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Review Article

Anti-Cancer (Novel Agents): A Review

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ABSTRACT

Cancer is a class of diseases characterized by out-of-control cell growth. Cancer cells damage the body by multiplying their cells uncontrollably to form masses of tissue named as tumor. Tumors cells can grow and interfere with the digestive, nervous, and circulatory systems, and they can release hormones that alter body function. Tumors that are severe to body are called cancerous tumors, and temporary cells that are affected to body are not harmful and called as benign tumors. Nearly 100's of cancers are known to be effecting the humans. According to this concern the presented review outlines the novel anticancer agents how they are useful, their mechanism, and chemistry has briefly discussed in this article, the main aim of these review is to evaluate the complete novel anticancer drugs under single review paper.

Keywords: Anti-Cancer, Chrmotherapy, malignant progression

INTRODUCTION

Cancer is the largest cause of death in the developed world. Cancer affects 1 in 3 people and is responsible for 25% of all deaths. Here are more than 100 different types of cancer. For example, lung cancer starts in the lung, and breast cancer starts in the breast. The spread of cancer from one part of the body to another is called metastasis.

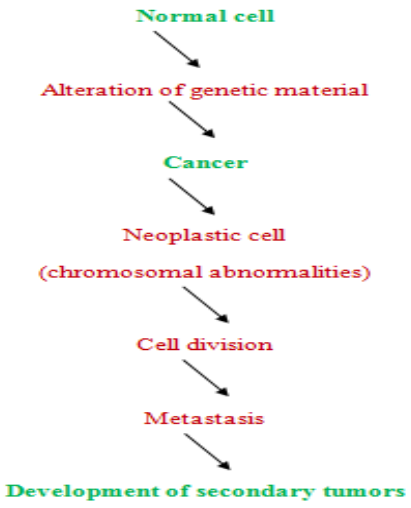
PERCENTAGE	CAUSE
30%	Smoking (lung, mouth, pharynx,larynx,esophagus etc;)
15%	Viruses (papillomavirusetc;)

Six characteristics of malignancies have been proposed:

- self-sufficiency in growth signalling
- insensitivity to anti-growth signals
- evasion of apoptosis
- enabling of a limitless replicative potential
- induction and sustainment of angiogenesis
- activation of metastasis and invasion of [1]

The progression from normal cells to cells that can form a discernible mass to outright cancer involves multiple steps known as malignant progression[2]

SCHEME OF CANCER CAUSES [3]:



ADVANCES IN CANCER CHEMOTHERAPY[3]:

SURGERY: BEFORE 1955
RADIOTHERAPY: 1955-1965

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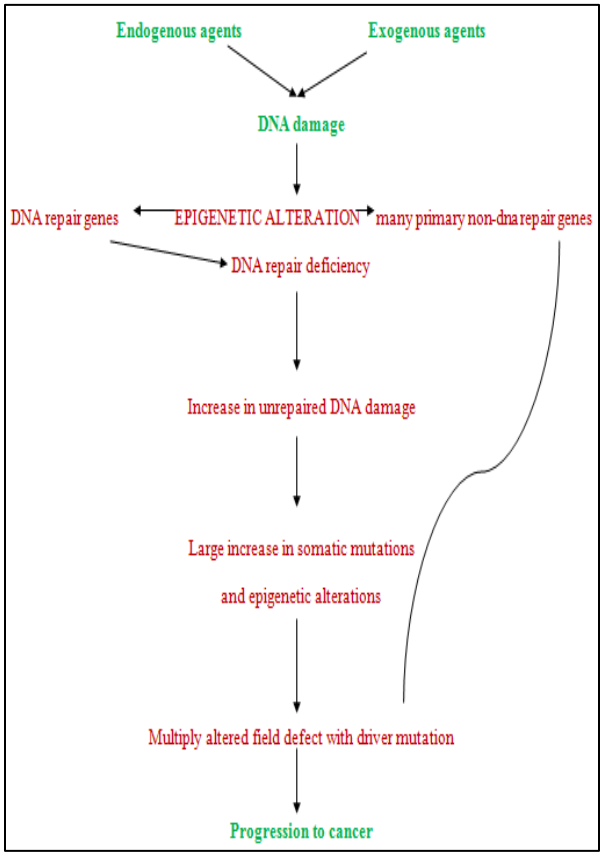
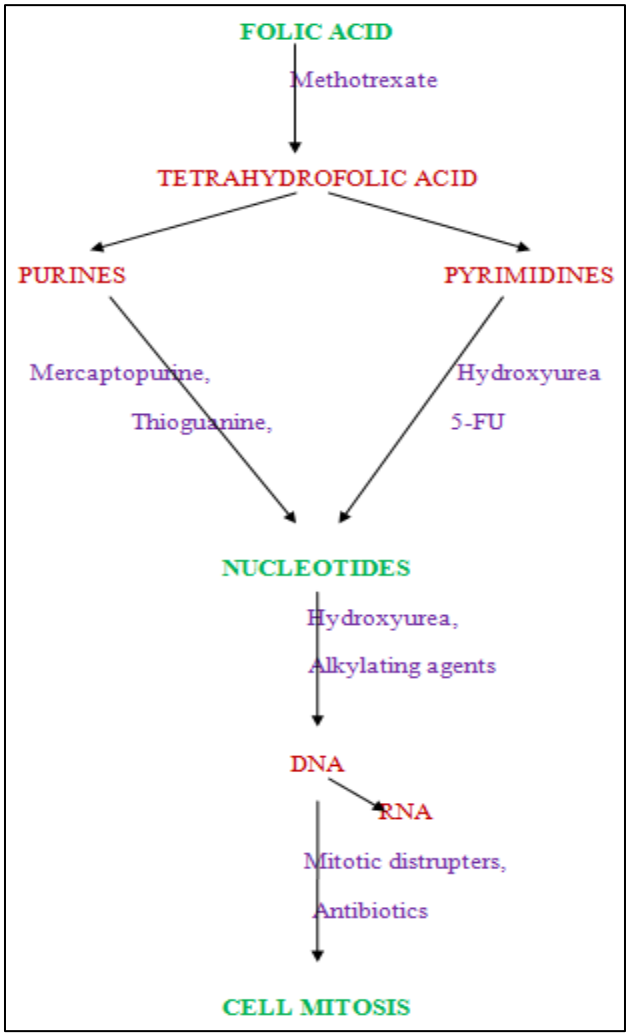
CHEMOTHERAPY: AFTER 1965
IMMUNOTHERAPY AND GENE THERAPY

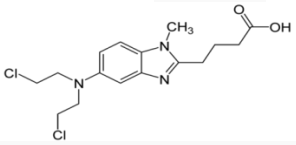
CELLULAR PATHWAY TO MALIGNANCE[4]:





GENERAL MECHANISM OF ANTICANCER DRUGS [5]:

ANTICANCER AGENTS

CYTOTOXIC AGENTS:				
ALKYLATING AGENTS:				
SNO	**DRUG**	**MECHANISM**	**USES**	**REFERENCE**
1	BENDAMUSTINE : TREANDA  4-[5-[bis(2-chloroethyl)amino]-1-methylbenzimidazol-yl]butanoic acid Formula: $C_{16}H_{21}Cl_2N_3O_2$ Mol. mass: 358.262 g/mol	(1) p53-dependent activation of DNA damage stress response and apoptosis, (2) inhibition of mitotic checkpoints, and (3) induction of mitotic catastrophe.[7]	Chronic lymphocytic leukemia, Hodgkin's disease, non-Hodgkin's lymphoma, multiple myeloma and lung cancer[6]	Kath R, [6] Leoni LM, et al [7]

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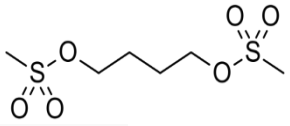
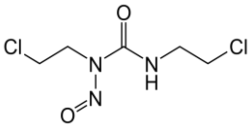
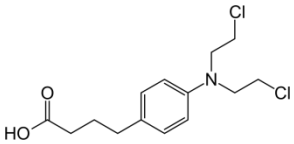
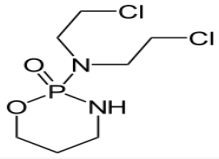
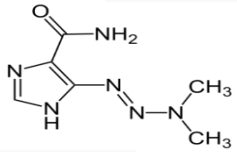
2	BUSULFAN : MYLERAN  butane-1,4-diyl dimethanesulfonate Formula: $C_6H_{14}O_6S_2$ Mol. mass: 246.304 g/mol	Results in the interference of DNA replication and RNA transcription, disruption of nucleic acid function undergoes apoptosis. [9]	-Chronic myeloid leukemia. -chronic myelogenous leukemia -lymphomas, myeloproliferative disorders. [8]	Lesurtel M, et al [8] Hall AG, et al [9]
3	CARMUSTINE : BICNU  1,3-Bis(2-chloroethyl)-1-nitrosourea Formula: $C_5H_9Cl_2N_3O_2$ Mol. mass: 214.05 g mol^{-1}	Inhibition of DNA synthesis, RNA production and RNA translation. Carmustine also binds and modifies (carbamoylates) glutathione reductase. This leads to cell death. [11]	Glioma, glioblastoma multiforme, medullo blastoma and astrocytoma multiple myeloma lymphoma [10]	"Carmustine – et al [10] Drablos F, et al [11]
4	CHLORAMBUCIL : LEUKERAN  4-[bis(2-chlorethyl)amino]benzenebutanoic acid Formula: $C_{14}H_{19}Cl_2NO_2$ Mol. mass: 304.212 g/mol	1) Preventing DNA Synthesis and RNA transcription from the affected DNA, 2) DNA damage 3) The induction of mispairing of the nucleotides leading to mutations. [13]	Non-Hodgkin lymphoma, Waldenström macroglobulinemia, polycythemia vera, trophoblastic neoplasms, ovarian carcinoma. [12]	Rai KR, et al [12] Begleiter A, et al [13]
5	CYCLOPHOSPHAMIDE : ENDOXAN  (RS)-N,N-bis(2-chloroethyl)-1,3,2-oxazaphosphinan-2-amine 2-oxide Formula: $C_7H_{15}Cl_2N_2O_2P$ Mol. mass: 261.086 g/mol	Mechanisms include: [14] Elimination of T regulatory cells (CD4+CD25+ T cells) Induction of T cell growth factors, such as type I IFNs, and/or	Numerous malignant processes and certain autoimmune diseases.	Sistigu A, et al [14]
6	DACARBAZINE : DTIC-DOME  5-(3,3-Dimethyl-1-triazenyl)imidazole-4-carboxamide Formula: $C_6H_{10}N_6O$	The mechanism of action is not known, but appears to exert cytotoxic effects via its action as an alkylating agent. Other theories include DNA synthesis inhibition by its action as a purine analog, [16]	Metastatic melanoma Hodgkin lymphoma [15]	fass.se [15] Lonn U,et al [16]

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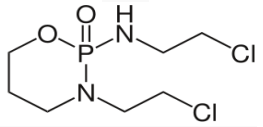
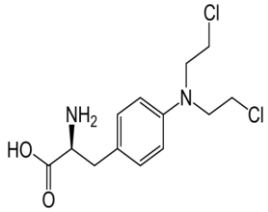
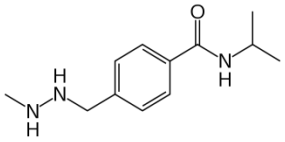
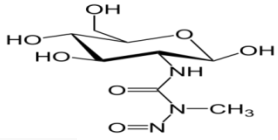
	Mol. mass: 182.18g/mol			
7	IFOSFAMIDE : IFEX  N-3-bis(2-chloroethyl)-1,3,2-oxazaphosphinan-2-amide-2-oxide Formula: $C_7H_{15}Cl_2N_2O_2P$ Mol. mass: 261.1 g mol^{-1}	The exact mechanism of ifosfamide has not been determined, but appears to be similar to other alkylating agents. The formation of inter and intra strand cross-links in the DNA results in cell death. [18]	Testicular cancer, Lymphoma , Soft tissue sarcoma, Osteogenic sarcoma , Cervical cancer, Ovarian cancer [17]	Jahnke K, et al [17] Dechant KL, et al [18]
8	MELPHALAN : ALKERAN  4-[bis(chloroethyl)amino]phenylalanine Formula: $C_{13}H_{18}Cl_2N_2O_2$ Mol. mass: 305.2 g/mol	Forming mono adducts and resulting in the DNA being fragmented, preventing DNA synthesis and RNA transcription from the affected DNA, [20]	Multiple myeloma and Ovarian cancer, malignant melanoma. [19]	Facon T, et al [19] Vasquez KM: et al [20]
9	PROCARBAZINE : MATULANE  N-isopropyl-4-[(2-methylhydrazino)methyl]benzamide Formula: $C_{12}H_{19}N_3O$ Mol. mass: 221.299 g/mol	Its mechanism of action is not fully understood. Metabolism yields azo-procarbazine and hydrogen peroxide which results in the breaking of DNA strands. [21]	Hodgkin's lymphoma	"WHO Model List of EssentialMedicines". Et al [21]
10	STREPTOZOCIN: ZANOSAR  2-Deoxy-2-({[methyl(nitroso)amino]carbonyl}amino)-β-D-glucopyranose. Formula: $C_8H_{15}N_3O_7$ Mol. mass: 265.221 g/mol	DNA damage induces activation of poly ADP-ribosylation, which is likely more important for diabetes induction than DNA damage itself.[3]	Metastatic cancer	Szkudelski T et al [22]
11	TEMOZOLOMIDE : TEMODAR	Temozolomide exhibits schedule-dependent anti-neoplastic activity by interfering with DNA replication. [24]	Oligodendroglioma brain tumors. melanoma[23]	Malcolm Stevens et al [23] Sitbon Sitruk,

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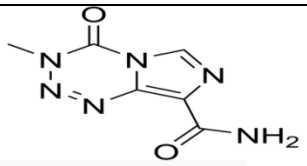
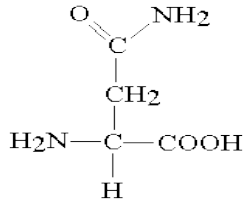
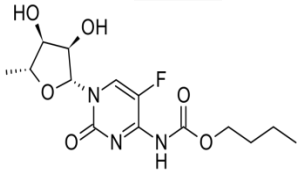
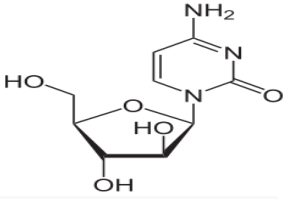
	 4-methyl-5-oxo-2,3,4,6,8-pentazabicyclo[4.3.0]nona-2,7,9-triene-9-carboxamide Formula: $C_6H_6N_6O_2$ Mol. mass: 194.151 g/mol			et al [24]
	ANTI- METABOLITES:			
12	ASPARAGINASE : ELSPAR  asparagine E. coli L-asparagine amidohydrolase Formula: $C_{1377}H_{2208}N_{382}O_{442}S_{17}$ Mol. mass: 31731.9 g/mol	Aspargine- →aspartate→aspargine synthatase→aspargine Aspargine(tumor cell=L-asparginase) →aspargine (protein synthesis)	Industrial and pharmaceutical purposes.	"WHO Model et al [21]
13	CAPECITABINE : XELODA  pentyl [1-(3,4-dihydroxy-5-methyltetrahydrofuran-2-yl)-5-fluoro-2-oxo-1H-pyrimidin-4-yl]carbamate Formula: $C_{15}H_{22}FN_3O_6$ Mol. mass: 359.35 g/mol	Thymidylate synthase inhibitor, hence inhibiting the synthesis of thymidine monophosphate (ThMP), the active form of thymidine which is required for the de novo synthesis of DNA and RNA during gene expression.	Colorectal cancer, Oesophageal cancer Gastric cancer Breast cancer	"Xeloda (capecitabine ….et al [25]
14	CYTARABINE: CYTOSAR-U  4-amino-1-[(2R,3S,4R,5R)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl] pyrimidin-2-one Formula: $C_9H_{13}N_3O_5$ Mol. mass: 243.217 g/mol	Inhibits both DNA[27] and RNA Polymerases and nucleotide reductase enzymes needed for DNA synthesis.	Acute myeloid leukaemia, acute lymphocytic leukaemia, lympho mas, [26]	Pigneux A, et al [26] Perry, Michael et al [27]

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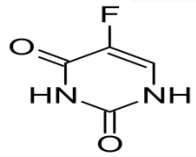
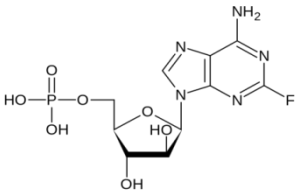
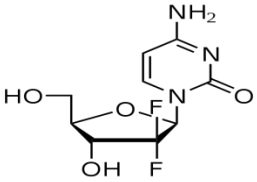
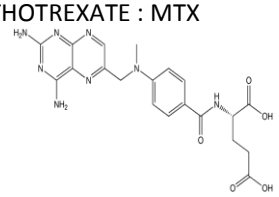
15	5- FLUORO URACIL : ADRUCIL  5-fluoro-1H,3H-pyrimidine-2,4-dione Formula: $C_4H_3FN_2O_2$ Mol. mass: 130.077 g/mol	Administration of 5-FU causes a scarcity in dTMP, so rapidly dividing cancerous cells undergo cell death via thymineless death. [29]	Anal, breast, colorectal,oesophageal, stomach, pancreatic and skin cancers [28]	Rossi, S, ed. Et al [28] Longley DB, et al [29]
16	FLUDARABINE : FLUDARA  [(2R,3R,4S,5R)-5-(6-amino-2-fluoro-purin-9-yl)- 3,4-dihydroxy-oxolan-2-yl]methoxyphosphonic acid Formula: $C_{10}H_{13}FN_5O_7P$ Mol. mass: 365.212 g/mol	Fludarabine inhibits DNA synthesis by interfering withribonucleotide reductase and DNA polymerase. It is active against both dividing and resting cells.	Hematological malignancies leukemias and lymphomas	Rai KR et al. [30]
17	GEMCITABINE : GEMZAR  4-amino-1-(2-deoxy-2,2-difluoro-β-D-erythro-pentofuranosyl)pyrimidin-2(1H)-on Formula: $C_9H_{11}F_2N_3O_4$ Mol. mass: 263.198 g/mol	The process arrests tumor growth. gemcitabine is the enzyme ribonucleotide reductase (RNR). The diphosphate analogue binds to RNR active site and inactivates the enzyme irreversibly. Once RNR is inhibited, the cell cannot produce the deoxy ribonucleotides required for DNA replication and repair, and cell apoptosis is induced.	Carcinomas: non-small cell lung cancer, pancreatic cancer, bladder cancer and breast cancer.	N. M. F. S. A. [31]
18	METHOTREXATE : MTX  N-(4-{[(2,4-Diamino-6-pteridinyl)methyl](methyl)amino}benzoyl)-L-glutamic acid Formula: $C_{20}H_{22}N_8O_5$ Mol. mass: 454.439301 Da	It is an inhibitor of tetrahydrofolate dehydrogenase and prevents the formation of tetrahydrofolate, necessary for synthesis of thymidylate, an essential component of DNA.	Neoplastic Diseases, Psoriasis Rheumatoid Arthritis	U.S. National Library of Medicine, [32]

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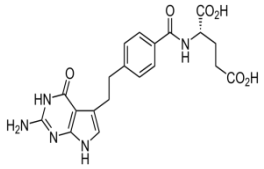
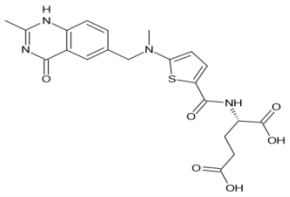
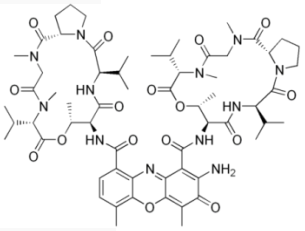
19	PEMETREXED: ALIMTA  (2S)-2-{[4-[2-(2-amino-4-oxo-1,7-dihydro pyrrolo[2,3-d]pyrimidin-5-yl)ethyl]benzoyl]amino} pentanedioic acid Formula: $C_{20}H_{21}N_5O_6$ Mol. mass: 427.411 g/mol	Pemetrexed prevents the formation of DNA andRNA, which are required for the growth and survival of both normal cells and cancer cells. [33]	Malignant Pleural Mesothelioma[34]	McLeod, et al [33] Manegold C et al [34]
20	RALTITREXED : TDX  N-[(5-{methyl[(2-methyl-4-oxo-1,4-dihydroquinazolin-6-yl)methyl]amino}-2-thienyl)carbonyl]-L-glutamic acid Formula: $C_{21}H_{22}N_4O_6S$ Mol. mass: 458.489 g/mol	Raltitrexed prevents the formation of DNA and RNA, which are required for the growth and survival of both normal cells and cancer cells. Inhibition of L1210 cell growth in culture IC_{50} = 9 nM, is one of the strongestantimetabolites in use.	malignant mesothelioma	Widemann BC, et al [35]
	ANTI-TUMOUR ANTIBIOTICS:			
21	ACTINOMYCIN D / DACTINOMYCIN : COSMEGEN  2-Amino-N,N'-bis[(6S,9R,10S,13R,18aS)-6,13-diisopropyl-2,5,9-trimethyl-1,4,7,11,14-pentaoxohexadecahydro-1H-pyrrolo[2,1-i][1,4,7,10,13]oxatetraazacyclohexadecin-10-yl]-4,6-dimethyl-3-oxo-3H-phenoxazine-1,9-dicarboxamide Formula: $C_{62}H_{86}N_{12}O_{16}$ Mol. mass: 1255.42 g/mol	Inhibit transcription. Actinomycin D binding DNA at the transcription initiation complex and preventing elongation of RNA chain by RNA polymerase.	Gestational trophoblastic neoplasia Wilms' tumor Rhabdomyosarcoma Ewing's sarcoma Malignant hydatidiform mole[36-41]	Sobell H- et al , Uberti, E. M. H et al [36-41]

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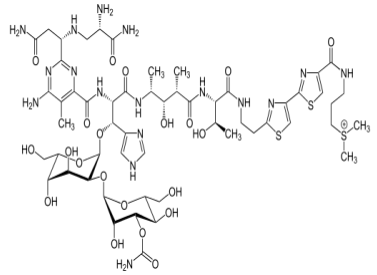
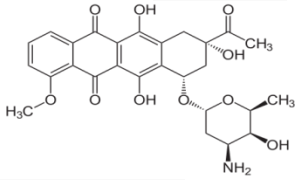
22	BLEOMYCIN : BLENOXANE  (3-{[(2'-{(5S,8S,9S,10R,13S)-15-{6-amino-2- [(1S)-3-amino-1-{[(2S)-2,3-diamino-3-oxopropyl]amino}-3-oxopropyl] -5-methylpyrimidin-4-yl}-13-[{[(2R,3S,4S,5S,6S)-3-{[(2R,3S,4S,5R,6R)-4-(carbamoyloxy)-3,5-dihydroxy-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yl]oxy} -4,5-dihydroxy-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yl]oxy} (1H-imidazol-5-yl)methyl]-9-hydroxy-5-[(1R)-1-hydroxyethyl]-8,10-dimethyl-4,7,12,15-tetraoxo-3,6,11,14-tetraazapentadec-1-yl}-2,4'-bi-1,3-thiazol-4-yl)carbonyl]amino}propyl)(dimethyl)sulfonium Formula: $C_{55}H_{84}N_{17}O_{21}S_3$ Mol. mass: 1415.551g/mol	Bleomycin may bind at specific sites in the DNA strand and induce scission by abstracting the hydrogen atom from the base, resulting in strand cleavage as the base undergoes a Criegee-type rearrangement, or forms an alkali-labile lesion. [42-44]	Hodgkin's lymphoma, plantar warts pleurodesis [42-44]	Lewis, TG et al - Hecht, e tal [42-44]
23	DAUNORUBICIN : CERUBIDINE  (8S,10S)-8-acetyl-10-[(2S,4S,5S,6S)-4-amino-5-hydroxy-6-methyl-oxan-2-yl]oxy-6,8,11-trihydroxy-1-methoxy-9,10-dihydro-7H-tetracene-5,12-dione Formula: $C_{27}H_{29}NO_{10}$ Mol. mass: 527.52 g/mol	Binds to every 3 base pairs and induces a local unwinding angle of 11°, but negligible distortion of helical conformation. It can also induce histone eviction from chromatin upon interc alation. [45-46]	Neuroblastoma, chronic myelogenous leukemia.	G J Quigley, et al - Pang B, et al [45-46]
24	DOXORUBICIN : ADRIAMYCIN			

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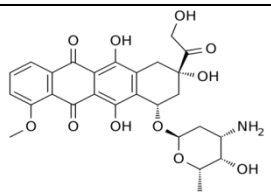
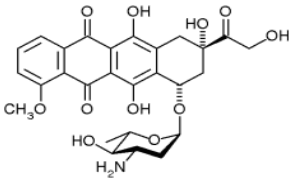
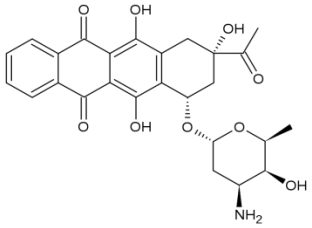
	 (7S,9S)-7-[(2R,4S,5S,6S)-4-amino-5-hydroxy-6-methyloxan-2-yl]oxy-6,9,11-trihydroxy-9-(2-hydroxyacetyl)-4-methoxy-8,10-dihydro-7H-tetracene-5,12-dione Formula: $C_{27}H_{29}NO_{11}$ Mol. mass: 543.52 g/mol	Induce histone eviction from chromatin. As a result, DNA damage response, epigenome and tr anscriptome are deregulated in doxorubicin-exposed cells. [48]	leukemias and Hod gkin's lymphoma, as well as cancers of the bladder, breast, stomach, lung, ovaries, thyroid, soft tissue sarcoma, multiple myeloma, [47]	Brayfield, A, et al [47] Pang B, et al [48]
25	EPIRUBICIN: ELLENCE  (8R,10S)-10-((2S,4S,5R,6S)-4-amino-5-hydroxy-6-methyltetrahydro-2H-pyran-2-yl)-6,8,11-trihydroxy-8-(2-hydroxyacetyl)-1-methoxy-7,8,9,10-tetrahydrotetracene-5,12-dione Formula: $C_{27}H_{29}NO_{11}$ Mol. mass: 543.519 g/mol	Acts by intercalating DNA strands . Intercalation results in complex formation which inhibits DNA and RNA synthesis. It also triggers DNA cleavage by topoisomerase II, resulting in mechanisms that lead to cell death.	Breast and ovarian cancer, gastric cancer, lung cancer and lymphomas.	Bonfante, V; et al [49]
26	IDARUBICIN : ZAVEDOS  (1S,3S)-3-acetyl-3,5,12-trihydroxy-6,11-dioxo-1,2,3,4,6,11-hexahydrotetracen-1-yl 3-amino-2,3,6-trideoxo-α-L-lyxo-hexopyranoside Formula: $C_{26}H_{27}NO_9$ Mol. mass: 497.494 g/mol	Prevents DNA from unwinding by interfering with the enzyme topoisomerase II. It also induces histoneeviction from chromatin.	Acute myeloid leukemia.	Pang B,et al [50]
27	MITOMYCIN : MITOMYCIN C	Mitomycin C is a potent DNA crosslinker chemotherapeutic agent in glaucoma surgery. [51-52]	Esophageal carcinoma bladder tumours anal cancers, and breast cancers	Tomasz, et al [51]

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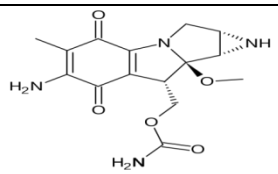
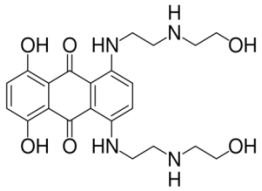
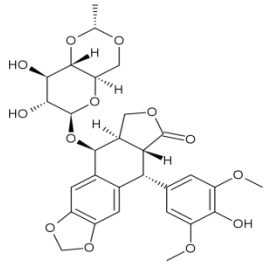
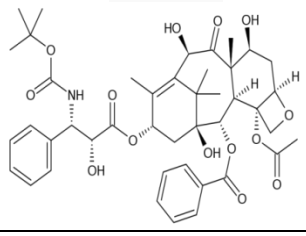
	 {11-Amino-7-methoxy-12-methyl-10,13-dioxo-2,5-diazatetracyclo[7.4.0.0^{2,7}.0^{4,6}]trideca-1(9),11-dien-8-yl}methyl carbamate Formula: $C_{15}H_{18}N_4O_5$ Mol. mass: 334.33 g mol^{-1}			Renault, et al [52]
28	MITOXANTRONE: NOVANTRONE  1,4-dihydroxy-5,8-bis[2-(2-hydroxyethylamino) ethylamino]-anthracene-9,10-dione Formula: $C_{22}H_{28}N_4O_6$ Mol. mass: 444.481 g/mol	Mitoxantrone is a type II topoisomerase inhibitor; it disrupts DNA synthesis andDNA repair in both healthy cells and cancer cells, by intercalation. between the DNA bases. [54]	Metastatic breast cancer, acute myeloid leukemia, and non-Hodgkin's lymphoma [53]	Parker C, et al [53] Mazerski J, et al [54]
PLANT ALKALOIDS/ MICROTUBULE INHIBITORS:				
29	ETOPOSIDE : ETOPOPHOS  4'-Demethyl-epipodophyllotoxin 9-[4,6-O-(R)-ethylidene-beta-D-glucopyranoside], 4' -(dihydrogen phosphate) Formula: $C_{29}H_{32}O_{13}$ Mol. mass: 588.557 g/mol	Prevents re-ligation of the DNA strands, and by doing so causes DNA strands to break. Cancer cells rely on this enzyme more than healthy cells, since they divide more rapidly. Therefore, this causes errors in DNA synthesis and promotes apoptosis of the cancer cell.	Kaposi's sarcoma, Ewing's sarcoma, lung cancer, testicular cancer, lymphoma, nonlymphocytic leu kemia, and glioblastoma multiforme.	Hande KR et al [55-57]
30	DOCETAXEL : TAXOTERE 	Binding stabilizes microtubules and prevents depolymerisation from calcium ions, decreased temperature and dilution, preferentially at the plus end of the microtubule. It has also been found to	Breast, colorectal, lung, ovarian, prostate, liver, renal, gastric, head and neck cancers, and melanoma [58]	Lyseng-et al [58] Yvon AM, et al [59]

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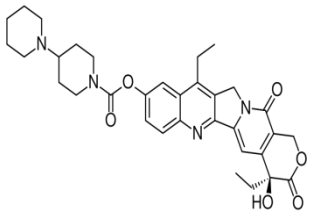
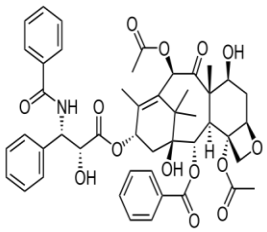
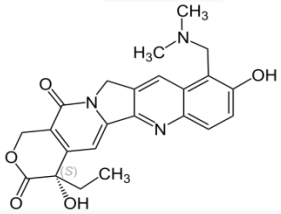
	1,7β,10β-trihydroxy-9-oxo-5β,20-epoxytax-11-ene-2α,4,13α-triyl 4-acetate 2-benzoate 13-{(2R,3S)-3-[(tert-butoxycarbonyl)amino]-2-hydroxy-3-phenylpropanoate Formula: $C_{43}H_{53}NO_{14}$ Mol. mass: 807.879 g/mol	lead to the phosphorylation of oncoprotein bcl-2, which is apoptosis-blocking in its oncoprotein form [59]		
31	IRINOTECAN : CAMPTOSAR  (S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo1H-pyrano[3',4':6,7]-indolizino[1,2-b]quinolin-9-yl-[1,4'bipiperidine]-1'-carboxylate Formula: $C_{33}H_{38}N_4O_6$ Mol. mass: 586.678 g/mol	Irinotecan prevents DNA from unwinding by inhibition of topoisomerase The inhibition of topoisomerase I by the active metabolite SN-38 eventually leads to inhibition of both DNA replication and transcription.	colon cancer	Pommier, Y., et al [60]
32	PACLITAXEL : TAXOL  (2α,4α,5β,7β,10β,13α)-4,10-bis(acetyloxy)-13-{[(2R,3S)- 3-(benzoylamino)-2-hydroxy-3-phenylpropanoyl]oxy}- 1,7-dihydroxy-9-oxo-5,20-epoxytax-11-en-2-yl benzoate Formula: $C_{47}H_{51}NO_{14}$ Mol. mass: 853.906 g/mol	Inhibit spindle function is generally attributed to its suppression of microtubule dynamics, Paclitaxel appears to suppress microtubule detachment from centrosomes, a process normally activated during mitosis. Paclitaxel binds to beta-tubulin subunits of microtubules.	Kaposi's sarcoma ovarian cancer.	Jordan et al [61-63]
33	TOPOTECAN : HYCAMTIN  (S)-10-[(dimethylamino)methyl]-4-ethyl-4,9-dihydroxy-1H-	Topotecan intercalates between DNA bases. This intercalation disrupts the DNA duplication machinery when it reaches a site where topotecan is intercalated. This disruption prevents DNA replication, and ultimately leads to cell	Ovarian cancer Cervical cancer Small cell lung cancer Neuroblastoma Brainstem glioma Ewing's sarcoma	Staker, B.L. et al [64]

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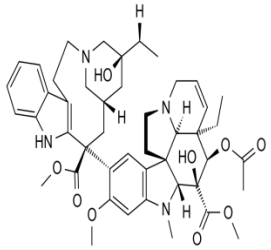
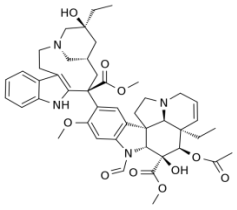
	pyrano[3',4':6,7]indolizino[1,2-b] quinoline-3,14(4H,12H)-dione monohydrochloride Formula: $C_{23}H_{23}N_3O_5$ Mol. mass: 457.9 g/mol	death.		
34	VINBLASTINE  dimethyl (2β,3β,4β,5α,12β,19α)-15-[(5S,9S)-5-ethyl-5-hydroxy-9-(methoxycarbonyl)-1,4,5,6,7,8,9,10-octahydro-2H-3,7-methanoazacycloundecino[5,4-b]indol- 9-yl]-3-hydroxy-16-methoxy-1-methyl-6,7-didehydroaspidospermidine-3,4-dicarboxylate Formula: $C_{46}H_{58}N_4O_9$ Mol. mass: 810.975 g/mol	Produce microtubule fragments by stimulating microtubule minus-end detachment from their organizing centers. Dose-response studies further indicate that enhanced microtubule detachment from spindle poles correlate best with cytotoxicity.	Hodgkin's lymphoma, non-small cell lung cancer,breast cancer, head and neck cancer, and testicular cancer.	Yang, H.; et al [65]
35	VINCRISTINE: ONCOVIN  (3aR,3a1R,4R,5S,5aR,10bR)-methyl 4-acetoxy-3a-ethyl-9-((5S,7S,9S)-5-ethyl-5-hydroxy-9-(methoxycarbonyl)-2,4,5,6,7,8,9,10-octahydro-1H-3,7-methano[1]azacycloundecino[5,4-b]indol-9-yl)-6-formyl-5-hydroxy-8-methoxy-3a,3a1,4,5,5a,6,11,12-octahydro-1H-indolizino[8,1-cd]carbazole-5-carboxylate Formula: $C_{46}H_{56}N_4O_{10}$ Mol. mass: 824.958 g/mol	Vincristine binds to tubulin dimers, inhibiting assembly of microtubule structures and arresting mitosis in metapha se. Because vincristine's mechanism of action targets all rapidly dividing cell types, it not only inhibits cancerous cells but can also affect the intestinal epithelium and bone marrow	Thrombotic thrombocytopenic purpura (TTP) or chronic idiopathic thrombocytopenic purpura	Brayfield, A, et al [66]
36	VINORELBINE : NAVELBINE			

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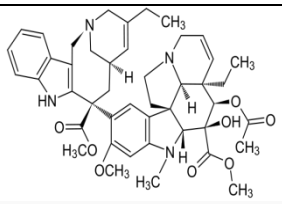
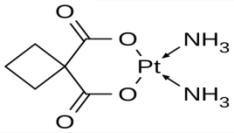
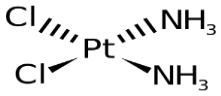
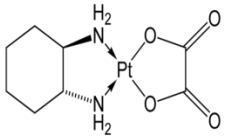
	 4-(acetyloxy)- 6,7-didehydro- 15-((2R,6R,8S)-4-ethyl- 1,3,6,7,8,9-hexahydro- 8-(methoxycarbonyl)- 2,6-methano- 2H-azecino(4,3-b)indol-8-yl)- 3-hydroxy- 16-methoxy- 1-methyl- methyl ester, Formula: $C_{45}H_{54}N_4O_8$ Mol. mass: 778.932 g/mol	Activity is due to inhibition of mitosis through interaction with tubulin.	Non-small-cell lung cancer and metastatic breast cancer. rhabdomyo sarcoma	Casanova, M; et al [67]
	DNA LINKING AGENTS:			
37	CARBOPLATIN : PARAPLATIN  cis-diammine(cyclobutane-1,1-dicarboxylate-O,O')platinum(II) Formula: $C_6H_{12}N_2O_4Pt$ Mol. mass: 371.249 g/mol	Aquation, or the like-cisplatin hypothesis. Activation, or the unlike-cisplatin hypothesis. while the latter hypothesis envisages a biological activation mechanism to release the active Pt2+ species.	Ovarian carcinoma, lung, head and neck cancers as well as endometrial, esophageal, bladder, breast and cervical	Wheate NJ, et al [68]
38	CISPLATIN : PLATINOL  (SP-4-2)-diammine dichloroplatinum(II) Formula: $H_6Cl_2N_2Pt$ Mol. mass: 300.01 g/mol	These platinum complexes react in vivo, binding to and causing crosslinking of DNA, which ultimately triggers apoptosis (program med cell death).	Small cell lung cancer, and ovarian cancer),lymphomas , and germ cell tumors	Praveen D*, et al [69]
38'	OXALIPLATIN : ELOXATIN  [(1R,2R)-cyclohexane-1,2-diamine](ethanedioato-O,O')platinum(II) Formula: $C_8H_{14}N_2O_4Pt$ Mol. mass: 397.2858 g/mol	Oxaliplatin forms both inter- and intra-strand cross links in DNA,which prevent DNA replication and transcription, causing cell death.	Colorectal cancer	Graham, et al [70]
	BIOLOGICAL AGENTS :			
39	BEVACIZUMAB : AVASTIN	Binds directly to VEGF to form a protein complex which is incapable of further binding to VEGF	Glioblastoma metastatic cancers colorectal	Los, M.; et al [71]

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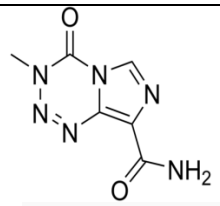
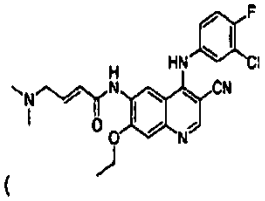
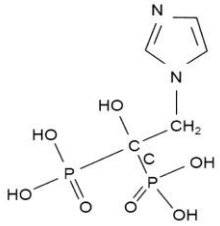
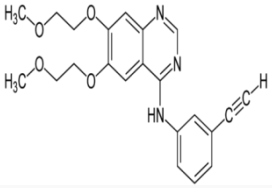
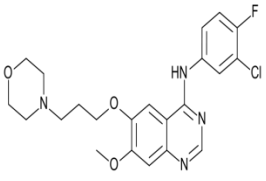
	 Formula: $C_{6638}H_{10160}N_{1720}O_{2108}S_{44}$ Mol. mass: approx. 149 k Da	receptor sites (which would initiate vessel growth) effectively reducing available VEGF. The Bevacizumab /VEGF complex is both metabolized and excreted directly.		
40	CETUXIMAB : ERBITUX  Formula: $C_{6484}H_{10042}N_{1732}O_{2023}S_{36}$ Mol. mass: 145781.6 g/mol	Binds to EGFR and turns off the uncontrolled growth in cancers with EGFR mutations. However, if the KRAS protein is mutated, cetuximab has been found not to work, mutated gene now does not respond to the EGFR receptor.	Metastatic colorectal cancer, metastatic non-small cell lung cancer	Micromedex Healthcare Series et al [72]
41	DENOSUMAB : XGEVA  Formula: $C_{6404}H_{9912}N_{1724}O_{2004}S_{50}$ Mol. mass: 144.7 kDa	Inhibits this maturation of osteoclasts by binding to and inhibiting RANKL.	Multiple myeloma and giant cell tumor of bone	McClung, et al [73]
42	ERLOTINIB:  N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy) quinazolin-4-amine Formula: $C_{22}H_{23}N_3O_4$ Mol. mass: 393.436 g/mol	Erlotinib is an EGFR inhibitor. inhibiting the ATP, formation of phosphotyrosine residues in EGFR is not possible and the signal cascades are not initiated.	Non-small cell lung cancer (NSCLC), pancreatic cancer	Raymond E, et al [74]
43	GEFITINIB: IRESSA  N-(3-chloro-4-fluoro-phenyl)-7-methoxy- 6-(3-morpholin-4-	Gefitinib inhibits EGFR tyrosine kinase by binding to the adenosine triphosphate (ATP)-binding site of the enzyme. Thus the function of the EGFR tyrosine kinase in activating the anti-apoptotic Ras signal transduction cascade is inhibited, and	Metastatic, unresectable NSCLC	Takimoto CH, Calvo E. et al [75]

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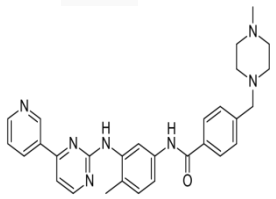
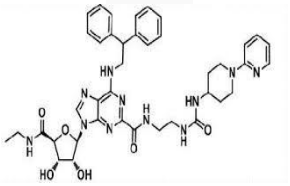
	ylpropoxy)quinazolin-4-amine Formula: $C_{22}H_{24}ClFN_4O_3$ Mol. mass: 446.902 g/mol	malignant cells are inhibited.		
44	IMATINIB: GLIVEC  4-[(4-methylpiperazin-1-yl)methyl]-N-(4-methyl-3-{[4-(pyridin-3-yl)pyrimidin-2-yl]amino}phenyl)benzamide Formula: $C_{29}H_{31}N_7O$ Mol. mass: 493.603 g/mol	Imatinib also inhibits the abl protein of non-cancer cells but cells normally have additional redundant tyrosine kinases which allow them to continue to function even if abl tyrosine kinase is inhibited. where it is unable to perform any of its normal anti-apoptopic functions. [76-77]	Chronic myelogenous leukemia (CML),gastrointestinal stromal tumors (GISTs) and a number of other malignancies.	Deininger MW, et al [76] Vigneri et al [77]
45	INTERFERON: **ROFERON A** Proteins made and released by host cells in response to the presence of pathogens such as viruses, bacteria, parasites or tumor cells. named after their ability to "interfere" with viral replication[78] Formula: $C_{908}H_{1408}N_{246}O_{253}S_6$ Mol. mass: 20011.0000	Interferon beta binds to type I interferon receptors (IFNAR1 and IFNAR2c) which activate two Jak (Janus kinase) tyrosine kinases (Jak1 and Tyk2). These transphosphorylate themselves and phosphorylate the receptors. The phosphorylated INFAR receptors then bind to Stat1 and Stat2 (signal transducers and activators of transcription) Interferon beta binds more stably to type I interferon receptors than interferon alpha. [79]	relapsing/remitting multiple sclerosis	de Weerd NA, et al [78] Russell-Harde D et al [79]
46	IPILIMUMAB : YERVOY  Formula: $C_{6572}H_{10126}N_{1734}O_{2080}S_{40}$ Mol. mass: 148 kDa	Ipilimumab is designed to block the activity of CTLA-4,	Non-small cell lung carcinoma (NSCLC), small cell lung cancer	Antoni Ribas et al [80]
47	LAPATINIB: TYKERB	Lapatinib inhibits receptor signal processes by binding to the ATP-binding pocket of the EGFR/HER2 protein kinase domain	Metastatic breast cancer	Dr. Angel Rodriguez [81]

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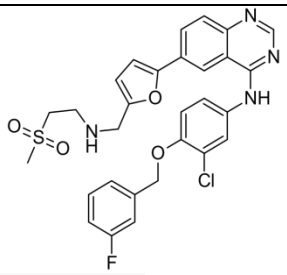
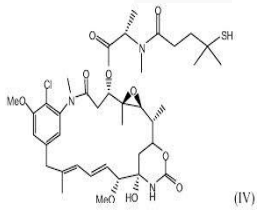
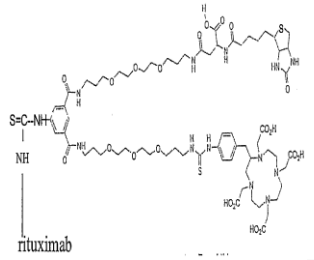
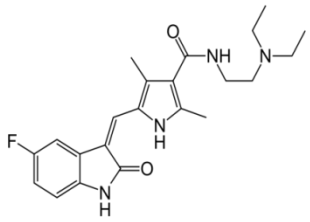
	 N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[(2-methylsulfonylethylamino)methyl]-2-furyl]quinazolin-4-amine Formula: $C_{29}H_{26}ClFN_4O_4S$ Mol. mass: 581.058 g/mol			
48	PANITUMUMAB : VECTIBIX  Formula: $C_{6398}H_{9878}N_{1694}O_{2016}S_{48}$ Mol. mass: 147 kDa	Panitumumab IS immunization of transgenic mice (XenoMouse) that are able to produce humanimmunoglobulin ligh t and heavy chains. B cells that produced an antibody against EGFR was selected and immortalized in Chinese hamster ovary (CHO) cells.	Metastatic colorectal cancer	U.S. Food and Drug Administration [82]
49	RITUXIMAB: RITUXAN  Formula: $C_{6416}H_{9874}N_{1688}O_{1987}S_{44}$ Mol. mass: 143859.7 g/mol	It elicits shedding of CD23. It downregulates the B cell receptor. It induces apoptosis of CD20+ cells.	Treat diseases which are characterized by having too many B cells, overactive B cells, or dysfunctional B cells.	T Shaw, J et al [83]
50	SUNITINIB: SUTENT  N-(2-diethylaminoethyl)-5-[(Z)-(5-fluoro-2-oxo-1H-indol-3-ylidene)methyl]-2,4-dimethyl-1H-	Sunitinib inhibits cellular signaling by targeting multiple receptor tyrosine kinases (RTKs). sunitinib inhibits other RTKs. These include the following:RET, CSF-1R, flt3	Gastrointestinal stromal tumor Pancreatic neuro-endocrine tumors Renal cell carcinoma	Pfizer, Inc, New York NY. [84]

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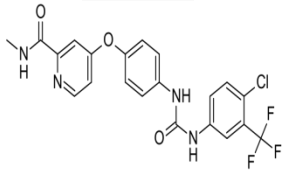
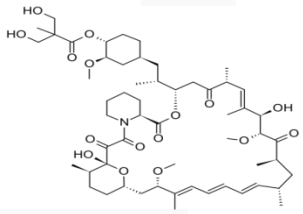
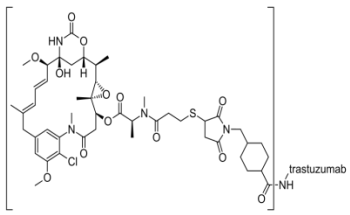
	pyrrole-3-carboxamide Formula: $C_{22}H_{27}FN_4O_2$ Mol. mass: 398.474 g/mol			
51	SORAFENIB: NEXAVAR  4-[4-[[4-chloro-3-(trifluoromethyl)phenyl]carbamoyl amino] phenoxy]-N-methyl-pyridine-2-carboxamide Formula: $C_{21}H_{16}ClF_3N_4O_3$ Mol. mass: 464.825 g/mol	Sorafenib is a small molecular inhibitor of several tyrosine protein kinases (VEGFR and PDGFR) and Raf kinases (more avidly C-Raf than B-Raf).	Renal cell carcinoma (RCC), unresectable hepat ocellular carcinomas(HCC) and thyroid cancer	Bleeding; including serious bleeds such as intracranial and intra-pulmonary bleeds [85]
52	TEMSIROLIMUS: TORISEL  (1R,2R,4S)-4-{(2R)-2-[(3S,6R,7E,9R,10R,12R,14S,15E,17E,19E,21S,23S,26R,27R,34aS)-9,27-dihydroxy-10,21-dimethoxy-6,8,12,14,20,26-hexamethyl-1,5,11,28,29-pentaoxo-1,4,5,6,9,10,11,12,13,14,21,22,23,24,25,26,27,28,29,31,32,33,34,34a-tetracosahydro-3H-23,27-epoxypyrido[2,1-c][1,4]oxazacyclohentriacontin-3-yl]propyl}-2-methoxycyclohexyl 3-hydroxy-2-(hydroxymethyl)-2-methylpropanoate Formula: $C_{56}H_{87}NO_{16}$ Mol. mass: 1030.28g/mol	Temsirolimus is a specific inhibitor of mTOR and interferes with the synthesis of proteins that regulate proliferation, growth, and survival of tumor cells.	Renal cell carcinoma	Wan, Xiaolin; et al [86]
53	TRASTUZUMAB: HERCLON  Formula: $C_{6470}H_{10012}N_{1726}O_{2013}S_{42}$ Mol. mass: 145531.5 g/mol	Trastuzumab binds to domain IV of the extracellular segment of the HER2/neu receptor. Cells treated with trastuzumab undergo arrest during the G1 phase of the cell cycle so there is reduced proliferation. induces some of its effect	HER2-positive breast cancer, [87]	Moja L, et al [87] Breast Cancer Care [88] Ménard, S; et al [89]

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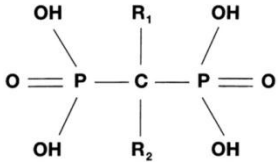
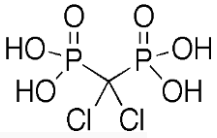
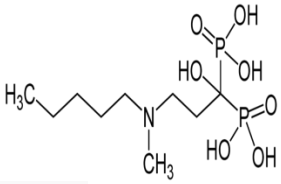
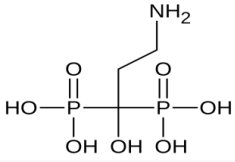
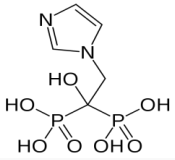
		by downregulation of HER2/neu [88-89]		
54	BISPHOSPHONATES: 	Bisphosphonates inhibit the digestion of bone by encouraging osteoclasts to undergo apoptosis, or cell death, thereby slowing bone loss.	osteoporosis osteitis deformans bone metastasis multiple,myeloma, hyper-parathyroidism,	Weinstein RS, et al [90]
55	CLODRONATE: CLODRONIC ACID  dichloro-phosphono-methyl)phosphonic acid Formula: $CH_4Cl_2O_6P_2$ Mol. mass: 244.892 g/mol	The exact mechanism of action of clodronate is not known, however it is known that it does not inhibit protein isoprenylation but can be metabolized intracellularly to a β-γ-methylene (AppCp-type) analog of ATP (AppCCl2p),	Osteoporosis in post-menopausal women	Lehenkari PP, et al [91]
56	IBANDRONIC ACID : BONIVA  1-hydroxy-3-[methyl(pentyl)amino]propane-1,1-diyl}bis(phosphonic acid) Formula: $C_9H_{23}NO_7P_2$ Mol. mass: 319.229 g/mol	Inhibits osteoclast activity and reduces bone resorption and turnover. In postmenopausal women, it reduces the elevated rate of bone turnover, leading to, on average, a net gain in bone mass.	Post-menopausal osteoporosis.	"boniva". The American Society of Health-System Pharmacists. [92] Epstein S, et al [93]
57	PAMIDRONATE: PAMIDRONIC ACID  (3-amino-1-hydroxypropane-1,1-diyl)bis(phosphonic acid) Formula: $C_3H_{11}NO_7P_2$ Mol. mass: 235.07 g/mol	Inhibition of bone resorption	Osteoporosis Paget's disease [94]	Zarychanski R, et al [94]
58	ZOLENDRONIC ACID: ZOLEDRONATE  [1-hydroxy-2-(1H-imidazol-1-yl)ethane-1,1-diyl]bis(phosphonic	Zoledronic acid slows down bone resorption, allowing the bone-forming cells time to rebuild normal bone and	Osteoporosis Paget's disease	Aclasta label-Australia [95]

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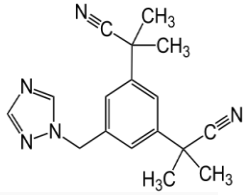
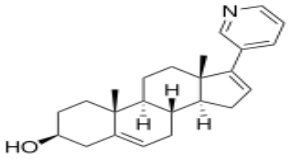
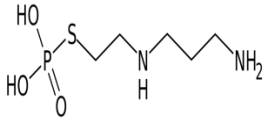
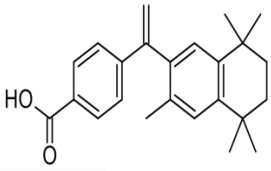
	acid) Formula: $C_5H_{10}N_2O_7P_2$ Mol. mass: 272.09 g/mol	allowing bone remodeling		
		HORMONES/OTHER:		
59	ANASTROZOLE: ARIMIDEX  2,2'-[5-(1H-1,2,4-triazol-1-ylmethyl)-1,3-phenylene]bis(2-methylpropanenitrile Formula: $C_{17}H_{19}N_5$ Mol. mass: 293.366 g/mol	Anastrozole binds reversibly to the aromatase enzyme through competitive inhibition, inhibits the conversion of androgens to estrogens in peripheral tissues (extra-gonadal)	Breast cancer in post menopausal women	Simpson ER et al [96]
60	ABIRATERONE: ZYTIGA  (3β)-17-(pyridin-3-yl)androsta-5,16-dien-3-ol Formula: $C_{24}H_{31}NO$ Mol. mass: 349.509 g/mol	Inhibition of CYP17 activity by abiraterone thus decreases circulating levels of testosterone	castration-resistant prostate cancer	Food and Drug Admin-istration[97] Attard G,et al [98]
61	AMIFOSTINE: ETHYOL  2-(3-aminopropylamino) ethylsulfanyl phosphonic acid Formula: $C_5H_{15}N_2O_3PS$ Mol. mass: 214.224 g/mol	Amifostine detoxifies reactive metabolites of platinum and alkylating agents, as well as scavenges free radicals. [99] Other possible effects include accelerated DNA repair, induction of cellular hypoxia, inhibition of apoptosis.	Xerostomia lung cancer	Kouvaris JR, et al [99]
62	BEXAROTENE: TARGRETIN  4-[1-(3,5,5,8,8-pentamethyltetralin-2-yl)ethenyl]benzoic acid Formula: $C_{24}H_{28}O_2$ Mol. mass: 348.478 g/mol	Bexarotene is a retinoid that selectively activates retinoid X receptors (RXRs), as opposed to the retinoic acid receptors which regulate cell differentiation and proliferation whereas RXRs regulate apoptosis. [100]	Alzheimer's disease non-small cell lung cancer and breast cancer.	Brunton, L; et al [100]
63	BICALUTAMIDE : CASODEX			

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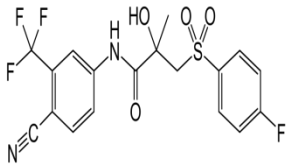
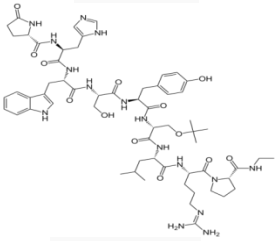
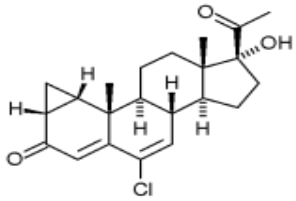
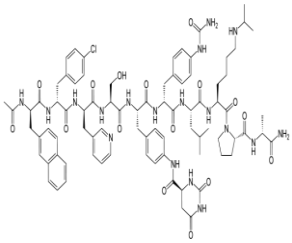
	 N-[4-cyano-3-(trifluoromethyl)phenyl]-3-[(4-fluorophenyl)sulfonyl]-2-hydroxy-2-methylpropanamide Formula: $C_{18}H_{14}F_4N_2O_4S$ Mol. mass: 430.373 g/mol	Bicalutamide acts as a pure anti-androgen by binding to the androgen receptor (AR) and preventing the activation of the AR and subsequent upregulation of androgen responsive genes by androgenic hormones. [101]	Andogen receptor positive ER-/PR- metastatic breast cancer[102]	Furr BJ et al [101] asco.org[102]
64	BUSERELIN: ETILAMIDE  Formula: $C_{62}H_{90}N_{16}O_{15}$ Mol. mass: 1299.48 g/mol	Buserelin desensitizes the GnRH receptor, reducing the amount of LH and testosterone. However, there is a concomitant surge in LH and testosterone levels with the decrease in androgens, so antiandrogens must administered. [103]	Prostate cancer or breast cancer endometriosis or ut erine fibroids	Kirby RS, et al [103]
65	CYPROTERONE  6-chloro-17-hydroxy-1α,2α-methylenepregna-4,6-diene-3,20-dione Formula: $C_{22}H_{27}ClO_3$ Mol. mass: 374.901 g/mol	Cyproterone is blockage of the binding of dihydrotestosterone to the specific receptors in the prostatic carcinoma cell. [105]	Antiandrogen and progestin. [104]	Index Nominum 2000: International Drug Directory. [104] Stadtler FA, et al [105]
66	DEGARELIX: FIRMAGON  Formula: $C_{82}H_{103}ClN_{18}O_{16}$ Mol. mass: 1630.75 g/mol	GnRH antagonists compete with natural GnRH for binding to GnRH receptors in the pituitary gland. This reversible blinding blocks the release of LH and FSH from the pituitary. The reduction in LH subsequently leads to a rapid and sustained suppression of testosterone release from the testes and subsequently reduces the size and growth of the prostate cancer. [107]	Prostate cancer [106]	Princivalle M, et al [106] Persson BE, et al [107]

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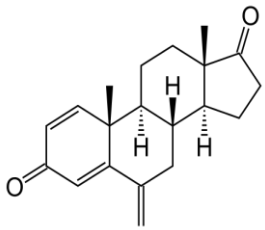
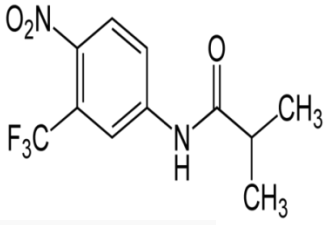
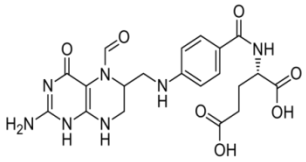
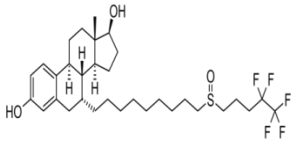
67	EXEMESTANE: AROMASIN  6-Methylideneandrosta-1,4-diene-3,17-dione Formula: $C_{20}H_{24}O_2$ Mol. mass: 296.403 g/mol	Principal enzyme that converts androgens to estrogens both in pre- and postmenopausal women. Exemestane is an irreversible, steroidal aromatase inactivator, lowers circulating estrogen concentrations in postmenopausal women, [109]	Advanced breast cancer in postmenopausal women [108]	Aromasin For Advanced Breast Cancer[108] Robinson A: et al [109]
68	FLUTAMIDE  2-methyl-N-[4-nitro-3-(trifluoromethyl)phenyl]-propanamide Formula: $C_{11}H_{11}F_3N_2O_3$ Mol. mass: 276.212 g/mol	Flutamide is a nonsteroidal antiandrogen that blocks the action of both endogenous and exogenous testosterone by binding to the androgen receptor. In addition Flutamide is a potent inhibitor of testosterone-stimulated prostatic DNA synthesis. [111]	Prostate cancer transsexual women[110]	Scher, Howard et al [110] Jack Lawrence et al [111]
69	FOLINIC ACID: LEUCOVORIN  2S)-2-{[4-[(2-amino-5-formyl-4-oxo-5,6,7,8-tetrahydro-1H-pteridin-6-yl)methylamino] benzoyl]amino}pentanedioic acid Formula: $C_{20}H_{23}N_7O_7$ Mol. mass: 473.44 g/mol	Folinic acid, therefore, allows for some purine/pyrimidine synthesis to occur in the presence of dihydrofolate reductase inhibition, so that some normal DNA replication processes can proceed. [112]	Colon cancer Toxoplasmosis-retinitis, Down's syndrome,	Ellis JM, et al [112]
70	FULVESTRANT: FASLODEX  (7α,17β)-7-{9-[(4,4,5,5,5-pentafluoropentyl)sulfinyl]nonyl}estra-1,3,5(10)-triene-3,17-diol Formula: $C_{32}H_{47}F_5O_3S$	fulvestrant binds to the receptors and down regulates them so that estrogen is no longer able to bind to these receptors. Second, fulvestrant degrades the estrogen receptors to which it is bound. Both of these	hormone receptor positive metastatic breast cancer in postmenopausal women [113]	Angela Mae et al [113] Kabos P, et al [114]

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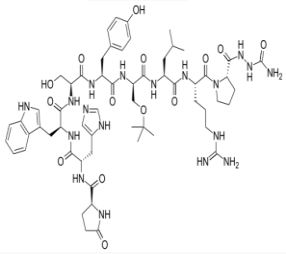
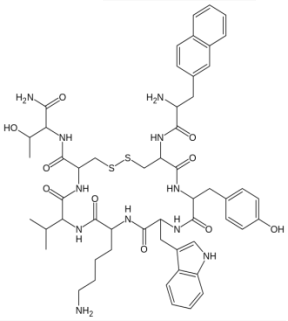
	Mol. mass: 606.772 g/mol	mechanisms inhibit the growth of tamoxifen-resistant as well as estrogen-sensitive human breast cancer cell lines. [114]		
71	GOSERELIN: ZOLADEX  N-(21-((1H-indol-3-yl)methyl)-1,1-diamino-12-(tert-butoxymethyl)-6-(2-(2-carbamoylhydrazinecarbonyl)cyclopentanecarbonyl)-15-(4-hydroxybenzyl)-18-(hydroxymethyl)-25-(1H-imidazol-5-yl)-9-isobutyl-8,11,14,17,20,23-hexaoxo-2,7,10,13,16,19,22-heptaazapentacos-1-en-24-yl)-5-oxopyrrolidine-2-carboxamide Formula: $C_{59}H_{84}N_{18}O_{14}$ Mol. mass: 1269.410 g/mol	Goserelin is a synthetic decapeptide analogue of LHRH. Goserelin acts as a potent inhibitor of pituitary gonadotropin secretion when administered in the biodegradable formulation. The result is sustained suppression of LH and serum testosterone levels. [116]	Breast and prostate cancer. [115]	FDA [115] Kripa S. et al [116]
72	LANREOTIDE : SOMATULINE  (4S,7S,10S,13R,16S,19S)-10-(4-aminobutyl)-19-[[(2R)-2-amino-3-naphthalen-2-yl-propanoyl]amino]-N-[(1S,2R)-1-carbamoyl-2-hydroxy-propyl]-16-[(4-hydroxyphenyl)methyl]-13-(1H-indol-3-ylmethyl)-6,9,12,15,18-pentaoxo-7-propan-2-yl-1,2-dithia-5,8,11,14,17-pentazacycloicosane-4-carboxamide	Lanreotide is a synthetic octapeptide analogue of somatostatin, an endogenous peptide present in several areas of the central nervous system and GI tract. It has inhibitory effects on different cell types and on endocrine, neuroendocrine, and exocrine mechanisms. [118]	Acromegaly carcinoid syndrome. [117]	"FDA [117] Tercica. Et al [118]

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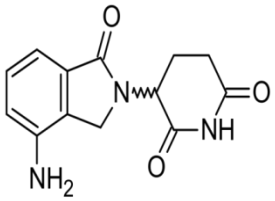
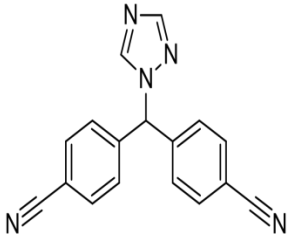
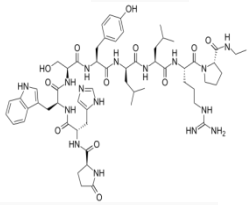
	Formula: $C_{54}H_{69}N_{11}O_{10}S_2$ Mol. mass: 1096.33 g/mol			
73	LENALIDOMIDE : REVLIMID  (RS)-3-(4-Amino-1-oxo 1,3-dihydro-2H-isoindol- 2-yl)piperidine-2,6-dione Formula: $C_{13}H_{13}N_3O_3$ Mol. mass: 259.261 g/mol	Three main activities: direct anti-tumor effect, inhibition of angiogenesis, and immunomodulatory role. [119]	Multiple myeloma Myelodysplastic syndromes Hodgkin's lymphoma,[15] as well as non-Hodgkin's lymphoma, chronic lymphocytic leukemia,	Vallet S, et al [119]
74	LETROZOLE: FEMARA  4,4'-((1H-1,2,4-triazol-1-yl)methylene)dibenzonitrile Formula: $C_{17}H_{11}N_5$ Mol. mass: 285.303 g/mol	Letrozole prevents the aromatase from producing estrogens by competitive, reversible binding to the heme of its cytochrome P450 unit. The action is specific, and letrozole does not reduce production of mineralo- or corticosteroids.	Ovarian stimulation gynecomastia azoospermia [120]	Haberfeld, H, ed. Et al [120]
75	LEUPRORELIN: LUPRON  N-[1-[[1-[[1-[[1-[[1-[[1-[[5-(diamino methylideneamino)-1-[2-(ethylcarbamoyl)pyrrolidin-1-yl]-1-oxo-pentan-2-yl]carbamoyl]-3-methyl-butyl]carbamoyl]-3-methyl-butyl]carbamoyl]-2-(4-hydroxyphenyl)ethyl] carbamoyl]-2-hydroxy-ethyl]carbamoyl]-2-(1H-indol-3-yl)ethyl]carbamoyl]-2-(3H-imidazol-4-yl)ethyl]-5-oxo-pyrrolidine-2-carboxamide Formula: $C_{59}H_{84}N_{16}O_{12}$ Mol. mass: 1209.4 g/mol	Indirectly downregulates the secretion of gonadotropins luteinizing hormone(LH) and follicle-stimulating hormone (FSH), leading to hypogonadism and thus a dramatic reduction in estradiol and testosteron e levels in both sexes	Paraphilias Alzheimer's disease	Badaru Aet al [121]

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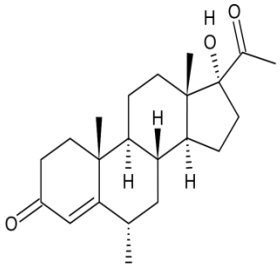
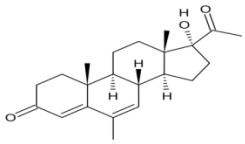
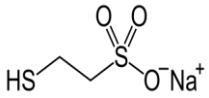
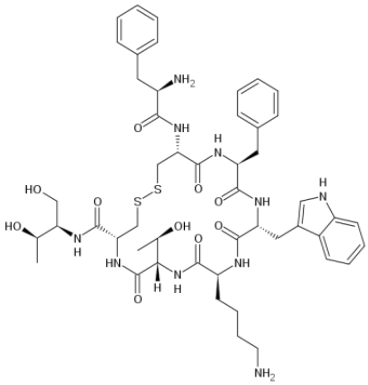
76	MEDROXYPROGESTERONE: MP  (6α)-17-hydroxy-6-methylpregn-4-ene-3,20-dione Formula: $C_{22}H_{32}O_3$ Mol. mass: 344.488 g/mol	Progestins diffuse freely into target cells in the female reproductive tract, mammary gland, hypothalamus, and the pituitary and bind to the progesterone receptor. Once bound to the receptor, progestins slow the frequency of release of gonadotropin releasing hormone (GnRH) from the hypothalamus and blunt the pre-ovulatory LH surge.	Endometriosis, endometrial and renal cell carcinomas, paraphilia in males,	Schindler AE et al [122]
77	MEGESTROL:  17-hydroxy-6-methylpregna-4,6-diene-3,20-dione Formula: $C_{22}H_{30}O_3$ Mol. mass: 342.472 g/mol	Involve suppression of luteinizing hormone by inhibition of pituitary function. megestrol's weight gain effect is related to its appetite-stimulant or metabolic effects rather than its glucocorticoid-like effects or the production of edema.	Metastatic breast cancer, endometrial cancer, and prostate cancer	Pascual Lopez A et al [123]
78	MESNA: MESNEX  sodium 2-sulfanylethanesulfonate Formula: $C_2H_5NaO_3S_2$ Mol. mass: 164.181 g/mol	Prophylactic agent to reduce the risk of hemorrhagic cystitis induced by ifosfamide.	Haemorrhagic cystitis and haematuria	World Health Organization. [124]
79	OCTREOTIDE : SANDOSTATIN  (4R,7S,10S,13R,16S,19R)-10-(4-aminobutyl)-19-[[(2R)-2-amino-3-phenyl-propanoyl]amino]-16-benzyl-N-[(2R,3R)-1,3-	Octreotide binds to somatostatin receptors. These receptors are coupled via pertussis toxin sensitive G proteins which lead to inhibition of adenylyl cyclase. Octreotide binding to these receptors also stimulates phosphotyrosine phosphatase and activation of the Na(+)/H(+) exchanger via pertussis toxin insensitive G proteins.	Acromegaly and gigantism, acute lymphoblastic leukemia	Lustig RH et al [125] Ruan W et al [126]

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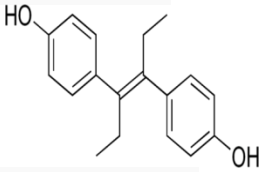
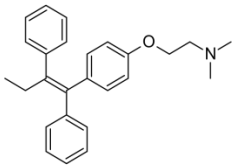
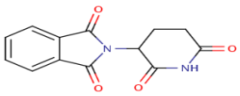
	dihydroxybutan-2-yl]-7-(1-hydroxyethyl)-13-(1H-indol-3-ylmethyl)-6,9,12,15,18-pentaoxo-1,2-dithia-5,8,11,14,17-pentazacycloicosane-4-carboxamide Formula: $C_{49}H_{66}N_{10}O_{10}S_2$ Mol. mass: 1019.24 g/mol			
80	STILBOESTROL: DIETHYLSTILBESTROL  4,4'-(3E)-hex-3-ene-3,4-diyldiphenol Formula: $C_{18}H_{20}O_2$ Mol. mass: 268.35 g/mol	Binding their receptors causes downstream increases the hepatic synthesis of sex hormone binding globulin (SHBG), decreasing the secretion of gonadotropin-releasing hormone (GnRH).	Gonorrheal vaginitis, atrophic vaginitis, menopausal symptoms, and postpartum lactation	Dutton DB et al [127] Baron S et al [128]
81	TAMOXIFEN: NOLVADEX  (Z)-2-[4-(1,2-diphenylbut-1-enyl)phenoxy]-N,N-dimethylethanamine Formula: $C_{26}H_{29}NO$ Mol. mass: 371.515 g/mol	Tamoxifen needs to block growth factor proteins such as ErbB2/HER2 because high levels of ErbB2 have been shown to occur in tamoxifen resistant cancers.	McCune-Albright syndrome Gynecomastia Angiogenesis and cancer Riedel's thyroiditis	USA [129] Osborne CK [130]
82	THALIDOMIDE: THALOMID  RS)-2-(2,6-dioxopiperidin-3-yl)-1H-isoindole-1,3(2H)-dione Formula: $C_{13}H_{10}N_2O_4$ Mol. mass: 258.23 g/mol–	Thalidomide can directly inhibit angiogenesis induced by bFGF or VEGF in vivo	Colorectal cancer Crohn's disease Rheumatoid arthritis, Behcet's syndrome	Franks et al [131] D'Amato RJ, et al [132]
83	TRIPTORELIN: TRELSTAR	Triptorelin is a synthetic luteinizing hormone releasing hormone (LHRH) analog triptorelin stimulates release of gonadotropins, luteinizing hormone (LH) and follicle-stimulating	Prostate cancer or breast cancer, precocious puberty,	Lahlou N, et al [133] Kalamazoo, MI et al [134]

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	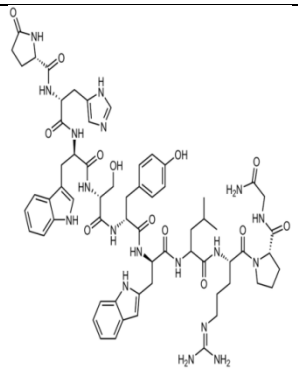 5-oxo-D-prolyl-L-histidyl-Ltryptophyl-L-seryl-Ltyrosyl-3-(1H-indol-2-yl)-L-alanylleucyl-L-arginyl-L-prolylglycinamide Formula: $C_{64}H_{82}N_{18}O_{13}$ Mol. mass: 1311.5 g/mol	hormone (FSH), from the anterior pituitary. Long-term, sustained use of triptorelin is associated with an early phase of increased LH and FSH levels, followed by their suppression		

PRINCIPLES OF ANTICANCER DRUGS (THERAPY)

S.NO	DESCRIPTION	TYPES
SURGICAL TREATMENT:	The removal of the tumor as a local pathological formation, but also the involvement of the whole organism. Effective easy to perform and economical.	Curative resection, Palliative surgery, Preventive surgery, Diagnostic surger, Cytoreductive surger, Cryosurgery [135]
RADIOTHERAPY:	Radiotherapy is based on the fact that ionizing radiation destroys tumor cells. X rays and gamma rays are able to penetrate the tissue depth, destroying tumor cells even from deep layers. Radiotherapy induces direct lesions in the DNA or biological molecules, which eventually affect DNA. These changes deregulate cell division, and daughter cells finally die.	Radiotherapy can be used in three modalities: curative radiotherapy; adjuvant radiotherapy; palliative radiotherapy [136]. Palliative radiotherapy Teleradiotherapy Brachytherapy Metabolic radiotherapy radiosensitivity of non-tumor tissues radiosensitivity of tumor tissues Canine tumors Tumors in felines
CHEMOTHERAPY:	Chemotherapy uses chemical substances that act electively on cells in mitosis, and antimitotic agents finally aim to destroy cancer cells. These substances have the great advantage that they do not act strictly locally on the primary neoplasm, and antimitotic agents perform a therapy of the potential or disseminated systemic disease.	Goldie-coldman model All anticancer agents [137]

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HYPERTHERMIA:	Hyperthermia therapy is used due to its cytotoxic effects and because it can be an adjuvant to chemotherapy and radiotherapy. However, it should be mentioned that the use of hyperthermia may also have undesired effects (inefficiency, toxicity, increased tolerance to heat and even the appearance of resistant cells).	Temperatures higher than 41°C induce lesions in tumor tissues, directly by cytotoxicity, and indirectly, by microcirculatory lesions. [138]
COMBINED TREATMENT:	The separate studies of the effects of hyperthermia and radiotherapy on tumor cells have led to the conclusion of the combination of the two beneficial results, based on the following reasons: High temperatures have cytotoxic effects on acidophilic cells in hypoxic condition. These findings correlated with the fact that hypoxic cells manifest a 2.5–3-fold increased resistance to destruction by radiation have determined the association of the two therapies. Hyperthermia increases the radiosensitivity of all cells and diminishes the repair of sublethal lesions induced by radiation. Hyperthermia is preferentially cytotoxic for cells in the S phase of the cell cycle, in contrast, these cells being almost radioresistant.	Combined hyperthermia-radiotherapy treatment Combined hyperthermia-chemotherapy treatment [138]
PHOTOTHERAPY:	Dynamic phototherapy refers to the use of hematoporphyrin or photofrin II preparations, at specific light wavelengths, in the detection and treatment of malignant solid tumors. Both the detection and treatment of tumors by the dynamic phototherapy technique depend on the character of the neoplasm and on the location of the preparation in the tumor. So, at a certain time after the intravenous injection of the preparation, this accumulates and is retained in a higher concentration in malignant tissues compared to normal tissues	Hematoporphyrin used in oncology. dihematoporphyrin ether, experimentally tested under the designation of photofrin II. The tumor can be located using hematoporphyrin, by lighting with 405 nm light, which has a fluorescence of approximately 630 nm (red-orange). [139]

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IMMUNOTHERAPY:	Immunotherapy is another modality of stimulating the host defense mechanisms, an anticancer strategy. Experiments and practical results have proved that immunotherapy alone has an inconsistent efficacy, while preceded by surgery for tumor volume reduction, by radiotherapy or chemotherapy, it has proved to be a valuable adjuvant in the treatment of neoplastic disease.	Preventive immunotherapy Non-specific active immunotherapy Specific active immunotherapy Specific passive immunotherapy Chemoimmunotherapy [140]

CONCLUSION

Many anti-cancer drugs have potentially deleterious, irreversible effects to the body parts. Patients at high risk should be identified early and different therapeutic treatments should be done by providing the proper anticancer agents. This review has discussed the medications that are helpful for the treatment of numerous cancers. And avoid the development of cell divisions by damaging the DNA, due to which treatment can be done in the systematic manner. According to FDA more than 100 cancers are going to arise in the future aspects. And also a brief detail has been discussed on the therapies that are used in cancer treatment.

↓ REFERENCES

1. Hanahan, Douglas; Weinberg, Robert A. "The hallmarks of cancer". Cell 100 January 7, 2000; (1): 57–70.
2. Hanahan, Douglas; Weinberg, Robert A. "Hallmarks of Cancer: The Next Generation" Cell, 2011; 144 (5): 646–74.
3. slideshare.net/intellifarhan390/anti-cancer-drugs-11444757
4. Baylin SB, Ohm JE. "Epigenetic gene silencing in cancer - a mechanism for early oncogenic pathway addiction?" Nature Reviews Cancer, February 2006; 6 (2): 107–16.
5. UC Davis ChemWiki by University of California
6. Kath R, Blumenstengel K, Fricke HJ, **Höffken** K. "Bendamustine monotherapy in advanced and refractory chronic lymphocytic leukemia". J. Cancer Res. Clin. Oncol, January 2001; 127 (1): 48–54.
7. Leoni LM, Bailey B, Reifert J, et al. Bendamustine (Treanda) displays a distinct pattern of cytotoxicity and unique mechanistic features compared with other alkylating agents. Clin Cancer Res, 2008; 14:309-17.
8. Lesurtel M, Graf R, Aleil B, Walther D, Tian Y, Jochum W, Gachet C, Bader M, Clavien P. "Platelet-derived serotonin mediates liver regeneration", 2006; Science 312 (5770): 104–7.
9. Hall AG, Tilby MJ: Mechanisms of action of, and modes of resistance to, alkylating agents used in the treatment of haematological malignancies. Blood Rev, 1992 Sep; 6(3):163-73.
10. "Carmustine - Compound Summary". PubChem Compound. USA: National Center for Biotechnology Information. 25 March 2005. Identification. Retrieved 11 April 2012.
11. Drablos F, Feyzi E, Aas Pa, Vaagbo CB, et al : Alkylating damage in DNA and RNA-Repair mechanisms and medical significance. Dna Repair (Amst), 2004 Nov 2; 3(11): 1389-407.
12. Rai KR, Peterson BL, Appelbaum FR, Kolitz J, Elias L, Shepherd L, Hines J, Threatte GA, Larson RA, Cheson BD, Schiffer CA. "Fludarabine compared with chlorambucil as primary therapy for chronic lymphocytic leukemia." N Engl J Med, 2000; 343(24): 1750–7

PHARMATUTOR
PHARMACY INFOPEDIA
ISSN: 2347-7881

13. Begleiter A, Mowat M, Israels LG, Johnson JB: Chlorambucil in chronic lymphocytic leukemia: mechanism of action. Leuk Lymphoma, 1996 oct; 23(3-4): 187-201.
14. Sistigu A, Viaud S, Chaput N, Bracci L, Proietti E, Zitvogel L. "Immunomodulatory effects of cyclophosphamide and implementations for vaccine design". Seminars in Immunopathology, July 2011; 33 (4): 369–83.
15.fass.se/LIF/produktfakta/audit_page.jsp?_sourcePage=%2Fproduktfakta%2Fartikel_produkt.jsp&docType=7&nplId=19971212000080
16. Lonn U, Lohn S: Prevention of dacarbazine damage of human neoplastic cell Dna b y aphidicolin. Cancer Res, 1987 Jan 1 ; 47(1); 26-30.
17. Jahnke K, Thiel E, Bechrakis NE, et al. "Ifosfamide or trofosfamide in patients with intraocular lymphoma". J. Neurooncol, Dec 2008; 93 (2): 213–7.
18. Dechant KL, Brogden RN, Pilkington T, Faulds D: Ifosfamide/mesna. A review of its antineoplastic activity, pharmacokinetic properties and therapeutic efficacy in cancer. Drugs, 1991 Sep; 42(3):428-67.
19. Facon T, Mary JY, Hulin C, et al. "Melphalan and prednisone plus thalidomide versus melphalan and prednisone alone or reduced-intensity autologous stem cell transplantation in elderly patients with multiple myeloma (IFM 99-06): a randomised trial", October 2007; Lancet 370 (9594): 1209–18.
20. Vasquez KM: Targeting and processing of site-specific DNA interstand crosslinks. Environ Mol Mutagen. 2010 Mar 1
21. "WHO Model List of EssentialMedicines". World Health Organization. October 2013. Retrieved 22 April 2014.
22. Szkudelski T. "The mechanism of alloxan and streptozotocin action in B cells of the rat pancreas." Physiol Res, 2001; 50 (6): 537–46.
23. Malcolm Stevens - interview, Cancer Research UK impact & achievements page
24. Sitbon Sitruk, L.; Sanson, M.; Prades, M.; Lefebvre, G.; Schubert, B.; Poirot, C. "Chimiothérapie a gonadotoxicité inconnue et preservation de la fertilite : Exemple du témozolomide". Gynécologie Obstétrique & Fertilite, 2010; 38 (11): 660–662.
25. "Xeloda (capecitabine) dosing, indications, interactions, adverse effects, and more". Medscape Reference. WebMD. 25 January 2014.
26. Pigneux A, Perreau V, Jourdan E, et al. "Adding lomustine to idarubicin and cytarabine for induction chemotherapy in older patients with acute myeloid leukemia: the BGMT 95 trial results". Haematologica, October 2007; 92(10): 1327–34.
27. Perry, Michael J. The Chemotherapy source book. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins, 2008; p. 80.
28. Rossi, S, ed. Australian Medicines Handbook (2013 ed.). Adelaide: The Australian Medicines Handbook Unit Trust, 2013.
29. Longley DB, Harkin DP, Johnston PG "5-fluorouracil: mechanisms of action and clinical strategies". Nat. Rev. Cancer, May 2003; 3 (5): 330–8.
30. Rai KR et al. Fludarabine compared with chlorambucil as primary therapy for chronic lymphocytic leukemia. N Engl J Med, 2000; 343:1750-7
31. N. M. F. S. A. Cerqueira, P. A. Fernandes, M. J. Ramos "Understanding ribonucleotide reductase inactivation by gemcitabine". Chemistry: A European Journal, 2007; 13 (30): 8507–15.
32. U.S. National Library of Medicine, 8600 Rockville Pike, Bethesda, MD 20894 National Institutes of Health, Health & Human Services
33. McLeod, Howard L.; James Cassidy, Robert H. Powrie, David G. Priest, Mark A. Zorbas, Timothy W. Synold, Stephen Shibata, Darcy Spicer, Donald Bissett, Yazdi K. Pithavala, Mary A. Collier, Linda J.

PHARMATUTOR
PHARMACY INFOPEDIA
ISSN: 2347-7881

Paradiso, John D. Roberts "Pharmacokinetic and Pharmacodynamic Evaluation of the Glycinamide Ribonucleotide Formyltransferase Inhibitor AG2034".Clinical Cancer Research; Clinical Trials, July 2000; 6 (7): 2677–84.
34. Manegold C "Pemetrexed (Alimta, MTA, multitargeted antifolate, LY231514) for malignant pleural mesothelioma". Semin. Oncol, August 2003; 30 (4 Suppl 10): 32–6.
35. Widemann BC, Balis FM, Godwin KS, McCully C, Adamson PC."The plasma pharmacokinetics and cerebrospinal fluid penetration of the thymidylate synthase inhibitor raltitrexed (Tomudex) in a nonhuman primate model". Cancer Chemother. Pharmacol, 1999; 44 (6): 439–43.
36. Sobell H, "Actinomycin and DNA transcription". Proceedings of the National Academy of Sciences of the United States of America, 1985; 82 (16): 5328–31.
37. Turan T, Karacay O, Tulunay G, Boran N, Koc S, Bozok S, Kose M "Results with EMA/CO (etoposide, methotrexate, actinomycin D, cyclophosphamide, vincristine) chemotherapy in gestational trophoblastic neoplasia". Int J Gynecol Cancer, 2006; 16(3): 1432–8.
38. Abd El-Aal H, Habib E, Mishrif M "Wilms' Tumor: The Experience of the Pediatric Unit of Kasr El-Aini Center of Radiation Oncology and Nuclear Medicine (NEMROCK)". J Egypt Natl Canc Inst, 2005; 17 (4): 308–11.
39. Khatua S, Nair C, Ghosh K "Immune-mediated thrombocytopenia following dactinomycin therapy in a child with alveolar rhabdomyosarcoma: the unresolved issues". J Pediatr Hematol Oncol, 2004; 26 (11): 777–9.
40. Jaffe, N.; Paed, D.; Traggis, D.; Salian, S.; Cassady, J. R"Improved outlook for Ewing's sarcoma with combination chemotherapy (vincristine, actinomycin D and cyclophosphamide) and radiation therapy". Cancer, 1976; 38 (5): 1925–1930.
41. Uberti, E. M. H.; Fajardo, M. D. C.; Ferreira, S. V. V. R.; Pereira, M. C. V.; Seger, R. C.; Moreira, M. A. L. R.; Torres, M. D.; De Nápoli, G.; Schmid, H. "Reproductive outcome after discharge of patients with high-risk hydatidiform mole with or without use of one bolus dose of actinomycin D, as prophylactic chemotherapy, during the uterine evacuation of molar pregnancy". Gynecologic Oncology, 2009; 115 (3): 476–481.
42. Lewis, TG; Nydorf, ED "Intralesional bleomycin for warts: a review.". Journal of Drugs in Dermatology, 2006; 5 (6): 499–504.
43. Shaw, P; Agarwal, R "Pleurodesis for malignant pleural effusions". In Shaw, Paul HS. Cochrane Database of Systematic Reviews (1), 2004;
44. Hecht, SM "Bleomycin: new perspectives on the mechanism of action". J. Nat. Prod, 2000; 63: 158–168.
45. G J Quigley, A H Wang, G Ughetto, G van der Marel, J H van Boom, and A Rich "Molecular structure of an anticancer drug-DNA complex: daunomycin plus d(CpGpTpApCpG)". PNAS, December 1980; 77 (12): 7204–7208.
46. Pang B, Qiao X, Janssen L, Velds A, Groothuis T, Kerkhoven R, Nieuwland M, Ovaa H, Rottenberg S, van Tellingen O, Janssen J, Huijgens P, Zwart W, Neefjes J "Drug-induced histone eviction from open chromatin contributes to the chemotherapeutic effects of doxorubicin". Nature Communications, 2013; 4: 1908.
47. Brayfield A, ed."Doxorubicin". Martindale: The Complete Drug Reference. Pharmaceutical Press, 19 December 2013 Retrieved 15 April 2014
48. Pang B, Qiao X, Janssen L, Velds A, Groothuis T, Kerkhoven R, Nieuwland M, Ovaa H, Rottenberg S, van Tellingen O, Janssen J, Huijgens P, Zwart W, Neefjes J "Drug-induced histone eviction from open chromatin contributes to the chemotherapeutic effects of doxorubicin". Nature Communications, 2013.

PHARMATUTOR
PHARMACY INFOPEDIA
ISSN: 2347-7881

4 (5): 1908.
49. Bonfante, V; Bonadonna, G; Villani, F; Martini, A "Preliminary clinical experience with 4-epidoxorubicin in advanced human neoplasia".Recent results in cancer research, 1980. 74: 192–9.
50. Pang B, Qiao X, Janssen L, Velds A, Groothuis T, Kerkhoven R, Nieuwland M, Ovaa H, Rottenberg S, van Tellingen O, Janssen J, Huijgens P, Zwart W, Neefjes J "Drug-induced histone eviction from open chromatin contributes to the chemotherapeutic effects of doxorubicin". Nature Communications, 2013. 4: 1908
51. Tomasz, Maria "Mitomycin C: small, fast and deadly (but very selective)."Chemistry and Biology, September 1995. 2 (9): 575–579.
52. Renault, J.; Baron, M; Mailliet P. et al. Heterocyclic quinones 2. Quinoxaline-5,6-(and 5-8)-diones - Potential antitumoral agents. Eur. J. Med. Chem. 1981.16, 6, 545–550,
53. Parker C, Waters R, Leighton C, Hancock J, Sutton R, Moorman AV, Ancliff P, Morgan M, Masurekar A, Goulden N, Green N, Révész T, Darbyshire P, Love S, Saha V "Effect of mitoxantrone on outcome of children with first relapse of acute lymphoblastic leukaemia (ALL R3): an open-label randomised trial". Lance 2010. t 376 (9757): 2009–2017
54. Mazerski J, Martelli S, Borowski E "The geometry of intercalation complex of antitumor mitoxantrone and ametantrone with DNA: molecular dynamics simulations". Acta Biochim. Pol, 1998; 45 (1): 1–11
55. Hande KR "Etoposide: four decades of development of a topoisomerase II inhibitor". Eur. J. Cancer 1998; 34 (10): 1514–21.
56. Pommier Y, Leo E, Zhang H, Marchand C "DNA topoisomerases and their poisoning by anticancer and antibacterial drugs". Chem. Biol. 2010. 17 (5): 421–33.
57. Gordaliza M, García PA, del Corral JM, Castro MA, Gómez-Zurita MA "Podophyllotoxin: distribution, sources, applications and new cytotoxic derivatives". Toxicon, 2004; 44 (4): 441–59.
58. Lyseng-Williamson KA, Fenton C "Docetaxel: a review of its use in metastatic breast cancer". Drugs 2005. 65 (17): 2513–31
59. Yvon AM, Wadsworth P, Jordan MA "Taxol Suppresses Dynamics of Individual Microtubules in Living Human Tumor Cells". Mol. Biol. Cell April 1999; 10 (4): 947–59.
60. Pommier, Y., Leo, E., Zhang, H., Marchand, C.. DNA topoisomerases and their poisoning by anticancer and antibacterial drugs. Chem. Biol. 2010; 17: 421-433.
61. Jordan, MA; Wilson, L "Microtubules as a target for anticancer drugs". Nature reviews. Cancer 2004; 4 (4): 253–65.
62. Ganguly, A; Yang, H; Cabral, F "Paclitaxel-dependent cell lines reveal a novel drug activity".Molecular cancer therapeutics 2010; 9 (11): 2914–23..
63. Lowe, J; Li, H; Downing, KH; Nogales, E "Refined structure of $alpha;$beta;-tubulin at 3.5 p resolution1".Journal of Molecular Biology 2001; 313 (5): 1045–57.
64. Staker, B.L. et al "The mechanism of topoisomerase I poisoning by a camptothecin analog". PNAS 2002; 99 (24): 15387–15392
65. Yang, H.; Ganguly, A.; Cabral, F. "Inhibition of Cell Migration and Cell Division Correlate with Distinct Effects of Microtubule Inhibiting Drugs" (pdf). Journal of Biological Chemistry 2010; 285 (42): 32242–32250.
66. Brayfield, A, ed. "Vincristine". Martindale: The Complete Drug Reference. Pharmaceutical Press. 13 December 2013; Retrieved 15 April 2014.
67. Casanova, M; Ferrari, A; Spreafico, F; Terenziani, M; Massimino, M; Luksch, R; Cefalo, G; Polastri, D et al. "Vinorelbine in previously treated advanced childhood sarcomas: Evidence of activity in

PHARMATUTOR
PHARMACY INFOPEDIA
ISSN: 2347-7881

rhabdomyosarcoma". Cancer 2002; 94 (12): 3263–8.
68. Wheate NJ, Walker S, Craig GE, Oun R "The status of platinum anticancer drugs in the clinic and in clinical trials". Dalton Transactions September 2010; 39 (35): 8113–27.
69. Praveen D*, Ranadheer Chowdary P, "A review on the use of Bleomycin-Cisplatin-Vinblastine combinations in therapy of testicular cancer" ,Indian Journal of Research in Pharmacy and Biotechnology, IJRPB 1(6) , November – December 2013, 793- 796
70. Graham, Joanne; Mushin, Mohamed; Kirkpatrick, Peter January 2004. "Oxaliplatin". Nature Reviews Drug Discovery 3 (1): 11–2.
71. Los, M.; Roodhart, J. M. L.; Voest, E. E. "Target Practice: Lessons from Phase III Trials with Bevacizumab and Vatalanib in the Treatment of Advanced Colorectal Cancer". The Oncologist 2007; 12 (4): 443–50.
72. Micromedex Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically
73. McClung, Michael R.; Lewiecki, E. Michael; Cohen, Stanley B.; Bolognese, Michael A.; Woodson, Grattan C.; Moffett, Alfred H.; Peacock, Munro; Miller, Paul D. et al. "Denosumab in Postmenopausal Women with Low Bone Mineral Density". New England Journal of Medicine 354 , 2006; (8): 821–31.
74. Raymond E, Faivre S, Armand J "Epidermal growth factor receptor tyrosine kinase as a target for anticancer therapy".Drugs. 2000; 60 Suppl 1: 15–23; discussion 41–2.
75. Takimoto CH, Calvo E. "Principles of Oncologic Pharmacotherapy" in Pazdur R, Wagman LD, Camphausen KA, Hoskins WJ (Eds) Cancer Management: A Multidisciplinary Approach. 11 ed. 2008.
76. Deininger MW, Druker BJ "Specific targeted therapy of chronic myelogenous leukemia with imatinib". Pharmacol. Rev. 55, September 2003; (3): 401–23.
77. Vigneri P, Wang JY "Induction of apoptosis in chronic myelogenous leukemia cells through nuclear entrapment of BCR-ABL tyrosine kinase". Nat Med. February 2001, 7 (2): 228–34.
78. de Weerd NA, Samarajiwa SA, Hertzog PJ "Type I interferon receptors: biochemistry and biological functions". J Biol Chem, 2007. 282 (28): 20053–20057.
79. Russell-Harde D, Wagnere TC, Perez HD, Cronze E: Formation of a uniguely stable type-1 interferon receptor complex by interferon beta is dependent upon particular interactions between interferon beta and its receptor and independent of tyrosine phosphorylation Biochem Biophys Res Commun. 1999 Feb 16; 255(2): 539-44
80. Antoni Ribas "Tumor immunotherapy directed at PD-1". New England Journal of Medicine, 28 June 2012; 366 (26): 2517–9
81. Dr. Angel Rodriguez "New type of drug shrinks primary breast cancer tumors significantly in just six weeks; research provides leads to a new target in cancer treatment – the cancer stem cell" April 2008.
82. U.S. Food and Drug Administration
83. T Shaw, J Quan, and M Totoritis, "B cell therapy for rheumatoid arthritis: the rituximab (anti-CD20) experience", Ann Rheum Dis. 2003 Nov; 62 (Suppl 2): ii55–ii59.
84. "Prescribing information for Sutent (sunitinib malate)". Pfizer, Inc, New York NY.
85. Bleeding; including serious bleeds such as intracranial and intrapulmonary bleeds
86. Wan, Xiaolin; Shen, Na; Mendoza, Arnulfo; Khanna, Chand; Helman, Lee J. "CCI-779 Inhibits Rhabdo myosarcoma Xenograft Growth by an Antiangiogenic Mechanism Linked to the Targeting of mTOR/Hif-1α/VEGF Signaling". Neoplasia, 2006. 8 (5): 394–401.
87. Moja L, Tagliabue L, Balduzzi S, et al. "Trastuzumab containing regimens for early breast cancer". Cochrane Database Syst Rev 4: 2012.
88. "Breast Cancer Care Trastuzumab factsheet". Breast Cancer Care. Retrieved 22 Oct2013.

PHARMATUTOR
PHARMACY INFOPEDIA
ISSN: 2347-7881

89. Ménard, S; Pupa SM, Campiglio M, Tagliabue E "Biologic and therapeutic role of HER2 in cancer". Oncogene 22, 2003; (42): 6570–6578.
90. Weinstein RS, Roberson PK, Manolagas SC "Giant osteoclast formation and long-term oral bisphosphonate therapy". N. Engl. J. Med. Jan 2009; 360 (1): 53–62.
91. Lehenkari PP, Kellinsalmi M, Napankangas JP, Ylitalo KV, Monkkonen J, Rogers MJ, Azhayev A, Vaananen HK, Hassinen IE: Further insight into mechanism of action of clodronate: inhibition of mitochondrial ADP/ATP translocase by a nonhydrolyzable, adenine-containing metabolite. Mol Pharmacol. 2002 May; 61(5):1255-62
92. "boniva". The American Society of Health-System Pharmacists. Retrieved 3 April 2011.
93. Epstein S, Zaidi M: Biological properties and mechanism of action of ibandronate: application to the treatment of osteoporosis. Bone. 2005 Oct; 37(4):433-40.
94. Zarychanski R, Elphee E, Walton P, Johnston J "Osteonecrosis of the jaw associated with pamidronate therapy." Am J Hematol 81, 2006; (1): 73–5.
95. Aclasta label- Australia
96. Simpson ER "Sources of estrogen and their importance". The Journal of Steroid Biochemistry and Molecular Biology86, 2003; (3–5): 225–30.
97. "FDA approves Zytiga for late-stage prostate cancer"(Press release). Food and Drug Administration (FDA). 2011-04-28.
98. Attard G, Belldegrun AS, de Bono JS "Selective blockade of androgenic steroid synthesis by novel lyase inhibitors as a therapeutic strategy for treating metastatic prostate cancer". BJU Int. Dec 2005; 96 (9): 1241–6.
99. Kouvaris JR, Kouloulias VE, Vlahos LJ "Amifostine: the first selective-target and broad-spectrum radioprotector". Oncologist June 2007; 12(6): 738–47
100. Brunton, L; Chabner, B; Knollman, B Goodman and Gilman's The Pharmacological Basis of Therapeutics (in English) (12th ed.). New York: McGraw-Hill Professional. 2010.
101. Furr BJ "The development of Casodex (bicalutamide): preclinical studies". Eur. Urol. 1996; 29 Suppl 2, 83–95.
102. asco.org/ASCOv2/Meetings/Abstracts?&vmview=abst_detail_view&confID=114&abstractID=94715
103. Kirby RS, Fitzpatrick JM, Clarke N: Abarelix and other Gonadotrophin-releasing hormone antagonists in prostate cancer. BJU Int. 2009 Dec; 104(11): 1580-4
104. Index Nominum 2000: International Drug Directory. Taylor & Francis US. 2000. p. 289. Retrieved 29 May 2012.
105. Stadtler FA, Langner V: The effect of cyproterone and gonadotrophins on the adrenal gland of juvenile and adult rats. A morphological and morphometrical study. Pathol Res Pract. 1985 Mar; 179 (4-5):493-8.
106. Principalle M, Broqua P, White R, et al Rapid suppression of plasma testosterone levels and tumor growth in the dunning rat model treated with degarelix, a new gonadotropin-releasing hormone antagonist. J. Pharmacol. Exp. Ther. Mar 2007. 320: 1113-8.
107. Persson BE, Kold Olesen T, Jensen JK: Degarelix: a new approach for the treatment of prostate cancer. Neuroendocrinology.2009; 90(3):235-44. Epub 2009 Jul 14.
108. Aromasin For Advanced Breast Cancer
109. Robinson A: A review of the use of exemestane in early breast cancer. Ther Clin Risk Manag. 2009 Feb; 5(1):91-8. Epub 2009 Mar 26.
110. Scher, Howard I. "Hyperplastic and Malignant Diseases of the Prostate". In Dennis L. Kasper, Anthony S. Fauci, Dan L. Longo, Eugene Braunwald, Stephen L. Hauser, & J. Larry Jameson (Eds.),

PHARMATUTOR
PHARMACY INFOPEDIA
ISSN: 2347-7881

Harrison's Principles of Internal Medicine (16th edition), New York: McGraw-Hill. 2005. pp. 548–9.
111. Jack Lawrence James, Louis Frank Molnar, Jr., Tania E. Toney-Parker, "Processes for preparing flutamide compounds and compounds prepared by such processes." U.S. Patent US 6,228,401, issued Nov, 1976.
112. Ellis JM, Tan HK, Gilbert RE, et al ."Supplementation with antioxidants and folinic acid for children with Down's syndrome: randomised controlled trial". BMJ 336 (7644): 594–7. Mar2008.
113. Angela Mae Obermiller, PharmD; and Mehmet Sitki Copur, MD "The Longstanding Quest for a Better Endocrine Therapy Continues High-Dose Fulvestrant: Have We Found Its Effective Dose, Combination, Setting, or Sequence?".Contemporary Oncology, 2011. 3 (1).
114. Kabos P, Borges VF: Fulvestrant: a unique antiendocrine agent for estrogen-sensitive breast cancer. Expert Opin Pharmacother. 2010 Apr;11(5):807-16
115. FDA Approval for Zoladex 3.6 mg
116. Kripa S. Srivastava, Matthew R. Davis, "Solid Phase Peptide for the Production of Goserelin." U.S. Patent US20100311946, issued Dec 09, 2010.
117. "FDA Approves New Drug to Treat Rare Disease, Acromegaly" (Press release). U.S. Food and Drug Administration. August 30, 2007. Retrieved 2007-09-06.
118. Tercica. SOMATULINE product monograph. Brisbane, California; 1 Aug 2007
119. Vallet S, Palumbo A, Raje N, Boccadoro M, Anderson KC "Thalidomide and lenalidomide: Mechanism-based potential drug combinations". Leukemia & Lymphoma, July 2008. 49 (7): 1238–45.
120. Haberfeld, H, ed. (Austria-Codex (in German) (2009/2010 ed.). Vienna: Osterreichischer Apothekerverlag. 2009.
121. Badaru A, Wilson DM, Bachrach LK, et al. "Sequential comparisons of one-month and three-month depot leuprolide regimens in central precocious puberty". The Journal of Clinical Endocrinology and Metabolism May 2006. 91 (5): 1862–7.
122. Schindler AE, Campagnoli C, Druckmann R, Huber J, Pasqualini JR, Schweppe KW, Thijssen JH: Classification and pharmacology of progestins. Maturitas. 2008 Sep-Oct; 61(1-2):171-80.
123. Pascual Lopez A, Roque i Figuls M, Urrutia Cuchi G, Berenstein EG, Almenar Pasies B, Balcells Alegre M, Herdman M: Systematic review of megestrol acetate in the treatment of anorexia-cachexia syndrome. J Pain Symptom Manage. 2004 Apr; 27(4):360-9.
124. "WHO Model List of EssentialMedicines". World Health Organization. October 2013. Retrieved 22 Apr 2014.
125. Lustig RH, Hinds PS, Ringwald-Smith K, Christensen RK, Kaste SC, Schreiber RE, Rai SN, Lensing SY, Wu S, Xiong X "Octreotide therapy of pediatric hypothalamic obesity: a double-blind, placebo-controlled trial". J. Clin. Endocrinol. Metab. June 2003. 88 (6): 2586–92.
126. Ruan W, Fahlbusch F, Clemmons DR, Monaco ME, Walden PD, Silva AP, Schmid HA, Kleinberg DL: SOM230 inhibits insulin-like growth factor-I action in mammary gland development by pituitary independent mechanism: mediated through somatostatin subtype receptor 3? Mol Endocrinol. 2006 Feb; 20(2):426-36. Epub 2005 Oct 13.
127. Dutton DB Worse than the disease: pitfalls of medical progress. Cambridge: Cambridge University Press, 1988.
128. Baron S, Escande A, Alberola G et al,: estrogen receptor alpha and the activating protein-1 complex cooperate during insulin-like growth factor-I-induced transcriptional activation of the pS2/TFF1 gene. J Biol Chem. 2007 Apr 20; 282 (16): 11732-41 Epub 2007 Feb 22
129. USA (2012-10-19). "Tamoxifen treatment of pr... [J Pediatr Endocrinol Metab. 1999 Sep-Oct] - PubMed - NCBI". Ncbi.nlm.nih.gov. Retrieved 2013-01-06.

ISSN: 2347-7881

130. Osborne CK, Bardou V, Hopp TA, Chamness GC, Hilsenbeck SG, Fuqua SA, Wong J, Allred DC, Clark GM, Schiff R, "Role of the estrogen receptor coactivator AIB1 (SRC-3) and HER-2/neu in tamoxifen resistance in breast cancer". J. Natl. Cancer Inst. March 2003. 95 (5): 353–61
131. Franks ME, Macpherson GR, Figg WD "Thalidomide". Lancet, May 2004.363 (9423): 1802–1811.
132. D'Amato RJ, Loughnan MS, Flynn E, Folkman J "Thalidomide is an inhibitor of angiogenesis". Proceedings of the National Academy of Sciences of the United States of America 1994, 91 (9): 4082–4085
133. Lahlou N, Carel JC, Chaussain JL, Roger M "Pharmacokinetics and pharmacodynamics of GnRH agonists: clinical implications in pediatrics". J Pediatr Endocrinol Metab. July 2000. 13 Suppl 1: 723–37.
134. Product Information: Trelstar Depot, triptorelin pamoate. Pharmacia & Upjohn, Kalamazoo, MI, PI reviewed 09/2000.
135. Magnol JP, Achache S. Cancerologie vétérinaire et comparée. Maloine Editeur; Paris: 1983.
136. Mc Knight JA, Mauldin GN, Mc Entee MC, Meleo KA, Patnaik AK. Radiation treatment for incompletely resected soft – tissue sarcomas in dogs. J. Am. Vet. Med. Assoc. 2000; 217 (2):205–210.
137. Theilen GH, Madewell BR, Carter SK. Chemotherapy. In: Theilen, Madewell, editors. Veterinary Cancer Medicine. Lea & Febiger; Philadelphia: 1987a. pp. 157–166.
138. Dewhirst MW. Hyperthermia. In: Theilen, Madewell, editors. Veterinary Cancer Medicine. Lea & Febiger; Philadelphia: 1987. pp. 197–214.
139. Hetzel FW. Phototherapy. In: Theilen, Madewell, editors. Veterinary Cancer Medicine. Lea & Febiger; Philadelphia: 1987. pp. 215–218.
140. Theilen GH, Madewell BR. Clinical Applications of Cancer Chemotherapy. In: Theilen, Madewell, editors. Veterinary Cancer Medicine. Lea & Febiger; Philadelphia: 1987a. pp. 183–196.