≪ TETRAHYDROISOQUINOLINE ALKALOIDAL COMPOUNDS WITH MACROCYCLIC SCAFFOLD EXHIBITING ANTI–TUMOR ACTIVITIES≫
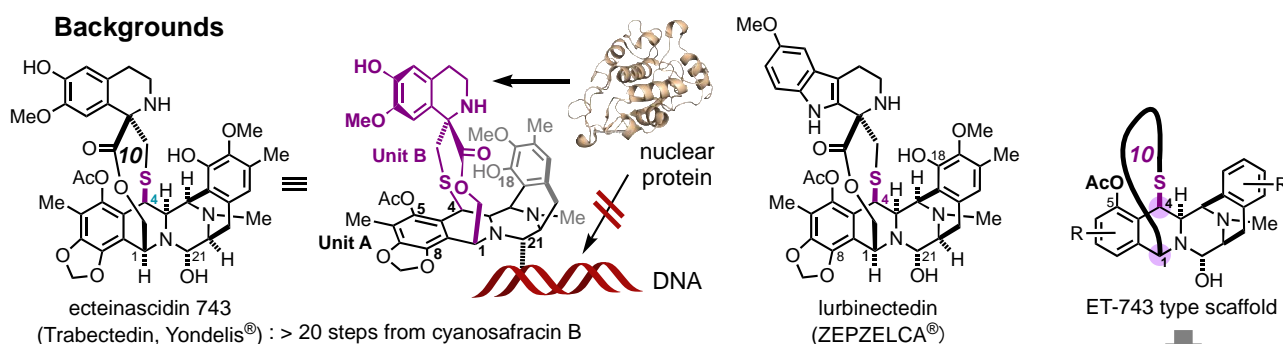
＜Invention Overview＞
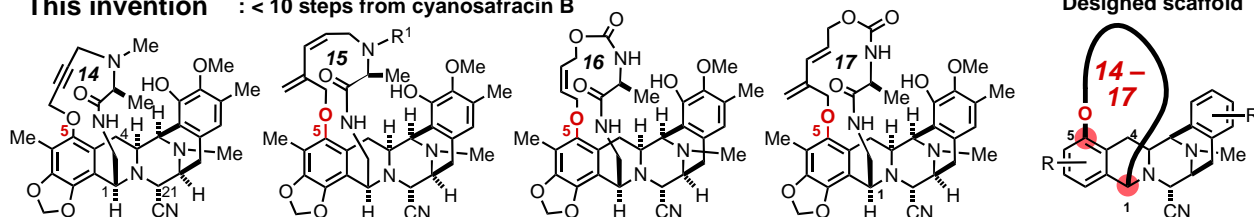
■ Tetrahydroisoquinoline Alkaloids

Ecteinascidin743 (ET-743), a natural product isolated from a marine sponge, has been clinically applied as an antitumor agent (Trabectedin, the trade name "Yondelis"). Structurally, ET-743 can be divided into 2 parts, a core scaffold (unit A) consisting of two tetrahydroisoquinoline (THIQ) rings, and a 10-membered macrolactone ring with an additional THIQ moiety (unit B). Unit A recognizes DNA duplexes through hydrogen bonds and alkylates at minor groove of DNA sequence-selectively. Unit B, meanwhile, is thought to inhibit the approach of nucleic proteins (e.g., transcription factor, DNA-repair proteins) to DNA, and thereby inducing DNA double-strand break and cell death. A synthetic derivative, lurbinectedin (ZEPZELCA), bearing a tetrahydro-ß-carboline ring in place of the THIQ ring on unit B, has also been approved as a chemotherapeutic agent for small cell lung cancer. Based on the structural and mechanistic insights into the potent and unique anti-cancer agent ET-743, diversification of unit B is a promising approach to generate novel antitumor agents targeting DNA–protein interactions. However, the commercialized semisynthetic process of ET-743 requires more than 20-step chemical conversions starting from cyanosafracin B obtained from microbial cultures, which makes it difficult to modify the structure of unit B.

Exploiting our experimental findings, we designed an unnatural, novel macrocyclic scaffold connecting C1 and C5 hydroxyl group of unit A, instead of C4 position in ET-743. This design enabled rapid synthesis of a series of drug lead candidates ranging from 14 to 17 membered macrocycles exhibiting comparable antitumor activity with ET-743. This versatile synthetic platform with significantly fewer number of steps also allowed flexible modification of unit B by just a single step appendage reaction (such as [4+2] cycloaddition).

Backgrounds

ecteinascidin 743
(Trabectedin, Yondelis®) : > 20 steps from cyanosafracin B

lurbinectedin
(ZEPZELCA®)

ET-743 type scaffold

This invention : < 10 steps from cyanosafracin B

Designed scaffold

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■Evaluation of anti-cancer activity

These structurally simplified macrocyclic compounds can be synthesized within 10 steps in a time- and cost-efficient manner. Antitumor activities (GI_{50} values) of the synthetic compounds were evaluated against 39 cancer cell lines (JFCR39). Most of the macrocyclic compounds generated in this invention exhibit superior antitumor activities compared to the natural product, cyanosafracin B and synthetic intermediates without the macrocyclic scaffold. Notably, several synthetic compounds (e. g. TFR5) exhibited very potent antitumor activity comparable to approved drugs, ET-743 and lurbinectedin.
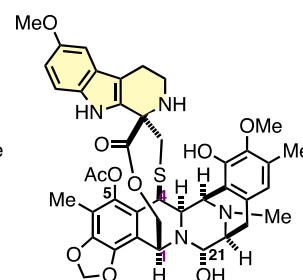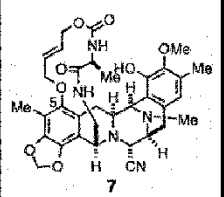

More potent activities rather than approved drugs
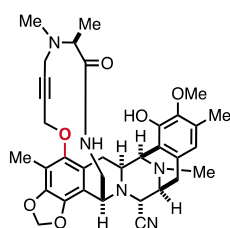
invented compound (TFR5)
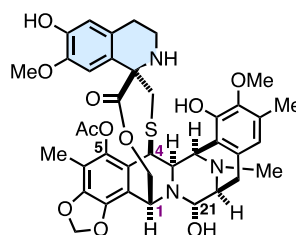
ecteinascidin 743 (Yondelis®)

lurbinectedin (ZEPZELCA®)

GI_{50}: 50% growth inhibitory concentration		GI_{50}	GI_{50}	GI_{50}
Breast cancer cell lines	MCF-7	**0.67 nM**	2.6 nM	1.7 nM
	MDA-MB-231	**2.3 nM**	3.9 nM	3.4 nM
Colorectal cancer cell lines	HT-29	**2.0 nM**	9.8 nM	2.4 nM
	HCT-116	**2.4 nM**	4.9 nM	6.4 nM
Lung cancer cell lines	NCI-H23	2.6 nM	2.1 nM	5.3 nM
	NCI-H460	2.8 nM	1.8 nM	1.5 nM

Modification of macrocyclic structure (unit B) of ET-743 allowed development of the systematic collections of novel anti-tumor drug candidates. This synthetic platform rapidly generates more than 10 kinds of skeletally diverse macrocyclic compounds capable of further structural modifications exploiting the preinstalled functional groups (secondary amine, conjugated diene, and alkyne). The versatile and flexible synthetic platform enables rational structural diversification of the complex macrocyclic structures, while maintaining potent antitumor activities with inhibition of DNA–nuclear protein interactions.

＜Inventor＞

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Assistant Professor, Ryo Tanifuji, The University of Tokyo

＜Public Information＞
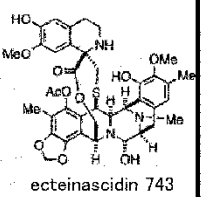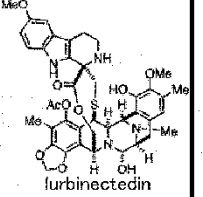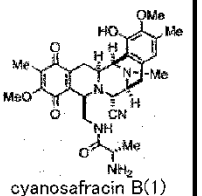
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Supplemental Data

Table1 :antitumor activity [nM] of Compound 29 (GI_{50} value: 50% growth inhibitory concentration)

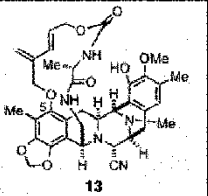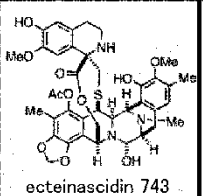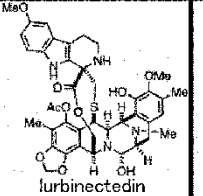|		7	ecteinascidin 743	lurbinectedin	cyanosafracin B(1)
breast cancer cells	HBC-4	28			59
	BSY-1	19			34
	HBC-5	79			62
	MCF-7	17	2.6	1.7	52
	MDA-MB-231	32	3.9	3.4	130
central nervous system cancer cells	U251	39			370
	SF-268	89			370
	SF-295	240			500
	SF-539	35			180
	SNB-75	61			150
	SNB-78	45			63
colorectal cancer cells	HCC2998	69			350
	KM-12	58			530
	HT-29	58	9.8	2.4	190
	HCT-15	310			390
	HCT-116	51	4.9	6.4	290
lung cancer cells	NCI-H23	140	2.1	5.3	290
	NCI-H226	260			310
	NCI-H522	21			43
	NCI-H460	270	1.8	1.5	400
	A549	480	10.4	1.3	1600
	DMS273	82			270
	DMS114	14			35
melanoma cells	LOX-IMVI	19			61
cervical cancer cells	OVCAR-3	41			130
	OVCAR-4	390			290
	OVCAR-5	240			390
	OVCAR-8	200			290
	SK-OV-3	420			540
kidney cancer cells	RXF-631L	240			400
	ACHN	300			320
gastric cancer cells	St-4	300			430
	MKN1	36			52
	MKN-B	280			170
	MKN-A	260			250
	MKN45	47			300
	MKN74	370			310
prostate cancer cells	DU-145	430			490
	PC-3	240			290

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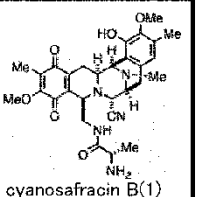Table2 :antitumor activity [nM] of Compound 29 (GI_{50} value: 50% growth inhibitory concentration)

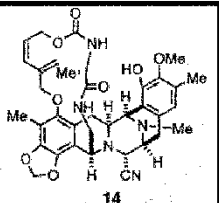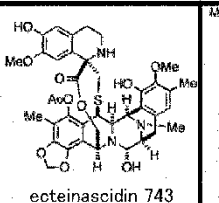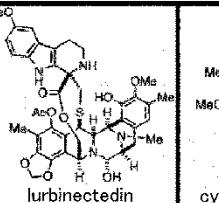|		13	ecteinascidin 743	lurbinectedin	cyanosafracin B(1)
breast cancer cells	HBC-4	120			59
	BSY-1	32			34
	HBC-5	92			62
	MCF-7	50	2.6	1.7	52
	MDA-MB-231	95	3.9	3.4	130
central nervous system cancer cells	U251	220			370
	SF-268	350			370
	SF-295	490			500
	SF-539	120			180
	SNB-75	120			150
	SNB-78	100			63
colorectal cancer cells	HCC2998	250			350
	KM-12	290			530
	HT-29	200	9.8	2.4	190
	HCT-15	1500			390
	HCT-116	220	4.9	6.4	290
lung cancer cells	NCI-H23	350	2.1	5.3	290
	NCI-H226	530			310
	NCI-H522	40			43
	NCI-H460	620	1.8	1.5	400
	A549	3400	10.4	1.3	1600
	DMS273	320			270
	DMS114	37			35
melanoma cells	LOX-IMVI	57			61
cervical cancer cells	OVCAR-3	290			130
	OVCAR-4	1400			290
	OVCAR-5	580			390
	OVCAR-8	310			290
	SK-OV-3	440			540
kidney cancer cells	RXF-631L	460			400
	ACHN	520			320
gastric cancer cells	St-4	420			430
	MKN1	220			52
	MKN-B	360			170
	MKN-A	540			250
	MKN45	250			300
	MKN74	280			310
prostate cancer cells	DU-145	830			490
	PC-3	450			290

Table3 :antitumor activity [nM] of Compound 29 (GI_{50} value: 50% growth inhibitory concentration)

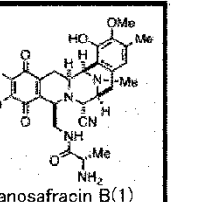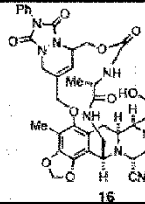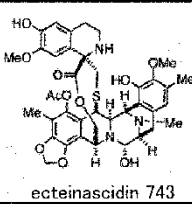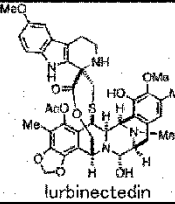|		14	ecteinascidin 743	lurbinectedin	cyanosafracin B(1)
breast cancer cells	HBC-4	19			59
	BSY-1	10			34
	HBC-5	15			62
	MCF-7	10	2.6	1.7	52
	MDA-MB-231	17	3.9	3.4	130
central nervous system cancer cells	U251	27			370
	SF-268	39			370
	SF-295	49			500
	SF-539	17			180
	SNB-75	14			150
	SNB-78	34			63
colorectal cancer cells	HCC2998	34			350
	KM-12	30			530
	HT-29	22	9.8	2.4	190
	HCT-15	98			390
	HCT-116	23	4.9	6.4	290
lung cancer cells	NCI-H23	34	2.1	5.3	290
	NCI-H226	38			310
	NCI-H522	10			43
	NCI-H460	57	1.8	1.5	400
	A549	280	10.4	1.3	1600
	DMS273	29			270
	DMS114	10			35
melanoma cells	LOX-IMVI	12			61
cervical cancer cells	OVCAR-3	25			130
	OVCAR-4	38			290
	OVCAR-5	47			390
	OVCAR-8	34			290
	SK-OV-3	59			540
kidney cancer cells	RXF-631L	48			400
	ACHN	38			320
gastric cancer cells	St-4	36			430
	MKN1	26			52
	MKN-B	34			170
	MKN-A	54			250
	MKN45	21			300
	MKN74	41			310
prostate cancer cells	DU-145	52			490
	PC-3	47			290

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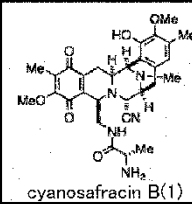Table4 :antitumor activity [nM] of Compound 29 (GI$_{50}$ value: 50% growth inhibitory concentration)

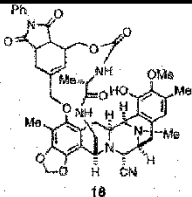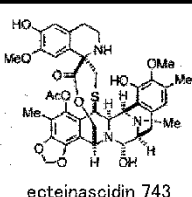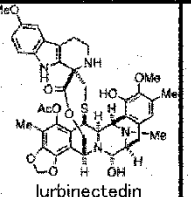|		16	ecteinascidin 743	lurbinectedin	cyanosafracin B(1)
breast cancer cells	HBC-4	5.2			59
	BSY-1	3.1			34
	HBC-5	6.9			62
	MCF-7	4.4	2.6	1.7	52
	MDA-MB-231	6.7	3.9	3.4	130
central nervous system cancer cells	U251	5.8			370
	SF-268	13			370
	SF-295	29			500
	SF-539	8.2			180
	SNB-75	9.9			150
	SNB-78	7.5			63
colorectal cancer cells	HCC2998	17			350
	KM-12	14			530
	HT-29	7.3	9.8	2.4	190
	HCT-15	43			390
	HCT-116	9.3	4.9	6.4	290
lung cancer cells	NCI-H23	20	2.1	5.3	290
	NCI-H226	25			310
	NCI-H522	2.4			43
	NCI-H460	36	1.8	1.5	400
	A549	51	10.4	1.3	1600
	DMS273	15			270
	DMS114	3.8			35
melanoma cells	LOX-IMVI	3.3			61
cervical cancer cells	OVCAR-3	6.4			130
	OVCAR-4	38			290
	OVCAR-5	31			390
	OVCAR-8	21			290
	SK-OV-3	34			540
kidney cancer cells	RXF-631L	35			400
	ACHN	25			320
gastric cancer cells	St-4	37			430
	MKN1	4.8			52
	MKN-B	30			170
	MKN-A	29			250
	MKN45	7.1			300
	MKN74	32			310
prostate cancer cells	DU-145	41			490
	PC-3	26			290

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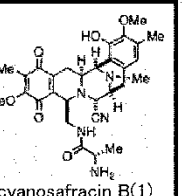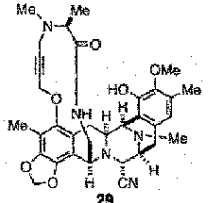Table5 :antitumor activity [nM] of Compound 29 (GI$_{50}$ value: 50% growth inhibitory concentration)

		18	ecteinascidin 743	lurbinectedin	cyanosafracin B(1)
breast cancer cells	HBC-4	30			59
	BSY-1	19			34
	HBC-5	38			62
	MCF-7	22	2.6	1.7	52
	MDA-MB-231	41	3.9	3.4	130
central nervous system cancer cells	U251	50			370
	SF-268	74			370
	SF-295	300			500
	SF-539	33			180
	SNB-75	50			150
	SNB-78	40			63
colorectal cancer cells	HCC2998	95			350
	KM-12	100			530
	HT-29	72	9.8	2.4	190
	HCT-15	630			390
	HCT-116	74	4.9	6.4	290
lung cancer cells	NCI-H23	110	2.1	5.3	290
	NCI-H226	280			310
	NCI-H522	20			43
	NCI-H460	260	1.8	1.5	400
	A549	540	10.4	1.3	1600
	DMS273	100			270
	DMS114	12			35
melanoma cells	LOX-IMVI	27			61
cervical cancer cells	OVCAR-3	43			130
	OVCAR-4	350			290
	OVCAR-5	280			390
	OVCAR-8	130			290
	SK-OV-3	410			540
kidney cancer cells	RXF-631L	310			400
	ACHN	240			320
gastric cancer cells	St-4	300			430
	MKN1	50			52
	MKN-B	160			170
	MKN-A	210			250
	MKN45	78			300
	MKN74	120			310
prostate cancer cells	DU-145	330			490
	PC-3	170			290
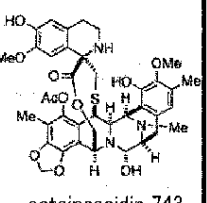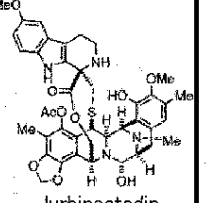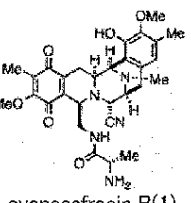
Table6 :antitumor activity [nM] of Compound 29 (GI$_{50}$ value: 50% growth inhibitory concentration) TFR5

		29	ecteinascidin 743	lurbinectedin	cyanosafracin B(1)
breast cancer cells	HBC-4	1.5			59
	BSY-1	0.60			34
	HBC-5	1.8			62
	MCF-7	0.67	2.6	1.7	52
	MDA-MB-231	2.3	3.9	3.4	130
central nervous system cancer cells	U251	1.4			370
	SF-268	2.8			370
	SF-295	3.4			500
	SF-539	1.3			180
	SNB-75	1.3			150
	SNB-78	3.1			63
colorectal cancer cells	HCC2998	2.8			350
	KM-12	3.1			530
	HT-29	2.0	9.8	2.4	190
	HCT-15	3.9			390
	HCT-116	2.4	4.9	6.4	290
lung cancer cells	NCI-H23	2.6	2.1	5.3	290
	NCI-H226	2.5			310
	NCI-H522	0.60			43
	NCI-H460	2.8	1.8	1.5	400
	A549	3.4	10.4	1.3	1600
	DMS273	1.1			270
	DMS114	0.89			35
melanoma cells	LOX-IMVI	0.59			61
cervical cancer cells	OVCAR-3	2.6			130
	OVCAR-4	3.5			290
	OVCAR-5	3.2			390
	OVCAR-8	2.6			290
	SK-OV-3	5.7			540
kidney cancer cells	RXF-631L	3.1			400
	ACHN	2.2			320
gastric cancer cells	St-4	3.8			430
	MKN1	2.3			52
	MKN-B	3.0			170
	MKN-A	3.5			250
	MKN45	1.3			300
	MKN74	3.7			310
prostate cancer cells	DU-145	3.5			490
	PC-3	3.0			290
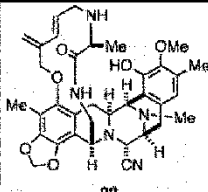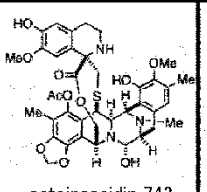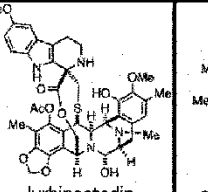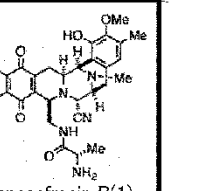
＜For inquiries, contact＞

Table7 :antitumor activity [nM] of Compound 29 (GI_{50} value: 50% growth inhibitory concentration)

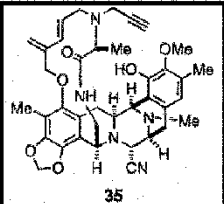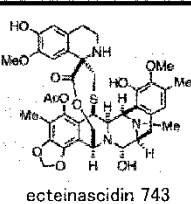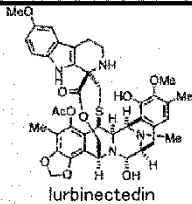|		33	ecteinascidin 743	lurbinectedin	cyanosafracin B(1)
breast cancer cells	HBC-4	32			59
	BSY-1	18			34
	HBC-5	40			62
	MCF-7	26	2.6	1.7	52
	MDA-MB-231	52	3.9	3.4	130
central nervous system cancer cells	U251	55			370
	SF-268	110			370
	SF-295	270			500
	SF-539	46			180
	SNB-75	96			150
	SNB-78	83			63
colorectal cancer cells	HCC2998	140			350
	KM-12	110			530
	HT-29	86	9.8	2.4	190
	HCT-15	400			390
	HCT-116	87	4.9	6.4	290
lung cancer cells	NCI-H23	93	2.1	5.3	290
	NCI-H226	260			310
	NCI-H522	25			43
	NCI-H460	260	1.8	1.5	400
	A549	360	10.4	1.3	1600
	DMS273	140			270
	DMS114	31			35
melanoma cells	LOX-IMVI	31			61
cervical cancer cells	OVCAR-3	70			130
	OVCAR-4	400			290
	OVCAR-5	310			390
	OVCAR-8	180			290
	SK-OV-3	500			540
kidney cancer cells	RXF-631L	300			400
	ACHN	260			320
gastric cancer cells	St-4	270			430
	MKN1	68			52
	MKN-B	220			170
	MKN-A	330			250
	MKN45	41			300
	MKN74	260			310
prostate cancer cells	DU-145	370			490
	PC-3	190			290

Table8 :antitumor activity [nM] of Compound 29 (GI$_{50}$ value: 50% growth inhibitory concentration)

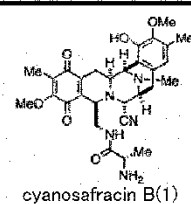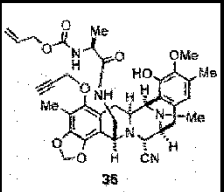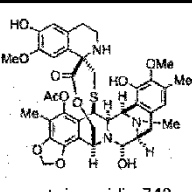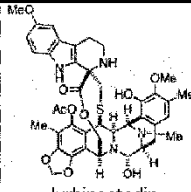|		35	ecteinascidin 743	lurbinectedin	cyanosafracin B(1)
breast cancer cells	HBC-4	2.2			59
	BSY-1	1.3			34
	HBC-5	2.7			62
	MCF-7	0.87	2.6	1.7	52
	MDA-MB-231	2.7	3.9	3.4	130
central nervous system cancer cells	U251	2.5			370
	SF-268	3.3			370
	SF-295	3.8			500
	SF-539	2.2			180
	SNB-75	1.7			150
	SNB-78	3.4			63
colorectal cancer cells	HCC2998	3.6			350
	KM-12	3.8			530
	HT-29	3.2	9.8	2.4	190
	HCT-15	4.5			390
	HCT-116	2.7	4.9	6.4	290
lung cancer cells	NCI-H23	3.5	2.1	5.3	290
	NCI-H226	2.7			310
	NCI-H522	1.1			43
	NCI-H460	3.4	1.8	1.5	400
	A549	7.2	10.4	1.3	1600
	DMS273	2.5			270
	DMS114	1.2			35
melanoma cells	LOX-IMVI	1.7			61
cervical cancer cells	OVCAR-3	3.2			130
	OVCAR-4	3.6			290
	OVCAR-5	3.3			390
	OVCAR-8	3.1			290
	SK-OV-3	6.5			540
kidney cancer cells	RXF-631L	2.9			400
	ACHN	3.1			320
gastric cancer cells	St-4	3.8			430
	MKN1	2.7			52
	MKN-B	3.5			170
	MKN-A	3.7			250
	MKN45	2.7			300
	MKN74	4.5			310
prostate cancer cells	DU-145	3.8			490
	PC-3	3.3			290

＜For inquiries, contact＞
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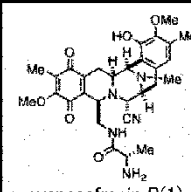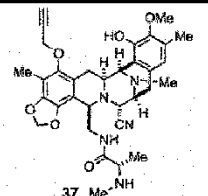Table9 :antitumor activity [nM] of Compound 29 (GI$_{50}$ value: 50% growth inhibitory concentration)
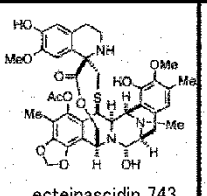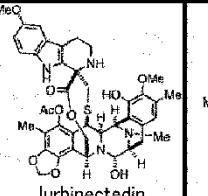
		35	ecteinascidin 743	lurbinectedin	cyanosafracin B(1)
breast cancer cells	HBC-4	3.5			59
	BSY-1	3.3			34
	HBC-5	7.6			62
	MCF-7	2.9	2.6	1.7	52
	MDA-MB-231	4.4	3.9	3.4	130
central nervous system cancer cells	U251	4.9			370
	SF-268	6.3			370
	SF-295	17			500
	SF-539	4.3			180
	SNB-75	7			150
	SNB-78	5.7			63
colorectal cancer cells	HCC2998	6.9			350
	KM-12	9			530
	HT-29	5.7	9.8	2.4	190
	HCT-15	29			390
	HCT-116	5.9	4.9	6.4	290
lung cancer cells	NCI-H23	13	2.1	5.3	290
	NCI-H226	23			310
	NCI-H522	2.4			43
	NCI-H460	30	1.8	1.5	400
	A549	38	10.4	1.3	1600
	DMS273	6.8			270
	DMS114	3			35
melanoma cells	LOX-IMVI	2.8			61
cervical cancer cells	OVCAR-3	4.8			130
	OVCAR-4	25			290
	OVCAR-5	20			390
	OVCAR-8	7.9			290
	SK-OV-3	25			540
kidney cancer cells	RXF-631L	39			400
	ACHN	22			320
gastric cancer cells	St-4	25			430
	MKN1	4.1			52
	MKN-B	25			170
	MKN-A	15			250
	MKN45	4.2			300
	MKN74	20			310
prostate cancer cells	DU-145	32			490
	PC-3	17			290

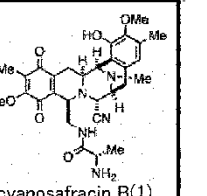Table10 :antitumor activity [nM] of Compound 29 (GI$_{50}$ value: 50% growth inhibitory concentration)

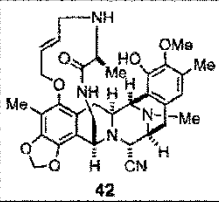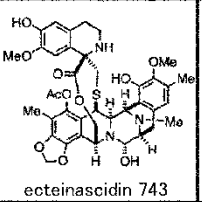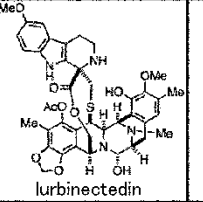|		37	ecteinascidin 743	lurbinectedin	cyanosafracin B(1)
breast cancer cells	HBC-4	42			59
	BSY-1	26			34
	HBC-5	100			62
	MCF-7	33	2.6	1.7	52
	MDA-MB-231	77	3.9	3.4	130
central nervous system cancer cells	U251	110			370
	SF-268	250			370
	SF-295	460			500
	SF-539	69			180
	SNB-75	100			150
	SNB-78	92			63
colorectal cancer cells	HCC2998	210			350
	KM-12	200			530
	HT-29	93	9.8	2.4	190
	HCT-15	480			390
	HCT-116	140	4.9	6.4	290
lung cancer cells	NCI-H23	270	2.1	5.3	290
	NCI-H226	280			310
	NCI-H522	28			43
	NCI-H460	410	1.8	1.5	400
	A549	1500	10.4	1.3	1600
	DMS273	270			270
	DMS114	29			35
melanoma cells	LOX-IMVI	40			61
cervical cancer cells	OVCAR-3	160			130
	OVCAR-4	450			290
	OVCAR-5	440			390
	OVCAR-8	230			290
	SK-OV-3	580			540
kidney cancer cells	RXF-631L	370			400
	ACHN	260			320
gastric cancer cells	St-4	400			430
	MKN1	220			52
	MKN-B	340			170
	MKN-A	370			250
	MKN45	180			300
	MKN74	330			310
prostate cancer cells	DU-145	440			490
	PC-3	350			290

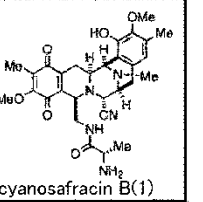Table11 :antitumor activity [nM] of Compound 29 (GI_{50} value: 50% growth inhibitory concentration)
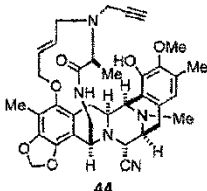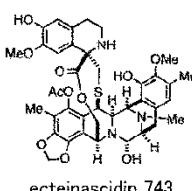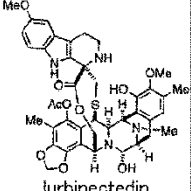
		42	ecteinascidin 743	lurbinectedin	cyanosafracin B(1)
breast cancer cells	HBC-4	<10			59
	BSY-1	<10			34
	HBC-5	17			62
	MCF-7	<10	2.6	1.7	52
	MDA-MB-231	<10	3.9	3.4	130
central nervous system cancer cells	U251	13			370
	SF-268	27			370
	SF-295	38			500
	SF-539	17			180
	SNB-75	<10			150
	SNB-78	11			63
colorectal cancer cells	HCC2998	18			350
	KM-12	19			530
	HT-29	13	9.8	2.4	190
	HCT-15	47			390
	HCT-116	21	4.9	6.4	290
lung cancer cells	NCI-H23	31	2.1	5.3	290
	NCI-H226	30			310
	NCI-H522	<10			43
	NCI-H460	22	1.8	1.5	400
	A549	110	10.4	1.3	1600
	DMS273	16			270
	DMS114	<10			35
melanoma cells	LOX-IMVI	<10			61
cervical cancer cells	OVCAR-3	15			130
	OVCAR-4	55			290
	OVCAR-5	47			390
	OVCAR-8	34			290
	SK-OV-3	49			540
kidney cancer cells	RXF-631L	34			400
	ACHN	42			320
gastric cancer cells	St-4	37			430
	MKN1	18			52
	MKN-B	25			170
	MKN-A	36			250
	MKN45	16			300
	MKN74	35			310
prostate cancer cells	DU-145	58			490
	PC-3	40			290

Table12 :antitumor activity [nM] of Compound 29 (GI$_{50}$ value: 50% growth inhibitory concentration)

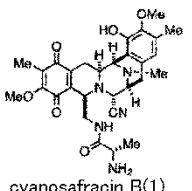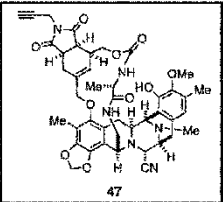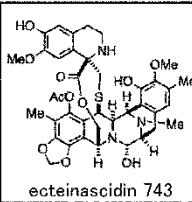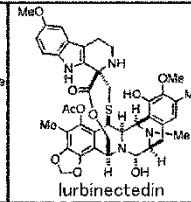|		44	ecteinascidin 743	lurbinectedin	cyanosafracin B(1)
breast cancer cells	HBC-4	<10			59
	BSY-1	<10			34
	HBC-5	<10			62
	MCF-7	<10	2.6	1.7	52
	MDA-MB-231	<10	3.9	3.4	130
central nervous system cancer cells	U251	<10			370
	SF-268	<10			370
	SF-295	<10			500
	SF-539	<10			180
	SNB-75	<10			150
	SNB-78	<10			63
colorectal cancer cells	HCC2998	<10			350
	KM-12	<10			530
	HT-29	<10	9.8	2.4	190
	HCT-15	<10			390
	HCT-116	<10	4.9	6.4	290
lung cancer cells	NCI-H23	<10	2.1	5.3	290
	NCI-H226	<10			310
	NCI-H522	<10			43
	NCI-H460	<10	1.8	1.5	400
	A549	<10	10.4	1.3	1600
	DMS273	<10			270
	DMS114	<10			35
melanoma cells	LOX-IMVI	<10			61
cervical cancer cells	OVCAR-3	<10			130
	OVCAR-4	<10			290
	OVCAR-5	<10			390
	OVCAR-8	<10			290
	SK-OV-3	<10			540
kidney cancer cells	RXF-631L	<10			400
	ACHN	<10			320
gastric cancer cells	St-4	<10			430
	MKN1	<10			52
	MKN-B	<10			170
	MKN-A	<10			250
	MKN45	<10			300
	MKN74	<10			310
prostate cancer cells	DU-145	<10			490
	PC-3	<10			290

＜For inquiries, contact＞

Table13 :antitumor activity [nM] of Compound 29 (GI_{50} value: 50% growth inhibitory concentration)

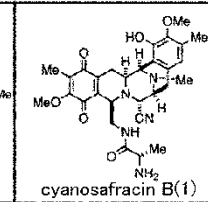|		47	ecteinascidin 743	lurbinectedin	cyanosafracin B(1)
breast cancer cells	HBC-4	200			59
	BSY-1	150			34
	HBC-5	300			62
	MCF-7	63	2.6	1.7	52
	MDA-MB-231	160	3.9	3.4	130
central nervous system cancer cells	U251	350			370
	SF-268	620			370
	SF-295	1800			500
	SF-539	290			180
	SNB-75	330			150
	SNB-78	260			63
colorectal cancer cells	HCC2998	410			350
	KM-12	450			530
	HT-29	490	9.8	2.4	190
	HCT-15	2200			390
	HCT-116	450	4.9	6.4	290
lung cancer cells	NCI-H23	850	2.1	5.3	290
	NCI-H226	2300			310
	NCI-H522	29			43
	NCI-H460	630	1.8	1.5	400
	A549	3900	10.4	1.3	1600
	DMS273	450			270
	DMS114	31			35
melanoma cells	LOX-IMVI	160			61
cervical cancer cells	OVCAR-3	330			130
	OVCAR-4	3500			290
	OVCAR-5	2800			390
	OVCAR-8	1100			290
	SK-OV-3	3900			540
kidney cancer cells	RXF-631L	2100			400
	ACHN	2800			320
gastric cancer cells	St-4	2200			430
	MKN1	290			52
	MKN-B	730			170
	MKN-A	1400			250
	MKN45	470			300
	MKN74	1600			310
prostate cancer cells	DU-145	3900			490
	PC-3	1500			290

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