[0028] None of the teachings of prior art provide for a therapeutic estradiol derivative with favorable side effect profile that can be used for these types of conditions.

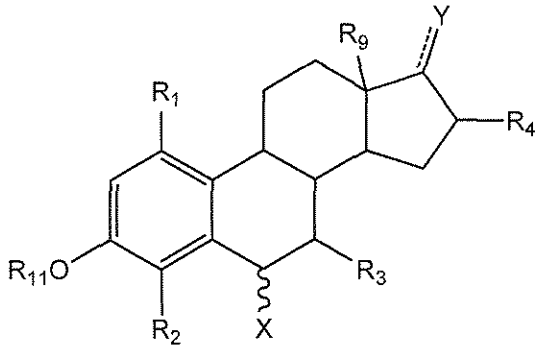
SUMMARY ~~OF THE INVENTION~~

[0029] In light of the foregoing, the present ~~invention~~disclosure is directed towards chemotherapeutic compounds, compositions and methods for their use and preparation, thereby overcoming various deficiencies and shortcomings of the prior art, including those outlined above. Accordingly, it is one object of the present ~~invention~~disclosure to ~~provide~~describe compounds useful in the treatment of estrogen-dependent conditions and tumors which provide a better patient tolerance, prognosis and compliance.

[0030] Another object of the present ~~invention~~disclosure is to ~~provide~~describe compounds and methods for the treatment of estrogen-independent tumors with compounds having substantially less side effects than those currently available to the patients.

[0031] Yet another objective of the present ~~invention~~disclosure is to ~~provide~~describe for compounds and alternative modes of treatment of tissues afflicted with hyperproliferative conditions, including viral and bacterial infections.

[0031a] In one aspect, the present invention refers to a compound of formula:



wherein

R_1, R_2, R_3 and R_4 are independently selected from hydrogen, C_1-C_6 alkyl, halo, a sulfate, a glucuronide, -OH, a bulky group, aryl, cycloalkyl, heteroaryl, heterocycloalkyl, $-N(CH_2)_n$, a phosphate group, and a phosphinate group;

R_6 is selected from H, C_1-C_6 alkyl, sulfate, and glucuronide;

R_9 is selected from hydrogen, halogen or alkyl;

R_{11} is selected from H, C_1-C_6 alkyl, a sulfate, a glucoronide, and $-SO_2NH_2$;

X is selected from C_2-C_{12} alkenyl, C_2-C_{12} alkynyl, $-(CH_2)_q$-O-CH_3, $-(CH_2)_q$-O-$(CH_2)_nCH_3$, $(CH_2)_m$-S-CH_3, $-(CH_2)_m$-S-$(CH_2)_nCH_3$, $-(CH_2)_m$-NH-$(CH_2)_nCH_3$, $-C_2$-C_8 alkenyl-O-$(CH_2)_nCH_3$, $-C_2$-C_8 alkenyl-S-$(CH_2)_nCH_3$, $-C_2$-C_8 alkenyl-N-$(CH_2)_nCH_3$, $-C_2$-C_8 alkynyl-O-$(CH_2)_nCH_3$, $-C_2$-C_8 alkynyl-S-$(CH_2)_nCH_3$, and $-C_2$-C_8 alkynyl-N-$(CH_2)_nCH_3$, ;

Y is selected from hydrogen, $-OCO(R_6)$ and -OH;

m is an integer between 1-20;

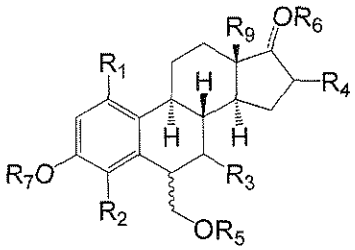
n is an integer between 0-8;

q is an integer from 2-20;and

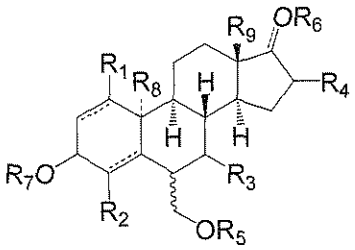
the ~~wavy~~ symbol represents any type of bond regardless of the stereochemistry;

and the respective enantiomers, stereochemical isomers, hydrates, solvates, tautomers and pharmaceutically acceptable salts thereof.

[0032] The present ~~invention~~disclosure includes any one of the following sets of compounds represented in Formulas I-IV. One ~~aspect of the present invention~~example pertains to a compound of Formula I and II.



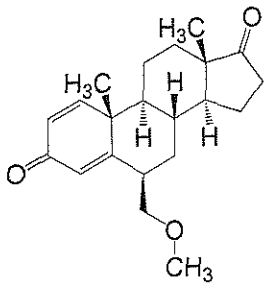
(I)



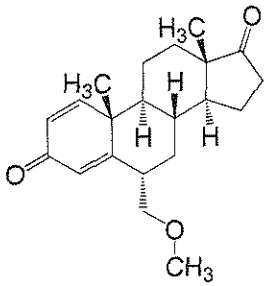
(II)

wherein R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8 and R_9 are independently selected from the group consisting of hydrogen, C_1 to C_6 alkyl or substituted alkyl, halogen, sulfate, and glucuronide moieties; and the ---- symbol represents either a single or a double bond and when the ---- symbol is a double bond and forms a keto group at position 3 or 17, then no R_7 or R_6 is present, respectively; the symbol --- represent the presence or absence of a bond at position 10; and the ~~~ symbol represents any type of bond regardless of the stereochemistry. The compounds also embrace the enantiomers, other stereochemical isomers, hydrates, solvates, tautomers and pharmaceutically acceptable salts thereof.

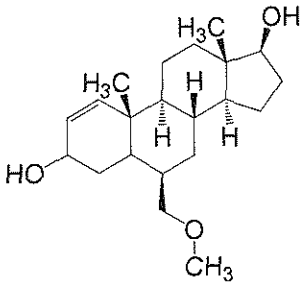
[0033] In another ~~aspect of the invention~~example, compounds having Formula III are described, wherein R_5 is as described above.



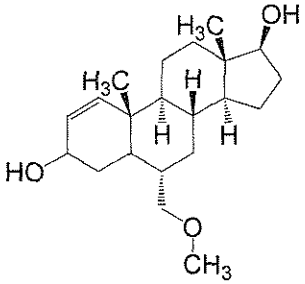
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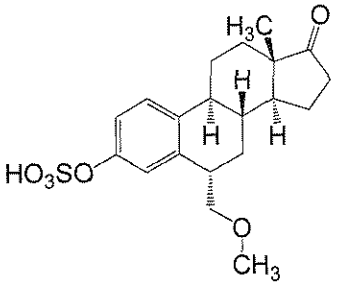
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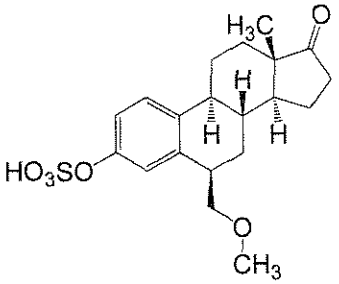
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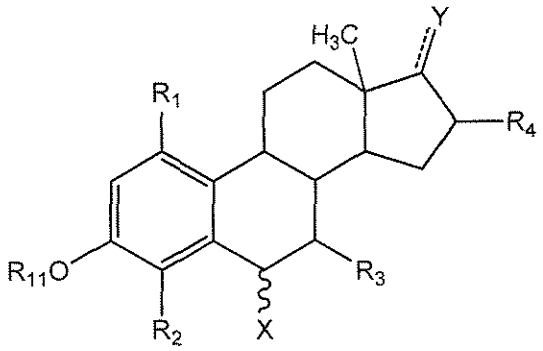


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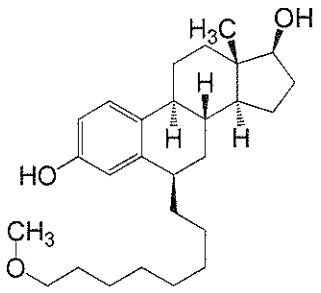
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[0035] Another ~~aspect of the present invention~~example pertains to amine derivatives of the compounds of Formulas (I) - (III). In at least this ~~aspect~~example of the ~~invention~~disclosure, amine moieties are placed in suitable positions on the molecular core to improve physical and clinical properties. Formula (IV) represents a general core structure for the present ~~invention~~disclosure. Formula (IV) depicts compounds having the structure:

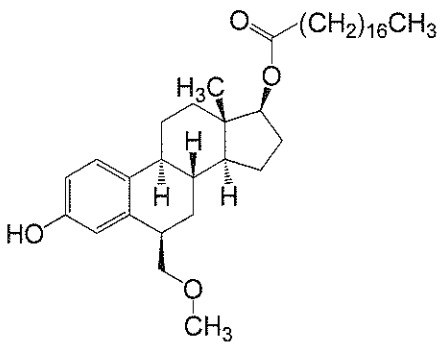


(IV)

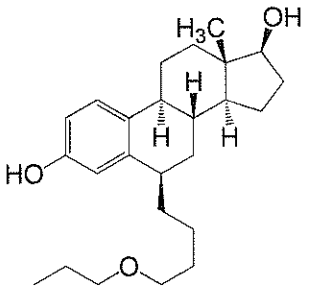
wherein R_1, R_2, R_3 and R_4 are independently hydrogen, C_1-C_6 alkyl, halo, a sulfate, a glucuronide, -OH, a bulky group, aryl, cycloalkyl, heteroaryl, heterocycloalkyl, -$N(CH_2)_n$; a phosphate group, and a phosphinate group; R_{11} is



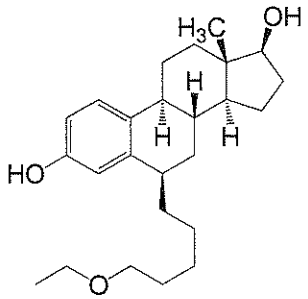
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[0036a] In another aspect, the present invention refers to a compound selected from the group consisting of:

(6*S*,8*R*,9*S*,10*R*,13*S*,14*S*)-17-hydroxy-6-(methoxymethyl)-10,13-dimethyl-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-3*H*-cyclopenta[a]phenanthren-3-one;

(6*R*,8*R*,9*S*,10*R*,13*S*,14*S*)-17-hydroxy-6-(methoxymethyl)-10,13-dimethyl-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-3*H*-cyclopenta[a]phenanthren-3-one,

(6*R*,8*R*,9*S*,10*R*,13*S*,14*S*)-6-(methoxymethyl)-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthrene-3,17-diol

(6*S*,8*R*,9*S*,13*S*,14*S*)-6-(hydroxymethyl)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthrene-3,17-diol,

(6*S*,8*R*,9*S*,13*S*,14*S*)-6-((aminooxy)methyl)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthrene-3,17-diol,

(6*R*,8*R*,9*S*,13*S*,14*S*)-6-(((methoxymethyl)amino)methyl)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthrene-3,17-diol,

(6*S*,8*R*,9*S*,13*S*,14*S*)-6-(((methoxymethyl)amino)methyl)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthrene-3,17-diol,

1-((((6*R*,8*R*,9*S*,13*S*,14*S*)-3,17-dihydroxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-6-yl)methyl)amino)propan-2-one,

1-((((6*S*,8*R*,9*S*,13*S*,14*S*)-3,17-dihydroxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-6-yl)methyl)amino)propan-2-one,

(6*R*,8*R*,9*S*,13*S*,14*S*)-3-hydroxy-6-(methoxymethyl)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-17-yl stearate,

(6*R*,8*R*,9*S*,10*R*,13*S*,14*S*)-6-(methoxymethyl)-10,13-dimethyl-7,8,9,10,11,12,13,14,15,16-decahydro-3*H*-cyclopenta[*a*]phenanthrene-3,17(6*H*)-dione,

(6*S*,8*R*,9*S*,10*R*,13*S*,14*S*)-6-(methoxymethyl)-10,13-dimethyl-7,8,9,10,11,12,13,14,15,16-decahydro-3*H*-cyclopenta[*a*]phenanthrene-3,17(6*H*)-dione,

(6*R*,8*R*,9*S*,10*R*,13*S*,14*S*)-6-(methoxymethyl)-10,13-dimethyl-4,5,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-3*H*-cyclopenta[*a*]phenanthrene-3,17-diol,

(6*S*,8*R*,9*S*,13*S*,14*S*)-6-(methoxymethyl)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl hydrogen sulfate,

cc) (6*R*,8*R*,9*S*,13*S*,14*S*)-6-(methoxymethyl)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl hydrogen sulfate, and

(6*R*,8*S*,9*S*,14*S*)-6-(methoxymethyl)-2-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthrene-3,17-diol.

[0037] In another ~~aspect~~example of the ~~invention~~disclosure, methods of inhibiting growth of cancer cells comprising providing to a patient a prodrug of Formulas I-IV are described. As such, the compounds of the present ~~invention~~disclosure may be used for administration in a mammalian subject in the form of a drug, prodrug or active metabolite. However, it is envisioned that such compounds are most effective when incorporated into nanoparticles, liposomes or polymeric matrix systems or other delivery systems which are capable of being directly delivered to a solid mass or be targeted to tissues of interest via suitable targeting agents.

[0037a] In yet another aspect, the present invention refers to the use of a therapeutically effective amount of a compound as defined above in the manufacture of a medicament for inhibiting growth of cancer cells, wherein the use comprises to provide a growth of cancer cells; and to contact said cancer cells with a compound as defined above.

[0038] The present ~~invention~~disclosure also relates to a method of therapeutically treating cancer in a mammalian subject (e.g., a human patient). In this ~~aspect~~example of the ~~invention~~disclosure, methods are provided for inhibiting tumor or cancerous cell growth within the mammalian subject. In such a method, the cells are exposed to or contacted with a compound of fourmuls I-IV as described herein or

pharmaceutically acceptable enantiomers, other stereochemical isomers, hydrates, solvates, tautomers, or salts thereof, as shown herein. In a specific, non-limiting ~~embodiment~~example of the methods of the present ~~invention~~disclosure, a compound of Formula (I)-(IV) is used to therapeutically treat an identified cancer state as described herein. In another specific non-limiting ~~embodiment~~example of the methods of the present ~~invention~~disclosure, a composition comprising a compound of Formula (I)-(IV) is used to therapeutically treat an identified cancer state as described herein.

[0039] At least another ~~aspect~~example of the ~~invention~~disclosure concerns delivery systems that allows conversion of suitable analogues which can be converted to a specified active compound *in vivo* after it is administered to the patient for exerting its therapeutic activity.

[0040] The compounds of the present ~~invention~~disclosure may be used to treat any tumor which may be either directly or indirectly effected by hormonal and/or estrogen-related activity, including but not in any way limited to solid tumors associated with breast, pancreatic, lung, colon, prostate, ovarian cancers, as well as brain, liver, spleen, kidney, lymph node, small intestine, blood cells, bone, stomach, endometrium, testicular, ovary, central nervous system, skin, head and neck, esophagus, or bone marrow cancer; as well as hematological cancers, such as leukemia, acute promyelocytic leukemia, lymphoma, multiple myeloma, myelodysplasia, myeloproliferative disease, or refractory anemia.

[0041] The compounds of the present ~~invention~~disclosure may also be used in combination-based therapeutic cancer treatments in a mammalian subject. Such methods may comprise administration of a compound of Formulas (I)-(IV) in combination with other adjunct cancer therapies,

such as chemotherapy, radiotherapy, gene therapy, hormone therapy and other cancer therapies known in the art.

[0042] Any of the compounds of the present ~~invention~~disclosure may be contemplated for administration to the mammalian subject in the form of a drug, prodrug or even active metabolite. In the methods of treatment of the present ~~invention~~disclosure, the term "administering" shall encompass the treatment of the various conditions described with the compound specifically disclosed or with a compound which may not be specifically disclosed, but which converts to the specified compound *in vivo* after administration to the patient and exhibits therapeutic activity.

[0043] Other objects, features, benefits and advantages of the present ~~invention~~disclosure will be apparent from this summary and the following descriptions of certain embodiments, and will be readily apparent to those skilled in the art having knowledge of various chemotherapeutic compounds, methods and/or modes of operation.

DETAILED DESCRIPTION OF THE INVENTION

[0044] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as is commonly understood by one of skill in the art to which this invention belongs and shall be understood to have the meanings described below. All publications and patents referred to herein are incorporated by reference in their entirety. Unless otherwise specified, a reference to a particular compound includes all such isomeric forms, including racemic and other mixtures thereof. Unless otherwise specified, a reference to a particular compound also includes ionic, salt, solvate