, glucuronic acid, galacturonic acid, or derivatives thereof, or combinations thereof.

A composition comprising an effective amount of compound selected from the above formula or a salt, ester, metabolite or derivative thereof can be used as a medicament for blocking the invasion, migration, metastasis of cancer cells, inhibiting tumor or cancer cell growth and for treating cancer, wherein the cancers comprise breast cancer, leukocytic cancer, liver cancer, ovarian cancer, bladder cancer, prostatic cancer, skin cancer, bone cancer, brain cancer, leukemia cancer, lung cancer, colon cancer, CNS cancer, melanoma cancer, renal cancer, cervical cancer, esophageal cancer, testicular cancer, spleenic cancer, kidney cancer, lymphhatic cancer, pancreatic cancer, stomach cancer and thyroid cancer.

This invention provides a composition for inhibiting cancer invasion, cancer cell invasion, comprising a compound, wherein the compound is a triterpene, which comprises at least two side chains which comprise angeloyl groups, wherein the side chains are at adjacent carbon in *trans* configuration. In an embodiment, the side chains are at alternate carbon in *cis* configuration. In an embodiment, the side chains are at alternate carbon in *trans* configuration. In an embodiment, an angeloyl, acetyl, tigloyl, senecioyl, is attached to the side chains. In an embodiment, an acyl is attached to the side chains. In an embodiment, an unsaturated group is attached to the side chains. In an embodiment, the side chains are at non-adjacent carbons in *cis* or *trans* configuration. In an embodiment, the side chains comprise a functional group capable of performing the functions of an angeloyl group.

This invention provides a composition comprising the compounds provided in the invention for treating cancers; for inhibiting viruses; for preventing cerebral aging; for improving memory; improving cerebral functions; for curing enuresis, frequent micturition, urinary incontinence, dementia, Alzheimer's disease, autism, brain trauma, Parkinson's disease or other diseases caused by cerebral dysfunctions; for treating arthritis, rheumatism, poor circulation, arteriosclerosis, Raynaud's syndrome, angina pectoris, cardiac disorder, coronary heart disease, headache, dizziness, kidney disorder; cerebrovascular diseasea; inhibiting NF-Kappa B activation; for treating brain edema, severe acute respiratory syndrome, respiratory viral diseases, chronic venous insufficiency, hypertension, chronic venous disease, oedema, inflammation, hemonhoids, peripheral edema formation, varicose vein disease, flu, post traumatic edema and postoperative swelling; for inhibiting blood clots, for inhibiting ethanol absorption; for lowering blood sugar; for regulating adrenocorticotropin and corticosterone levels. This invention provides a composition for AntiMS, antianeurysm, antiasthmatic, anti-oedematous, anti-inflammatory, antibradykinic, anticapillarihemorrhagic, anticephalagic, anticervicobrachialgic, antieclamptic, antiedemic, antiencaphalitic, antiepiglottitic, antiexudative, antiflu, antifracture, antigingivitic, antihematomic, antiherpetic, antihistaminic, antihydrathritic, antimeningitic, antioxidant, antiperiodontic, antiphlebitic, antipleuritic, antiraucedo, antirhinitic, antitonsilitic, antiulcer, antivaricose, antivertiginous, cancerostatic, corticosterogenic, diuretic, fungicide, hemolytic, hyaluronidase inhibitor, lymphagogue, natriuretic, pesticide, pituitary stimulant, thymolytic, vasoprotective, inhibiting leishmaniases, modulating adhesion or angiogenesis of cancer cells, antiparasitic; increase the

expression of the genes: ANGPT2, DDIT3, LIF and NFKB1Z, and manufacturing an adjuvant composition and venotonic treatment.

Alkenyl means unsaturated linear or branched structures and combinations thereof, having formula R2C=CR2, one or more double bonds therein. Examples of alkenyl groups include vinyl, propenyl, isopropenyl, butenyl, s- and t-butenyl, pentenyl, hexenyl, butadienyl, pentadienyl, and hexadienyl.

An aryl is a functional group of organic molecule derived from an aromatic compound such as benzene, a 6-14 membered carbocyclic aromatic ring system comprising 1-3 benzene rings. If two or more aromatic rings are present, then the rings are fused together, so that adjacent rings share a common bond. Examples include phenyl and naphthyl. The aryl group may be substituted with one or more substitutes independently selected from halogen, alkyl or alkoxy.

Acyl is a functional group which can be obtained from an organic acid by the removal of the carboxyl. Acyl groups can be written using the general formula -COR, where there is a double bond between the carbon and oxygen. The names of acyl groups typically end in -yl, such as formyl, acetyl, propionyl, butyryl and benzoyl.
Benzoyl is one of the acyls, C_6H_5COR, obtained from benzoic acid by the removal of the carboxyl.

A heterocyclic compound is a compound containing a heterocyclic ring which refers to a non-aromatic ring having 1-4 heteroatoms, said ring being isolated or fused to a second ring selected from 3- to 7-membered alicyclic ring containing 0-4 heteroatoms，aryl and heteroaryl，wherein heterocyclic compounds include pyrrolidinyl，pipyrazinyl，morpholinyl，trahydrofuranyl，imidazolinyl，thiomorpholinyl，and the like.
Heterocyclyl groups are derived from heteroarenes by removal of a hydrogen atom from any ring atom.

Alkanoyl is the general name for an organic functional group RCO-, where R represents hydrogen or an alkyl group. Examples of alkanoyls are acetyl，propionoyl，butyryl，isobutyryl, pentanoyl and hexanoyl.

Alkenoyl is an alkenylcarbonyl in which the alkenyl is defined above. Examples are pentenoyl(tigloyl) and hexenoyl(angeloyl).

Alkyl is a radical containing only carbon and hydrogen atoms arranged in a chain, branched, cyclic or bicyclic structure or their combinations, having 1-18 carbon atoms. Examples include but are not limited to methyl, ethyl, propyl isopropyl, butyl, s- and t-butyl, pentyl, hexyl, heptyl, octyl, nonyl, undecyl, dodecyl, tridecyl, tetradecyl, pentadecyl, cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl.

Benzoyl alkyl substituted alkanoyl refers to straight or branched alkanoyl substituted with at least one benzoyl and at least one alkyl, wherein the benzoyl is attached to a straight or branched alkyl. An example of a benzoyl alkyl substituted alkanoyl is benzoyl methyl isobutanoyl.

A sugar moiety is a segment of molecule comprising one or more sugars or derivatives thereof or alduronic acid thereof.

Isobutyryl is a synonym of 2-Methylpropanoyl

(Y)Y3, Y and Y3 represent the same compound.

YM and (ACH-Y) represent the same compound.

Connecting moiety is a substructure or a group of atoms which connect the functional group to a core compound. Example: angeloyl group is connected by a sugar moiety to a triterpene core.

Building blocks are triterpene, acetyl, angeloyl, tigloyl, senecioyl, alkyl, dibenzoyl, benzoyl, methylbutanoyl, methylpropanoyl, alkanoyl, alkenoyl, benzoyl alkyl substituted alkanoyl, alkanoyl substituted phenyl, alkenoyl substituted phenyl, aryl, acyl, heterocylic, heteroraryl and alkenylcarbonyl

In the presented experiments, concentrations of drug that inhibit 15% cell-growth or less (i.e. 85% of control or above) as compared to the no-drug control (DMSO) are considered non-cytotoxic concentrations. In an embodiment, the concentrations of drug that inhibit 10% cell-growth or less (i.e. 90% of control or above) as compared to the no-drug control (DMSO) are considered non-cytotoxic concentrations. In an embodiment, the concentrations of drug that inhibit 5% cell-growth or less (i.e. 95% of control or above) as compared to the no-drug control (DMSO) are considered non-cytotoxic concentrations. In an embodiment, the concentrations of drug that inhibit 20% cell-

growth or less (i.e. 80% of control or above) as compared to the no-drug control (DMSO) are considered non-cytotoxic concentrations. In an embodiment, the concentrations of drug that inhibit 25% cell-growth or less (i.e. 75% of control or above) as compared to the no-drug control (DMSO) are considered non-cytotoxic concentrations. In an embodiment, the concentrations of drug that inhibit 30% cell-growth or less as compared to the no-drug control (DMSO) are considered non-cytotoxic concentrations. In an embodiment, the concentrations of drug that inhibit 45% cell-growth or less as compared to the no-drug control (DMSO) are considered non-cytotoxic concentrations.

The triterpene compound or compounds selected from this invention can be administered to a subject in need thereof, treating the subject, wherein including preventing canceror, or providing an adjuvant effect to the subject, or inhibiting the initation or promotion of cancer, or killing the cancer/tumor cells, or inhibiting cancer cell invasion. In an embodiment the compounds inhibit the activation of nuclear factor-kB, wherein inhibiting the localization or wherein binding the DNA. In an embodiment the compounds induce apoptosis in cancer cells.

Table 1 to 12, Effect of Y and YM on gene expression (Table of 1 to 12 PCT/US2008/002086, 1188-ALA-PCT, filed February 15, 2008 are incorporated herein by reference) Table 13 to 19, Effect of Y and YM on gene expression (Table of 13 to 19 PCT/US2009/034115, 1188-D-PCT, filed February 15, 2008 are incorporated herein by reference)

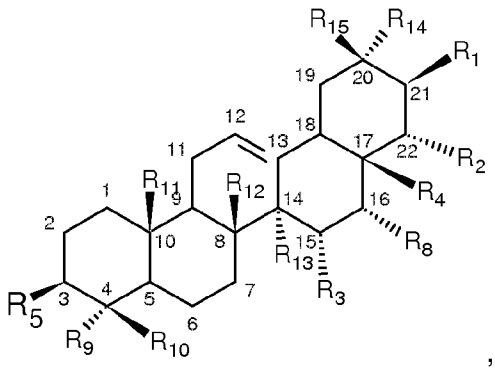
Determination of gene expression by Real-time PCR method (Brilliant QPCR, Agilent Technologies): The real-time polymerase chain reactions further confirm the results obtained from micro array analysis. The Real-time PCR results (shown below) confirmed that Compound Y3 and YM increase the expression of the genes: ANGPT2, DDIT3, LIF and NFKB1Z, wherein the results in Table 19-21 disclosed in PCT/US09/34115, filed February 13, 2009 are incorporated herein by reference.

The saponins are partially hydrolyzed into a mixture of products which can be separated by HPLC. Specific partial hydrolysis of saponins can also be achieved with enzymes. The glycosidases catalyze the hydrolysis of the glycosidic linkage. Galactosidase is an enzyme which catalyzes the hydrolysis of galactosides. Glucosidase is an enzyme

which breaks glucose from saponin. Other enzyme examples are xylanases, lactase, amylase, chitinase, sucrase, maltase, and neuraminidase.

The sugar moiety of the triterpenoid saponin (example Xanifolia Y) can be removed by acid hydrolysis. The synthetic compound of ACH-Y is obtained. ACH-Y is a triterpene with acyl groups but no sugar moiety. The acyl group of the saponin (example Xanifolia Y) can be removed by alkaline hydrolysis. The synthetic compound AKOH-Y can be obtained. AKOH-Y is a pentacyclic triterpene with sugar moieties. A pentacyclic triterpene can be obtained by acid and alkaline hydroysis of saponins from natural sources. A pentacyclic triterpene can be obtained by synthetic methods (Reference: Surendra et al., Rapid and Enantioselective Synthetic Approches to Germanicol and Other Pentacyclic Triterpenes, Journal of the American Chemical Society, 2008, 130(27), 8865-8869). Pentacyclic triterpenes with sugar moieties can also be obtained by synthesis (Reference: Ple et al., Synthesis of L-arabinopyranose containing hederagenin saponins, Tetrahedron 61 (2005) 4347-4362). Acylation is the process of adding an acyl group to a compound. The Friedel-Crafts reaction is an example of this process. An active compound can be obtained by acylating a pentacyclic triterpene. In an embodiment, acylating C21 and C22 of a pentacyclic triterpene produce compounds for inhibiting cancer invasion, cells invasion or cancer cell invasion. In an embodiment, modification of sugar moiety(ies) at C3 can affect the activities of pentacyclic triterpene, wherein the triterpene has acyl group(s), wherein the acyl group(s) may be at C21, 22, or 28. In an embodiment, a sugar moiety is at C21, 22, or 28, wherein the sugar moiety is substituted with 2 acyl groups. In an embodiment, acylating the compounds of (A), (B), (C), (D), (F), (G), (H), produce the compounds for inhibiting cancer invasion, cells invasion or cancer cell invasion; cancer metastasis; or cancer growth The building blocks in the present application are used to synthesise active saponins.

Acylating the compound (G) with angeloyl or tigloyl group gives the following compounds



,(K),

wherein R1, R2, R5, R8 represent OH or O-angeloyl; R3 represents OH, H or O-angeloyl; R4, R10 represent CH3, CH2OH or CH2Oangeloyl; R9, R11, R12, R13, R14, R15 represent CH3; or wherein R1, R2, R5, R8 represent OH or O-tigloyl; R3 represents OH, H or O- tigloyl; R4, R10 represent CH3, CH2OH or CH2O tigloyl; R9, R11, R12, R13, R14, R15 represent CH3; wherein the compounds inhibit cancer invasion, cells invasion or cancer cell invasion.

EXPERIMENTAL DETAILS

Experiment details of herb extraction, analysis of extract components by HPLC, determination of the cell-growth activity effected by Xanifolia Y with cells derived from different human organs using MTT Assay, purification of the bioactive components from plant extract, fractionation of plant extracts with FPLC, isolation of component Ys with preparative HPLC, determination of the chemical structure, cell experiments and animal studying are disclosed in PCT/US05/31900, U.S. Serial No. 11/289142, U.S. Serial 10/906303, U.S. Serial No. 11/131551 and U.S. Serial Nos.11/683198, filed on March 7, 2007, PCT/US2007/077273, filed August 30, 2007, U.S. Serial No. 60/890380, filed on February 16, 2007, U.S. Nos. 60/947,705, filed on July 3, 2007, PCT/US2008/002086, 1188-ALA-PCT, filed February 15, 2008, App'l No. PCT/US09/34115, filed February 13, 2009, the contents of which are incorporated herein by reference. Experiments 1-23 of PCT/US2008/002086, 1188-ALA-PCT, filed February 15, 2008 are incorporated herein by reference.

Experiment 1: Removal of the sugar moiety from saponin by acid hydrolysis

15mg saponin was dissolved in 1ml of Methanol. 1ml of 2N HCl was then added. The mixture was refluxed in 80C water bath for 5 hours. The solution was then neutralized by adding 2ml of 1N NaOH (to final pH 4-6). The aglycone was then extracted with ethylacetate 3ml x 2. The extracts were collected and pooled. Further isolation of aglycone (sugar-removed saponin) was achieved by HPLC with isocratic elution of 80-100% acetonitrile.

Experiment 2: Removal of the acyl group by alkaline hydrolysis

Methods: 20mg of saponin was dissolved in 0.5ml of 1N NaOH. The solution was incubated in 80C water bath for 4 hours. It was cooled to room temperature before neutralized with 0.5ml 1N HCl (adjust pH to about 3). The mixture was extracted with 2 ml 1-butanol 3 times. The butanol fractions were collected and lyophilized. The

hydrolyzed saponin with further purified with HPLC in a C-18 column eluted with 25% acetonitrile.

Experiment 3: Adding the acyl group to triterpene by esterification

Method: 40 mg of triterpene core (fraction IV) was dissolved in 1 ml pyridine in a 50 ml tube. Reaction is started by adding 0.2 ml of acyl chloride (Tigloyl chloride or angeloyl chloride). The mixture is stirred for 3 days at room temperature. At the end of reaction, 3 ml of NaHCO3 is slowly added to the reaction mixture. The solution is then extracted 3 times with 10 ml of ethyl acetate which is then evaporated under vacuum and at 45C and lyophilization. The reaction product is dissolved in 80% acetonitrile – 0.005% Trifluoroacetic acid. The active esterification products are purified with HPLC.

Experiment 4: Inhibition of cell invasion by Xanifolia Y10

Method: The BD BioCoatTM MatrigelTM Invasion Chamber system provides cells with the conditions that allow assessment of their invasive property in vitro.

A. Growth curves of ES2 cells:

1. ES2 cells (10K per well) were seeded in a 96-wells plate overnight.
2. Cultures were replaced with medium containing Saponin Y10 (0, 5, 7.5 and 10ug/ml).
3. Growth of cells was determined with MTT assay after 1, 2 and 3 days of cultures.

Results: (also see Figure 1)

1. After 24 hours, the growth of ES2 cells is inhibited in the presence of Y10.
2. The degree of inhibition increases with doses of Y10.
3. There are no dead cells observed with less than 10 ug/ml of Y10.
4. Accordingly, 10 ug/ml of Y10 or less is non-cytotoxic.

B. Invasion assay:

1. The Matrigel system consists of an upper chamber which is separated from the lower chamber with a membrane and a thin layer of reconstituted basement membrane (BD BioCoatTM MatrigelTM invasion Chamber system).
2. Both upper and lower chambers contain RPMI1640 medium with 10% FBS and SaponinY10 (0.8ug/ml). For controls, DMSO was used instead of saponin Y10.
3. Equal numbers (10K or 20K per well) of ES2 cells were applied into the upper chambers of all wells (for both drug- and DMSO-treated).

4. After 23 hours of incubation, invasive ES2 cells that passed through the membrane (and attached at the bottom of membrane) were fixed (methanol), stained (1% Toluidine Blue) and counted.

Results:

Number of Cells applied to chamber 20K

	Number of cells which passed through the membrane	
DMSO	312	
DMSO	184	
DMSO	313	
	270	Average
Y10 (8ug/ml)	22	
Y10 (8ug/ml)	31	
Y10 (8ug/ml)	17	
	23	Average
	9	% Y treated cells passed membrane

The invasion assay experiments were repeated 5 times.

The results of experiments for % Y treated cells passed membrane are 7%, 9%, 22%, 25%, 28%

1. It was found that ES2 cells are invasive in control DMSO samples.
2. It was found that cells treated with saponin Y10 lost invasion ability.
3. At a non-cytotoxic concentration of 8 ug/ml, averaging of 5 experiments, 18% cells (compared to DMSO control) passed through the membrane, giving an 82% inhibition of cell invasion.

Experiment 5: Inhibition of invasion in ES2 cells (ovary) by Xanifolia (drugs)

(A) Determination of drug concentration used in Invasion Assay:

Purpose: To determine the non-cytotoxic concentrations of individual drugs that are used for the invasion assay.

Methods: Human cancer cells (from ovary, bladder, lung, brain, skin, prostate, bone, kidney, cervix and pancreas) were exposed to different drug concentrations for 1 and 2 days. The growth of cells was measured by MTT assay.

Result presentation: The optical density (O.D.) of the MTT product (formazan) reflecting cell growth in cells after drug-treatment of day 0, 1 and 2 were measured and plotted

(growth curves). Concentrations of drug that inhibit 15% cell-growth or less (i.e. 85% of control or above) as compared to the no-drug control (DMSO) are considered non-cytotoxic concentrations. .

Procedure:

1. Cells (5-10K per well) were seeded in a 96-wells plate overnight.
2. Culture medium was replaced with fresh medium containing different drugs (Xanifolia).
3. The drug concentrations selected depends on the xanifolia-Y being used (from 6 to 30ug/ml).
4. DMSO was used as the no-drug control.
5. Cells were incubated for 1 and 2 days.
6. Cell growth was measured with MTT assay after 0, 1 or 2 days of incubation. To measure cell growth, the cell cultures were incubated with MTT (3-[4, 5-Dimethylthiazol-2-yl]-2, 5-diphenyl-tetrazolium bromide) (0.5 mg/ml) for 1 h and the formazan formed was dissolved with DMSO. The optical density (O.D.) of formazan at 490 nm was measured.
7. The O.D. of samples was plotted against the time (days) of incubation (Growth curves).

Summary of Growth Curves studies of cells with MTT assay

Cells	ES2
Medium	RPMI 1640
# cells per well	10K
Days of incubation	1 to 2

Results:

Based on the growth curves, the concentration of drugs that has no effect on cell growth or reduces 15% or less of control, after 1 day incubation are listed in the following table. These drug concentrations (ug/ml) (or less) are considered as non-cytotoxic are then employed in the invasion assay (Matrigel).

Drug	X	Y0	Y1	Y3	Y7	ACH-Y3	AKOH-Y3	bES	M10
ug/ml	10	10	10	6	10	15	30	20	10

(B) Determination of cell invasion by Matrigel assay:

Methods:

1. The Matrigel system consists of an upper and a lower chamber which is separated with a membrane containing a thin layer of reconstituted basement membrane materials (BD BioCoatTM MatrigelTM invasion Chamber system).
2. Both upper and lower chambers were filled with specific culture medium (according to the requirement of individual cell lines) also containing 10% FBS.
3. Three to five chambers were used per sample in which different drug (xanifolia-Ys) was added in both upper and lower chambers.
4. A non-cytotoxic drug concentration (determined by the growth curves) was employed in this assay. DMSO was used as the non-drug control.
5. Equal numbers (usually 20K per well) of cells were applied into the upper chamber.
6. After 24 hours of incubation, invasive cells that passed through the membrane from the upper chamber to the lower chamber and attached at the bottom of membrane were fixed (with methanol), then stained (with 1% Toluidine Blue), air dry and their numbers were counted.
7. The percentage of invasive cells (as compared to DMSO control) was calculated.

Results:

The percentage of cells (compared to control) that passed the membrane at certain drug concentration is listed in the table.

Summary of Matrigel invasion studies

Cells: ES2 (ovary)

Cell concentration per cup (3 cups per sample): 20K

Incubation time: 1 day

Xanifolia or DMSO	concentration (ug/ml)	% cells passed membrane compared to DMSO	p value compared to DMSO
DMSO	10	100	
X	10	42.4	0.047
Y0	10	28.1	0.063
Y1	10	47.6	0.023
Y3	10	14.2	0.004
Y7	10	27.2	0.009
ACH-Y	10	26.2	0.01
AKOH-Y	160	70.7	0.03
bES	20	52.9	0.002

M10	10	13	0.003

Results:

1. Most of the xanifolia drugs are effective at inhibiting ES2 cells invasion activity.
2. Y3 and M10 are the most potent, only 13-14 % cells (compare to control) passed the membrane at drug concentration 10ug/ml.
3. Y7, Y0 and ACH-Y are next in potency; X, Y1and bES are less effective.
4. AKOH is not effective. Even with 160 ug/ml of the drug, 70% of cells passed the membrane.

Experiment 6: Inhibition of invasion in TB9 cells (bladder) by Xanifolia (Drug)

Method and procedures are same as experiment 5

Summary of Growth Curves studies of cells with MTT assay

Cells	TB9
Medium	RPMI 1640
# cells per well	10K
Days of incubation	2
Concentration of xanifolia-Y	0, 5 and 10 ug/ml

Results and conclusion:

Based on the growth curves, the concentration (ug/ml) of individual drugs that does not affect cell growth or reduces less than 15% of control growth, after 1 day of incubation are:

Drug	X	Y0	Y1	Y3	Y7	ACH-Y3	AKOH-Y3	bES	M10
ug/ml	10	10	10	5	10	10	80	10	5

Summary of Matrigel invasion studies

Cells: TB9 (bladder)

Cell concentration per cup (3 cups per sample): 20K

Incubation time: 1 day

Xanifolia or DMSO	concentration (ug/ml)	% cells passed membrane compared to DMSO	p value compared to DMSO
DMSO		100	
X	10	29	0.0148
Y0	10	7.7	0.0022
Y1	10	7.7	0.0021
Y3	5	6.6	0.0009

Y7	10	6.1	0.0002
ACH-Y	10	2.7	0.0007
AKOH-Y	80	93.1	0.37
bES	10	62.6	0.0434
M10	5	13.2	0.0012

Results:

1. The results show that Y0, Y1, Y3, Y7, M10, ACH-Y3, and X are effective at inhibiting TB9 cells' invasion activity.
2. AKOH is not effective. At drug concentration 80 ug/ml, 93% cells (compared to control) passed the membrane.

Experiment 7: Inhibition of invasion in H460 cells (Lung) by Xanifolia (Drug)

Method and procedures are same as experiment 5

Cells	H460 (Lung)
Medium	RPMI 1640
# cells per well	5K
Days of incubation	2
Concentration of drug	0, 5, 10 and 15 ug/ml

Results and conclusion:

Based on the growth curves, the concentration of individual drugs that does not affect the cell growth or reduces less than 15% of control growth, after 1 day of incubation are:

Drug	X	Y0	Y1	Y3	Y7	ACH-Y3	AKOH-Y3	bES	M10
ug/ml	15	10	15	10	15	10	120	15	10

Summary of Matrigel invasion studies

Cells: H460 (Lung)

Cell concentration per cup (3 cups per sample): 25K

Incubation time: 2 days

Xanifolia(Drug) or DMSO	concentration (ug/ml)	% cells passed membrane compared to DMSO	p value compared to DMSO
DMSO		100	
X	10	48	0.004
Y0	10	18	0.0003
Y1	10	28	0.001

Y3	10	21	0.032
Y7	15	20	0.0003
ACH-Y	10	8	0.0004
AKOH-Y	10	114	0.383
bES	15	77	0.09
M10	10	11	0.0002

Results:

1. The drug concentration and the percentage of cells (compared to control) that passed the membrane are listed in the table.
2. Y0, Y1, Y3, Y7, ACH-Y and M10 are effective at inhibiting H460 cells invasion. X and bES are less effective.
3. AKOH is not effective.

Experiment 8: Inhibition of invasion in T98G cells (brain) by Xanifolia (Drug)

Method and procedures are same as experiment 5

Cells	T98G (brain)
Medium	MEM eagle's Plus
# cells per well	5K
Days of incubation	2
Concentration of drug	0, 5, 10 and 15 ug/ml

Results and conclusion:

Based on the growth curves, the concentration of individual drugs that does not affect the cell growth or reduces less than 15% of control growth, after 1 day of incubation are:

Drug	X	Y0	Y1	Y3	Y7	ACH-Y3	AKOH-Y3	bES	M10
ug/ml	15	15	15	10	15	10	120	15	10

Summary of Matrigel invasion studies

Cells: T98G (brain)

Cell concentration per cup (3 cups per sample): 20K

Incubation time: 1 day

Xanifolia(Drug) or DMSO	concentration (ug/ml)	% cells passed membrane compared to DMSO	p value compared to DMSO
DMSO		100	
X	15	32	0.02

Y1	15	45	0.07
Y3	10	22	0.02
Y7	15	35	0.03
ACH-Y	10	15	0.01
AKOH-Y	16	85	0.32
M10	10	12	0.02

Results:

1. The drug concentration and the percentage of cells (compared to control) that passed the membrane are listed in table.
2. These results indicate that X, Y1, Y3, Y7, ACH-Y and M10 inhibit T98G cell invasion activity.
3. AKOH is not effective.

Experiment 9: Inhibition of invasion in SK-MEL5 cells (skin) by Xanifolia (Drug)

Method and procedures are same as experiment 5

Cells	SK-MEL5 cells (skin)
Medium	MEM eagle's Plus
# cells per well	5K
Days of incubation	2
Concentration of drug	0, 5, 10 and 15 ug/ml

Results and conclusion:

Base on the growth curves, the concentration of individual drugs that does not affect the cell growth or reduces less than 15% of control growth, after 1 day of incubation are:

Drug	X	Y0	Y1	Y3	Y7	ACH-Y3	AKOH-Y3	bES	M10
ug/ml	10	10	10	5	10	5	15	15	10

Summary of Matrigel invasion studies

Cells: SK (skin)

Cell concentration per cup (3 cups per sample): 20K

Incubation time: 2 days

Xanifolia(Drug) or DMSO	concentration (ug/ml)	% cells passed membrane compared to DMSO	p value compared to DMSO
DMSO		100	
X	10	62.2	0.023
Y0	10	31.9	0.006

Y1	10	52.2	0.007
Y3	5	28.6	0.0003
ACH-Y	10	19.1	0.001
AKOH-Y	10	106.4	0.43
bES	10	54.1	0.011
M10	5	37.3	0.0012

Results:

1. The drug concentration and the percentage of cells (compared to control) that passed the membrane are listed in table.
2. It is concluded that X, Y0, Y1, Y3, ACH-Y, bES and M10 inhibit SK cells invasion activity with various degree of potency.
3. AKOH-Y has no significant effect.

Experiment 10: Inhibition of invasion in DU145 cells (Prostate) by Xanifolia(Drug)

Method and procedures are same as experiment 5

Cells	DU145 cells (Prostate)
Medium	McCoy 5A
# cells per well	5K
Days of incubation	2
Concentration of drug	0, 5,10 and 15 ug/ml

Results and conclusion:

Based on the growth curves, the concentration of individual drugs that does not affect the cell growth or reduces less than 15% of control growth, after 1 day of incubation are:

Drug	X	Y0	Y1	Y3	Y7	ACH-Y3	AKOH-Y3	bES	M10
ug/ml	15	15	15	10	15	10	15	15	10

Summary of Matrigel invasion studies

Cells: DU145 (prostate)

Cell concentration per cup (3 cups per sample): 20K

Incubation time: 2 days

Xanifolia(Drug) or DMSO	concentration (ug/ml)	% cells passed membrane compared to DMSO	p value compared to DMSO
DMSO		100	
X	15	9.1	0.0001

Y3	10	18	0.03
ACH-Y3	10	5.4	0.0009
M10	10	40	0.062

Results:

1. The drug concentration and the percentage of cells (compared to control) that passed the membrane are listed in table.
2. It is concluded that X, Y3, ACH-Y and M10 inhibit invasion of DU145 cells.

Experiment 11: Inhibition of invasion in U2OS cells (bone) by Xanifolia (Drug)

Method and procedures are same as experiment 5

Cells	U2OS (bone)
Medium	McCoy 5A
# cells per well	5K
Days of incubation	2
Concentration of drug	0, 5, 10 and 15ug/ml

Results and conclusion:

Based on the growth curves, the concentration of individual drugs that does not affect the cell growth or reduces less than 15% of control growth, after 1 day of incubation are:

Drug	**X**	**Y0**	**Y1**	**Y3**	**Y7**	**ACH-Y3**	**AKOH-Y3**	**bES**	**M10**
ug/ml	**5**	**10**	**10**	**5**	**10**	**10**	**10**	**20**	**10**

Summary of Matrigel invasion studies

Cells: U2OS (bone)

Cell concentration per cup (3 cups per sample): 20K

Incubation time: 1 day

Xanifolia(Drug) or DMSO	concentration (ug/ml)	% cells passed membrane compared to DMSO	p value compared to DMSO
DMSO		100	
X	5	47	0.017
Y0	10	27	9E-04
Y1	10	27	0.001
Y3	5	12	0.0007
Y7	10	31	0.007
ACH-Y	10	12	0.042

AKOH-Y	10	172	0.013
bES	20	0.6	0.0003
ES-core	20	74	0.0753
M10	5	30	0.0003
M10	10	0	0.01

Results:

1. It is concluded that X, Y0, Y1, Y3, Y7, ACH-Y, bES and M10 inhibit invasion of U2OS cells
2. AKOH-Y and ES-core have no significant effect.

Experiment 12: Inhibition of invasion in A498 cells (kidney) by Xanifolia(Drug)

Method and procedures are same as experiment 5

Cells	**A498 cells (kidney)**
Medium	MEM
# cells per well	5K
Days of incubation	2
Concentration of drug	0, 5, 10 and 15 ug/ml

Results and conclusion:

Based on the growth curves, the concentration of individual drugs that does not affect the cell growth or reduces less than 15% of control growth, after 1 day of incubation are:

Drug	**X**	**Y0**	**Y1**	**Y3**	**Y7**	**ACH-Y3**	**AKOH-Y3**	**bES**	**M10**
ug/ml	**15**	**20**	**15**	**10**	**20**	**15**	**20**	**20**	**15**

Summary of Matrigel invasion studies

Cells: A498 cells (kidney)

Cell concentration per cup (3 cups per sample): 20K

Incubation time: 1 day

Xanifolia(Drug) or DMSO	concentration (ug/ml)	% cells passed membrane compare to DMSO	p value compare to DMSO
DMSO		100	
X	15	29	0.04
Y0	20	28	0.036
Y1	15	9.4	0.002
Y3	10	13.8	0.002
Y7	20	0	0
ACH-Y	15	23.4	0.004

AKOH-Y	20	92	0.397
bES	20	11.7	0.002
M10	15	0	0

Results:

1. It is concluded that X, Y0, Y1, Y3, ACH-Y, and bES inhibit invasion of A498 cells
2. Y7 and M10 have 100% inhibition at the stated concentrations.
3. AKOH-Y has no significant effect.

Experiment 13: Inhibition of invasion in HeLa cells (cervix) by Xanifolia(Drug)

Method and procedures are same as experiment 5

Cells	HeLa cells (cervix)
Medium	MEM
# cells per well	5K
Days of incubation	2
Concentration of xanifolia-Y	0, 10, 15 and 20ug/ml

Results and conclusion:

Based on the growth curves, the concentration of individual drugs that does not affect the cell growth or reduces less than 15% of control growth, after 1 day of incubation are:

Drug	**X**	**Y0**	**Y1**	**Y3**	**Y7**	**ACH-Y3**	**AKOH-Y3**	**bES**	**M10**
ug/ml	**20**	**20**	**20**	**15**	**15**	**10**	**20**	**20**	**10**

Summary of Matrigel invasion studies

Cells: HeLa cells (cervix)

Cell concentration per cup (3 cups per sample): 25K

Incubation time: 3 day

Xanifolia(Drug) or DMSO	concentration (ug/ml)	% cells passed membrane compared to DMSO	p value compared to DMSO
DMSO		100	
X	20	5	0.0005
ACH-Y	10	13	0.0006
AKOH-Y	20	98	0.487
bES	20	52	0.013
M10	10	8	0.003

Results:

1. It is concluded that X, ACH-Y, bES and M10 inhibit invasion of HeLa cells
2. AKOH-Y has no significant effect.

Experiment 14: Inhibition of invasion in Capan cells (pancreas) by Xanifolia (Drug)

Method and procedures are same as experiment 5

Cells	Capan cells (pancreas)
Medium	RPMI
# cells per well	5K
Days of incubation	2
Concentration of drug	0, 5, 10 and 15ug/ml

Results and conclusion:

Based on the growth curves, the concentration of individual drugs that does not affect the cell growth or reduces less than 15% of control growth, after 1 day of incubation are:

Drug	X	Y0	Y1	Y3	Y7	ACH-Y3	AKOH-Y3	bES	M10
ug/ml	15	15	15	10	15	15	15	15	10

Summary of Matrigel invasion studies

Cells: Capan cells (pancreas)

Cell concentration per cup (3 cups per sample): 50K

Incubation time: 3 day

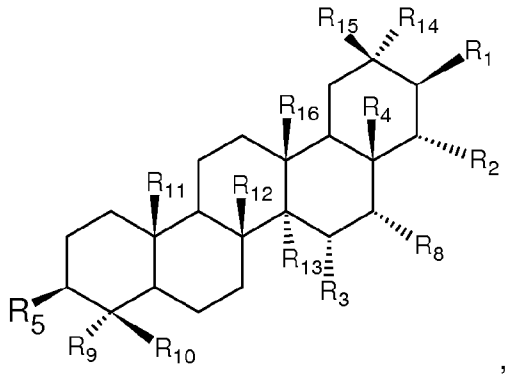
Xanifolia(Drug) or DMSO	concentration (ug/ml)	% cells passed membrane compared to DMSO	p value compared to DMSO
DMSO		100	
X	15	29	0.002
Y1	15	29	0.014
Y3	5	16	0.0007
Y7	15	13	0.0005
ACH-Y	15	2	0.00032
AKOH-Y	15	72	0.028
M10	10	17	0.00061

Results:

1. It is concluded that X, Y1, Y3, Y7, ACH-Y, AKOH and M10 inhibit Capan cells invasion activity.
2. AKOH has no significant effect.

What is claimed is:

1. A use of compound for the manufacture of medicament for inhibiting cancer invasion, cell invasion or cancer cell invasion, with an effective amount of an isolated, purified or synthesized compound, or its salt, or ester thereof, selected from the formula:



, also named (1E), wherein

R1 is selected from hydrogen, hydroxyl, O-angeloyl, O-tigloyl, O-senecioyl, O-alkyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-alkanoyl substituted phenyl, O-alkenoyl substituted phenyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, and derivatives thereof;

R2 is selected from hydrogen, hydroxyl, O-angeloyl, O-tigloyl, O-senecioyl, O-alkyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-alkanoyl substituted phenyl, O-alkenoyl substituted phenyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, and derivatives thereof;

R4 represents CH3, CHO, CH_2R6 or COR6, wherein R6 is selected from hydroxyl, O-angeloyl, O-tigloyl, O-senecioyl, O-alkyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-alkanoyl substituted phenyl, O-alkenoyl substituted phenyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, and derivatives thereof; R3 is H or OH; R8 is H or OH; R16 is H ,or R4 and R16 may form an oxygen bridge with divalent radical formula of –CH2-O-, CH(OH)-O- or C(=O)-O-, wherein the –O- may be replaced with –NH- or – S - ; wherein when the C12-13 of ring 3 of the triterpene has a double bond then R16 is absent; R5 is a hydrogen, hydroxyl, heterocyclic or O-sugar moiety(ies), wherein the sugar moiety(ies) is/are selected from a group consisting of glucose, galactose, rhamnose, arabinose, xylose, fucose, allose, altrose, gulose, idose, lyxose, mannose, psicose, ribose, sorbose, tagatose, talose, fructose, alduronic acid, glucuronic acid, galacturonic acid, and derivatives or combination thereof; wherein R9, R10, R11, R12, R13, R14, R15 are independently attached a group selecting from CH_3, CH_2OH, CHO, COOH, COO-alkyl, COO-aryl, COO-

heterocyclic, COO-heteroaryl, CH_2Oaryl, CH_2O- heterocyclic, CH_2O- heteroaryl, alkyls group, hydroxyl, acetyl group; wherein at least two of R1, R2 and R6 are compriseing a group selected from O-angeloyl, O-tigloyl, O-senecioyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, and derivatives thereof; or at least one of R1, R2, and R4 is a sugar moiety substituted with at least two groups selected from a group consisting of angeloyl, acetyl, tigloyl, senecioyl, benzoyl, dibenzoyl, alkanoyl, alkenoyl, benzoyl alkyl substituted alkanoyl, aryl, acyl, heterocylic, heteroraryl, and a derivative thereof; or wherein R4 is CH_2R6, wherein R1 and R2 independently consists an O-angeloyl group, or at least two of R1, R2 and R6 are O-angeloyl or at least one of R1, R2 or R6 is a sugar moiety with two O-angeloyls; or wherein R5 is/are a hydrogen, hydroxyl, O-sugar moiety(ies) wherein the sugar moiety(ies) selected from the following sugars and alduronis acids: glucose, galactose, rhamnose, arabinose, xylose, fucose, allose, altrose, gulose, idose, lyxose, mannose, psicose, ribose, sorbose, tagatose, talose, fructose, glucuronic acid, galacturonic acid; or their derivatives thereof, or the combination thereof; wherein the sugar preferably comprises glucuronic acid, arabinose and galactose; or wherein R5 is/are sugar moiety(ies) selected from a group consisting of glucose, galactose, arabinose, alduronic acid, glucuronic acid, galacturonic acid, and a derivative or combination thereof.

2. The use of claim 1, wherein at least one of R1 and R2 of the compound is selected from O-acetyl, O-angeloyl, O-tigloyl, O-senecioyl, O-dibenzoyl, and O-benzoyl, or at least one of R1 and R2 is a sugar moiety substituted with two groups selecting from acetyl, angeloyl, tigloyl, senecioyl, dibenzoyl, benzoyl; R5 is a hydrogen or sugar moiety(ies), wherein the sugar moiety(ies) is/are selected from a group of glucose, galactose, arabinose and derivatives thereof, wherein the derivatives are acid, ester and salt.

3. The use of claim 1, wherein R5 is a hydroxyl.

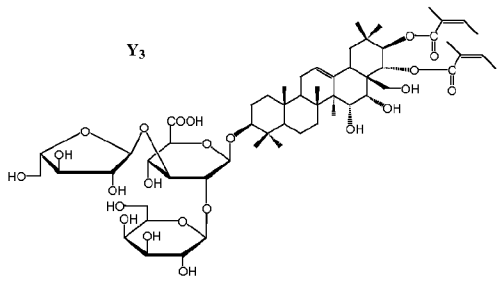
4. The use of claim 1, wherein the cancer is selected from breast cancer, leukocytic cancer, liver cancer, ovarian cancer, bladder cancer, prostatic cancer, skin cancer, bone cancer, brain cancer, leukemia cancer, lung cancer, colon cancer, CNS cancer, melanoma cancer, renal cancer, cervical cancer, esophageal cancer, testicular cancer, spleenic cancer, kidney cancer, lymphhatic cancer,

pancreatic cancer, stomach cancer and thyroid cancer; wherein the cell is selected from breast cell, leukocytic cell, liver cell, ovarian cell, bladder cell, prostatic cell, skin cell, bone cell, brain cell, leukemia cell, lung cell, colon cell, CNS cell, melanoma cell, renal cell, cervical cell, esophageal cell, testicular cell, spleenic cell, kidney cell, lymphhatic cell, pancreatic cell, stomach cell and thyroid cell.

5. The use of claim 1, wherein inhibiting cancer invasion, cell invasion, cancer cell invasion, includes increasing expression of the genes of DDIT3, LIF and NFKB1Z.

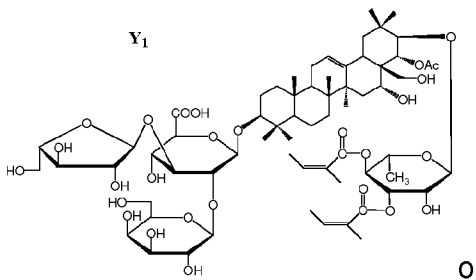
6. The use of claim 1, wherein the compound is selected from the following:

a) An isolated, purified or synthesized compound having structure Xanifolia(Y),



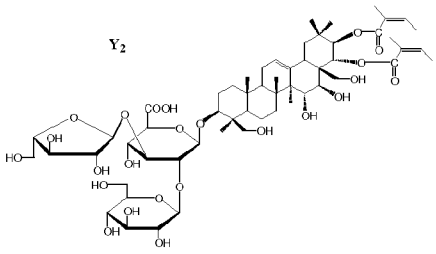
or chemical name: 3-O-[β-D-galactopyranosyl (1→2)]-α-L-arabinofuranosy (1→3)-β-D-glucuronopyranosyl-21,22-O-diangeloyl-3β, 15α, 16α, 21β, 22α, 28-hexahydroxyolean-12-ene;

b) An isolated, purified or synthesized compound having structure Xanifolia (Y1),



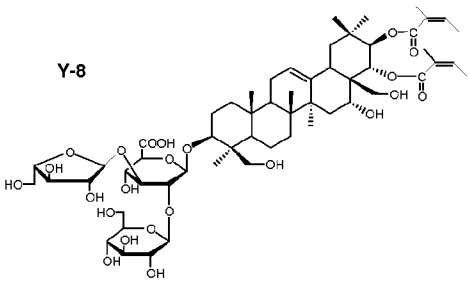
or chemical name: 3-O-[β-D-galactopyranosyl (1→2)]-α-L-arabinofuranosyl (1→3)-β-D-glucuronopyranosyl-21-O-(3,4-diangeloyl)-α-L-rhamnophyranosyl-22-O-acetyl-3β,16α, 21β, 22α, 28-pentahydroxyolean-12-ene;

c) An isolated, purified or synthesized compound having structure Xanifolia (Y2),



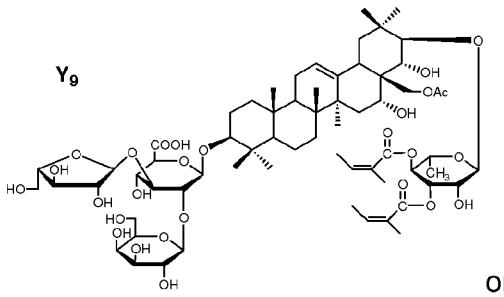
or chemical name: 3-O-[β-D-glucopyranosyl-(1→2)]-α-L-arabinofuranosy (1→3)-β-D-glucuronopyranosyl-21,22-O-diangeloyl-3β, 15α, 16α, 21β, 22α, 24β, 28-heptahydroxyolean-12-ene;

d) An isolated, purified or synthesized compound having structure Xanifolia (Y8),



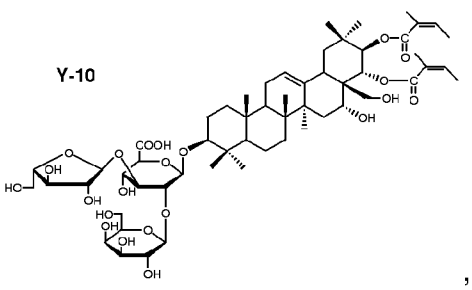
or chemical name: 3-*O*-[*β*-glucopyranosyl (1→2)]-*α*-arabinofuranosyl (1→3)-*β*-glucuronopyranosyl-21, 22-*O*-diangeloyl-3*β*, 16*α*, 21*β*, 22*α*, 24*β*, 28-hexahydroxyolean-12-ene;

e) An isolated, purified or synthesized compound having structure Xanifolia (Y9),



or chemical name: 3-*O*-[*β*-galactopyranosyl (1→2)]-*α*-arabinofuranosyl (1→3)-*β*-glucuronopyranosyl-21-*O*-(3,4-diangeloyl)-*α*-rhamnopyranosyl-28-*O*-acetyl-3*β*, 16*α*, 21*β*, 22*α*, 28-pentahydroxyolean-12-ene; and

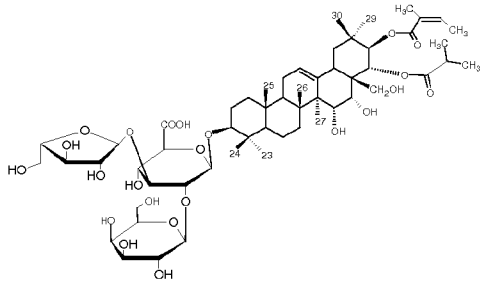
f) An isolated, purified or synthesized compound having structure Xanifolia (Y10),



, or chemical name:

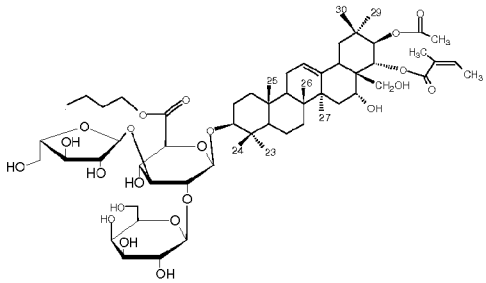
3-*O*-[*β*-galactopyranosyl (1→2)]-*α*-arabinofuranosyl (1→3)-*β*-glucuronopyranosyl-21, 22-*O*-diangeloyl-3*β*, 16*α*, 21*β*, 22*α*, 28-pentahydroxyolean-12-ene.

g) An isolated, purified or synthesized compound having structure Xanifolia (Y0),



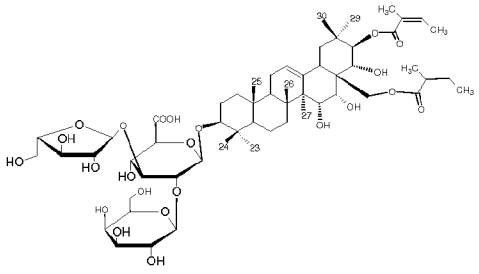
, or chemical name: 3-O-[β-D-galactopyranosyl(1→2)]-α-L-arabinofuranosyl(1→3)-β-D-glucuronopyranosyl-21-O-angeloyl, 22-O-(2-methylpropanoyl)-3β, 15α, 16α, 21β, 22α, 28-hexahydroxyolean-12-ene,

h) An isolated, purified or synthesized compound having structure Xanifolia (X),



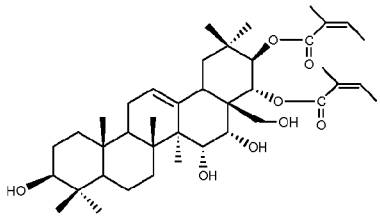
, or chemical name: 3-*O*-{[*β*-D-galactopyranosyl (1→2)]-[*α*-L-arabinofuranosyl (1→3)]- *β*-D-glucuronopyranoside butyl ester}-21-*O*-acetyl-22-*O*- angeloyl- 3*β*,16*α*,21*β*,22*α*,28-pentahydroxyolean-12-ene.

i) An isolated, purified or synthesized compound having structure (Y7),

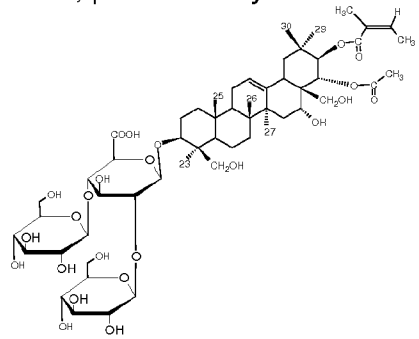


, or chemical name: 3-*O*-[*β*-D-galactopyranosyl-(1→2)]-*α*-L-arabinofuranosyl-(1→3)-*β*-D--glucuronopyranosyl-21-*O*-angeloyl-28-*O*-2-methylbutanoyl-3*β*, 15 *α*, 16*α*, 21*β*, 22*α*, 28-hexahydroxyolean-12-ene

j) An isolated, purified or synthesized compound having structure (ACH-Y):



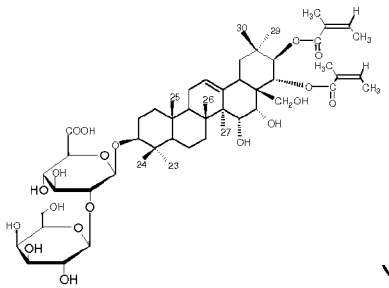
k) An isolated, purified or synthesized compound having structure:



or chemical name:

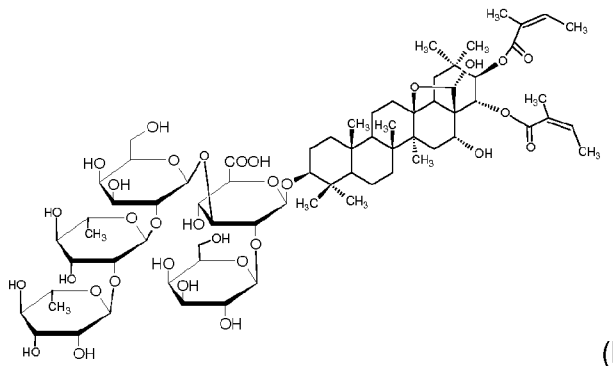
3-*O*-[*β*-glucopyranosyl (1→2)]- *β*-arabinofuranosyl (1→4)-*β*- glucuronopyranosyl -21-*O*-angeloyl-22-O-acteyl-3*β*, 16*α*, 21*β*, 22*α*, 24*β*, 28-hexahydroxyolean-12-ene;

(l) An isolated, purified or synthesized compound having structure:



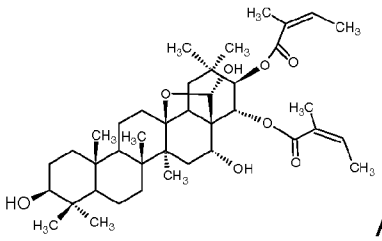
Y5

(m) An isolated, purified or synthesized compound having structure:



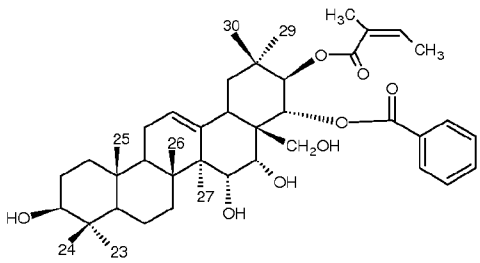
(M10) ,

(n) An isolated, purified or synthesized compound having structure:



ACH-M10

(o) An isolated, purified or synthesized compound having structure:



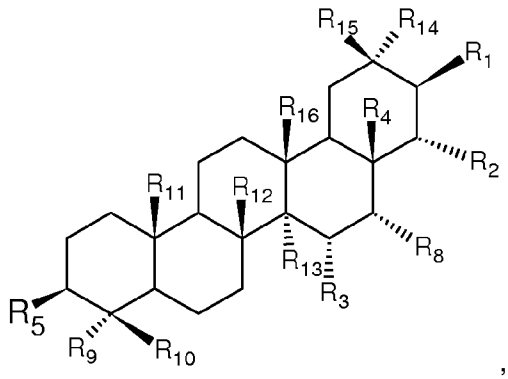
ACH-Z4

7. The use of claim 1, further comprising a pharmaceutically acceptable carrier or diluent.

8. The use of claim 1, wherein the said compound is present in a concentration of 0.01 ug/ml to 40ug/ml, or wherein said compound is present in a concentration of 0.01 ug/ml to 30ug/ml, or wherein said compound is present in a concentration of 0.01 ug/ml to 10ug/ml, or wherein said compound is present in a concentration of 0.01 ug/ml to 5ug/ml, or wherein said compound is present in a concentration of 5 ug/ml to 10ug/ml, or wherein said compound is present in a concentration of 0.1 ug/ml to 5ug/ml, or wherein said compound is present in a concentration of 0.1 ug/ml to 7.5ug/ml, or wherein said compound is present in a concentration of 0.1 ug/ml to 10ug/ml, or wherein said compound is present in a concentration of 0.1 ug/ml to 15ug/ml, or wherein said compound is present in a concentration of 0.1 ug/ml to 20ug/ml, or wherein said compound is present in a concentration of 0.1 ug/ml to 30ug/ml, or wherein said compound is present in a concentration of 1 ug/ml to 5ug/ml, or wherein said compound is present in a concentration of 1 ug/ml to 7.5ug/ml, or wherein said compound is present in a concentration of 1 ug/ml to 10ug/ml, or wherein said compound is present in a concentration of 1 ug/ml to 15ug/ml, or wherein said compound is present in a concentration of 1 ug/ml to 20ug/ml, or wherein said compound is present in a concentration of 1 ug/ml to 30ug/ml, or wherein said compound is present in a concentration of 3 ug/ml to 5ug/ml, or wherein said compound is present in a concentration of 3 ug/ml to 7.5ug/ml, or wherein said compound is present in a concentration of 3 ug/ml to 10ug/ml, or wherein said compound is present in a concentration of 3

ug/ml to 15ug/ml, or wherein said compound is present in a concentration of 3 ug/ml to 20ug/ml, or wherein said compound is present in a concentration of 3 ug/ml to 30ug/ml; or present in a concentration of 4 ug/ml to 5ug/ml, or wherein said compound is present in a concentration of 4 ug/ml to 7.5ug/ml, or wherein said compound is present in a concentration of 4 ug/ml to 10ug/ml, or wherein said compound is present in a concentration of 4 ug/ml to 15ug/ml, or wherein said compound is present in a concentration of 4 ug/ml to 20ug/ml, or wherein said compound is present in a concentration of 4 ug/ml to 30ug/ml, or present in a concentration of 5 ug/ml to 8ug/ml, or wherein said compound is present in a concentration of 5 ug/ml to 9ug/ml, or wherein said compound is present in a concentration of 5 ug/ml to 10ug/ml, or wherein said compound is present in a concentration of 5 ug/ml to 15ug/ml, or wherein said compound is present in a concentration of 5 ug/ml to 20ug/ml, or wherein said compound is present in a concentration of 5 ug/ml to 30ug/ml, or present in a concentration of 7 ug/ml to 8ug/ml, or wherein said compound is present in a concentration of 7 ug/ml to 9ug/ml, or wherein said compound is present in a concentration of 7 ug/ml to 10ug/ml, or wherein said compound is present in a concentration of 7 ug/ml to 15ug/ml, or wherein said compound is present in a concentration of 7 ug/ml to 20ug/ml, or wherein said compound is present in a concentration of 7 ug/ml to 30ug/ml; or wherein administration is by intravenous drip: 0.003-0.03mg/kg body weight of compound dissolved in 250ml of 10% glucose solution or in 250ml of 0.9% NaCl solution, or by intravenous injection: 0.003-0.03mg/kg body weight per day of compound dissolved in 10-20ml of 10% glucose solution or of 0.9% NaCl solution, or 0.01-0.03mg/kg body weight of compound dissolved in 250ml of 10% glucose solution or in 250ml of 0.9% NaCl solution, or by intravenous injection: 0.01-0.03mg/kg body weight per day of compound dissolved in 10-20ml of 10% glucose solution or of 0.9% NaCl solution, or 0.01-0.05mg/kg body weight of compound dissolved in 250ml of 10% glucose solution or in 250ml of 0.9% NaCl solution, or by intravenous injection: 0.01-0.05mg/kg body weight per day of compound dissolved in 10-20ml of 10% glucose solution or of 0.9% NaCl solution.

9. A method for inhibiting cancer invasion, cell invasion or cancer cell invasion, comprising contacting said cell with an effective amount of an isolated, purified or synthesized compound, or its salt, or ester thereof, selected from the formula:



, also named (1E), wherein

R1 is selected from hydrogen, hydroxyl, O-angeloyl, O-tigloyl, O-senecioyl, O-alkyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-alkanoyl substituted phenyl, O-alkenoyl substituted phenyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, and derivatives thereof;

R2 is selected from hydrogen, hydroxyl, O-angeloyl, O-tigloyl, O-senecioyl, O-alkyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-alkanoyl substituted phenyl, O-alkenoyl substituted phenyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, and derivatives thereof;

R4 represents CH3, CHO, CH_2R6 or COR6, wherein R6 is selected from hydroxyl, O-angeloyl, O-tigloyl, O-senecioyl, O-alkyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-alkanoyl substituted phenyl, O-alkenoyl substituted phenyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, and derivatives thereof; R3 is H or OH; R8 is H or OH; R16 is H ,or R4 and R16 may form an oxygen bridge with divalent radical formula of –CH2-O-, CH(OH)-O- or C(=O)-O-, wherein the –O- may be replaced with –NH- or – S - ; wherein when the C12-13 of ring 3 of the triterpene has a double bond then R16 is absent; R5 is a hydrogen, hydroxyl, heterocyclic or O-sugar moiety(ies), wherein the sugar moiety(ies) is/are selected from a group consisting of glucose, galactose, rhamnose, arabinose, xylose, fucose, allose, altrose, gulose, idose, lyxose, mannose, psicose, ribose, sorbose, tagatose, talose, fructose, alduronic acid, glucuronic acid, galacturonic acid, and derivatives or combination thereof; wherein R9, R10, R11, R12, R13, R14, R15 are independently attached a group selecting from CH_3, CH_2OH, CHO, COOH, COO-alkyl, COO-aryl, COO-heterocyclic, COO-heteroaryl, CH_2Oaryl, CH_2O- heterocyclic, CH_2O- heteroaryl, alkyls group, hydroxyl, acetyl group; wherein at least two of R1, R2 and R6 are compriseing a group selected from O-angeloyl, O-tigloyl, O-senecioyl, O-dibenzoyl, O-benzoyl, O-alkanoyl, O-alkenoyl, O-benzoyl alkyl substituted O-alkanoyl, O-aryl, O-acyl, O-heterocylic, O-heteroraryl, and derivatives thereof; or

at least one of R1, R2, and R4 is a sugar moiety substituted with at least two groups selected from a group consisting of angeloyl, acetyl, tigloyl, senecioyl, benzoyl, dibenzoyl, alkanoyl, alkenoyl, benzoyl alkyl substituted alkanoyl, aryl, acyl, heterocylic, heteroraryl, and a derivative thereof; or wherein R4 is CH_2R6, wherein R1 and R2 independently consists an O-angeloyl group, or at least two of R1, R2 and R6 are O-angeloyl or at least one of R1, R2 or R6 is a sugar moiety with two O-angeloyls; or wherein R5 is/are a hydrogen, hydroxyl, O-sugar moiety(ies) wherein the sugar moiety(ies) selected from the following sugars and alduronis acids: glucose, galactose, rhamnose, arabinose, xylose, fucose, allose, altrose, gulose, idose, lyxose, mannose, psicose, ribose, sorbose, tagatose, talose, fructose, glucuronic acid, galacturonic acid; or their derivatives thereof, or the combination thereof; wherein the sugar preferably comprises glucuronic acid, arabinose and galactose; or wherein R5 is/are sugar moiety(ies) selected from a group consisting of glucose, galactose, arabinose, alduronic acid, glucuronic acid, galacturonic acid, and a derivative or combination thereof.

10. The method of claim 9, wherein at least one of R1 and R2 of the compound is selected from O-acetyl, O-angeloyl, O-tigloyl, O-senecioyl, O-dibenzoyl, and O-benzoyl, or at least one of R1 and R2 is a sugar moiety substituted with two groups selecting from acetyl, angeloyl, tigloyl, senecioyl, dibenzoyl, benzoyl; R5 is a hydrogen or sugar moiety(ies), wherein the sugar moiety(ies) is/are selected from a group of glucose, galactose, arabinose and derivatives thereof, wherein the derivatives are acid, ester and salt.

11. The method of claim 9, wherein R5 is a hydroxyl.

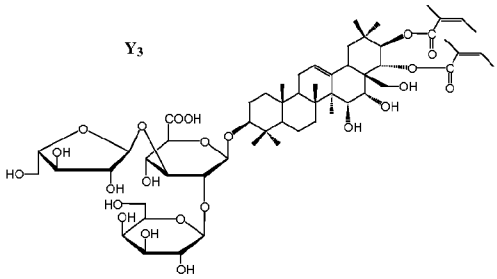
12. The method of claim 9, wherein the cancer is selected from breast cancer, leukocytic cancer, liver cancer, ovarian cancer, bladder cancer, prostatic cancer, skin cancer, bone cancer, brain cancer, leukemia cancer, lung cancer, colon cancer, CNS cancer, melanoma cancer, renal cancer, cervical cancer, esophageal cancer, testicular cancer, spleenic cancer, kidney cancer, lymphhatic cancer, pancreatic cancer, stomach cancer and thyroid cancer; wherein the cell is selected from breast cell, leukocytic cell, liver cell, ovarian cell, bladder cell, prostatic cell, skin cell, bone cell, brain cell, leukemia cell, lung cell, colon cell, CNS cell, melanoma cell, renal cell, cervical cell, esophageal cell, testicular cell,

spleenic cell, kidney cell, lymphhatic cell, pancreatic cell, stomach cell and thyroid cell.

13. The method of claim 9, wherein inhibiting cancer invasion, cell invasion, cancer cell invasion, includes increasing expression of the genes of DDIT3, LIF and NFKB1Z.

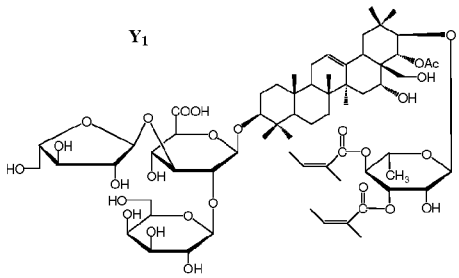
14. The method of claim 9, wherein the compound is selected from the following:

a) An isolated, purified or synthesized compound having structure Xanifolia(Y),



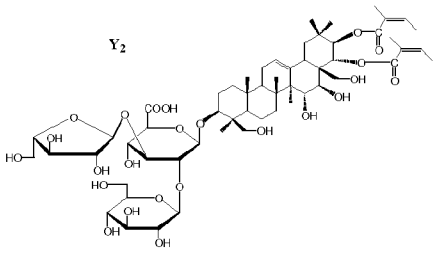
or chemical name: 3-O-[β-D-galactopyranosyl (1→2)]-α-L-arabinofuranosy (1→3)-β-D-glucuronopyranosyl-21,22-O-diangeloyl-3β, 15α, 16α, 21β, 22α, 28-hexahydroxyolean-12-ene;

b) An isolated, purified or synthesized compound having structure Xanifolia (Y1),



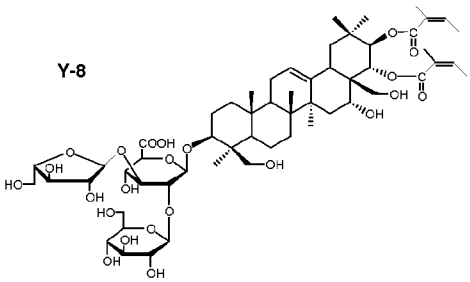
or chemical name: 3-O-[β-D-galactopyranosyl (1→2)]-α-L-arabinofuranosyl (1→3)-β-D-glucuronopyranosyl-21-O-(3,4-diangeloyl)-α-L-rhamnophyranosyl-22-O-acetyl-3β,16α, 21β, 22α, 28-pentahydroxyolean-12-ene;

c) An isolated, purified or synthesized compound having structure Xanifolia (Y2),



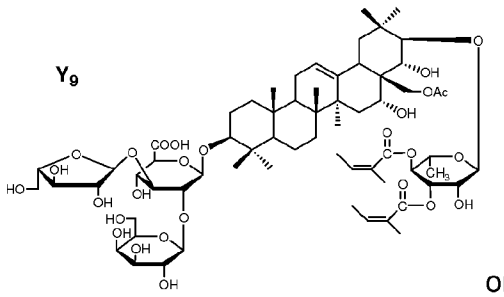
or chemical name: 3-O-[β-D-glucopyranosyl-(1→2)]-α-L-arabinofuranosy (1→3)-β-D-glucuronopyranosyl-21,22-O-diangeloyl-3β, 15α, 16α, 21β, 22α, 24β, 28-heptahydroxyolean-12-ene;

d) An isolated, purified or synthesized compound having structure Xanifolia (Y8),



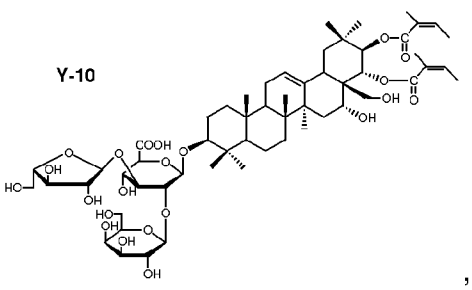
or chemical name: 3-*O*-[*β*-glucopyranosyl (1→2)]-*α*-arabinofuranosyl (1→3)-*β*-glucuronopyranosyl-21, 22-*O*-diangeloyl-3*β*, 16*α*, 21*β*, 22*α*, 24*β*, 28-hexahydroxyolean-12-ene;

e) An isolated, purified or synthesized compound having structure Xanifolia (Y9),



or chemical name: 3-*O*-[*β*-galactopyranosyl (1→2)]-*α*-arabinofuranosyl (1→3)-*β*-glucuronopyranosyl-21-*O*-(3,4-diangeloyl)-*α*-rhamnopyranosyl-28-*O*-acetyl-3*β*, 16*α*, 21*β*, 22*α*, 28-pentahydroxyolean-12-ene; and

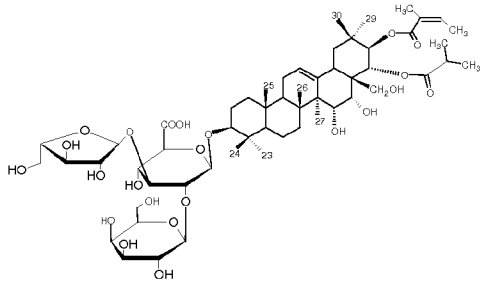
f) An isolated, purified or synthesized compound having structure Xanifolia (Y10),



, or chemical name:

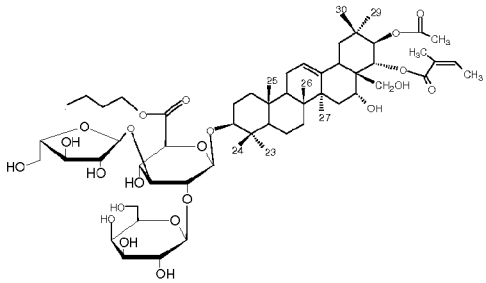
3-*O*-[*β*-galactopyranosyl (1→2)]-*α*-arabinofuranosyl (1→3)-*β*-glucuronopyranosyl-21, 22-*O*-diangeloyl-3*β*, 16*α*, 21*β*, 22*α*, 28-pentahydroxyolean-12-ene.

g) An isolated, purified or synthesized compound having structure Xanifolia (Y0),



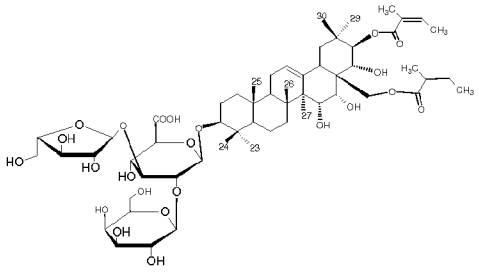
, or chemical name: 3-O-[β-D-galactopyranosyl(1→2)]-α-L-arabinofuranosyl(1→3)-β-D-glucuronopyranosyl-21-O-angeloyl, 22-O-(2-methylpropanoyl)-3β, 15α, 16α, 21β, 22α, 28-hexahydroxyolean-12-ene,

h) An isolated, purified or synthesized compound having structure Xanifolia (X),



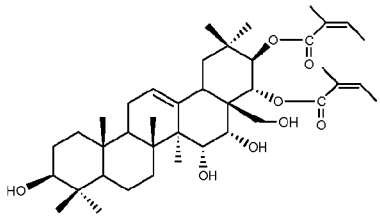
, or chemical name: 3-*O*-{[*β*-D-galactopyranosyl (1→2)]-[*α*-L-arabinofuranosyl (1→3)]- *β*-D-glucuronopyranoside butyl ester}-21-*O*-acetyl-22-*O*- angeloyl- 3*β*,16*α*,21*β*,22*α*,28-pentahydroxyolean-12-ene.

i) An isolated, purified or synthesized compound having structure (Y7),

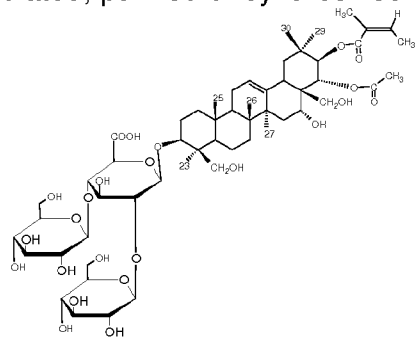


, or chemical name: 3-*O*-[*β*-D-galactopyranosyl-(1→2)]-*α*-L-arabinofuranosyl-(1→3)-*β*-D--glucuronopyranosyl-21-*O*-angeloyl-28-*O*-2-methylbutanoyl-3*β*, 15 *α*, 16*α*, 21*β*, 22*α*, 28-hexahydroxyolean-12-ene

j) An isolated, purified or synthesized compound having structure (ACH-Y):



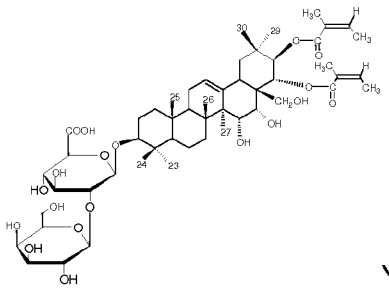
k) An isolated, purified or synthesized compound having structure:



or chemical name:

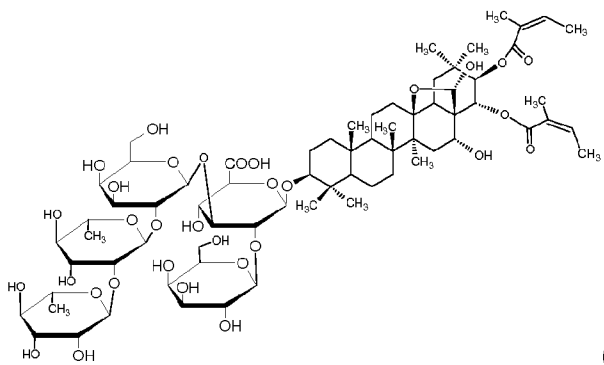
3-*O*-[*β*-glucopyranosyl (1→2)]- *β*-arabinofuranosyl (1→4)-*β*- glucuronopyranosyl -21-*O*-angeloyl-22-O-acteyl-3*β*, 16*α*, 21*β*, 22*α*, 24*β*, 28-hexahydroxyolean-12-ene;

(l) An isolated, purified or synthesized compound having structure:



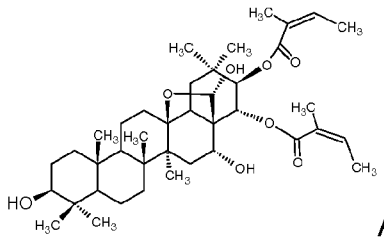
Y5

(m) An isolated, purified or synthesized compound having structure:



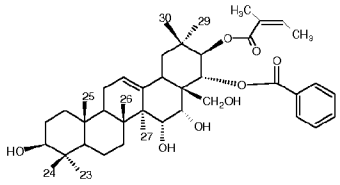
(M10) ,

(n) An isolated, purified or synthesized compound having structure:



ACH-M10

(o) An isolated, purified or synthesized compound having structure:



ACH-Z4

15. The method of claim 9, further comprising a pharmaceutically acceptable carrier or diluent.

16. The method of claim 9, wherein the said compound is present in a concentration of the said compound is present in a concentration of 0.01 ug/ml to 40ug/ml, or wherein the said compound is present in a concentration of 0.01 ug/ml to 30ug/ml, or wherein the said compound is present in a concentration of 0.01 ug/ml to 10ug/ml, or wherein the said compound is present in a concentration of 0.01 ug/ml to 5ug/ml, or wherein the said compound is present in a concentration of 5 ug/ml to 10ug/ml, or wherein the said compound is present in a concentration of 0.1 ug/ml to 5ug/ml, or wherein the said compound is present in a concentration of 0.1 ug/ml to 7.5ug/ml, or wherein the said compound is present in a concentration of 0.1 ug/ml to 10ug/ml, or wherein the said compound is present in a concentration of 0.1 ug/ml to 15ug/ml, or wherein the said compound is present in a concentration of 0.1 ug/ml to 20ug/ml, or wherein the said compound is present in a concentration of 0.1 ug/ml to 30ug/ml, or wherein the said compound is present in a concentration of 1 ug/ml to 5ug/ml, or wherein the said compound is present in a concentration of 1 ug/ml to 7.5ug/ml, or wherein the said compound is present in a concentration of 1 ug/ml to 10ug/ml, or wherein the said compound is present in a concentration of 1 ug/ml to 15ug/ml, or wherein the said compound is present in a concentration of 1 ug/ml to 20ug/ml, or wherein the said compound is present in a concentration of 1 ug/ml to 30ug/ml, or wherein the said compound is present in a concentration of 3 ug/ml to 5ug/ml, or wherein the said compound is present in a concentration of 3 ug/ml to 7.5ug/ml, or wherein the said compound is present in a concentration of 3 ug/ml to 10ug/ml, or wherein the said compound is present in a concentration of 3

ug/ml to 15ug/ml, or wherein the said compound is present in a concentration of 3 ug/ml to 20ug/ml, or wherein the said compound is present in a concentration of 3 ug/ml to 30ug/ml; or present in a concentration of 4 ug/ml to 5ug/ml, or wherein the said compound is present in a concentration of 4 ug/ml to 7.5ug/ml, or wherein the said compound is present in a concentration of 4 ug/ml to 10ug/ml, or wherein the said compound is present in a concentration of 4 ug/ml to 15ug/ml, or wherein the said compound is present in a concentration of 4 ug/ml to 20ug/ml, or wherein the said compound is present in a concentration of 4 ug/ml to 30ug/ml, or present in a concentration of 5 ug/ml to 8ug/ml, or wherein the said compound is present in a concentration of 5 ug/ml to 9ug/ml, or wherein the said compound is present in a concentration of 5 ug/ml to 10ug/ml, or wherein the said compound is present in a concentration of 5 ug/ml to 15ug/ml, or wherein the said compound is present in a concentration of 5 ug/ml to 20ug/ml, or wherein the said compound is present in a concentration of 5 ug/ml to 30ug/ml, or present in a concentration of 7 ug/ml to 8ug/ml, or wherein the said compound is present in a concentration of 7 ug/ml to 9ug/ml, or wherein the said compound is present in a concentration of 7 ug/ml to 10ug/ml, or wherein the said compound is present in a concentration of 7 ug/ml to 15ug/ml, or wherein the said compound is present in a concentration of 7 ug/ml to 20ug/ml, or wherein the said compound is present in a concentration of 7 ug/ml to 30ug/ml; or wherein administration is by intravenous drip: 0.003-0.03mg/kg body weight of compound dissolved in 250ml of 10% glucose solution or in 250ml of 0.9% NaCl solution, or by intravenous injection: 0.003-0.03mg/kg body weight per day of compound dissolved in 10-20ml of 10% glucose solution or of 0.9% NaCl solution, or 0.01-0.03mg/kg body weight of compound dissolved in 250ml of 10% glucose solution or in 250ml of 0.9% NaCl solution, or by intravenous injection: 0.01-0.03mg/kg body weight per day of compound dissolved in 10-20ml of 10% glucose solution or of 0.9% NaCl solution, or 0.01-0.05mg/kg body weight of compound dissolved in 250ml of 10% glucose solution or in 250ml of 0.9% NaCl solution, or by intravenous injection: 0.01-0.05mg/kg body weight per day of compound dissolved in 10-20ml of 10% glucose solution or of 0.9% NaCl solution.

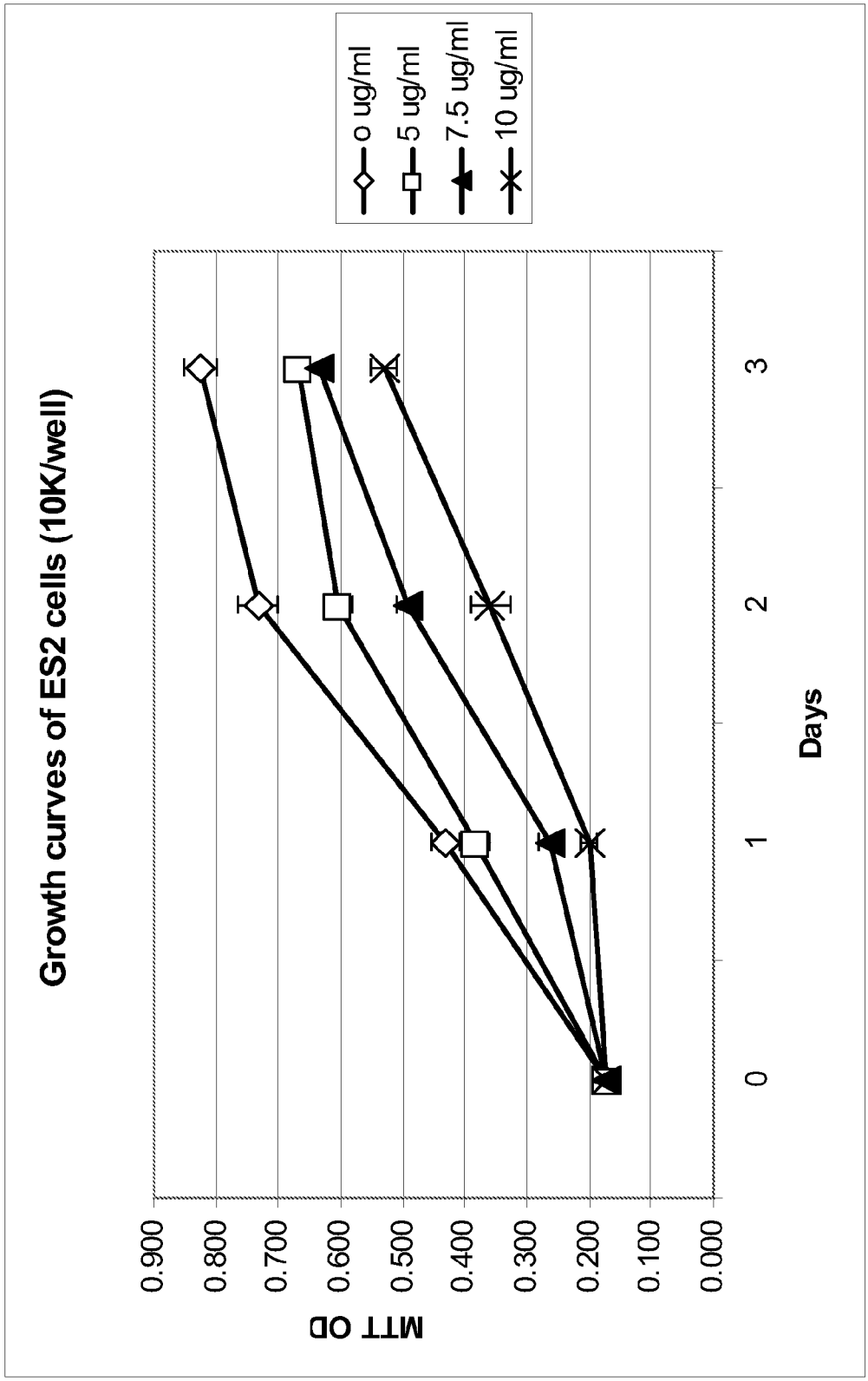


Figure 1
Growth of ES2 (ovary) cells in presence of compound Y10

Figure 2
Growth curves of ES2 (ovary) cells in the presence of drugs

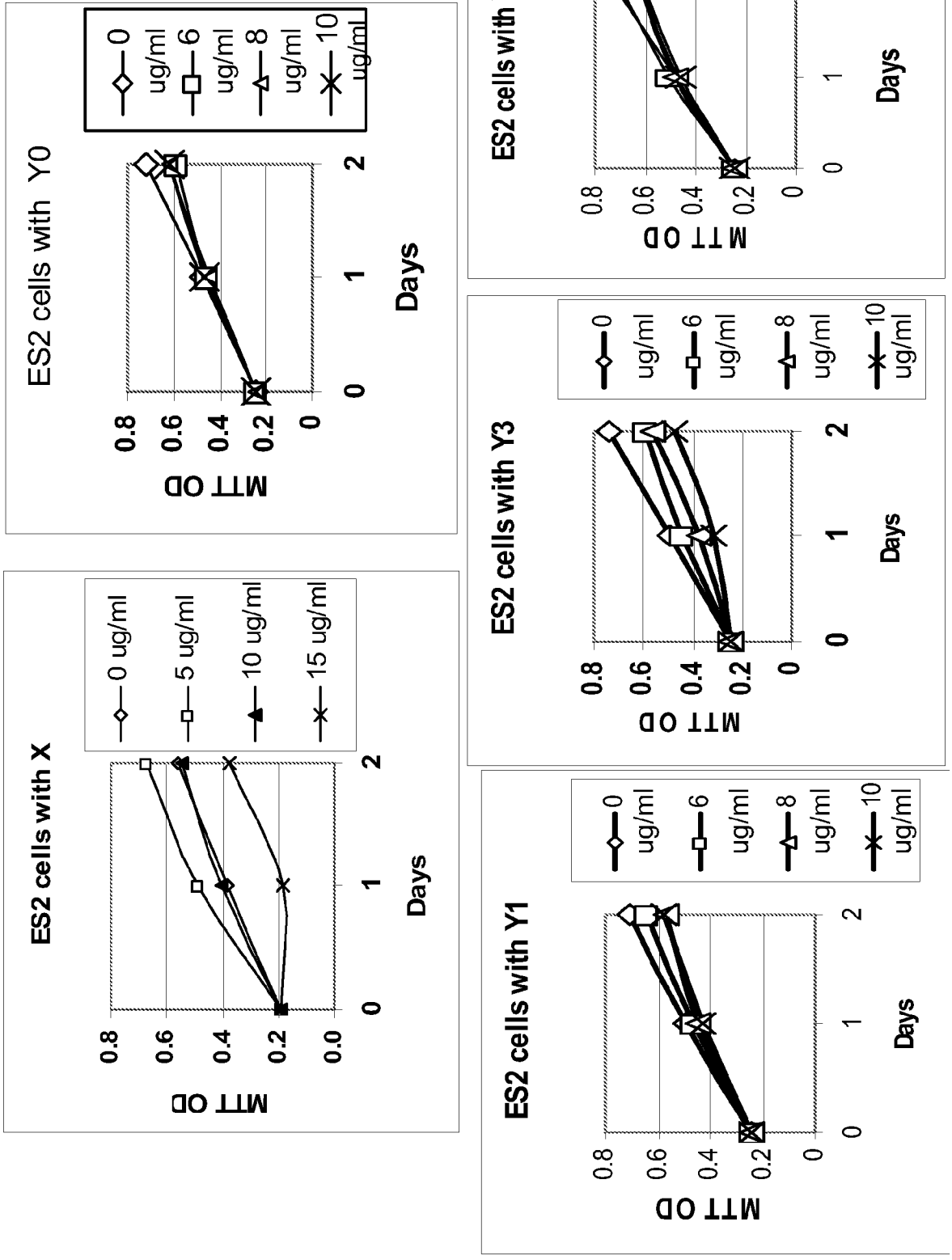


Figure 3
Growth curves of ES2 (ovary) cells in the presence of drugs

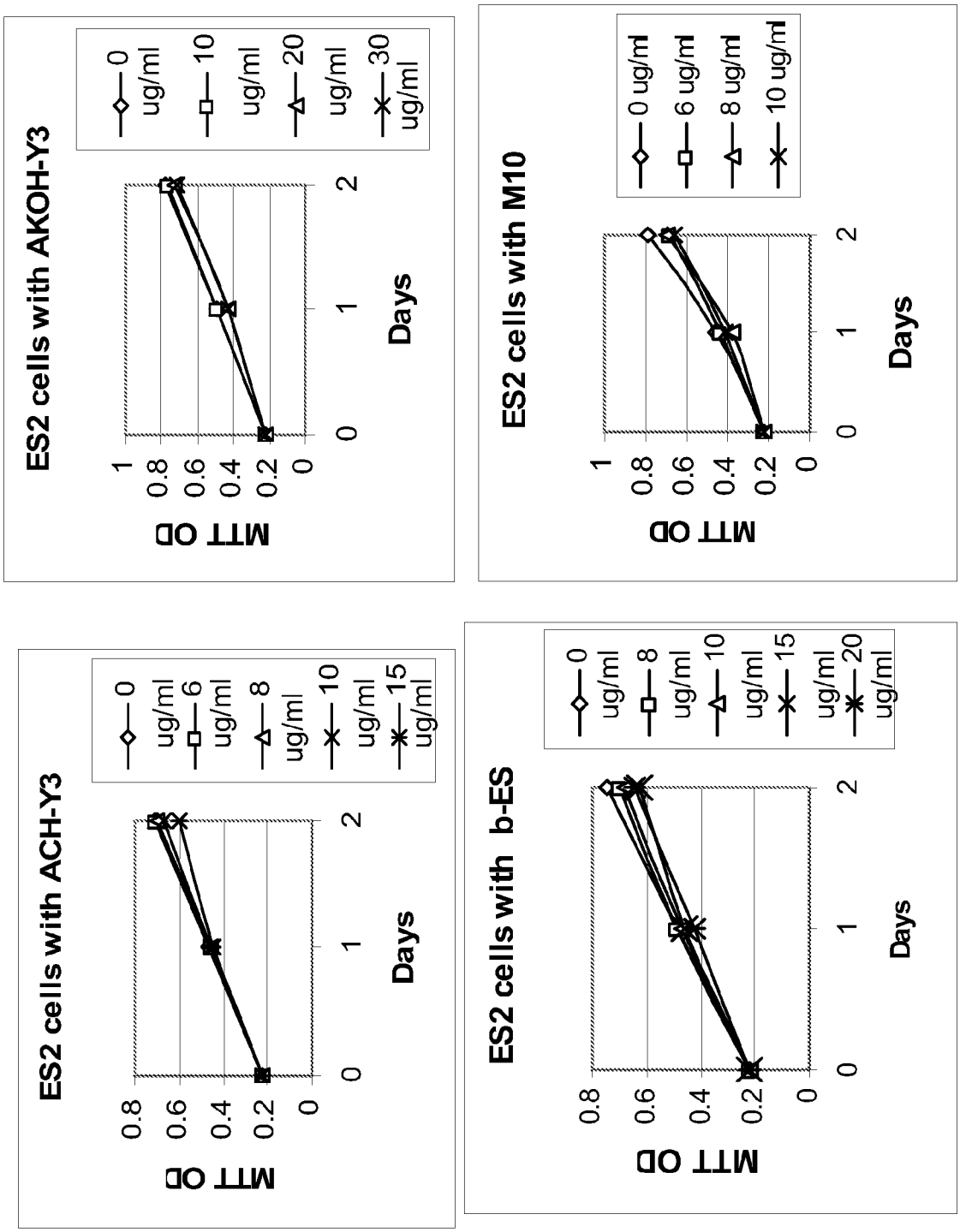


Figure 4
Growth curves of TB9 cells (bladder) in the presence of drugs

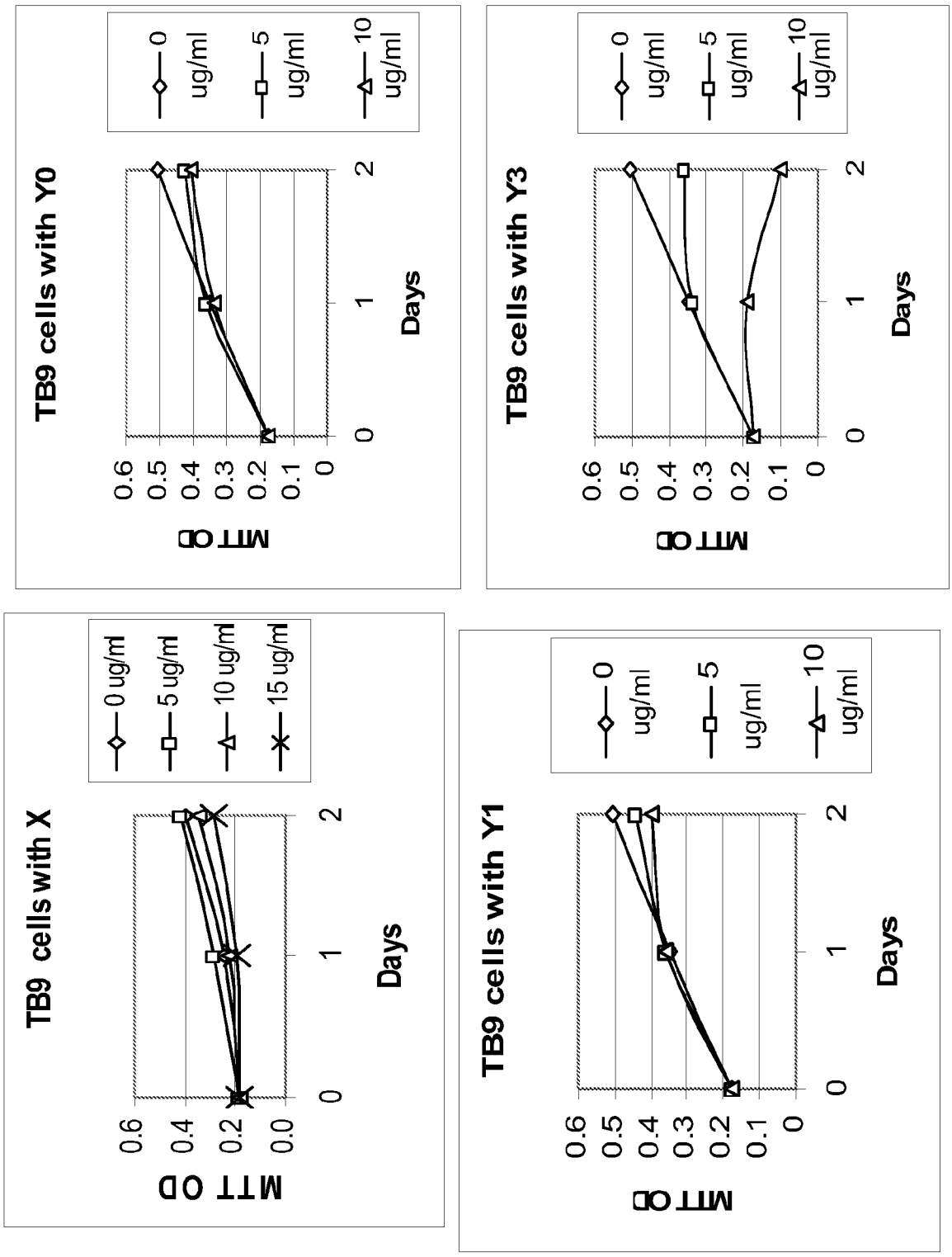


Figure 5
Growth curves of TB9 cells (bladder) in the presence of drugs

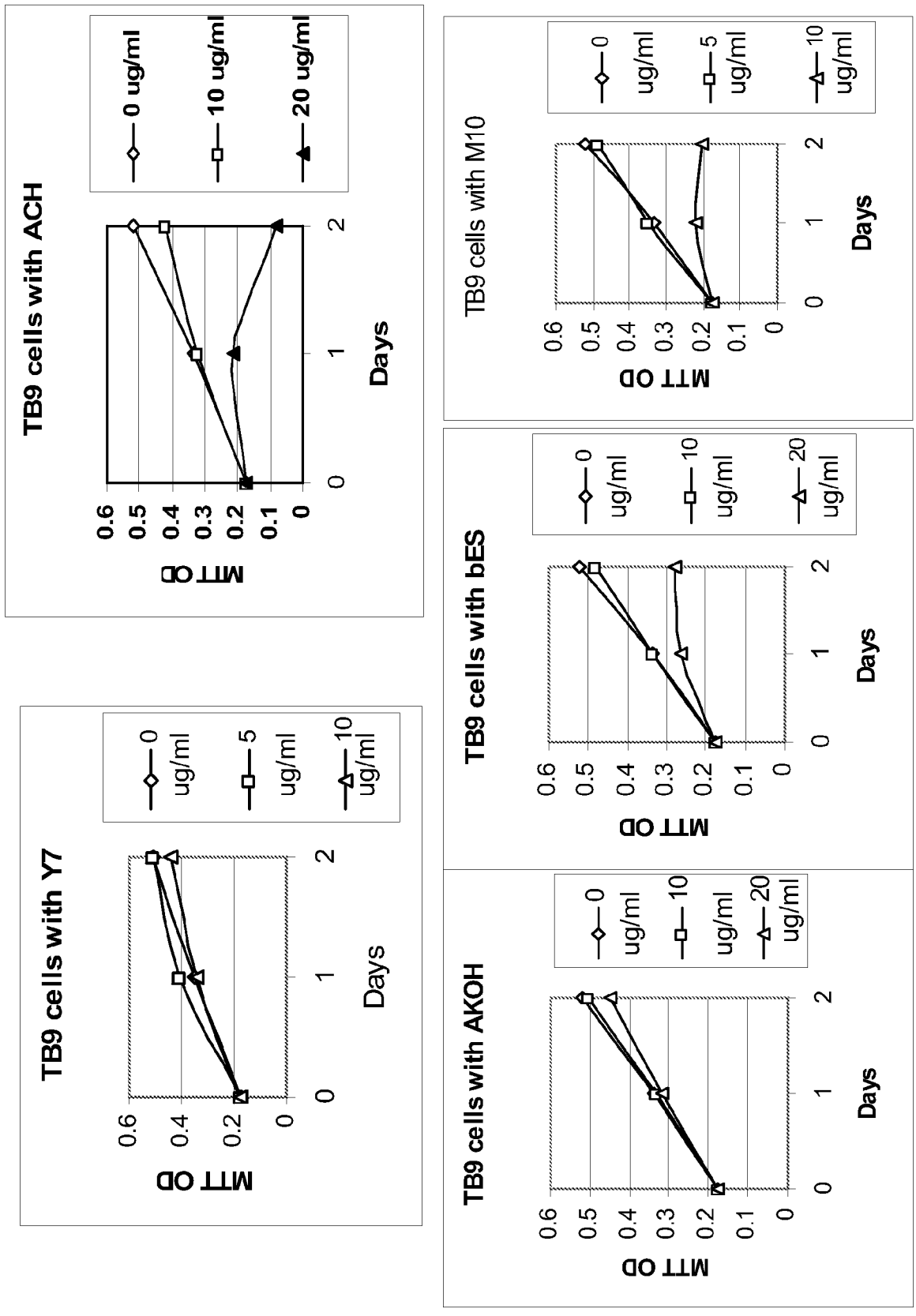


Figure 6
Growth curves of H460 cells (lung) in the presence of drugs

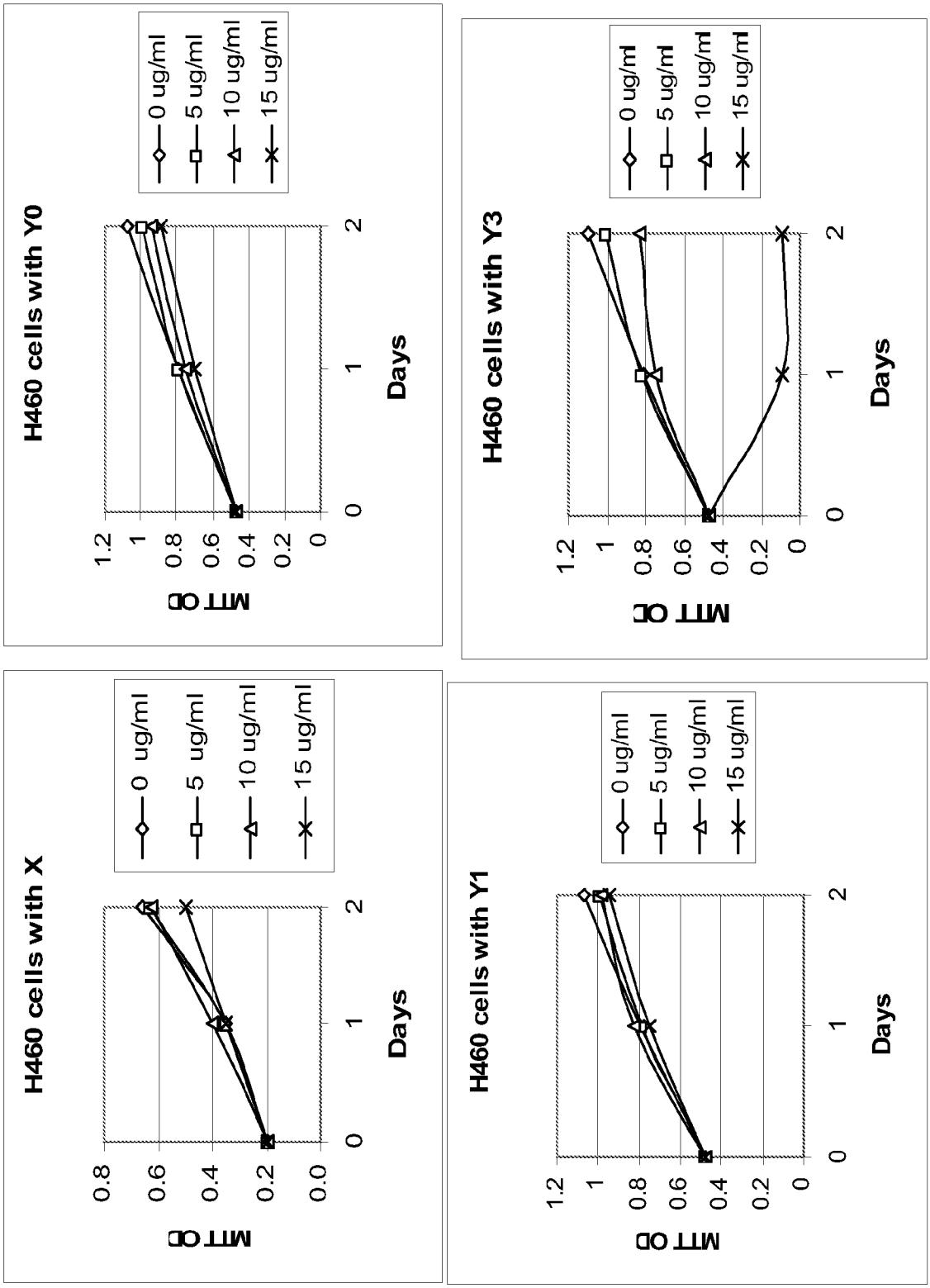


Figure 7
Growth curves of H460 cells (lung) in the presence of drugs

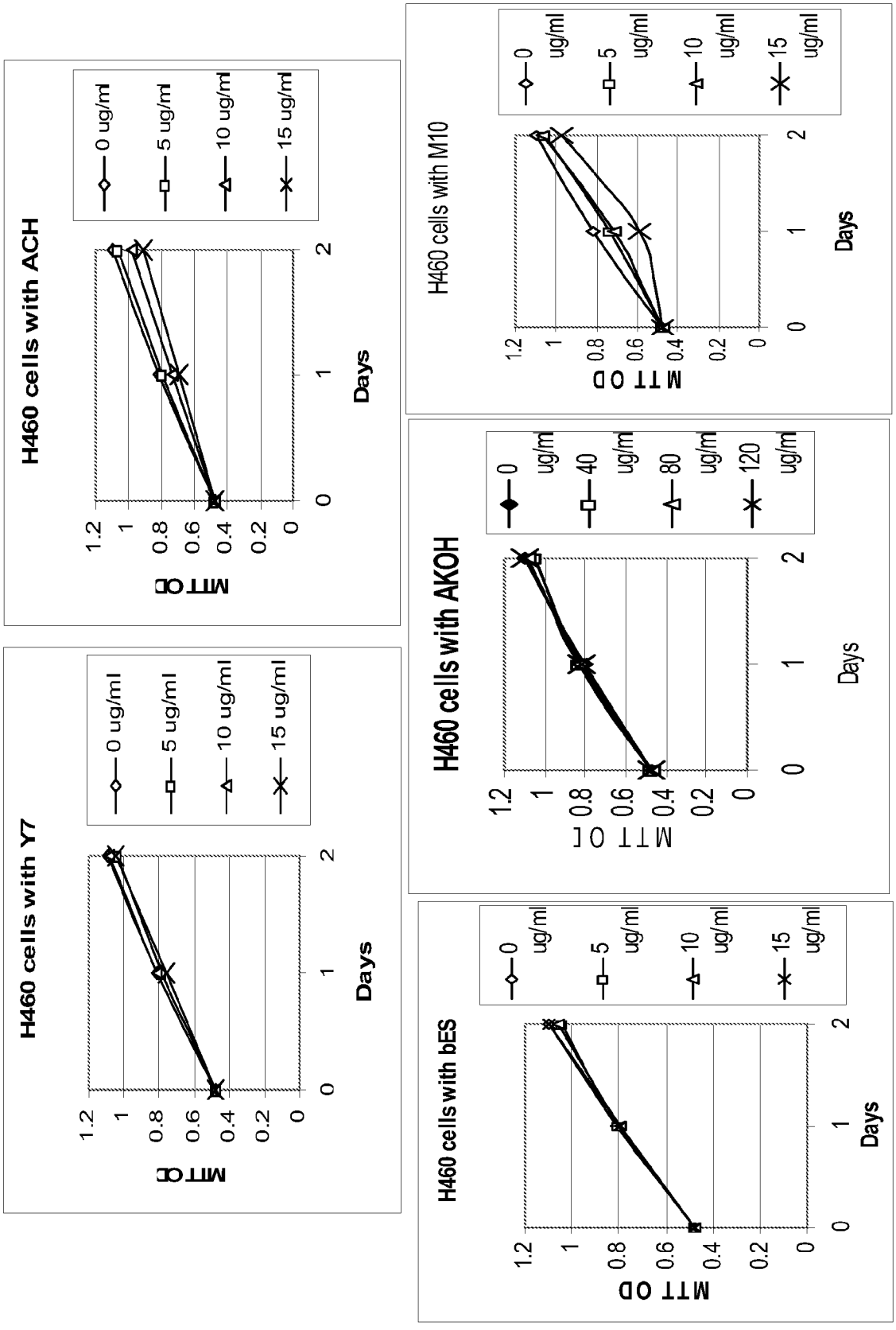


Figure 8
Growth curves of T98G cells (brain) in the presence of drugs

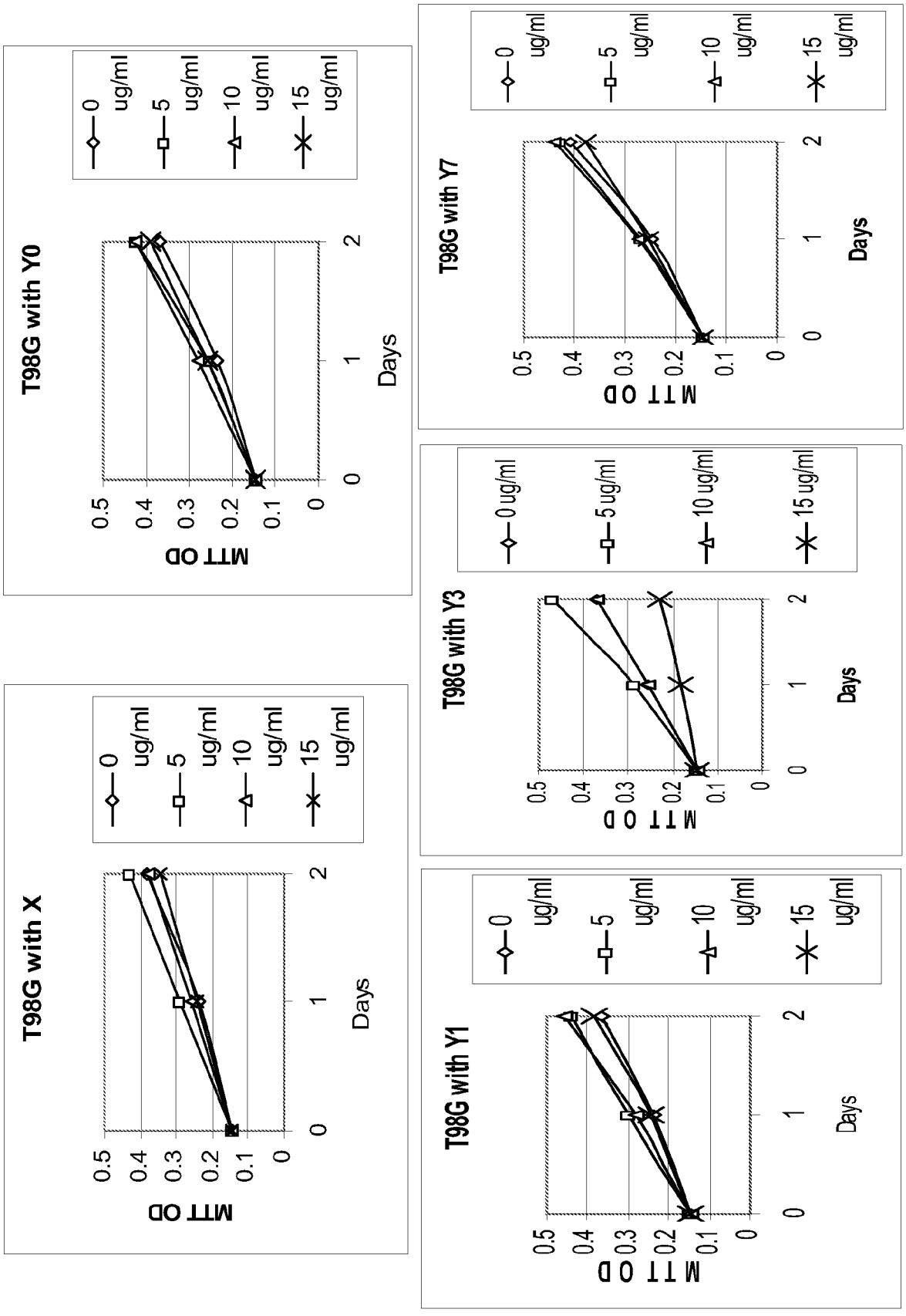


Figure 9
Growth curves of T98G cells (brain) in the presence of drugs

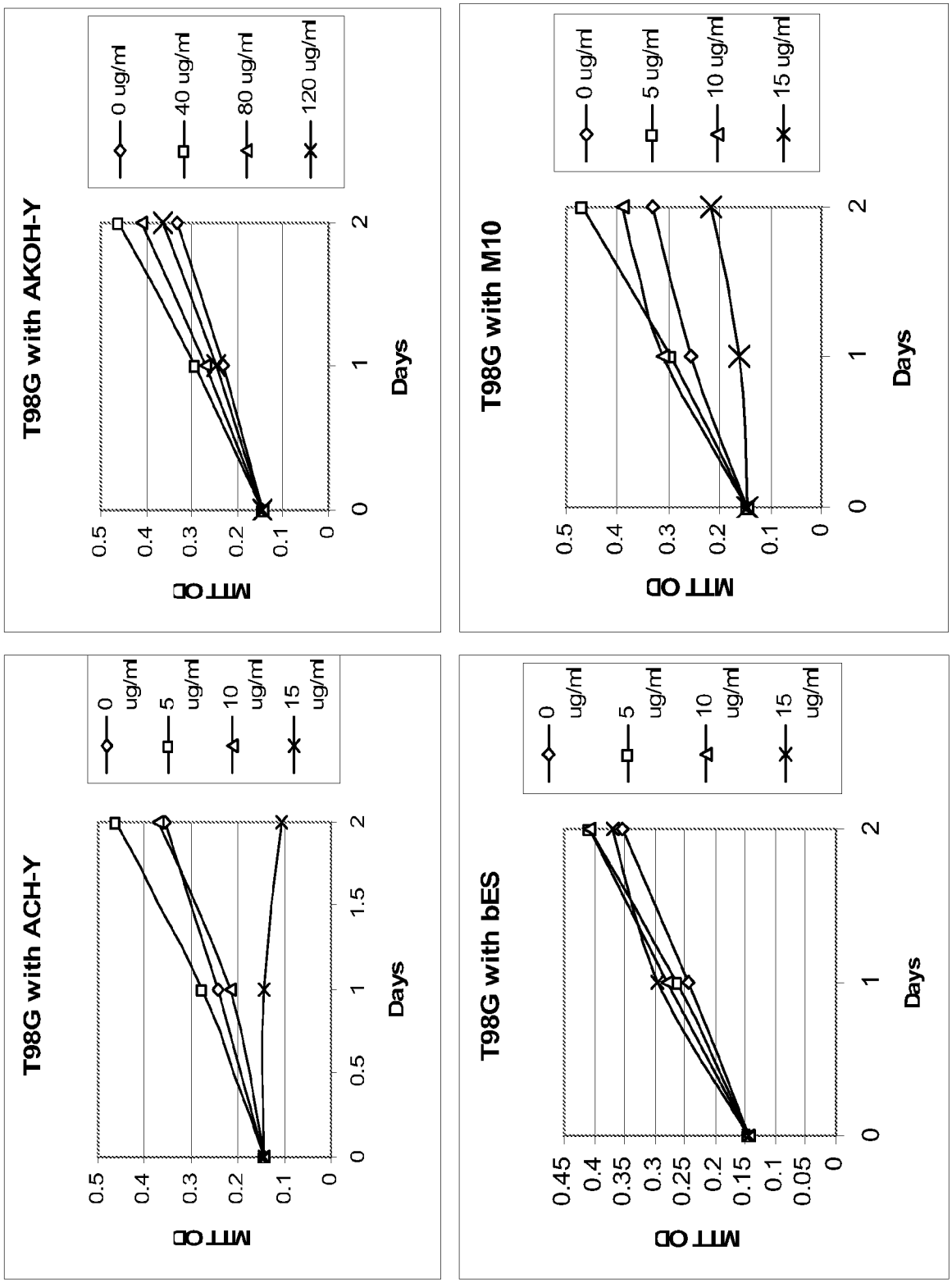


Figure 10
Growth curves of U2OS cells (bone) in the presence of drugs

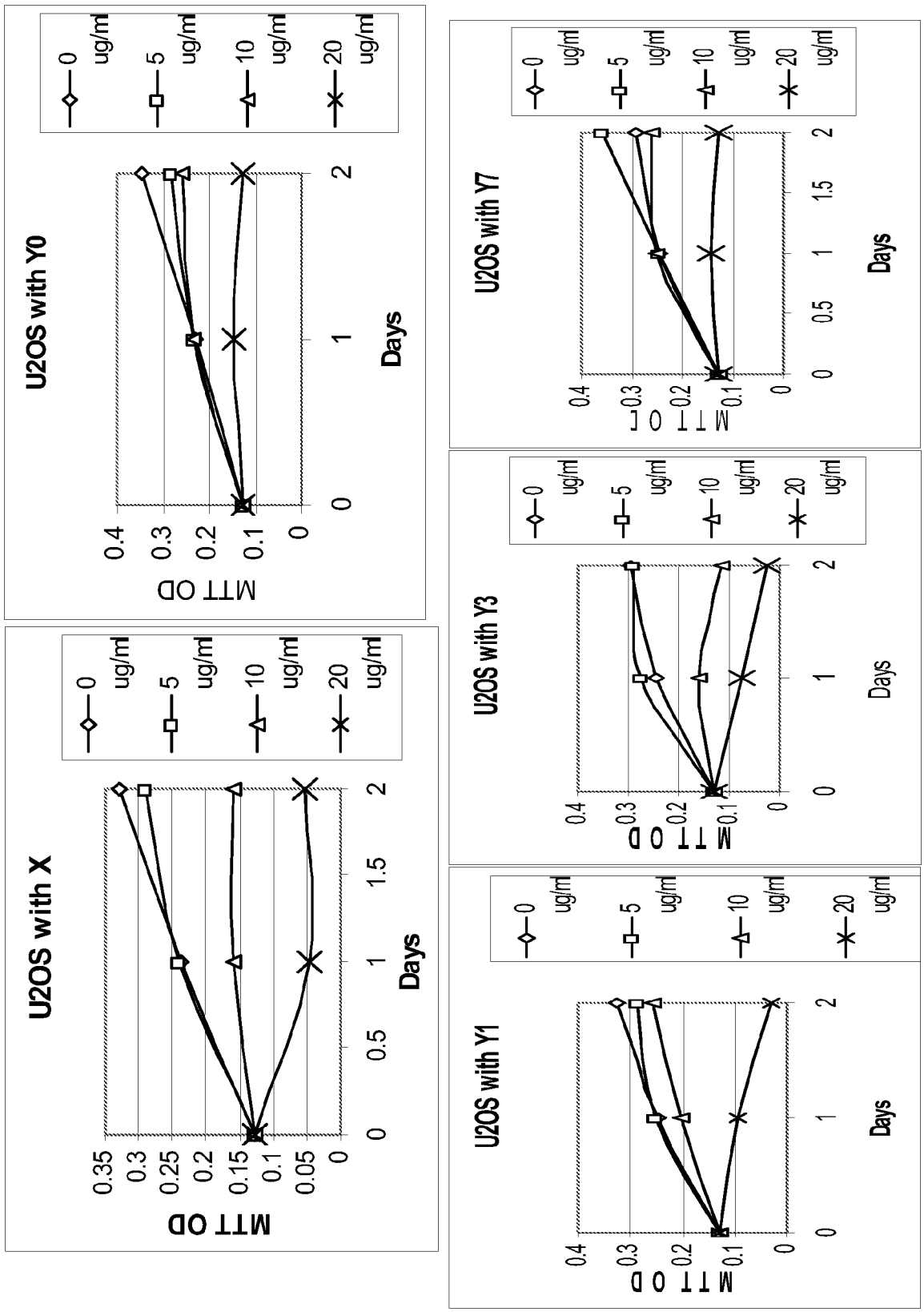
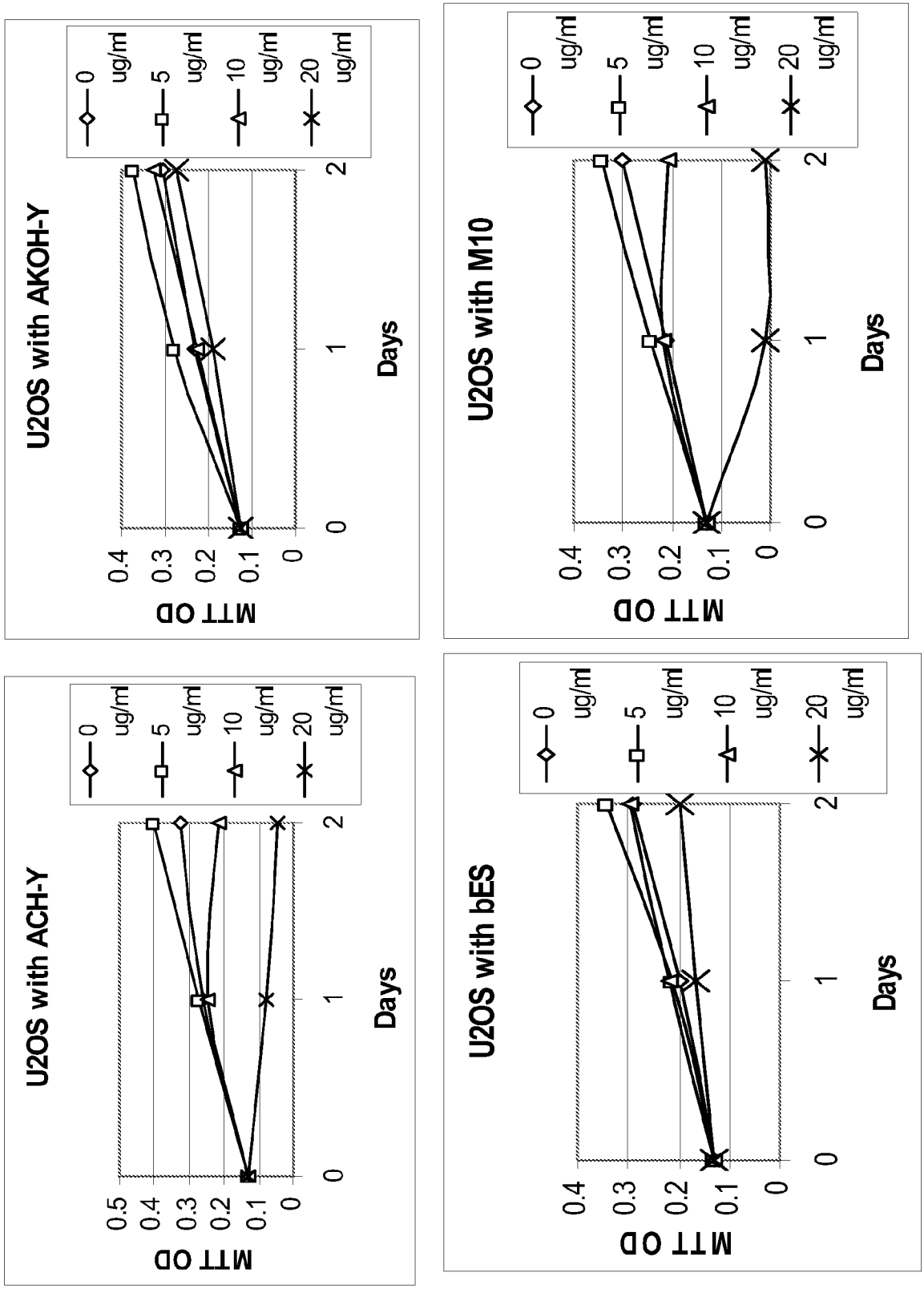


Figure 11
Growth curves of U2OS cells (bone) in the presence of drugs



INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 10/42240

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A01N 43/04 (2010.01)
USPC - 514/33
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
USPC: 514/33

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
WEST: DB=PGPB,USPT,USOC,EPAB,JPAB
Google: Scholar/Patents: glucopyranosyl arabinofuranosyl sugar angeloyl ovarian breast cancer xanifolia gene expression chemotherapy upregulation GADD153 saponin triterpene

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2007/0161580 A1 (CHAN et al) 12 July 2007 (12.07.2007) abstract; para [0083];[0084];[0087];[0091]-[0097]; [0104]-[0105];[0110];[0114]-[0119] ; [0183];[0336]-[0343]; Figures 2, 3 and 7	1-16

☐ Further documents are listed in the continuation of Box C. ☐

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
24 August 2010 (24.08.2010)	02 SEP 2010
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (July 2009)