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The usefulness of cyclic diamidines with different core-substituents as antitumor agents

Jarosław Spychała*

Department of Chemistry, Adam Mickiewicz University, Grunwaldzka 6, 60-780 Poznań, Poland

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ABSTRACT

A series of related polycationic compounds has been screened for potential antitumor activity by the NCI's in vitro testing (one dose primary anticancer assay and the NCI-60 full panel screening). The GI_{50} values of triazines **3** and **4** are on average 1.9 μ M and 2.4 μ M, respectively. Furan **8** deserves mention too (1.9 μ M). The biological test results showed that carbazole **10** possessed cytotoxic activity in the nanomolar range, much better than the other compounds tested, only against several cancer cell lines: CCRF-CEM, HL-60(TB), MOLT-4, NCI-H522, COLO 205, SF-268, but the average GI₅₀ value was higher (15 μ M). The activity appears closely dependent on the core-shape and length of the bisimidazoline molecules (important for both high cytotoxicity and DNA binding). The mechanism of DNA minor-groove binding of diamidines **1–12**, based on the anticancer parameters, is highly probable.

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1. Introduction

Anticancer drugs have been classified as antitumor antibiotics, antimetabolites, antitubulin agents, topoisomerase inhibitors, and alkylating agents [1–5]. They often exhibit multiple mechanisms of action in tumor cells. During the past few decades, simple and cyclic amidines and their derivatives have been widely tested as antitumor agents in vitro and in vivo treatment [6–23]. Other exemplary compounds, containing the amidine N=C-N unit (e.g., pyrimidines, purines, triazines, guanidines, ureas), are usually considered separately.

From a general structure-activity standpoint, the above groups of amidines demonstrate that the structural variations can result in significant changes in specificity and potency with regard to anticancer activity. The active bisamidines increase the denaturation temperature of the calf thymus DNA (stimulate topoisomerase II—mediated DNA cleavage). A general strategy for the synthesis of drugs having a specific activity has been elaborated [20,24].

Hydrogen bond formation is involved in many biological processes. A model has been described for the biological activity against *Giardia lamblia* in which only one nitrogen atom of both amidine groups is in hydrogen bonding distance to the thymine O2 atom at AT rich sites of the minor-groove of DNA and the two

* Fax: +48 618658008.

E-mail address: jjspychala@wp.pl

cationic groups lie between phosphate groups on each strand of the duplex [24,25]. The complex results in the inhibition of the microbial topoisomerase II enzyme. Other findings of a molecular modeling study are in agreement with the crystal structure described [26].

Additional bifurcated hydrogen bonding interactions between the indole NH hydrogen and the thymine O2-carbonyl groups overstabilize the B-form helix and increase the $\Delta T_{\rm m}$ values of the DAPI-DNA complex [27]. The complexation can occur in vivo and it causes inhibition of DNA synthesis at therapeutic levels in humans, in treatment of far advanced cancer cases.

The amidinium moiety is known to contribute to the stabilization of DNA recognition element through electrostatic and hydrogen bonding interactions [28–32]. Therefore, hydrogen bonds are frequently used as recognition elements due to their directionality. The strategy approach for the development of new drugs for the treatment of diseases, which are induced by RNA viruses, is based on the design of agents which bind to specific stem or loop units in the viral RNA genome [33,34].

The binding affinities and specificities observed suggest that the incorporation of a variety of moieties will lead to substances that interact with RNA targets. This approach greatly expands the utility of the amidines and related polycationic compounds for the construction of drugs in general. Hydrogen bonding is an attractive approach to the biological activity [35]. If there is the right size of a drug, the hydrogen bonds become stronger.





It has been shown that various bisamidines can be effective for opportunistic infections and as antifungal, antileishmanial, antiplasmodial, antiprotozoal, and antitrypanosomal agents [36–43]. The structures, which possess adequate proportions of interactions among DNA [44] (e.g., Berenil, DAPI, Furamidine DB75, Hoechst 33258, Pentamidine), are mainly related to several antibiotics [45,46] (Amidinomycin, Anthelvencin A and B, Congocidin, Distamycin A, Kikumycin A and B, Noformycin) and their derivatives [32,47,48].

The radius of curvature of several defined groups in the mimic molecule shows that the shape of the latter affects the strength of nucleic acid binding. Therefore, many classes of drugs have substantial curvature, high DNA affinity, binding to the minor-groove, and interference with DNA-associated enzymes. Very often, the cytotoxicity remains at the micromolar level and confirms the results provided by the $T_{\rm m}$ studies [20].

This paper highlights usefulness in medicinal chemistry of the direct reaction of formation of cyclic amidines and secondary amides from nitriles. The practical value of this complex reaction has been demonstrated by preparation of some bisimidazolines [49] and tetrahydropyrimidines [50]. The reaction is an alternative method to the existing methodologies based on sulfur containing reagents [9,51–57].

In several papers, the formation of a range of cyclic amidines from thioamides or imidates has been described [58,59]. Both thioamides and nitriles were important synthetic intermediates for the preparation of simple amidines [60–62]. This paper describes the practical results obtained from anticancer screening of the products of the cited reactions. The presence of cationic groups and other core structural features make these compounds very suitable probes for nucleic acid binding modes. Therefore, it is desirable to

 Table 1

 Growth percentages of 1–13 (one dose primary anticancer assay)

Compound	NSC Number	NCI-H460 (Lung)	MCF7 (Breast)	SF-268 (CNS)
1	NSC 710604	12	10	8
2	NSC 710605	23	17	30
3	NSC 710607	-90	-79	-85
4	NSC 710608	-90	-91	-96
5	NSC 711986	20	14	31
6	NSC 711987	20	7	36
7	NSC 711989	-74	-74	-66
8	NSC 714616	8	-74	14
9	NSC 714620	29	49	57
10	NSC 715653	-80	3	-45
11	NSC 715654	-48	-33	-49
12	NSC 717052	9	16	72
13	NSC 717046	100	98	102

Table 2

design strong DNA binders by means of various anticancer parameters.

2. Materials and methods

2.1. Materials

Melting points were uncorrected and determined on a Boetius melting point apparatus. NMR spectra were recorded on a Varian Gemini (300 MHz) spectrometer with D₂O solutions using TMS as the internal standard. High-resolution mass spectra were obtained using an AMD 402 or 602 mass spectrometer in the El or FAB mode, respectively. Thin layer chromatography was performed with Merck silica gel 60 F₂₅₄ plates (0.25 mm thickness). The reagents were purchased from Aldrich. Compounds **1–11** are the author samples in the literature cited [9,24,42,49]. All final compounds were dried in an oven at 120 °C for several hours and then stored in a vacuum desiccator over P₂O₅.

2.2. Representative procedures for the preparation of amidines **12** and **13**

Polycationic compounds containing an α , α' -xylene linker have been found to exhibit various inhibitory effects [34,63]. Monocyclam and bicyclam have proven to be effective against HIV-1 and HIV-2 and have been tested in clinical trials [64–66]. They interfere with nucleic acid binding *via* non-covalent interactions. All xylene and toluene derivatives described in this paper were prepared following the synthetic way outlined in Fig. 2.

The syntheses of the cyclic amidines were previously disclosed by the author [49]. To illustrate the methodology, the synthetic scheme and experimental procedures for the representative compounds **12** and **13** are included. As starting compounds, the appropriate nitriles and diaminoalkanes, saturated with hydrogen sulfide, have been used for their preparation.

2.2.1. (±)-N,N-Bis[4-(4,5-dihydro-4-methyl-1H-imidazol-2-yl) benzyl]-4,4 -propylenebispiperidine tetrahydrochloride (**12**)

Starting from 4,4′-propylenebispiperidine and α -bromo-*p*-tolunitrile, *N*,N′-bis(4-cyanobenzyl)-4,4′-propylenebispiperidine (mp 128 °C) was obtained by refluxing the reaction mixture in methanol in the presence of potassium carbonate [49]. The reaction of the bisnitrile with the (±)-1,2-diaminopropane-H₂S reagent in ethanol was carried out under literature conditions [49] and the title compound was obtained (90%): mp > 30 °C; ¹H NMR δ 1.24–1.48 (m, 14H), 1.50 (d, 6H, *J* = 6.3 Hz, CH₃), 1.63 (m, 2H), 2.19 (m, 4H), 3.08 (m, 3H), 3.55 (m, 3H), 3.76 (dd, 2H, *J* = 11.3, 8.0 Hz, imidazoline), 4.28 (t, 2H, *J* = 11.3 Hz, imidazoline), 4.45 (s, 4H, NCH₂),

Overview of the results of the in vitro antitumor screening	for compounds 1–12 schedu	iled automatically for evaluation	against the full panel of abou	it 60 human tumor cell lines

Compound	No. of the cell lines investigated	Number of the cell lines giving log GI_{50} , log TGI, and log $LC_{50} < -4$						
		-log GI ₅₀	–log GI ₅₀		–log TGI		-log LC ₅₀	
		No.	Range	No.	Range	No.	Range	
1	58	43	4.06-4.75	15	4.01-4.41	2	4.06-4.07	
2	58	45	4.04-4.70	11	4.00-4.30	0	<4.00	
3	58	58	4.78-6.44	58	4.45-5.78	49	4.05-5.31	
4	58	58	4.63-6.07	58	4.22-5.66	52	4.06-5.31	
5	58	38	4.09-4.88	3	4.17-4.23	0	<4.00	
6	58	48	4.00-5.24	12	4.01-4.41	2	4.01-4.05	
7	58	57	4.12-4.86	49	4.02-4.53	23	4.01-4.26	
8	58	58	4.55-5.92	54	4.10-5.60	49	4.24-5.30	
9	58	43	4.01-5.65	2	4.02-4.87	0	<4.00	
10	57	50	4.11-8.00	5	4.20-8.00	3	4.04-7.25	
11	57	52	4.09-5.76	35	4.02-4.72	12	4.01-4.21	
12	59	41	4.07-4.83	20	4.04-4.54	7	4.01-4.25	

4.55-4.72 (m, 2H, imidazoline), 7.78 (d, 4H, J = 8.5 Hz), 7.95 (d, 4H, 8.3 Hz); ¹³C NMR δ 22.7, 25.4, 32.0, 35.5, 37.7, 54.3, 55.9, 56.5, 62.6, 126.8, 131.7, 135.0, 138.1, 167.6; LRMS (EI): 554 (24), 382 (25), 381 (86), 174 (100),

158 (15); HRMS (EI): M⁺, found 554.4067. C₃₅H₅₀N₆ requires 554.4097.

2.2.2. 1,3,6,8-Tetrakis(1,4,5,6-tetrahydro-2-pyrimidinyl)pyrene tetrahydrochloride (13)

This compound was prepared by analogy to the 2-imidazoline homologues [49] from 1,3,6,8-tetracyanopyrene and 1,3-diamino-

> 2HCI 1





2.3. Determination of growth percentages in the 3-cell line, one dose primary anticancer assay

As a primary screening, compounds 1-13 were submitted to the National Cancer Institute (NCI) cell line screen for evaluation of

















Fig. 1. Compounds 1-11, active against most tumor cell lines, may serve as useful lead compounds for the search of more powerful anticancer agents. The presence of opposite cationic groups in the molecule is essential for cytotoxicity.

their anticancer activity [67]. From the data analysis [68] it follows that approximately 95% of the actives from the 60 cell line screen can be identified using only three cell lines. Thus a 48 h continuous drug exposure protocol and a protein-binding dye sulforhodamine B (SRB) were used to estimate cell growth. In a preliminary test at a single concentration (100 μ M) against three human cell lines (NCI-H460 lung cancer, MCF7 breast cancer, and SF-268 glioma), a compound is considered active when it reduces the growth of any of the cell lines to 32% or less.

By these criteria, 12 compounds reported were active (six compounds: **3**, **4**, **7**, **8**, **10**, and **11** with negative numbers indicate cell kills) and passed on for evaluation in the full panel of 57–59 human tumor cell lines. Pyrene **13**, which bears four tetrahydropyrimidine groups on the pyrene residue, did not inhibit growth of the tumor cells. The results of **1–13** are summarized in Table 1.

2.4. Methodology of the NCI-60 in vitro cancer screening

The panel is organized into nine subpanels representing diverse histologies: leukemia, melanoma, and cancers of lung, colon, kidney, ovary, breast, prostate, and central nervous system [68]. The test compounds **1–12** were dissolved in DMSO and evaluated using five concentrations at 10-fold dilutions, the highest being 10^{-4} M and the others being 10^{-5} , 10^{-6} , 10^{-7} , and 10^{-8} M. Table 2 reports the results obtained with this test expressed as the $-\log$ of the molar concentration that inhibited the cell growth by 50% (pGI₅₀), that caused total cytostasis (pTGI, total growth inhibition), or that killed half of the cells (pLC₅₀) when compared with values of untreated control cells. For the calculation of the MG_MID values, insensitive cell lines are included with the highest test concentration.

3. Results and discussion

A current trend in chemical modifications has appending the examples that have already been tested. Efforts were directed towards extending the approach to the synthesis of other biologically interesting antibiotic analogues. Molecules used in the present assay and their numbering are given in Figs. 1–2. Since it has been well known that amidines in general exhibit biological and pharmacological activities, it was interesting to investigate the anticancer properties of some polycationic molecules and to compare their activities with the relevant literature data.

Consequently, the parent structures are altered by varying the core-substituents (shape of the molecules). On the basis of the growth inhibition parameters, a structure-activity relationship

was obtained. Overall, the results show that the presence of amidinium groups is not the unique requirement for the compounds to induce activity. Inactive tetraamidine **13** led to consider the shape of molecules responsible for the activity exerted by the compounds.

Most cell lines were sensitive to the agents. It appeared, as indicated in Table 2, that weak structural modifications were responsible for the activity variation. The range between the least sensitive and most sensitive cell lines was about 1–2 log units for **3**, **4**, **6**, **8**, **9**, **10**, and **11**. The range was smaller, less than 1 log unit, for the other compounds. Thus, the growth inhibition results allow classification of the compounds according to their activity profiles.

Averaged values, designated as mean graph midpoints (MG_MID), are calculated for each of the three parameters mentioned by averaging the log parameters of all cell lines. All anticancer agents possessed three different average potencies at the parameters pGI_{50} , pTGI, and pLC_{50} , respectively: **1** (4.33, 4.06, 4.00), **2** (4.34, 4.03, 4.00), **3** (5.73, 5.17, 4.54), **4** (5.62, 5.13, 4.59), **5** (4.30, 4.01, 4.00), **6** (4.41, 4.04, 4.00), **7** (4.66, 4.29, 4.05), **8** (5.72, 5.31, 4.73), **9** (4.28, 4.02, 4.00), **10** (4.83, 4.15, 4.11), **11** (4.77, 4.21, 4.02), **12** (4.37, 4.09, 4.01).

Among all compounds, the data for selected members **1**, **2**, **3**, **4**, **8**, and **10** are summarized in Table 3. The assays of **3** and **4** were repeated once; other compounds were assayed once. At the pGI_{50} endpoint isomers **3** and **4** were of approximately equal overall potency; the ranges of the $-\log$ molar concentrations for all cell lines were from 4.78 to 6.44 for **3** (average 5.73) and 4.63 to 6.07 for **4** (average 5.62), compared to the average potency of **8**, which was 5.72, ranging from 4.55 to 5.92.

For the most active compounds, there were considerable differences between log GI_{50} and log LC_{50} values (MG_MID parameters). At the pTGI endpoint the average log molar potencies were very close to the pLC_{50} in most cases. The ranges at the pTGI between the least sensitive and the most sensitive cell lines were tighter than the ranges seen at the pGI_{50} , though the overall patterns showed less difference among the cell lines of the same tumor, except for **10** (data shown in Tables 2–3).

The average TGI values for triazines **3** and **4** were 6.8 μ M and 7.4 μ M, respectively. The hexahydrobenzimidazolyl to tetrahydropyrimidinyl change in **8** (4.9 μ M) to **9** (95.5 μ M) causes such a large increase in the TGI. The ΔT_m data from biophysical studies with DNA and **8** (ΔT_m 24.5 °C) or **9** ($\Delta T_m > 28$ °C) [24] show that these compounds exhibit dissimilar binding affinities. It is reflected in their different dose response curves (Fig. 3). These results support



Fig. 2. Representative syntheses of 12 and 13. Reagents: (A) K₂CO₃, MeOH; (B) H₂NCH₂CH(CH₃)NH₂-H₂S, EtOH; (C) Br₂, CCl₄; (D) Cu₂(CN)₂, quinoline; (E) H₂N(CH₂)₃NH₂-H₂S.

Table 3

Inhibition of in vitro cancer lines by active compounds **1**, **2**, **3**, **4**, **8**, and **10** (-log GI₅₀ > 4.00 for active compounds)

27.86(24.5) CRF-FCM (430), FS2 (446), MOT-4 (421), RPMI-5226 (4.44), SK (4.37) Non-small cell lung cancer A59(MCC (-400), BVX (-400), HOP-62 (439), HOP-82 (439), NCI-H226 (4.25), NCI-H22 (4.43), NCI-H322M (4.43), NCI-H422 (4.43), NCI-H322M (4.43), NCI-H422 (4.43), NCI-H322M (4.43), NCI-H422 (4.43), NCI-H322M (4.43), NCI-H426 (4.55), NCI-H32 (4.43), NCI-H322M (4.43), NCI-H322M (4.43), NCI-432 (4.43), NCI-H322M (4.43), NCI-432 (4.44), NCI-432 (4.45), NCI-H32 (4.4	Panel	Cell lines (cytotoxicity: -log GI ₅₀ > 4.00)
Lankernia CERF-EDM (<4.00), IK-552 (4.46), MCIT-4 (4.2), RPM-B226 (4.44), SR (4.37) Non-small cell lung concer F439 (4.20), INC 24 (4.00), INC 24 (4.00), INC 24 (2.43), NCI-1123 (4.43), NCI-1123 (4.43), NCI-1150 (4.53), NCI-1126 (4.53), NCI-1123 (4.43), NCI-1126 (4.53), INCI-1126 (4.54), INCI-1166 (4.54), INCI-1166 (4.54), INCI-1166 (4.55), INCI-1266 (4.53), INCI-1460 (4.50),	2,7-Bis(4,5-dihydro-4-methyl-1	H-imidazol-2-yl)fluorene dihydrochloride (1)
Non-small cell lung cancer ASB(MCC (-4.00), EVX (-4.00), HOH-82 (4.39), HOH-82 (-4.00), NCI-426 (4.25), NCI-426 (4.25), SCI-420 (-4.25) COID 205 (4.3), FBS (4.41), SWI-19 (4.45), WRI-15 (-4.00), HTD 5 (-4.00), SWI-E2 (-4.00), UACC-37 (-4.49), UACC-42 (-4.54) Oratin cancer CROV (1-(4.00), WCAR-3 (-4.05), WAI-15 (-4.00), RXF 393 (-4.00), SWIE2 (-4.32), TK-10 (-4.00), UACC-37 (-4.49), UACC-42 (-4.54) Prostate cancer PTS-0 (-4.55), MAB (-4.00), ACHN (-4.00), CAK-1 (-4.00), RXF 393 (-4.00), SWIE2 (-4.32), TK-10 (-4.00), UO-31 (-4.00) Prostate cancer PC-3 (-4.35), UACLARR-RES (-4.00), MAH-Re31/ATC (-4.47), IRS 5787 (-4.23), MAL-N (-4.45), MAL-N (-4.00), T-47D Prostate cancer PC-3 (-4.35), UCLARR-RES (-4.00), MAH-Re31/ATC (-4.47), INS 5787 (-4.12), IND-NB-435 (-4.59), MAL-N (-4.60), T-47D CMD 27 (-5.7), CALARR-RES (-4.00), MAH-Re31/ATC (-4.47), INS 5787 (-4.12), IND-123 (-4.45), NCI-H322 (M-4.6), NCI-H460 (-4.51), NCI-H32 (-4.51), NCI-H322 (M-4.6), NCI-H460 (-4.51), NCI-H322 (-4.51), NCI-H32 (-4.51), NCI-H	Leukemia	CCRF-CEM (<4.00), K-562 (4.46), MOLT-4 (4.42), RPMI-8226 (4.44), SR (4.37)
Colon currer ED22 (145) COS cancer COS (2014) COS cancer COS (2014) COS cancer COS (2014) COS cancer COS (2014) COS (2014) COS (2014) Protate cancer PS6-0 (425), MAR (>4.00), CAR-1 (<4.00), CAR-1 (<4.00), SN12C (4.23), TR-10 (<4.00), UD-31 (<4.00)	Non-small cell lung cancer	A549/ATCC (<4.00), EKVX (<4.00), HOP-62 (4.39), HOP-92 (<4.00), NCI-H226 (4.25), NCI-H23 (4.43), NCI-H322M (4.63), NCI-H460 (4.58), NCI- H220 (4.25), NCI-H23 (4.43), NCI-H322M (4.63), NCI-H460 (4.58), NCI-H260 (4.58), NCI-H270
CMS enter SP-208 (4.53), SP-205 (4.14), SNB-19 (4.44), SNB-75 (4.27), L021 (4.71), L021 (4.72),	Colon cancer	H322 (4:05) COLO 205 (4:27) HCC-2998 (4:74) HCT-116 (4:50) HCT-15 (<4:00) HT29 (4:21) KM12 (4:69) SW-620 (4:25)
Melanoma LOX, IMV (42), MALME-3M, 422, M14 (440), SK-MEL-2 (442), SK-MEL-2 (406), SK-MEL-2 (443), SK-OV-3 (442) Renal cancer R56-0 (426), A488 (<400), ACH (<400), CAK-1 (<400), RXF 393 (<400), SN 12 (<432), TK-10 (<400), UO-31 (<400)	CNS cancer	SF-268 (4.25), SF-295 (4.14), SNB-19 (4.44), SNB-75 (4.27), U251 (4.71)
Ovaria cancer IGR001 (1 IGR001 (2 IGR001 (2 IGR001 (2 IGR001 ACM (2 <thigr01 (2<="" acm="" th=""> <thigr01 (2<="" acm="" th=""> <</thigr01></thigr01>	Melanoma	LOX IMVI (4.33), MALME-3M (4.72), M14 (4.40), SK-MEL-2 (4.63), SK-MEL-28 (4.06), SK-MEL-5 (4.14), UACC-257 (4.49), UACC-62 (4.54)
Renal cancer 786-0 (4.26), Ad98 (4.00), ACM-1 (4.400), RXF 393 (4.200), SN12C (4.32), TK-10 (4.00), ID-31 (4.400) Prostate cancer NCF7 (4.75), NO1/ADR.RES (4.00), MDA-MB-231/ATCC (4.47), HS 578T (4.42), MDA-MB-435 (4.59), MDA-N (4.46), BT-549 (4.400), T47D (4.45) Streast cancer NCF7 (4.75), NO1/ADR.RES (4.00), MDA-MB-231/ATCC (4.47), HS 578T (4.42), MDA-MB-435 (4.45), NCI-H322M (4.46), NCI-H460 (4.51), NCI-H322M (4.50), NCI-H460 (4.51), NCI-H322M (4.45), NCI-S (4.45), SKB-25 (4.40), NCI-H460 (4.51), NCI-H322M (4.45), NCI-S (4.45)	Ovarin cancer	IGROV1 (<4.00), OVCAR-3 (4.68), OVCAR-4 (4.72), OVCAR-5 (<4.00), OVCAR-8 (4.43), SK-OV-3 (4.42)
Prostate cancer PC-3 (4.36), DOI-145 (4.18) Breast cancer MCF7 (4.75), NCI/NERRS (4-400), MDA-MB-231/ATCC (4.47), HS 578T (4.42), MDA-MB-435 (4.59), MDA-N (4.46), BT-549 (4-400), T-47D (4.45) Breast cancer CCRF-CEM (4.32), K-562 (4.51), MOI-74 (4.50), RPMI-8226 (4.60), SR (4.49) Non-small cell lung cancer CSR/ATCC (4-40), ENCV (4.22), HOP-52 (4.47), HOP-92 (4.40), NCI-H226 (4.31), NCI-H23 (4.45), NCI-H322M (4.60), NCI-H460 (4.51), NCI-H522 (4.52), SV-620 (4.46) State and Cancer COID 205 (4.55), ENC-2998 (4.58), HCT-116 (4.48), HTC-15 (4.400), HT29 (4.49), KM12 (4.55), SW-620 (4.46) CNS cancer SF-268 (4.46), SF-295 (4.400), SNB-19 (4.45), SNB-75 (4.400), US3 (4.460), SNC44 (4.48), SNR-48 (4.43), SK-MEL-5 (4.22), UACC-257 (4.51), UACC-62 (4.60) Ovarin cancer ICROVI (4.400), OVCAR-3 (4.45), OVCAR-4 (4.48), OVCAR-5 (4.400), NC2A-88 (4.43), SNR-26 (4.00), U-0.1 (4.00) Preast cancer PC-3 (4.40), DU-145 (4.40), MDA-MB-231/ATCC (4.41), HS 578T (4.19), MDA-MB-435 (4.48), MDA-N (4.40), BT-549 (4.400), T-47D Freast cancer MCF7 (4.40), NC1/ARERS (4-400, MDA-MB-231/ATCC (4.41), HS 578T (4.19), MDA-MB-435 (4.48), MDA-N (4.40), BT-549 (4.400), T-47D Freast cancer MCF7 (4.40), NC1/ARERS (4-400, MDA-MB-231/ATCC (4.41), HS 578T (4.19), MDA-MB-435 (4.48), MDA-N (4.40), BT-549 (4.400), T-47D freast cancer MCF7 (4.40), MLR-SM (6.59), MALC (4.51), NCT-4226 (5.53) MCF7 (CG4), NC1/ARERS (4.50), MDA-MB-231/ATCC (4.41), HS 578T (4.19), MDA-MB	Renal cancer	786-0 (4.26), A498 (<4.00), ACHN (<4.00), CAKI-1 (<4.00), RXF 393 (<4.00), SN12C (4.32), TK-10 (<4.00), UO-31 (<4.00)
Disease catter MCP (47.5), MC(ADR-REG (44.00), MD-MB-23) [ATC (44.7), R5 37.61 (44.2), MD-MB-435 (43.5), MD-MB 435 (44.6), R1-44.6), R1-44.6) 2.7-Bis (4.5-dib)dro-4-4-dimethyl- H-imitable-2-yllphorene dihydrochloride (2) Interventia CCRF-CCRH (43.2), CSC (46.1), MD1-4 (45.5), RNF-18-226 (46.0), SR (4.49) Non-small cell lung cancer A549/ATC (-4.00), EVX (42.2), HOP-52 (44.7), HDP-92 (40.4), NT29 (4.49), KM12 (4.5), SV-620 (4.46) Norain cancer COLO 205 (45.5), HCC-2988 (45.8), HCT-116 (4.48), HCT-15 (-4.00), HT29 (4.49), KM12 (4.5), SV-620 (4.46) Melanoma LOX IMVI (4.43), MAIR-3M (4.61), MH (4.45.5), SK-75 (4.40), USX (4.61), SK-MEL 28 (4.41), SK-0V-1 (4.55) Melanoma LOX IMVI (4.43), MAIR-3M (4.43), VCRA4 (4.48), OVCRA5 (-4.00), ND2-KHEL 38 (4.41), SK-0V-1 (4.55) Melanoma LOX IMVI (4.43), MAIR-34 (4.43), OVCRA4 (4.43), OVCRA5 (-4.00), ND2-MB-231/ATCC (4.41), HS 578T (4.19), MDA-MB-435 (4.48), MDA-N (4.40), BT-549 (-4.00), T-47D Retait cancer PC-3 (4.40), DU-45 (-400) Retait (-4.41), R-422 (5.55) Non-small cell lung cancer A569/ATC (-6.02) RS (5.41), ST-116 (6.20), HCT-15 (5.11), HT2 (5.26), NDA-MB-435 (4.48), MDA-N (4.40), BT-549 (-4.00), T-47D (4.23) MCF7 (4.63), ND/ADR-RES (-4.00), MDA-MB-231/ATCC (4.41), HS 578T (4.19), MDA-MB-435 (4.83), MDA-MB (4.60), S6.90, NC1+522 (5.97) COBC CCM (6.33), LEX (4.53), SCMC (5.56), HD-62 (5.52), HD-62 (5.55	Prostate cancer	PC-3 (4.36), DU-145 (4.18)
2.7.Big 4.5-dibydro-4.4.dimethyl-11-inidaol-2-yl fluorene dibydrochloride [2] Lenkemia CCR-CEM (4.22), K-562 (4.61), MOLT-4 (4.50), RFMI-8226 (4.60), SR (4.49) Non-small cell lung cancer CGP-CEM (4.22), K-562 (4.51), MOLT-4 (4.50), RFMI-8226 (4.64), NCI-H226 (4.45), NCI-H322M (4.60), NCI-H460 (4.51), NCI-H522 (4.32) Colo cancer COL 200 (4.55), HCC-2998 (4.58), HCT-116 (4.48), HCT-15 (<4.00), HT29 (4.49), SKM-12 (4.45), SKM-620 (4.46)	Breast cancer	MLC1 (4.75), NCI/ADR-RES (<4.00), MDA-MB-231/ATCC (4.47), HS 5781 (4.42), MDA-MB-435 (4.59), MDA-N (4.46), BT-549 (<4.00), T-47D (4.46), MDA-MB-231/ATCC (4.47), HS 5781 (4.42), MDA-MB-435 (4.59), MDA-N (4.46), BT-549 (<4.00), T-47D (4.46), MDA-MB-231/ATCC (4.47), HS 5781 (4.42), MDA-MB-435 (4.59), MDA-N (4.46), BT-549 (<4.00), T-47D (4.46), MDA-MB-231/ATCC (4.47), HS 5781 (4.42), MDA-MB-435 (4.59), MDA-N (4.46), BT-549 (<4.00), T-47D (4.46), MDA-MB-231/ATCC (4.47), HS 5781 (4.42), MDA-MB-435 (4.59), MDA-N (4.46), BT-549 (<4.00), T-47D (4.46), MDA-MB-231/ATCC (4.47), HS 5781 (4.42), MDA-MB-435 (4.59), MDA-N (4.46), BT-549 (<4.00), T-47D (4.46), MDA-MB-435 (4.59), MDA-N (4.46), BT-549 (<4.00), T-47D (4.46), MDA-MB-435 (4.59), MDA-N (4.5
2.7-884.3-200/07-4.4-ametry: In-Imitador-2-9/juliorene anyotochanice (2) possible (4.40), SR (4.49) Non-small cell lung cancer A549/NEC (4.400), KWX (4.22), HOP-62 (4.47), HOP-92 (4.04), NCI-H226 (4.31), NCI-H22 (4.45), NCI-H322M (4.60), NCI-H460 (4.51), NCI-H322 (4.20), SK (4.40), SK (4.40), SK (4.40), SK (4.40), SK (4.40), SK (4.40), SK (4.45), SK (4.41), SK (4.45), SK (4.45), SK (4.41), SK (4.45), SK (4.41), SK (4.45), SK (4.41), SK	2.7 Dis(4.5 dilation 4.4 dimeth	
Constrained	2,7-Bis(4,5-ainyaro-4,4-aimethy	y_{1} - 1/1imiadzoi-2-y/j/jiuorene ainyarocnionae (Z) $CCRE_CEM (4.32) K-552 (4.61) MOIT_4 (4.50) ROMI_8226 (4.60) SR (4.49)$
 HS22 (4.52) HS2 (4.53) HS2 (4.53) HS2 (4.53) HS2 (4.54) HS2 (4.55) HS2 (4.54) HS2 (4.55) HS2 (4.55)	Non-small cell lung cancer	6549/ATCC (<4.00), EKVX (4.22), HOP-62 (4.47), HOP-92 (4.04), NCI-H26 (4.31), NCI-H23 (4.45), NCI-H322M (4.60), NCI-H460 (4.51), NCI-
Colon cancer COLO 205 (455), HCC-2998 (445), HCC-116 (448), HCT-15 (440), HT29 (445), KM12 (455), SW-620 (446) CNS cancer SP-268 (446), ST-259 (4400), SNE 19 (445), SNF-76 (440), U25 (446) Melanoma LOX IMVI (443), MALME-39M (461), M14 (435), SK-MEL-2 (470), SK-MEL-28 (441), SK-MEL-5 (422), UACC-257 (451), UACC-62 (460) Ovarin cancer PC-6 (430), A498 (4.11), ACHN (400), CAKL-1 (440), RXF 393 (4400), SN12C (4.44), TK-10 (440), UO-31 (440) Breast cancer MCF (463), NCI/ADR-RES (4400), MDA-MB-231/ATCC (4.41), HS 5787 (419), MDA-MB-435 (4.48), MDA-N (4.40), BT-549 (4.00), T-47D (4.21) 4.6-Bis [3-(4.5-dihydro-4-methyl-1 H-imidizob-2-yl)phenyl]-2-dimethylamino-1,3.5-triazine tetrahydrochloride (3) Feakeria CCRF-CEM (633), HL-60(TB) (5.59), K-562 (521), MOLT-4 (6.44), RPMI-8226 (5.50), NCI-14520 (5.69), NCI-14522 (5.67), NCI-1523 (5.60), NCI-14522 (5.97) Colon cancer SF-268 (5.56), NEC 2595 (5.36), SF-553 (5.34), SF-36 (5.35), MEL-32 (5.60), NCI-1422 (5.60), NCI-1452 (5.60), NCI-1452 (5.65), VACC-25 (5.65), VACC-25 (5.65), VACC-25 (5.73) Ovarin cancer R26 (5.60), NCI-2595 (5.36), SF-350 (5.34), SK-91 (5.60), NCI-259 (5.65), NCI-1452 (5.66), NCI (5.37) Melanoma UX IMVI (5.36), MALM-3 (5.27), VACR-4 (5.47), NCR-48 (5.61), NCI-25 (5.65), MDA-NB (5.83), NCI-3469 (5.73) Ovarin cancer SF-268 (5.66), SF-25 (5.36), SF-350 (SCAR + (5.64)), SF-351 (5.55), MDA-NB (5.82), NCI-359 (5.73), NCI-350 (5.73), NCI-350 (5.73), NCI-350 (5.73), NCI-350 (5.73), NCI-350 (5.73), NCI-350 (5.74), NCI +46	0	H522 (4.52)
CNS cancer SF-286 (446), SF-295 (-400), SNE-19 (445), SNE-75 (-404), U251 (446) Welanoma LDX INW1 (433), MALME-30 (445), SNE-162 (404), U251 (445), SK-MEL-28 (441), SK-MEL-5 (422), UACC-257 (451), UACC-62 (460) Ovarin cancer ICROVI (-400), OVCAR-3 (445), OVCAR-4 (448), OVCAR-5 (-400), SNL-28 (441), SK-MEL-5 (422), UACC-257 (451), UACC-62 (460) Prostate cancer 786-0 (430), 498 (411), ACIN (-400), CKI-1 (-400), RXF 393 (-400), SNL2C (-444), TK-10 (-400), UO-31 (-400) Prostate cancer PC-3 (-400), DU-145 (-4.00) Breast cancer NC7 (463), NCI/ADR-RES (-4.00), MDA-MB-231/ATCC (4.41), HS 578T (4.19), MDA-MB-435 (4.48), MDA-N (4.40), BT-549 (-4.00), T-47D (-4.21) 4.6-Bis [3-(4.5-dihydro-4-methyl-1H-imidazol-2-yl)phenyl-2-dimethylamino-1,3-5-triazine tetrahydrocholoide (3) Eukemia CRF-CEM (-633), HL-607B (-560), NS-526 (-513), MOLT-4 (-404), RFM-3226 (-555) Non-small cell lung cancer A549/ATCC (553), HD-762 (-522), HDP-92 (-563), NC1-H322 (-58), KML (-58), NC1-H460 (-569), NC1-H522 (-597) Colon cancer COLO 205 (-500), HC-2989 (-534), HC-116 (-564), HCT-15 (-500), NC1-H322M (-589), KNC1-H460 (-561), MACC-62 (-5,73) Ovarin cancer IGROVI (-533), OVCAR-3 (-567), OVCAR-4 (-591), NC1-H23 (-540), NC4-E23 (-569), UACC-257 (-565), UACC-62 (-5,73) Ovarin cancer IGROVI (-533), OVCAR-3 (-567), OVCAR-4 (-593), ST-575, SN12C (-591), TK-10 (-563), UO-31 (-548) Prostate cancer P6-0 (-567), A498 (-563), ACH (-57), SN12C (-591), TK-10 (-563), UO-31 (-548) Prostate cancer P6-0 (-567), A498 (-563), MDA-MB-231/ATCC (-580), HS 7517 (-555), MDA-MB-435 (-582), MDA-N (-582), BT-549 (-5.43), T-470 (-5.67) A6-Bis/4-(-4,-5,-dihydro	Colon cancer	COLO 205 (4.55), HCC-2998 (4.58), HCT-116 (4.48), HCT-15 (<4.00), HT29 (4.49), KM12 (4.55), SW-620 (4.46)
Melanoma LOX IMVI (443), MALME-3M (461), M14 (435), SK-MEL-2 (4.70), SK-MEL-2 (4.72), SK-MEL-5 (4.22), UACC-327 (4.51), UACC-62 (4.60) Ovarin cancer T68-0 (4.30), A98 (4.11), ACHN (4.40), CAKL-1 (4.40), RKF 393 (4.00), SN12C (4.44), TK-10 (4.00), UO-31 (4.400) Prostate cancer PC-3 (4.40), DL-145 (4.40) MDA-MB-231 (ATCC (4.41), HS 578T (4.19), MDA-MB-435 (4.48), MDA-N (4.40), BT-549 (4.40), T-47D (4.21) 46-Bis [3-(4.5-dilydro-4-methyl-1H-imidazol-2-yl)phenyl]-2-dimethylamino-1.3.5-triazine tetrahydrochloride (3) CCRF-CEM (6.33), HL-60(TB) (5.60), K-562 (6.21), MOLT-4 (6.44), RTM-1822 (5.55) Non-small cell lung cancer SF-268 (5.56), SEX (5.55) (5.60), K-562 (5.21), MOLT-4 (6.44), RTM-1822 (5.55) Colo cancer COLO 206 (5.90), HCC-2998 (5.34), HCT-116 (6.26), HCT-15 (5.01), HT29 (5.88), KM12 (5.81), SW-620 (6.12) Cols cancer SF-268 (5.56), SF-295 (5.36), SF-359 (5.34), SF-35 (5.36), SC-46E (5.63), SC-46E (5.63), SC-46E (5.63), UACC-257 (5.65), UACC-62 (5.73) Ovarin cancer ICROVIC (5.30), OVCRA* (5.47), VOCRA* (5.53), OVCRA* (5.44), SC-W-3 (5.69), UACC-257 (5.63), UACC-62 (5.73) Ovarin cancer PC-3 (6.31), ML-145 (5.66) SC-30, SC-30, SC-30, SC-30, SC-30, SC-30, SC-30, SC-30, SC-30, UO-31 (5.84) Prostate cancer PC-3 (6.31), ML-145 (5.60), VOCRA* (5.53), NOA-MB-435 (5.85), MDA-N (5.82), UC-31 (5.84) Prostate cancer PC-3 (6.31), ML-145 (5.60), NCCA+2 (5.53), MOL-44 (5.73), NC+1423 (5.83), SC-04 (5.53)	CNS cancer	SF-268 (4.46), SF-295 (<4.00), SNB-19 (4.45), SNB-75 (4.04), U251 (4.66)
Ovann cancer DKDVT (44,00), DUCAR-3 (44.8), DUCAR-4 (44.8), DUCAR-5 (43.0), DUSAR (44.4), TK-10 (44.00), LD-31 (44.00) Prostate cancer PC-3 (44.4), DU-145 (44.00) BPC-3 (44.40), DU-145 (44.00) Prostate cancer PC-3 (44.4), DU-145 (44.00) BPC-3 (44.40), DU-145 (44.00) Prostate cancer PC-3 (44.4), DU-145 (44.00) BPC-3 (44.40), DU-145 (44.00) Prostate cancer PC-3 (44.4), DU-145 (44.00) BPC-3 (44.40), DU-145 (44.00) Prostate cancer PC-3 (44.4), DU-145 (44.00) BPC-3 (44.4), RN1 (44.00), RN1 (44.40),	Melanoma	LOX IMVI (4.43), MALME-3M (4.61), M14 (4.35), SK-MEL-2 (4.70), SK-MEL-28 (4.41), SK-MEL-5 (4.22), UACC-257 (4.51), UACC-62 (4.60)
Number Display Hole Display Hole <thdisplay hole<="" th=""> Display Hole</thdisplay>	Ovarin cancer Repal cancer	IGROVT (<4.00), OVCAR-3 (4.45), OVCAR-4 (4.48), OVCAR-5 (<4.00), OVCAR-8 (4.43), SK-0V-3 (4.35) 786.0 (4.30) Ad98 (411) ACTINI (4.40), OVCAR-5 (<4.00), SK-12 ((4.43), SK-0V-3 (4.35))
Breast cancer MCF7 (4.63), NCI/ADR-RES (<4.00), MDA-MB-231/ATCC (4.41), HS 578T (4.19), MDA-MB-435 (4.48), MDA-N (4.40), BT-549 (<4.00), T-47D (4.21) (4.21) (4.21) (4.21) (4.21) (4.21) (4.21) (4.21) (4.21) (4.21) (4.21) (4.21) (4.21) (4.21) (4.21) (4.21) (4.21) (4.21) (4.21) (4.21) (4.21) (4.21) (4.21) (4.21) (5.4), Structure (6.21), MOLT-4 (6.44), RPM-B226 (5.55) Non-small cell lung cancer S549/ATCC (5.53), EKX2 (5.56), HOF-62 (5.29), 216 (5.5), NOL-H3226 (5.69), NCL-H322 (5.69), NCL-H522 (5.69), NCL-H52 (5.62), NCL-H52 (5.62), NCL-H52 (5.63), NCL-H	Prostate cancer	PC-3 (4.40), DI-145 (4.11), TCHA (4.60), CHAI T (4.60), THE SSS (4.60), SHIZE (4.44), THE (4.60), COST (4.60)
(421) 4.6-Bis [3-(4.5-dillydro-4-metlyl-1-Hi-midazol-2-yllphenyl]-2-dimethylamino-1,3.5-triazine tetrahydrochloride (3) Leukemia CCRF-CEM (6.33), HL-60(TB) (5.69), K-562 (6.21), MOLT-4 (6.44), RPMI-8226 (5.55) Non-small cell lung cancer A549/ATCC (5.53), EKVV (5.56), HOP-62 (5.92), HOP-99 (5.63), NCI-H3223 (5.60), NCI-H322M (5.98), NCI-H460 (5.69), NCI-H522 (5.97) Colon cancer SF-268 (5.56), SF-295 (5.36), SF-393 (6.34), SNB-19 (6.07), SNB-75 (5.76), L251 (6.15) Melanoma LOX INV1 (5.96), MALME-3M (5.29), M14 (5.45), SK-MEL-2 (5.66), SK-MEL-3 (5.69), UACC-257 (5.65), UACC-62 (5.73) Ovarin cancer IGROV1 (5.53), OVCRA-3 (5.67), OVCRA+4 (5.91), OVCRA-5 (5.55), NVCA-8 (5.69), SK-0V-3 (5.69) Prostate cancer PC3 (6.13), DU-145 (5.66) Breast cancer MC77 (6.06), NCI/ADR-RES (4.78), MAD-MB-231/ATCC (5.86), HS 5781 (5.55), MDA-MB-435 (5.85), MDA-N (5.82), BT-549 (5.43), T-47D (5.67) Yons-mall cell lung cancer CCRF-CEM (6.06), H-60(TB) (5.58), K-562 (5.79), MOLT-4 (6.02), RPMI-8226 (5.37) Non-small cell lung cancer SF-268 (5.64), SF-295 (5.42), SF-593 (6.07), SRB-16 (5.47), SRB (5.25), MDA-MB-235 (5.83), MCH-493 (5.82) COlo 205 (5.53), HCC-298 (5.64), SK-642 (5.79), MOLT-4 (6.02), RPMI-8226 (5.37) Non-small cell lung cancer SF-268 (5.64), SF-295 (5.74), CCF-16 (5.81), HCT-15 (5.47), NF2 (5.28), NCI-4322M (5.79), NCI-H460 (5.45), NCI-H522 (5.82) COlo 205 (5.83), MCL-48 (5.63)	Breast cancer	MCF7 (4.63), NCI/ADR-RES (<4.00), MDA-MB-231/ATCC (4.41), HS 578T (4.19), MDA-MB-435 (4.48), MDA-N (4.40), BT-549 (<4.00), T-47D
4,6-Bis [3-(4,5-dihydro-4-methyl-1H-imidazol-2-yl)phenyl]-2-dimethylamino-1,3,5-triazine tetrahydrochloride (3) Leukemia CCRF-CEM (633), HL-60(TB) (556), K-552 (62.1), MOLT-4 (644), RNH-8226 (5.55) Non-small cell lung cance A549/ATCC (553), REVX (555), HOP-62 (553), NCH-1129 (5,60), NCI-H322 (5,99), NCI-H460 (5,69), NCI-H522 (5,97) Colon cancer COL 205 (5.90), HCC-2988 (5,94), HCT-116 (6,26), HCT-15 (5,01), HT29 (5,88), KML (5,81), SK-MEL-2 (5,66), UACC-257 (5,65), UACC-62 (5,73) Melanoma LOX IMVI (5,96), MALME-3M (5,29), M14 (5,45), SK-MEL-2 (5,66), SK-MEL-28 (5,44), SK-MEL-5 (5,69), UACC-257 (5,65), UACC-62 (5,73) Ovarin cancer GROV1 (5,53), OVCAR-3 (5,67), OVCAR-4 (5,91), OVCAR-8 (5,55), MOA-MB-435 (5,85), MDA-N (5,82), BT-549 (5,43), T-47D (5,67) Preast cancer PC-3 (6,13), DU-145 (5,66) Breast cancer VCF7 (6,06), NCI/JAPR-RES (4,78), MDA-MB-231/ATCC (5,86), HS 578T (5,55), MDA-MB-435 (5,85), MDA-N (5,82), BT-549 (5,43), T-47D (5,67) Non-small cell lung cancer A549/ATCC (5,46), HOP-62 (5,22), HOP-92 (5,70), NCI-H23 (5,44), NCI-H2322M (5,79), NCI-H460 (5,45), NCI-H522 (5,82) Colon cancer COL 205 (5,33), MALME-3M (5,42), M14 (5,46), SK-MEL-2 (5,69), SK-MEL-28 (5,43), SK-MEL-5 (5,50), UACC-257 (5,69), UACC-257 (5,79), UACF-25 (5,73), MDI-4 (5,74), SK-MEL-2 (5,74), SK-MEL-2 (5,73), SK-MEL-2 (5,73), SK-MEL-3 (5,74), MDA-N (5,77), BT-549 (5,40), T-470		(4.21)
Leukemia CCRF-CEM (6.33), IL-60(TB) (5.69), K-562 (6.21), MOLT-4 (6.44), RMI-8226 (5.55) Non-small cell lung cancer A549/ATCC (5.53), EVXX (5.56), HOP-62 (5.92), HOP-92 (5.63), NCI-H23 (5.60), NCI-H322M (5.98), NCI-H460 (5.69), NCI-H522 (5.97) Colo cancer SF-268 (5.56), SF-298 (5.34), ETT-116 (6.26), HCT-15 (5.01), HT29 (5.88), KM12 (5.81), SW-620 (6.12) CNS cancer SF-268 (5.56), ACHN (5.42), MIX (5.43), SKN-116 (6.26), SK-MEL-23 (5.64), SK-MEL-23 (5.69), UACC-257 (5.65), UACC-62 (5.73) Ovarin cancer T65-0 (5.67), A498 (5.63), ACHN (5.47), CAKL-1 (4.78), RXF 393 (5.57), SN122 (5.91), TK-10 (5.63), UO-31 (5.48) Prostate cancer PC3 (6.13), DU-145 (5.66) Breast cancer MCF7 (6.06), NCI/ABR-RES (4.78), MDA-MB-231/ATCC (5.86), HS 578T (5.55), MDA-MB-435 (5.85), MDA-N (5.82), BT-549 (5.43), T-47D (5.67) A6-BigH-4(4.5-dilydro-4-methyl-HI+imidaz0-2-yl)phenyl]-2-dimethylamino-1,3,5-triazine dihydrochloride (4) Leukemia CCRF-CEM (6.06), HL-60(TB) (5.58), K-562 (5.79), MOL-14 (6.02), RPMI-8226 (5.37) Non-small cell lung cancer SF-268 (5.64), SF-295 (5.42), SF-539 (6.07), SNB-19 (5.70), NCH-132 (5.54), NCI-H322 (5.79), NCI-H460 (5.45), NCI-H522 (5.82) Colon cancer SF-268 (5.64), SF-295 (5.42), SF-539 (6.07), SNB-19 (5.70), U251 (5.43), SK-MEL-3 (5.43), SK-MEL-3 (5.43), SK-MEL-5 (5.50), UACC-257 (5.69), UACC-62 (5.75) Ovarin cancer SF-268 (5.64), SF-295 (5.42), SF-539 (5.67), NCT-14 (5.74), NCH-28 (5.43), SK-MEL-3 (5.43), SK-MEL-5	4,6-Bis [3-(4,5-dihydro-4-methy	yl-1H-imidazol-2-yl)phenyl]-2-dimethylamino-1,3,5-triazine tetrahydrochloride (3)
Non-small cell lung cancer A549/ATCC (5:32), EKVX (5:56), HOP-62 (5:92), HOP-92 (5:30), NCI-H23 (5:60), NCI-H322M (5:88), NCI-H322 (5:81), SW-620 (6:12) CNS cancer SF-268 (5:56), SF-299 (5:34), ET-116 (6:26), HCI-15 (5:51), UACC (5:81), SW-620 (6:12) CNS cancer SF-268 (5:56), SF-299 (5:34), ET-116 (6:26), HCI-15 (5:51), UACC (5:81), SW-620 (6:12) Ovarin cancer IGROVI (5:50), UACC-315 (5:7), VCAR-4 (5:51), SV-MEL-23 (5:44), SK-MEL-3 (5:44), SK-MEL-5 (5:69), UACC-257 (5:55), UACC-62 (5:73) Ovarin cancer 786-0 (5:67), A498 (5:63), ACHN (5:47), CAK1-1 (4.78), RXF 393 (5:57), SN12C (5:91), TK-10 (5:63), UO-31 (5:48) Prostate cancer MCF7 (6:06), NCI/ADR-RES (4.78), MDA-MB-231/ATCC (5:86), HS 578T (5:55), MDA-MB-435 (5:85), MDA-N (5:82), BT-549 (5:43), T-47D (5:67) Non-small cell lung cancer CCRF-CEM (6:06), HL=60 (III) (5:58), K-562 (5:79), MOCT-4 (6:02), RPM-R326 (5:37) Non-small cell lung cancer CDS (5:93), HCC-2998 (5:70), HCT-116 (5:81), HCT-15 (4:77), HT29 (5:64), MM12 (5:75), SW-620 (5:82) COLs cos (5:93), HCC-2998 (5:70), HCT-116 (5:81), HCT-15 (4:77), HT29 (5:64), MM12 (5:75), W-620 (5:82) COS cancer CDL (5:83), MALME-30 (5:42), M14 (5:40), SK-MEL-2 (5:73), MD5 (5:30), UACC-257 (5:69), UACC-62 (5:75) Ovarin cancer FC-286 (5:63), ACHN (5:48), CAK1-1 (4:79), RXF 393 (5:59), SN-12 (5:43), SK-MEL-28 (5:33), SK-MEL-3 (5:30), MCI-42 (5:73), MD2 (5:69), TK-10 (5:57), UO-31 (5:31) Prostate cancer CCRV (5:75), HCOP-82 (5:82	Leukemia	CCRF-CEM (6.33), HL-60(TB) (5.69), K-562 (6.21), MOLT-4 (6.44), RPMI-8226 (5.55)
Colon cancer CoLO 205 (5.90), HCC-2998 (5.94), HCT-116 (5.26), HCT-15 (5.01), HT29 (5.88), KM12 (5.81), SW-620 (6.12) CNS cancer SF-268 (5.56), SF-295 (5.56), SF-295 (5.36), SF-39 (6.07), SNB-75 (5.76), U251 (6.15) Melanoma LOX INVI (5.96), MALME-3M (5.29), M14 (5.45), SK-MEL-2 (5.66), SK-MEL-28 (5.44), SK-MEL-5 (5.69), UACC-257 (5.65), UACC-62 (5.73) Orarin cancer IGROV1 (5.53), OVCAR-3 (5.67), OVCAR-4 (5.51), OVCAR-8 (5.55), OVCAR-8 (5.69), SK-OV-3 (5.69) Renal cancer PC-3 (6.13), DU-145 (5.66) Breast cancer PC-3 (6.13), DU-145 (5.66) Breast cancer MCF7 (6.06), NCI/ADR-RES (4.78), MDA-MB-231/ATCC (5.86), HS 578T (5.55), MDA-MB-435 (5.85), MDA-N (5.82), BT-549 (5.43), T-47D (5.67) 4.6-Big/4-(4.5-dihydro-4-methyl-1H-imidazol-2-yl)phenyl/2-dimethylamino-1,3.5-triazine dihydrochloride (4) Leukemia CCR-CEM (6.06), HL-60(TB) (5.58), K-562 (5.79), MOLT-4 (6.02), RPMI-8226 (5.37) Non-small cell lung cancer SP-268 (5.64), SF-295 (5.42), SF-539 (6.07), SNB-19 (5.72), SNB75 (5.78), U251 (5.94) Melanoma LOX INVI (5.83), MALME-3M (5.42), SK-MEL-2 (5.69), KM12 (5.75), SW-620 (5.82) CNS cancer SP-268 (5.64), SF-295 (5.42), SF-539 (6.07), SNB-19 (5.72), SNB75 (5.78), U251 (5.94) Melanoma LOX INVI (5.51), OVCAR-3 (5.68), OVCAR-4 (5.79), OVCAR-5 (5.41), OVCAR-8 (5.63), SK-OV-3 (5.71) Renal cancer 786-0 (5.62), A498 (5.60), ACHN (5.48), CAKL-1 (4.79), RXF 393 (5.59), SN122 (5.69), TK-10 (5.57), UC-257 (5.69), UACC-62 (5.75) Ovarin cancer 16ROV1 (5.51), OVCAR-3 (5.68), OVCAR-4 (5.79), OVCAR-5 (5.41), OVCAR-8 (5.63), SK-OV-3 (5.71) Renat cancer 786-0 (5.62), A498 (5.60), ACHN (5.48), CAKL-1 (4.79), RXF 393 (5.59), SN122 (5.69), TK-10 (5.57), UC-31 (5.31) Prostate cancer MCF7 (5.75), NCI/ADR-RES (4.63), MDA-MB-231/ATCC (5.84), HS 578T (5.54), MDA-MB-435 (5.81), MDA-N (5.67), BT-549 (5.40), T-47D (5.65) 2.3-Big/4-(4.5.67,8)-Hexahydro-Hi-hexaindazol-2-ylphenyl[furma dihydrochiorde (8) CCR-ECEM (5.75), HCCI (5.77), EVX (5.77), HOP-62 (5.82), HOT-15 (5.28), HT29 (5.66), KM12 (5.84), SW-620 (5.59) Non-small cell lung	Non-small cell lung cancer	A549/ATCC (5.53), EKVX (5.56), HOP-62 (5.92), HOP-92 (5.63), NCI-H23 (5.60), NCI-H322M (5.98), NCI-H460 (5.69), NCI-H522 (5.97)
Chs career Sh-259 (5.36), Sh-359 (6.34), SNB-19 (6.07), SNB-76 (2.76), U221 (6.15) Melanoma LOX IMVI (5.96), MAILME-3M (5.29), M14 (5.45), SK-MEL-2 (5.66), KK-MEL-28 (5.44), SK-MEL-26 (5.69), UACC-257 (5.65), UACC-62 (5.73) Ovarin cancer 786-0 (5.67), AV98 (5.63), ACHN (5.47), CAKL-1 (4.78), RXP 393 (5.57), SN12C (5.91), TK-10 (5.63), U0-31 (5.48) Prostate cancer PC-3 (6.13), DU-145 (5.66) Breast cancer MCF7 (6.06), NCI/ADR-RES (4.78), MDA-MB-231/ATCC (5.86), HS 578T (5.55), MDA-MB-435 (5.85), MDA-N (5.82), BT-549 (5.43), T-47D (5.67) A.6-Bigl4-(4,5-dihydro-4-methyl-1-H-imidazol-2-yl)phenyl]-2-dimethylamino-1,3,5-triazine dihydrochloride (4) Leukemia CCRF-CEM (6.06), HL-06(TB) (5.58), K-562 (5.79), MOLT-4 (6.02), RPMI-8226 (5.37) Non-small cell lung cancer COBO(TB) (5.58), MOP-62 (5.82), MOLT-4 (6.02), RPMI-8226 (5.37) Colo cancer COL0 205 (5.93), HCC-2998 (5.70), HCT-116 (5.81), HCT-15 (5.78), U251 (5.94) Melanoma LOX IMVI (5.83), MALME-3M (5.42), M14 (5.46), SK-MEL-2 (5.69), SK-MEL-28 (5.43), SK-MEL-2 (5.50), UACC-257 (5.69), UACC-62 (5.75) Ovarin cancer IGROVI (5.51), OVCAR-3 (5.68), OVCAR-4 (5.79), OVCAR-4 (5.54), NCV-48 (5.53), SK-OV-3 (5.71) Real cancer PG-3 (5.74), DU-145 (5.76) Real cancer PG-3 (5.74), DU-48 (5.66), ACHN (5.48), CAKI-1 (4.79), RXF 393 (5.59), SN12 (5.69), TK-10 (5.57), UO-31 (5.31) Prostate cancer	Colon cancer	COLO 205 (5.90), HCC-2998 (5.94), HCT-116 (6.26), HCT-15 (5.01), HT29 (5.88), KM12 (5.81), SW-620 (6.12)
International Interna International International<	CNS cancer Melanoma	SF-268 (5.56), 5F-259 (5.56), SF-359 (6.34), SIBE-19 (6.07), SIBE-75 (5.76), U251 (6.15) LOX IMVI (5.66), MALME-2M (5.26), MIE-19 (6.07), SEA (5.66), SEA (6.15), SEA (6.15), SEA (6.15), SEA (6.15), SEA
Renal cancer 786-0 (5.67), A498 (5.63), ACHN (5.47), CAK1-1 (4.78), RXF 393 (5.57), SN12 (5.51), TK-10 (5.63), UO-31 (5.48) Prostate cancer PC-3 (6.13), DU-145 (5.66) Breast cancer MCF7 (6.06), NCI/ADR-RES (4.78), MDA-MB-231/ATCC (5.86), HS 578T (5.55), MDA-MB-435 (5.85), MDA-N (5.82), BT-549 (5.43), T-47D (5.67) A/6-Bis/4-(4.5-dihydro-4-methyl-1H-imidazol-2-yl/phenyl]-2-dimethylamino-1,3,5-triazine dihydrochloride (4) Leukemia CCRF-CEM (6.06), HL-60(TB) (5.58), K-562 (5.79), MOLT-4 (6.02), RPMI-8226 (5.37) Non-small cell lung cancer OCJ0 (5.93), HCC-2998 (5.70), NCI-1423 (5.54), NCI-H322M (5.79), NCI-H460 (5.45), NCI-H522 (5.82) COlo cancer COLO 205 (5.93), HCC-2998 (5.70), NDCT-16 (4.77), HT29 (5.64), KM12 (5.75), SW-620 (5.82) CNS cancer SF-268 (5.64), SF-295 (5.42), SF-539 (6.07), SNB-19 (5.72), SNB75 (5.78), U251 (5.94) Melanoma LOX IMVI (5.83), MALME-3M (5.42), M14 (5.46), SK-MEL-2 (5.69), SK-MEL-28 (5.43), SK-MEL-5 (5.50), UACC-257 (5.69), UACC-62 (5.75) Ovarin cancer T86-0 (5.62), A498 (5.60), ACHN (5.48), CAKI-1 (4.79), RXF 393 (5.59), SN12C (5.69), TK-10 (5.57), UO-31 (5.31) Prostate cancer PC-3 (5.74), DU-145 (5.76) Breast cancer PC-3 (5.74), DU-145 (5.76) Breast cancer PC-3 (5.74), DU-145 (5.76) Breast cancer PC-3 (5.74), DU-145 (5.76) Nore-recor (5.50), NLO-HDPPHyl	Ovarin cancer	LOA INVI (J.53), OVCAR-3 (5 67) OVCAR-4 (5 91) OVCAR-5 (5 55) OVCAR-8 (5 69) SL-OV-3 (5 69)
Prostate cancer PC-3 (6,13), DU-145 (5,66) Breast cancer MCF7 (6,06), NCI/ADR-RES (4,78), MDA-MB-231/ATCC (5,86), HS 578T (5,55), MDA-MB-435 (5,85), MDA-N (5,82), BT-549 (5,43), T-47D (5,67) 4,6-Bis/4-(4,5-dihydro-4-methyl-H-inhimitazol-2-yl)phenyl/J2-dimethylamino-1,3,5-triazine dihydrochloride (4) Leukemia CCRF-CEM (6,06), HL-60(TB) (5,58), K-562 (5,79), MOLT-4 (6,02), RPMI-8226 (5,37) Non-small cell lung cancer A549/ATCC (5,47), EKVX (5,46), HOP-62 (5,82), HOP-92 (5,70), NCI-H23 (5,54), NCI-H322M (5,79), NCI-H460 (5,45), NCI-H522 (5,82) COlo cons cancer COLO 205 (5,93), HCC-2998 (5,70), HCT-116 (5,81), HCT-15 (4,77), HT29 (5,64), KM12 (5,75), SW-620 (5,82) CNS cancer SF-268 (5,64), SF-295 (5,42), SF-539 (6,07), SNB-19 (5,72), SNB75 (5,78), U251 (5,59) Ovarin cancer 786-0 (5,62), A498 (5,60), ACRH (5,48), CAR-4 (5,79), OVCAR-5 (5,41), OVCAR-8 (5,63), SK-MEL-2 (5,69), SK-MEL-2 (5,69), SK-MEL-3 (5,63), SK-MEL-3 (5,71), U0-31 (5,31) Prostate cancer PC-3 (5,74), DU-145 (5,76) Breast cancer PC-3 (5,74), DU-145 (5,76), MAD-MB-231/ATCC (5,84), HS 578T (5,54), MDA-MB-435 (5,81), MDA-N (5,67), BT-549 (5,40), T-47D (5,65) S2-5Bis/4-(-4,5,6,78,9-hexab/dvI+h-benzimidazol-2-yl)phenyl/furan dihydrochloride (8) CCRF-CEM (5,77), HCM (5,77), HDP-62 (5,82), HOCP-92 (5,84), NCI-H226 (5,73), NCI-H322 M (5,87), NCI-H460 (5,74), NCI-H522 (5,79) Colon cancer COL0 205 (5,82), HCC-2998 (5,89), HCT-116 (5,82), HCT-15 (5,28), HT2-9 (5,86),	Renal cancer	786-0 (5.67), A498 (5.63), ACHN (5.47), CAKI-1 (4.78), RXF 393 (5.57), SN12C (5.91), TK-10 (5.63), UO-31 (5.48)
Breast cancer MCF7 (6.06), NCI/ADR-RES (4.78), MDA-MB-231/ATCC (5.86), HS 578T (5.55), MDA-MB-435 (5.85), MDA-N (5.82), BT-549 (5.43), T-47D (5.67) 4.6-Bigl=4.(4,5-dihydro-4-methyl-1H-imidazol-2-yl)phenyl]-2-dimethylamino-1,3,5-triazine dihydrochloride (4) Leukemia CCRF-CEM (6.06), HL-60(TB) (5.58), K-562 (5.79), MOLT-4 (6.02), RPMI-8226 (5.37) Non-small cell lung cancer C549/ATCC (5.47), EKVX (5.46), HOP-62 (5.82), HOP-92 (5.70), NCI-H32 (5.54), NCI-H322M (5.79), NCI-H460 (5.45), NCI-H522 (5.82) Colo accer COLO 205 (5.93), HCC-2998 (5.70), HCT-116 (5.81), HTC-15 (4.77), HT29 (5.64), KM12 (5.75), SW-620 (5.82) CNS cancer SF-268 (5.64), SF-295 (5.42), SF-39 (6.07), SNB-19 (5.72), SNB75 (5.78), U251 (5.94) Melanoma LOX IMVI (5.83), MALME-3M (5.42), M14 (5.46), SK-MEL-2 (5.69), SK-MEL-28 (5.43), SK-0V-3 (5.71) Real cancer 786-0 (5.62), A498 (5.60), ACHN (5.48), CARI-1 (4.79), RXF 393 (5.59), SN12C (5.69), TK-10 (5.57), UO-31 (5.31) Prostate cancer PC-3 (5.75), NCI/ADR-RES (4.63), MDA-MB-231/ATCC (5.84), HS 578T (5.54), MDA-MB-435 (5.81), MDA-N (5.67), BT-549 (5.40), T-470 (5.65) S2,5-Bis[4-(4,5,6,7,8,9-hexahydro-1H-benzimidazol-2-yl)phenyl[furan dihydrochloride (8) CCRF-CEM (5.75), NCI/ADR-RES (4.63), MDA-MB-231/ATCC (5.84), HS 578T (5.53), NCI-H32 (5.80), NCI-H322M (5.87), NCI-H460 (5.74), NCI-H522 (5.79) Colon cancer CCRF-CEM (5.75), HL-60(TB) (5.64), K-562 (5.85), MOLT-4 (5.74), RPMI-8226 (5.75) Non-small cell lung cancer	Prostate cancer	PC-3 (6.13), DU-145 (5.66)
4,6-Bis[4-(4,5-dihydro-4-methyl-1H-imidazol-2-yl)phenyl]-2-dimethylamino-1,3,5-triazine dihydrochloride (4) Leukemia CCRF-CEM (6.06), HL-60(TB) (5.58), K-562 (5.79), MOLT-4 (6.02), RPMI-8226 (5.37) Non-small cell lung cancer COL0 205 (5.33), HCC-2998 (5.70), HOT-16 (5.81), HCT-15 (4.77), HT29 (5.64), KM12 (5.75), SW-620 (5.82) CNS cancer SF-268 (5.64), SF-295 (5.42), SF-539 (6.07), SNB-19 (5.72), SNB75 (5.78), U251 (5.94) Melanoma LOX INVI (5.83), MALME-3M (5.42), M14 (5.46), SK-MEL-2 (5.69), SK-MEL-28 (5.43), SK-OUC-257 (5.69), UACC-257 (5.69), UACC-62 (5.75) Ovarin cancer ICROVI (5.51), OVCAR-3 (5.68), OVCAR-4 (5.79), OVCAR-5 (5.41), OVCAR-8 (5.63), SK-OU-3 (5.71) Renal cancer 786-0 (5.62), A498 (5.60), ACHN (5.48), CAKL-1 (4.79), RXF 393 (5.59), SN12C (5.69), TK-10 (5.57), UO-31 (5.31) Prostate cancer PC-3 (5.74), DU-145 (5.76) Breast cancer MCF7 (5.75), NCI/ADR-RES (4.63), MDA-MB-231/ATCC (5.84), HS 578T (5.54), MDA-MB-435 (5.81), MDA-N (5.67), BT-549 (5.40), T-47D (5.65) 2,5-Bis[4-(4,5,6,7,8,9-hexabydro-1H-benzimidazol-2-yl)phenylfuran dihydrochloride (8) Eukemia Cell-CEM (5.75), NL-60(TB) (5.58), MCI-4 (5.78), MCI-4 (5.74), RPMI-8226 (5.75) Non-small cell lung cancer S49/ATCC (5.77), EKVX (5.77), HOP-62 (5.82), HOP-92 (5.84), NCI-H226 (5.73), NCI-H322 M (5.87), NCI-H460 (5.74), NCI-H522 (5.79) Colon cancer COLO 205 (5.82), HCC-2998 (5.89), HCT-116 (5.82), HCT-15 (5.28), HT29 (5.86), KM12 (5.84), SW-620 (5.59) <td>Breast cancer</td> <td>MCF7 (6.06), NCI/ADR-RES (4.78), MDA-MB-231/ATCC (5.86), HS 578T (5.55), MDA-MB-435 (5.85), MDA-N (5.82), BT-549 (5.43), T-47D (5.67)</td>	Breast cancer	MCF7 (6.06), NCI/ADR-RES (4.78), MDA-MB-231/ATCC (5.86), HS 578T (5.55), MDA-MB-435 (5.85), MDA-N (5.82), BT-549 (5.43), T-47D (5.67)
Leukemia CCRF-CEM (6.06), HL-60(TB) (5.58), K-562 (5.79), MOLT-4 (6.02), RPMI-8226 (5.37) Non-small cell lung cancer A549/ATCC (5.47), EKVX (5.46), HOP-62 (5.82), HOP-92 (5.70), NCI-H23 (5.54), KM12 (5.75), SW-620 (5.82) CNS cancer SF-268 (5.64), SF-295 (5.42), SF-539 (6.07), SNB-19 (5.72), SNB75 (5.78), U251 (5.94) Melanoma LOX IMVI (5.83), MALME-3M (5.42), M14 (5.46), SK-MEL-2 (5.69), SK-MEL-28 (5.43), SK-MEL-5 (5.50), UACC-257 (5.69), UACC-62 (5.75) Ovarin cancer IGROV1 (5.51), OVCAR-3 (5.68), OVCAR-4 (5.79), OVCAR-5 (5.41), OVCAR-8 (5.63), SK-OVC-3 (5.71) Preata cancer PC-3 (5.74), DU-145 (5.76) Breast cancer PC-3 (5.74), DU-145 (5.76) Pc-3 (5.74), DU-145 (5.76) MCF7 (5.75), NCI/ADR-RES (4.63), MDA-MB-231/ATCC (5.84), HS 578T (5.54), MDA-MB-435 (5.81), MDA-N (5.67), BT-549 (5.40), T-47D (5.65) 2,5-Bis/4-(4,5,6,7,8,9-hexahyto-1H-benzimidazol-2-yi)phenyl/jturan dihydrochloride (8) Leukemia CCRF-CEM (5.57), HL-60(TB) (5.64), K-562 (5.85), MOLT-4 (5.74), RPMI-8226 (5.75) Non-small cell lung cancer SF-268 (5.81), SF-299 (5.74), SF-539 (5.76), SNB-19 (5.82), HCT-15 (5.28), HC1-123 (5.80), NC1-H322M (5.87), NC1-H460 (5.74), NC1-H522 (5.79) Colon cancer COLO 205 (5.82), HCC-2998 (5.89), HCT-116 (5.82), HCT-15 (5.28), HT29 (5.86), KM12 (5.84), SW-620 (5.59) CNS cancer SF-268 (5.81), SF-295 (5.74), SF-539 (5.76), SNB-19 (5.83), SNB-75 (5.77), U251 (5.84)	4,6-Bis[4-(4,5-dihydro-4-methy	l-1H-imidazol-2-yl)phenyl]-2-dimethylamino-1,3,5-triazine dihydrochloride (4)
Non-small cell lung cancer A549/AICC (5.47), EKVX (5.46), HOP-62 (5.82), HOP-92 (5.70), NCI-H322 (5.54), NCI-H322 M (5.79), NCI-H406 (5.45), NCI-H522 (5.82) Colon cancer COLO 205 (5.93), HCC-2998 (5.70), HCT-116 (5.81), HCT-15 (4.77), HT29 (5.64), KM12 (5.75), SW-620 (5.82) Melanoma LOX IMVI (5.83), MALME-3M (5.42), SF-539 (6.07), SNB-19 (5.72), SNB75 (5.78), U251 (5.94) Melanoma LOX IMVI (5.83), MALME-3M (5.42), M14 (5.46), SK-MEL-2 (5.69), SK-MEL-28 (5.43), SK-OK-3 (5.71) Renal cancer 786-0 (5.62), A498 (5.60), ACHN (5.48), CAKI-1 (4.79), RXF 393 (5.59), SN12C (5.69), TK-10 (5.57), UO-31 (5.31) Prostate cancer PC-3 (5.74), DU-145 (5.76) Breast cancer MCF7 (5.75), NCI/ADR-RES (4.63), MDA-MB-231/ATCC (5.84), HS 578T (5.54), MDA-MB-435 (5.81), MDA-N (5.67), BT-549 (5.40), T-47D (5.65) 2,5-Bis/4-(4,5,6,7,8,9-hexahydro-1H-benzimidazol-2-yl)phenyllfuran dihydrochloride (8) Leukemia CCRF-CEM (5.75), HL-60(TB) (5.64), K-562 (5.85), MOLT-4 (5.74), RPMI-8226 (5.75) Non-small cell lung cancer SF-268 (5.81), SF-298 (5.74), SF-539 (5.76), SNB-19 (5.83), SNB-75 (5.77), U251 (5.84), SW-620 (5.59) COlon cancer COLO 205 (5.82), HCC-2998 (5.89), HCT-116 (5.82), HCT-15 (5.28), HT29 (5.86), KM12 (5.84), SW-620 (5.59) CNS cancer SF-268 (5.81), SF-295 (5.74), SF-539 (5.76), SNB-19 (5.83), SNB-75 (5.77), U251 (5.84) Melanoma LOX IMVI (5.81), MALME-3M (5.63), CAKI-1 (5.23), KT 393 (5.71), SNL2C (5.83), KMEL-5 (5.80), UACC-257	Leukemia	CCRF-CEM (6.06), HL-60(TB) (5.58), K-562 (5.79), MOLT-4 (6.02), PPMI-8226 (5.37)
Clob (2015) Clob (2015) <thclob (2015)<="" th=""> <thclob (2015)<="" th=""></thclob></thclob>	Non-small cell lung cancer	A549/AICC (5.47); EKVX (5.46); H0P-62 (5.82); H0P-92 (5.70); NCI-H23 (5.54); NCI-H322M (5.79); NCI-H460 (5.45); NCI-H522 (5.82) COLO 206 (5.62); UCC 2069 (5.70); UCC 116 (5.81); UCC 14 (4.77); UCC 04 (5.47); UCC 16 (5.9); NCI-H460 (5.45); NCI-H522 (5.82)
Construction Str. 205 (0.17, 0.1	CNS cancer	COLO 203 (3:35), FICC-2396 (3:70), FICT-116 (3:51), FICT-13 (4:77), FIZ2 (3:54), KM12 (3:75), SW-620 (3:62) SE-268 (5:64) SE-269 (5:47) SE-539 (6:77) SNE-19 (5:77) SIR75 (5:78) [1251 (5:94)
Ovarin cancer IGROV1 (5,51), OVCAR-3 (5,68), OVCAR-4 (5,79), OVCAR-5 (5,41), OVCAR-8 (5,63), SK-OV-3 (5,71) Renal cancer 786-0 (5,62), A498 (5,60), ACHN (5,48), CAKI-1 (4,79), RXF 393 (5,59), SN12C (5,69), TK-10 (5,57), UO-31 (5,31) Prostate cancer PC-3 (5,74), DU-145 (5,76) Breast cancer MCF7 (5,75), NCI/ADR-RES (4,63), MDA-MB-231/ATCC (5,84), HS 578T (5,54), MDA-MB-435 (5,81), MDA-N (5,67), BT-549 (5,40), T-47D (5,65) 2,5-Bis/4-(4,5,6,7,8,9-hexahydro-1H-benzimidazol-2-yl)phenyl]furan dihydrochloride (8) CCRF-CEM (5,75), HL-60(TB) (5,64), K-562 (5,85), MOLT-4 (5,74), RPMI-8226 (5,75) Non-small cell lung cancer A549/ATCC (5,77), EKVX (5,77), HOP-62 (5,82), HOP-92 (5,84), NCI-H23 (5,80), NCI-H322M (5,87), NCI-H460 (5,74), NCI-H522 (5,79) Colon cancer COLO 205 (5,82), HCC-2998 (5,89), HCT-116 (5,82), HCT-15 (5,28), HT29 (5,86), KM12 (5,84), SW-620 (5,59) CNS cancer SF-268 (5,81), SF-295 (5,74), SF-39 (5,76), SNB-19 (5,83), SNB-75 (5,77), U251 (5,84) Melanoma LOX IMVI (5,81), MALME-3M (5,76), M14 (5,78), SK-MEL-2 (5,74), SK-MEL-2 (5,79) Renal cancer 786-0 (5,83), A498 (5,54), ACHN (5,63), CAKI-1 (5,23), RXF 393 (5,71), SN12C (5,83), TK-10 (5,29), UACC-257 (5,76), UACC-62 (5,77) Ovarin cancer OVCAR-4 (5,81), OVCAR-5 (5,68), OVCAR-8 (5,75), SK-OV-3 (5,79) Renal cancer 786-0 (5,83), A498 (5,54), ACHN (5,63), CAKI-1 (5,23), RXF 393 (5,71), SN12C (5,83), TK-10 (5,29), U0-31 (5,53)	Melanoma	LOX INV (5.83), MALME-3N (5.42), M14 (5.46), SK-MEL-2 (5.9), SK-MEL-28 (5.43), SK-MEL-5 (5.50), UACC-257 (5.69), UACC-62 (5.75)
Renal cancer 786-0 (5.62), A498 (5.60), ACHN (5.48), CAKI-1 (4.79), RXF 393 (5.59), SN12C (5.69), TK-10 (5.57), UO-31 (5.31) Prostate cancer PC-3 (5.74), DU-145 (5.76) Breast cancer MCF7 (5.75), NCI/ADR-RES (4.63), MDA-MB-231/ATCC (5.84), HS 578T (5.54), MDA-MB-435 (5.81), MDA-N (5.67), BT-549 (5.40), T-47D (5.65) 2,5-Bis/4-(4,5,6,7,8,9-hexahyto-1H-benzimidazol-2-yl)phenyl]furan dihydrochloride (8) CCRF-CEM (5.75), HL-60(TB) (5.64), K-562 (5.85), MOLT-4 (5.74), RPMI-8226 (5.75) Non-small cell lung cancer A549/ATCC (5.77), EKVX (5.77), HOP-62 (5.82), HOP-92 (5.84), NCI-H226 (5.73), NCI-H322M (5.87), NCI-H460 (5.74), NCI-H522 (5.79) Colon cancer COLO 205 (5.82), HCC-2998 (5.89), HCT-116 (5.82), HCT-15 (5.28), HT29 (5.86), KM12 (5.84), SW-620 (5.59) CNS cancer SF-268 (5.81), SF-295 (5.74), SF-539 (5.76), SNB-19 (5.83), SNB-75 (5.77), U251 (5.84) Melanoma LOX IMVI (5.81), MALME-3M (5.76), M14 (5.78), SK-MEL-2 (5.74), SK-MEL-28 (5.74), SK-MEL-5 (5.80), UACC-257 (5.76), UACC-62 (5.77) Ovarin cancer OVCAR-3 (5.74), OVCAR-4 (5.81), OVCAR-5 (5.68), OVCAR-8 (5.75), SK-OV-3 (5.79) Renal cancer 786-0 (5.83), A498 (5.54), ACHN (5.63), CAKI-1 (5.23), RXF 393 (5.71), SN12C (5.83), TK-10 (5.29), UO-31 (5.53) Prostate cancer PC-3 (5.84), DU-145 (5.80) Breast cancer PC-3 (5.84), DU-145 (5.80) Breast cancer PC-3 (5.84), DU-145 (5.80) Breast cancer PC-3 (5.84),	Ovarin cancer	IGROV1 (5.51), OVCAR-3 (5.68), OVCAR-4 (5.79), OVCAR-5 (5.41), OVCAR-8 (5.63), SK-OV-3 (5.71)
Prostate cancer PC-3 (5.74), DU-145 (5.76) Breast cancer MCF7 (5.75), NCI/ADR-RES (4.63), MDA-MB-231/ATCC (5.84), HS 578T (5.54), MDA-MB-435 (5.81), MDA-N (5.67), BT-549 (5.40), T-47D (5.65) 2,5-Bis/4-(4,5,6,7,8,9-hexahydro-1H-benzimidazol-2-yl)phenyl/furan dihydrochloride (8) CCRF-CEM (5.75), HL-60(TB) (5.64), K-562 (5.85), MOLT-4 (5.74), RPMI-8226 (5.75) Non-small cell lung cancer CCRF-CEM (5.77), EKVX (5.77), HOP-62 (5.82), HOP-92 (5.84), NCI-H226 (5.73), NCI-H322M (5.87), NCI-H460 (5.74), NCI-H522 (5.79) Colon cancer COLO 205 (5.82), HCC-2998 (5.89), HCT-116 (5.82), HCT-15 (5.28), HT29 (5.86), KM12 (5.84), SW-620 (5.59) CNS cancer SF-268 (5.81), SF-295 (5.74), SF-539 (5.76), SNB-19 (5.83), SNB-75 (5.77), U251 (5.84) Melanoma LOX IMVI (5.81), MALME-3M (5.76), M14 (5.78), SK-MEL-2 (5.74), SK-MEL-28 (5.74), SK-MEL-5 (5.80), UACC-257 (5.76), UACC-62 (5.77) Ovarin cancer OVCAR-3 (5.74), OVCAR-4 (5.81), OVCAR-5 (5.68), OVCAR-8 (5.75), SK-OV-3 (5.79) Renal cancer 786-0 (5.83), A498 (5.54), ACHN (5.63), CAKI-1 (5.23), RXF 393 (5.71), SN12C (5.83), TK-10 (5.29), UO-31 (5.53) Prostate cancer PC-3 (5.84), DU-145 (5.80) Breast cancer PC-3 (5.84), DU-145 (5.80)	Renal cancer	786-0 (5.62), A498 (5.60), ACHN (5.48), CAKI-1 (4.79), RXF 393 (5.59), SN12C (5.69), TK-10 (5.57), UO-31 (5.31)
Breast cancer MCF7 (5.75), NCI/ADR-RES (4.63), MDA-MB-231/ATCC (5.84), HS 5/81 (5.54), MDA-MB-435 (5.81), MDA-N (5.67), B1-549 (5.40), 1-47D (5.65) 2,5-Bis/4-(4,5,6,7,8,9-hexahydro-1H-benzimidazol-2-yl)phenyl/furan dihydrochloride (8) Leukemia CCRF-CEM (5.75), HL-60(TB) (5.64), K-562 (5.85), MOLT-4 (5.74), RPMI-8226 (5.75) Non-small cell lung cancer A549/ATCC (5.77), EKVX (5.77), HOP-62 (5.82), HOP-92 (5.84), NCI-H226 (5.73), NCI-H23 (5.80), NCI-H322M (5.87), NCI-H460 (5.74), NCI-H522 (5.79) Colon cancer COLO 205 (5.82), HCC-2998 (5.89), HCT-116 (5.82), HCT-15 (5.28), HT29 (5.86), KM12 (5.84), SW-620 (5.59) CNS cancer SF-268 (5.81), SF-295 (5.74), SF-539 (5.76), SNB-19 (5.83), SNB-75 (5.77), U251 (5.84) Melanoma LOX IMVI (5.81), MALME-3M (5.76), M14 (5.78), SK-MEL-2 (5.74), SK-MEL-28 (5.74), SK-MEL-5 (5.80), UACC-257 (5.76), UACC-62 (5.77) Ovarin cancer OVCAR-3 (5.74), OVCAR-4 (5.81), OVCAR-5 (5.68), OVCAR-8 (5.75), SK-OV-3 (5.79) Renal cancer 786-0 (5.83), A498 (5.54), ACHN (5.63), CAKI-1 (5.23), RXF 393 (5.71), SN12C (5.83), TK-10 (5.29), UO-31 (5.53) Prostate cancer PC-3 (5.84), DU-145 (5.80) Breast cancer MCF7 (5.92), NCI/ADR-RES (4.55), MDA-MB-231/ATCC (5.82), HS 578T (5.81), MDA-MB-435 (5.73), MDA-N (5.78), BT-549 (5.67), T-47D (5.70) 3,6-Bis(4,5-dihydro-1H-imidazol-2-yl)-9-methylcarbazole dihydrochloride (10) Low amin CCRE-CEM (5.8 00) K 562 (4.58) MOLT-4 (6.20) RPML 8226 (4.61) SE (4.74) <td>Prostate cancer</td> <td>PC-3 (5.74), DU-145 (5.76)</td>	Prostate cancer	PC-3 (5.74), DU-145 (5.76)
2,5-Bis[4-(4,5,6,7,8,9-hexahydro-1H-benzimidazol-2-yl)phenyllfuran dihydrochloride (8) Leukemia CCRF-CEM (5.75), HL-60(TB) (5.64), K-562 (5.85), MOLT-4 (5.74), RPMI-8226 (5.75) Non-small cell lung cancer A549/ATCC (5.77), EVX (5.77), HOP-62 (5.82), HOP-92 (5.84), NCI-H22 (5.73), NCI-H23 (5.80), NCI-H322M (5.87), NCI-H460 (5.74), NCI-H522 (5.79) Colon cancer COLO 205 (5.82), HCC-2998 (5.89), HCT-116 (5.82), HCT-15 (5.28), HT29 (5.86), KM12 (5.84), SW-620 (5.59) CNS cancer SF-268 (5.81), SF-295 (5.74), SF-539 (5.76), SNB-19 (5.83), SNB-75 (5.77), U251 (5.84) Melanoma LOX IMVI (5.81), MALME-3M (5.76), M14 (5.78), SK-MEL-2 (5.74), SK-MEL-28 (5.74), SK-MEL-5 (5.80), UACC-257 (5.76), UACC-62 (5.77) Ovarin cancer OVCAR-3 (5.74), OVCAR-4 (5.81), OVCAR-5 (5.68), OVCAR-8 (5.75), SK-OV-3 (5.79) Renal cancer 786-0 (5.83), A498 (5.54), ACHN (5.63), CAKI-1 (5.23), RXF 393 (5.71), SN12C (5.83), TK-10 (5.29), UO-31 (5.53) Prostate cancer PC-3 (5.84), DU-145 (5.80) Breast cancer MCF7 (5.92), NCI/ADR-RES (4.55), MDA-MB-231/ATCC (5.82), HS 578T (5.81), MDA-MB-435 (5.73), MDA-N (5.78), BT-549 (5.67), T-47D (5.70) 3,6-Bis(4,5-dihydro-1H-imidazol-2-yl)-9-methylcarbazole dihydrochloride (10) Leukemia	Breast cancer	MCF7 (5.75), NCI/ADK-RES (4.63), MDA-MB-231/ATCC (5.84), HS 5781 (5.54), MDA-MB-435 (5.81), MDA-N (5.67), B1-549 (5.40), 1-47D (5.65)
Leukemia CCRF-CEM (5.75), HL-60(TB) (5.64), K-562 (5.85), MOLT-4 (5.74), RPMI-8226 (5.75) Non-small cell lung cancer A549/ATCC (5.77), EKVX (5.77), HOP-62 (5.82), HOP-92 (5.84), NCI-H226 (5.73), NCI-H23 (5.80), NCI-H322M (5.87), NCI-H460 (5.74), NCI-H522 (5.79) Colon cancer COLO 205 (5.82), HCC-2998 (5.89), HCT-116 (5.82), HCT-15 (5.28), HT29 (5.86), KM12 (5.84), SW-620 (5.59) CNS cancer SF-268 (5.81), SF-295 (5.74), SF-539 (5.76), SNB-19 (5.83), SNB-75 (5.77), U251 (5.84) Melanoma LOX IMVI (5.81), MALME-3M (5.76), M14 (5.78), SK-MEL-2 (5.74), SK-MEL-28 (5.74), SK-MEL-5 (5.80), UACC-257 (5.76), UACC-62 (5.77) Ovarin cancer OVCAR-3 (5.74), OVCAR-4 (5.81), OVCAR-5 (5.68), OVCAR-8 (5.75), SK-OV-3 (5.79) Renal cancer 786-0 (5.83), A498 (5.54), ACHN (5.63), CAKI-1 (5.23), RXF 393 (5.71), SN12C (5.83), TK-10 (5.29), UO-31 (5.53) Prostate cancer PC-3 (5.84), DU-145 (5.80) Breast cancer MCF7 (5.92), NCI/ADR-RES (4.55), MDA-MB-231/ATCC (5.82), HS 578T (5.81), MDA-MB-435 (5.73), MDA-N (5.78), BT-549 (5.67), T-47D (5.70) 3,6-Bis(4,5-dihydro-1H-imidazol-2-yl)-9-methylcarbazole dihydrochloride (10) Leukemia CCBF-CEM (>8 00) HL-60(TB) (>8 00) K 562 (4 58) MOLT-4 (6 20) RPML 8226 (4 61) SP (4 74)	2,5-Bis[4-(4,5,6,7,8,9-hexahydro	p-1H-benzimidazol-2-yl)phenyl]furan dihydrochloride (8)
Noti-shial cell fung cancer AS43/ATCC (5.77), EKVX (5.77), HOP-62 (5.82), HOP-92 (5.84), NCI-H226 (5.73), NCI-H25 (5.80), INCI-H25 (5.87), NCI-H252 (5.79) Colon cancer COLO 205 (5.82), HCC-2998 (5.89), HCT-116 (5.82), HCT-15 (5.28), HT29 (5.86), KM12 (5.84), SW-620 (5.59) CNS cancer SF-268 (5.81), SF-295 (5.74), SF-539 (5.76), SNB-19 (5.83), SNB-75 (5.77), U251 (5.84) Melanoma LOX IMVI (5.81), MALME-3M (5.76), M14 (5.78), SK-MEL-2 (5.74), SK-MEL-28 (5.74), SK-MEL-5 (5.80), UACC-257 (5.76), UACC-62 (5.77) Ovarin cancer OVCAR-3 (5.74), OVCAR-4 (5.81), OVCAR-5 (5.68), OVCAR-8 (5.75), SK-OV-3 (5.79) Renal cancer 786-0 (5.83), A498 (5.54), ACHN (5.63), CAKI-1 (5.23), RXF 393 (5.71), SN12C (5.83), TK-10 (5.29), UO-31 (5.53) Prostate cancer PC-3 (5.84), DU-145 (5.80) Breast cancer PC-3 (5.84), DU-145 (5.80) Breast cancer MCF7 (5.92), NCI/ADR-RES (4.55), MDA-MB-231/ATCC (5.82), HS 578T (5.81), MDA-MB-435 (5.73), MDA-N (5.78), BT-549 (5.67), T-47D (5.70) 3,6-Bis(4,5-dihydro-1H-imidazol-2-yl)-9-methylcarbazole dihydrochloride (10) Lowarmia CCPE-CEM (>8 00) K 562 (4 58) MOLT-4 (6 20) RPML 8226 (4 61) SP (4 74)	Leukemia	CCRF-CEM (5.75), HL-60(TB) (5.64), K-562 (5.85), MOLT-4 (5.74), RPMI-8226 (5.75)
Colon cancer COLO 205 (5.82), HCC-2998 (5.89), HCT-116 (5.82), HCT-15 (5.28), HT29 (5.86), KM12 (5.84), SW-620 (5.59) CNS cancer SF-268 (5.81), SF-295 (5.74), SF-539 (5.76), SNB-19 (5.83), SNB-75 (5.77), U251 (5.84) Melanoma LOX IMVI (5.81), MALME-3M (5.76), M14 (5.78), SK-MEL-2 (5.74), SK-MEL-28 (5.74), SK-MEL-5 (5.80), UACC-257 (5.76), UACC-62 (5.77) Ovarin cancer OVCAR-3 (5.74), OVCAR-4 (5.81), OVCAR-5 (5.68), OVCAR-8 (5.75), SK-OV-3 (5.79) Renal cancer 786-0 (5.83), A498 (5.54), ACHN (5.63), CAKI-1 (5.23), RXF 393 (5.71), SN12C (5.83), TK-10 (5.29), UO-31 (5.53) Prostate cancer PC-3 (5.84), DU-145 (5.80) Breast cancer PC-3 (5.84), DU-145 (5.80) Breast cancer MCF7 (5.92), NCI/ADR-RES (4.55), MDA-MB-231/ATCC (5.82), HS 578T (5.81), MDA-MB-435 (5.73), MDA-N (5.78), BT-549 (5.67), T-47D (5.70) 3,6-Bis(4,5-dihydro-1H-imidazol-2-yl)-9-methylcarbazole dihydrochloride (10) Low serial CCEPE-CEM (>8 00), K 562 (4 58), MOLT-4 (6 20), PRML 8226 (4 61), SP (4 74)	Non-small cell lung cancer	A549/ATCC (5.77), EKVX (5.77), HOP-62 (5.82), HOP-92 (5.84), NCI-H226 (5.73), NCI-H23 (5.80), NCI-H322M (5.87), NCI-H460 (5.74), NCI- H522 (5.73)
CNS cancer SF-268 (5.81), SF-295 (5.74), SF-599 (5.76), SNB-19 (5.83), SNB-75 (5.77), U251 (5.84) Melanoma LOX IMVI (5.81), MALME-3M (5.76), M14 (5.78), SK-MEL-2 (5.74), SK-MEL-28 (5.74), SK-MEL-5 (5.80), UACC-257 (5.76), UACC-62 (5.77) Ovarin cancer OVCAR-3 (5.74), OVCAR-4 (5.81), OVCAR-5 (5.68), OVCAR-8 (5.75), SK-OV-3 (5.79) Renal cancer 786-0 (5.83), A498 (5.54), ACHN (5.63), CAKI-1 (5.23), RXF 393 (5.71), SN12C (5.83), TK-10 (5.29), UO-31 (5.53) Prostate cancer PC-3 (5.84), DU-145 (5.80) Breast cancer PC-3 (5.84), DU-145 (5.80) Breast cancer MCF7 (5.92), NCI/ADR-RES (4.55), MDA-MB-231/ATCC (5.82), HS 578T (5.81), MDA-MB-435 (5.73), MDA-N (5.78), BT-549 (5.67), T-47D (5.70) 3,6-Bis(4,5-dihydro-1H-imidazol-2-yl)-9-methylcarbazole dihydrochloride (10) Lowkemia CCPE-CEM (>8 00), HL-60(TB) (>8 00), K 562 (4.58), MOLT-4 (6.20), PRML 8226 (4.61), SP (4.74)	Colon cancer	COLO 205 (5.82), HCC-2998 (5.89), HCT-116 (5.82), HCT-15 (5.28), HT29 (5.86), KM12 (5.84), SW-620 (5.59)
Melanoma LOX IMVI (5.81), MALME-3M (5.76), M14 (5.78), SK-MEL-2 (5.74), SK-MEL-28 (5.74), SK-MEL-5 (5.80), UACC-257 (5.76), UACC-62 (5.77) Ovarin cancer OVCAR-3 (5.74), OVCAR-4 (5.81), OVCAR-5 (5.68), OVCAR-8 (5.75), SK-OV-3 (5.79) Renal cancer 786-0 (5.83), A498 (5.54), ACHN (5.63), CAKI-1 (5.23), RXF 393 (5.71), SN12C (5.83), TK-10 (5.29), UO-31 (5.53) Prostate cancer PC-3 (5.84), DU-145 (5.80) Breast cancer MCF7 (5.92), NCI/ADR-RES (4.55), MDA-MB-231/ATCC (5.82), HS 578T (5.81), MDA-MB-435 (5.73), MDA-N (5.78), BT-549 (5.67), T-47D (5.70) 3,6-Bis(4,5-dihydro-1H-imidazol-2-yl)-9-methylcarbazole dihydrochloride (10) Lowkemia CCPE-CEM (>8 00), HL-60(TB) (>8 00), K 562 (4.58), MOLT-4 (6.20), PDML 8226 (4.61), SP (4.74).	CNS cancer	SF-268 (5.81), SF-295 (5.74), SF-539 (5.76), SNB-19 (5.83), SNB-75 (5.77), U251 (5.84)
Ovarin cancer OVCAR-3 (5.74), OVCAR-4 (5.81), OVCAR-5 (5.68), OVCAR-8 (5.75), SK-OV-3 (5.79) Renal cancer 786-0 (5.83), A498 (5.54), ACHN (5.63), CAKI-1 (5.23), RXF 393 (5.71), SN12C (5.83), TK-10 (5.29), UO-31 (5.53) Prostate cancer PC-3 (5.84), DU-145 (5.80) Breast cancer MCF7 (5.92), NC1/ADR-RES (4.55), MDA-MB-231/ATCC (5.82), HS 578T (5.81), MDA-MB-435 (5.73), MDA-N (5.78), BT-549 (5.67), T-47D (5.70) 3,6-Bis(4,5-dihydro-1H-imidazol-2-yl)-9-methylcarbazole dihydrochloride (10) Leukemia CCPE-CEM (>8 00), HL 60(TB) (>8 00), K 562 (4.58), MOLT-4 (6.20), PDML 8226 (4.61), SP (4.74)	Melanoma	LOX IMVI (5.81), MALME-3M (5.76), M14 (5.78), SK-MEL-2 (5.74), SK-MEL-28 (5.74), SK-MEL-5 (5.80), UACC-257 (5.76), UACC-62 (5.77)
Renal Cancer /86-0 (5.83), A498 (5.54), ACHN (5.63), CAKI-T (5.23), RXF 393 (5.71), SN12C (5.83), TK-T0 (5.29), UO-31 (5.53) Prostate cancer PC-3 (5.84), DU-145 (5.80) Breast cancer MCF7 (5.92), NCI/ADR-RES (4.55), MDA-MB-231/ATCC (5.82), HS 578T (5.81), MDA-MB-435 (5.73), MDA-N (5.78), BT-549 (5.67), T-47D (5.70) 3,6-Bis(4,5-dihydro-1H-imidazol-2-yl)-9-methylcarbazole dihydrochloride (10) CCPE-CEM (>8 00) HL-60(TB) (>8 00) K 562 (4.58), MOLT-4 (6.20) RPML 8226 (4.61) SP (4.74)	Ovarin cancer	0VCAR-3 (5.74), 0VCAR-4 (5.81), 0VCAR-5 (5.68), 0VCAR-8 (5.75), SK-0V-3 (5.79)
Prostate called PC-5 (3.64), DO-145 (3.60) Breast cancer MCF7 (5.92), NC1/ADR-RES (4.55), MDA-MB-231/ATCC (5.82), HS 578T (5.81), MDA-MB-435 (5.73), MDA-N (5.78), BT-549 (5.67), T-47D (5.70) 3,6-Bis(4,5-dihydro-1H-imidazol-2-yl)-9-methylcarbazole dihydrochloride (10) CCEP_CEM (58.00), HL_60(TB) (58.00), K 562 (4.58), MOLT-4 (6.20), PBML 8226 (4.61), SP (4.74)	Renal cancer	786-0 (5.83), A498 (5.54), ACHN (5.63), CAKI-1 (5.23), KXF 393 (5.71), SN12C (5.83), TK-10 (5.29), UO-31 (5.53)
3,6-Bis(4,5-dihydro-1H-imidazol-2-yl)-9-methylcarbazole dihydrochloride (10)	Breast cancer	PC=5 (3.64), DD=149 (3.60) MCF7 (5.92), NCI/ADR-RES (4.55), MDA-MB-231/ATCC (5.82), HS 578T (5.81), MDA-MB-435 (5.73), MDA-N (5.78), BT-549 (5.67), T-47D (5.70)
5,0 = $5,0$	2.6 Pic(4.5 dibudro 14 imidazo	(2 + 2) (mathulasharala dihudrashlarida (10)
	Leukemia	n-2-yi)-9-methytan bazone annyanotinoniae (10) CCRF-CFM (>8 00) H-60(TR) (>8 00) K-562 (4 58) MOIT-4 (6 20) RPMI-8226 (4 61) SR (4 74)
Non-small cell lung cancer A549/ATC (4.34), EKVX (4.77), H0P-62 (4.82), H0P-92 (4.87), NCI-H226 (4.52), NCI-H322M (4.90), NCI-H460 (5.27), NCI-	Non-small cell lung cancer	6549/ATCC (4.34), EKVX (4.77), HOP-62 (4.82), HOP-92 (4.87), NCI-H226 (4.52), NCI-H322M (4.90), NCI-H460 (5.27), NCI-
H522 (7.11)	0	H522 (7.11)
Colon cancer COLO 205 (6.14), HCT-116 (4.66), HCT-15 (<4.00), HT29 (5.11), KM12 (5.81), SW-620 (4.75)	Colon cancer	COLO 205 (6.14), HCT-116 (4.66), HCT-15 (<4.00), HT29 (5.11), KM12 (5.81), SW-620 (4.75)
CNS cancer SF-268 (7.33), SF-295 (4.37), SF-539 (4.53), SNB-19 (4.37), SNB-75 (4.11), U251 (4.83)	CNS cancer	SF-268 (7.33), SF-295 (4.37), SF-539 (4.53), SNB-19 (4.37), SNB-75 (4.11), U251 (4.83)
Meianoma LUX IMVI (4.31), MALME-3M (4.74), M14 (4.31), SK-MEL-2 (4.47), SK-MEL-28 (4.62), SK-MEL-5 (4.50), UACC-257 (4.36)	Melanoma Quarin cancor	LUX INVI (4.31), MALME-3M (4.74), M14 (4.31), SK-MEL-2 (4.47), SK-MEL-28 (4.62), SK-MEL-5 (4.50), UACC-257 (4.36)
Ovalin cancer IGROVI (4.01), OVCAR-3 (4.30), OVCAR-4 (4.07), OVCAR-3 (4.42), OVCAR-6 (4.34), SR-UV-3 (4.30) Renal cancer 786-0 (4.41) A498 (<4.00) ACHN (4.42) CAKI-1 (<4.00) RXF 393 (4.46) SN12C (5.20) TK-10 (4.22) HO-31 (4.25)	Renal cancer	1960) 1 (4.01), OVCAR-3 (4.30), OVCAR-4 (4.07), OVCAR-3 (4.42), OVCAR-8 (4.34), SR-UV-3 (4.30) 786-0 (4.41) A498 (<4.00) ACHN (4.42) CAKI-1 (<4.00) RXF 393 (4.46) SN12C (5.20) TK-10 (4.22) HO-31 (4.25)
Prostate cancer PC-3 (4.46), DU-145 (4.58)	Prostate cancer	PC-3 (4.46), DU-145 (4.58)
Breast cancer NCI/ADR-RES (<4.00), MDA-MB-231/ATCC (4.39), HS 578T (4.97), MDA-MB-435 (4.21), MDA-N (4.28), BT-549 (<4.00), T-47D (5.10)	Breast cancer	NCI/ADR-RES (<4.00), MDA-MB-231/ATCC (4.39), HS 578T (4.97), MDA-MB-435 (4.21), MDA-N (4.28), BT-549 (<4.00), T-47D (5.10)

the putative mechanism that minor-groove binding to DNA (topoisomerase inhibition) is a component of the anticancer activity.

The highest sensitivity of **10** described here was found for leukemia (CCRF-CEM, $GI_{50} < 0.01 \mu$ M; HL-60 (TB), $GI_{50} < 0.01 \mu$ M;

MOLT-4, GI₅₀ 0.6 μ M) (Fig. 4), non-small cell lung cancer (NCI-H522, GI₅₀ 0.08 μ M), colon cancer (COLO 205, GI₅₀ 0.7 μ M), and CNS cancer (SF-268, GI₅₀ 0.05 μ M), but the average GI₅₀ value was 15 μ M. Only three cancer cell lines possessed values repre-



Fig. 3. Dose–response curves of **8** (top) and **9** (bottom) for all nine subpanels of cell lines. Horizontal lines are provided at the PG (Percentage Growth) values of +50, 0, and -50. The concentrations corresponding to points where the curves cross these lines are the GI₅₀, TGI, and LC₅₀, respectively.

senting concentrations at which the PG is -50: CCRF-CEM, 0.2 μ M; HL-60(TB), 0.06 μ M; NCI-H460, 90 μ M. None of the three response parameters can be obtained by interpolation in several cases (the PGs in a given row exceed +50).

In the current article, the following has to be noted regarding the tumor cell growth inhibition data with two carbazoles. The substitution of the carbazole unit at the position 9 by the cyclohexylmethyl group led to less interesting compound **11** (the lowest Gl₅₀ is 1.7 μ M for COLO-205), nevertheless their average Gl₅₀ values were very close (17 μ M for **11**). Both carbazoles **10** (ΔT_m 24.0 °C [42]) and **11** (ΔT_m 16.8 °C [42]) possess the MG_MID parameters similar to **9**. The presence of two amidine groups is important concerning the activity of this class of derivatives, but care should be also taken to steric differences between the active compounds and to the distance of the cationic groups.

The activity may be due to a sufficient structural similarity to the amidine antibiotics (the pyrene series is not comparable in terms of structure-activity relationships). The average cytotoxic effects of **3**, **4**, and **8** against all cell lines investigated were comparable to those of *N*-alkylated furamidine derivatives [20]. They remain at the low-micromolar level and confirm the results provided by the previous $\Delta T_{\rm m}$ studies [24,34,42,53]. The high values indicate strong DNA affinities for these molecules.

It appeared that the most active compounds are DNA associated [69]. The poorer binding to DNA may be due to the presence of the out-of-shape less active molecules which prevent a suitable fit into the electronegative minor-groove of the DNA helix. In addition, some agents show significant affinity for RNA and have weaker affinity for DNA (nonspecific interaction mode) [34,53]. The discovery of antibiotic analogs with new selectivity patterns sets the stage for further effort to explore therapeutic potential, especially for AIDS-defining cancers [70].



Fig. 4. In vitro activity on leukemia cell lines. Triazine **3** (top), selected for further studies with the hollow fiber assay, in comparison with furan **8** (middle) and carbazole **10** (bottom).

4. Conclusion

In summary, the group of active compounds comprises 12 cyclic diamidines. Compounds **1–12** exhibited activity against most of cancer cell lines and, in particular, the in vitro anticancer data in the low-micromolar range prove usefulness of the cationic system in the design of active anticancer agents **3**, **4**, and **8**. Triazines **3** and **4** were the most promising agents (point of view of the NCI's Biological Evaluation Committee for Cancer Drugs), and carbazole **10** was of special interest because of its high activity in the nanomolar range against some cell lines: leukemia, non-small cell lung, colon, and CNS cell lines. Compounds **3**, **4**, and furan **8** exhibited activities against all tumor cell lines investigated.

The anticancer screening data presented are well correlated with mode of binding to DNA. They can be used to explore the strength of the DNA interactions by comparison of the NCI's activity profiles (all dose response curves). The strength of these interactions is likely a sum of both hydrogen bonding capabilities and the linker length (shape). Strong likeness among the cell line responses (MG_MID values) suggests that the compounds may be acting similarly through the same mechanism of action.

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