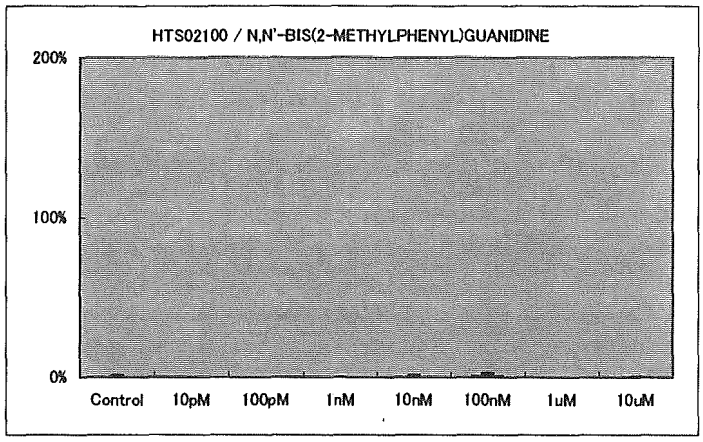
ERβ /HeLa

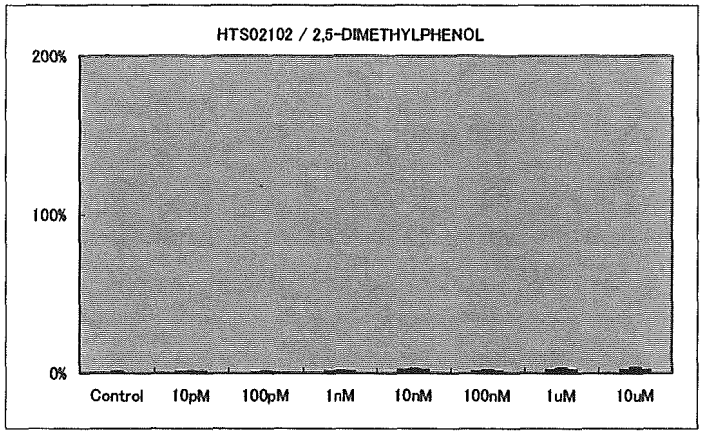
HTS02100
N,N'-BIS(2-METHYLPHENYL)GUANIDINE

PC50 (pM): -



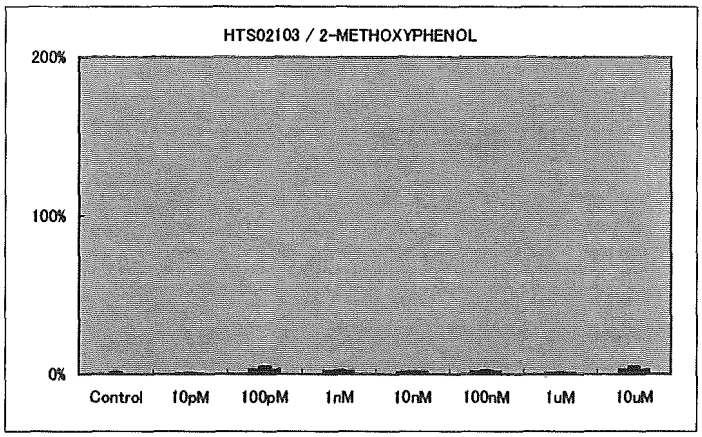
HTS02102
2,5-DIMETHYLPHENOL

PC50 (pM): -



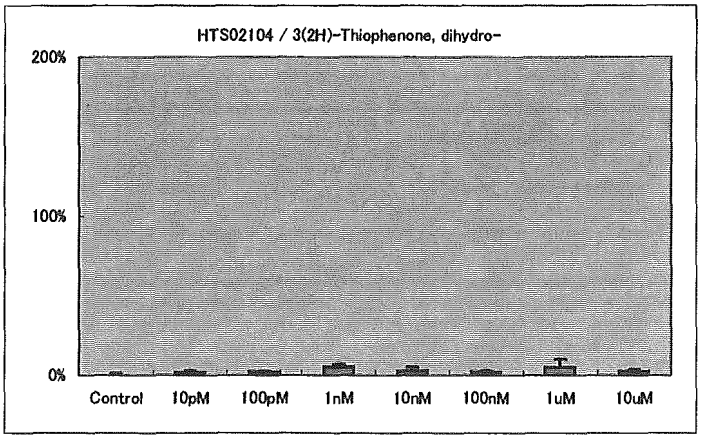
HTS02103
2-METHOXYPHENOL

PC50 (pM): -



HTS02104
3(2H)-Thiophenone, dihydro-

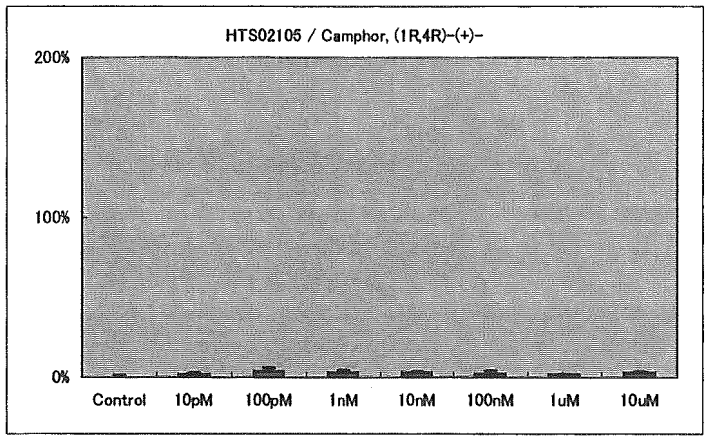
PC50 (pM): -



ERβ /HeLa

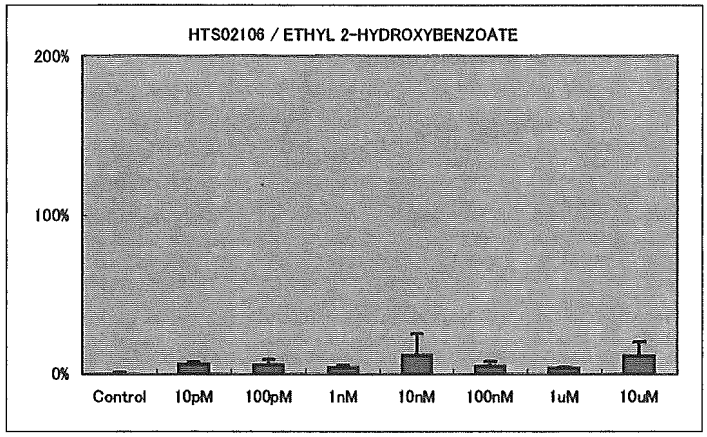
HTS02105
Camphor, (1R,4R)-(+)-

PC50 (pM): -



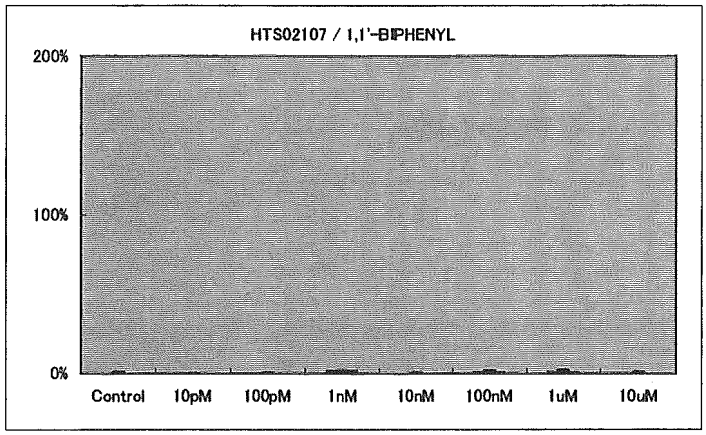
HTS02106
ETHYL 2-HYDROXYBENZOATE

PC50 (pM): -



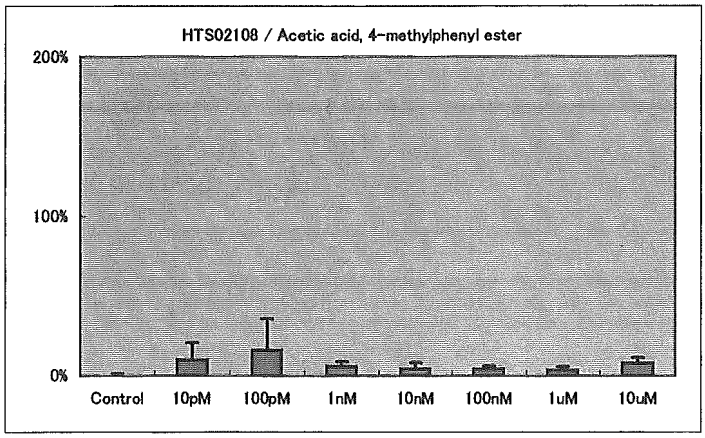
HTS02107
1,1'-BIPHENYL

PC50 (pM): -



HTS02108
Acetic acid, 4-methylphenyl ester

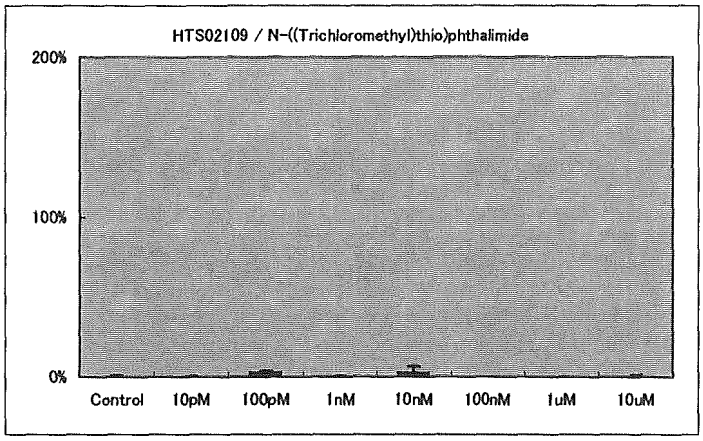
PC50 (pM): -



ERβ /HeLa

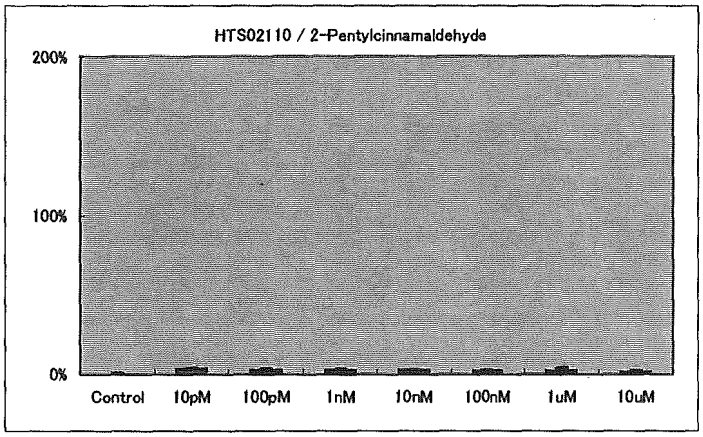
HTS02109
N-((Trichloromethyl)thio)phthalimide

PC50 (pM): -



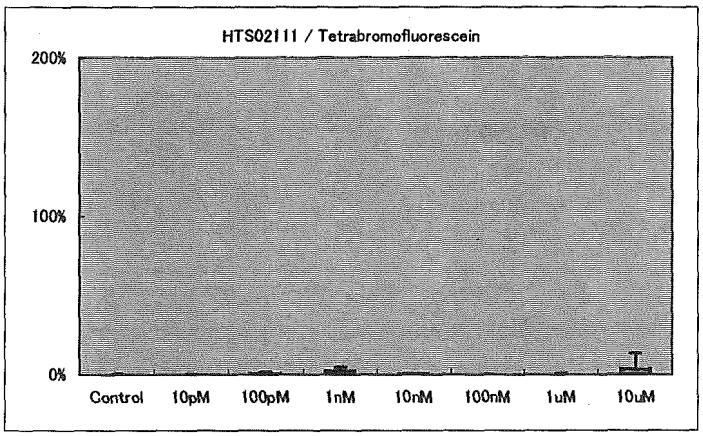
HTS02110
2-Pentylcinnamaldehyde

PC50 (pM): -



HTS02111
Tetrabromofluorescein

PC50 (pM): -



厚生労働科学研究費補助金(化学物質リスク研究事業)
生体の作用点、特に核内受容体及び関連転写因子群に着目した化学物質の
毒性発現機構の解明や毒性予測手法の開発を行う研究

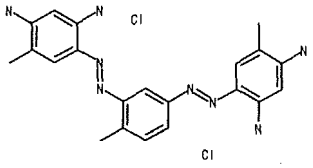
総括研究報告書　図表

(1)-2. アンドロゲン、甲状腺受容体レポーター遺伝子細胞系を用いた
高速自動分析系に関する研究
(主任研究者:大塚製薬ライフサイエンス時業務 EDC 分析センター委託業務)

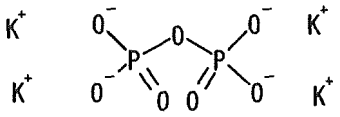
表 1　AR アゴニストアッセイの結果

Assay ID	name	CAS	PC50	PC10
AT101	1,3-Benzenediamine, 4,4'-_(4-methyl-1,3-phenyler	5421-66-9	-	3.96E-08
AT105	Pyrophosphoric acid, tetrapotassium salt	7320-34-5	-	1.95E-06

AT101



AT105



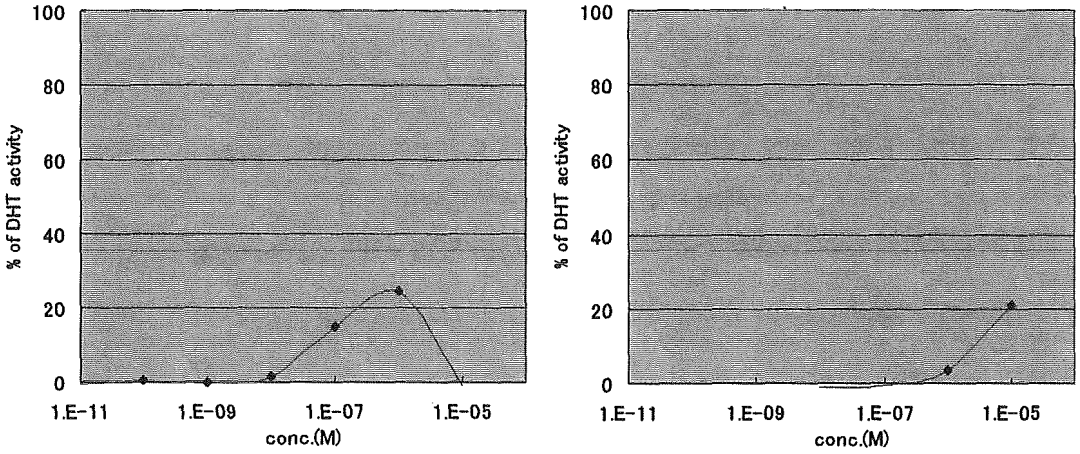
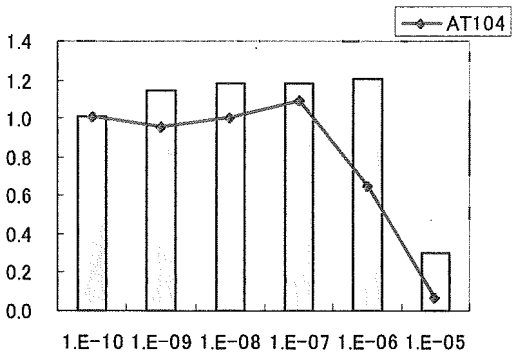


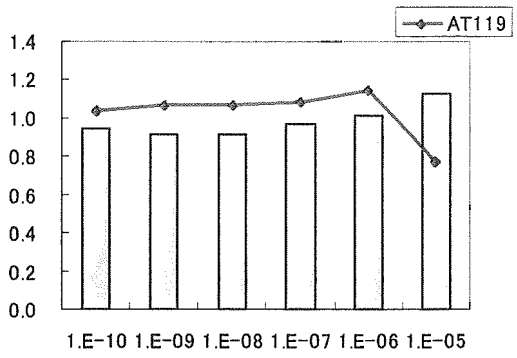
図 1　AR アゴニスト活性があった 2 物質の結果と化学構造

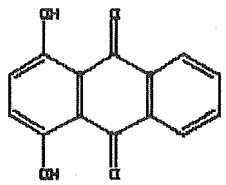
表 2　AR アンタゴニストアッセイの結果

Assay ID	name	CAS	IC50	IC20
AT126	Benzidine, 2,2',3,3',5,5',6,6'-octafluoro-	1038-66-0	3.6E-07	
AT104	Pyrethrins	8003-34-7	2.0E-06	
AT136	PROCHLORAZ	67747-09-5	2.09E-06	
AR146	Phenol, 4,4'-isopropylidenedi-	80-05-7	2.68E-06	
AR147	4,4'-Stilbenediol, alpha,alpha'-diethyl-	56-53-1	2.94E-06	
AR148	4,4'-Cyclohexylidenebisphenol	843-55-0	4.45E-06	
AT128	Benzidine, 3,3'-dimethyl-	119-93-7	4.9E-06	
AT127	Phenol, 4,4'-(diethylideneethylene)di-, diacetate	84-19-5	6.6E-06	
AR141	Capsaicin	404-86-4		4.8E-06
AT119	Anthraquinone, 1,4-dihydroxy-	81-64-1		6.96E-06

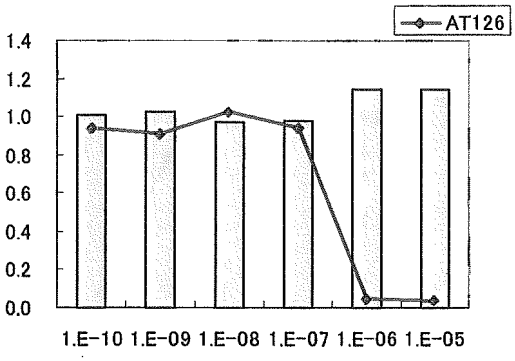


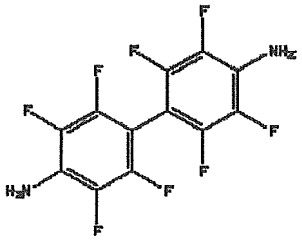
AT104
Pyrethrins （混合物）



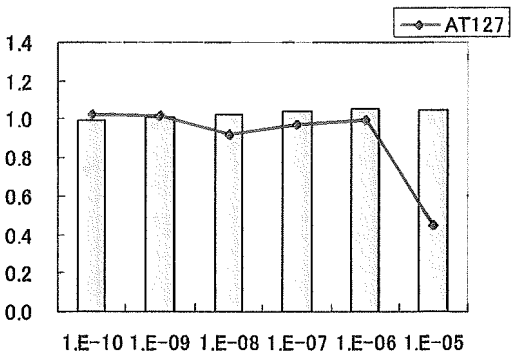


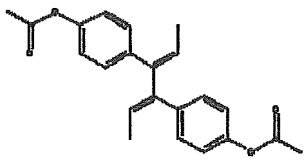
AT119
Anthraquinone, 1,4-dihydroxy-





AT126
Benzidine,
2,2',3,3',5,5',6,6'-octafluoro-

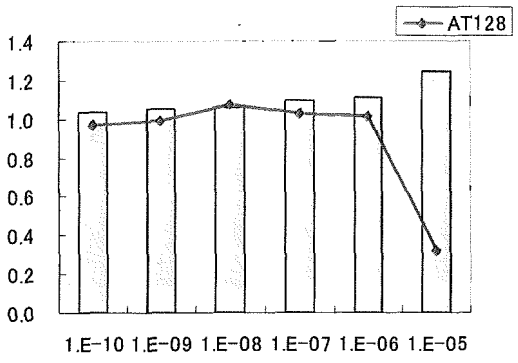


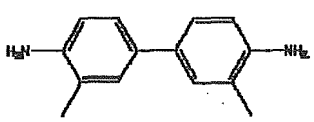


AT127
Phenol, 4,4'-(diethylideneethylene)di-,
diacetate

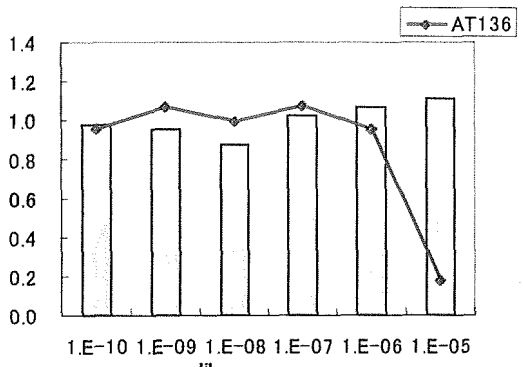
図２　AR アンタゴニスト活性とその化学構造（その１）

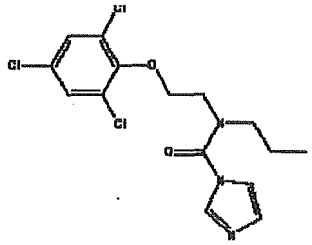
縦軸は相対活性（$5x10^{-10}$ M における DHT の活性を 1.0）、横軸は濃度（M）　を示す。



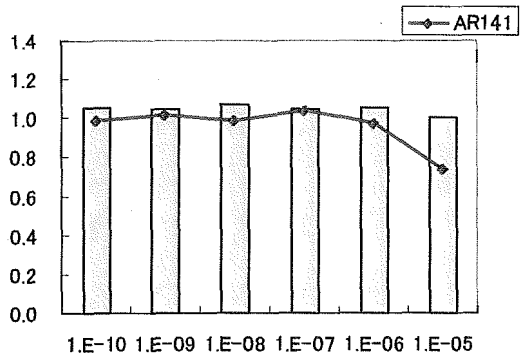


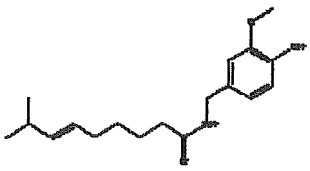
AT128
Benzidine, 3,3'-dimethyl-



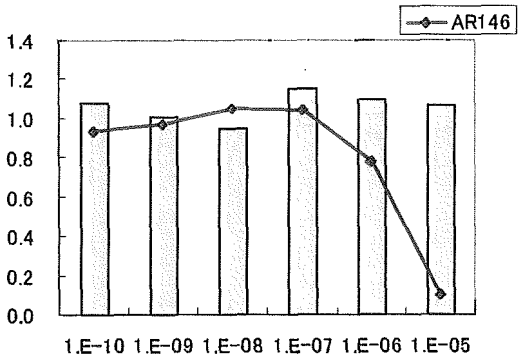


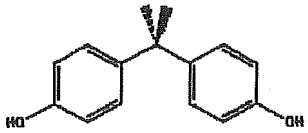
AT136
PROCHLORAZ





AR141
Capsaicin

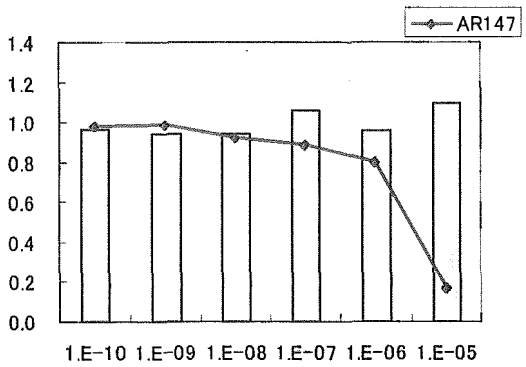


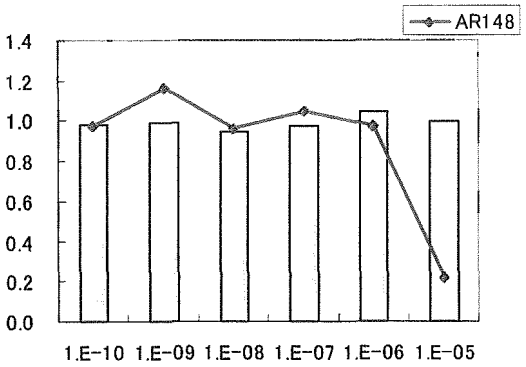


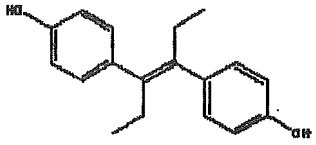
AR146
Phenol, 4,4'-isopropylidenedi-

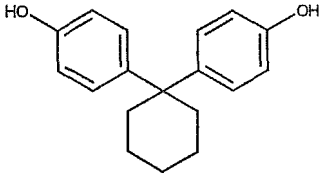
図２　ARアンタゴニスト活性とその化学構造（その２）

縦軸は相対活性（$5x10^{-10}$M における DHT の活性を 1.0)、横軸は濃度（M）　を示す。









AR147
4,4'-Stilbenediol,
alpha,alpha'-diethyl-

AR148
Phenol, 4,4'-isopropylidenedi-

図２　ARアンタゴニスト活性とその化学構造（その３）

縦軸は相対活性（$5x10^{-10}$ M におけるDHTの活性を1.0)、横軸は濃度（M）　を示す。

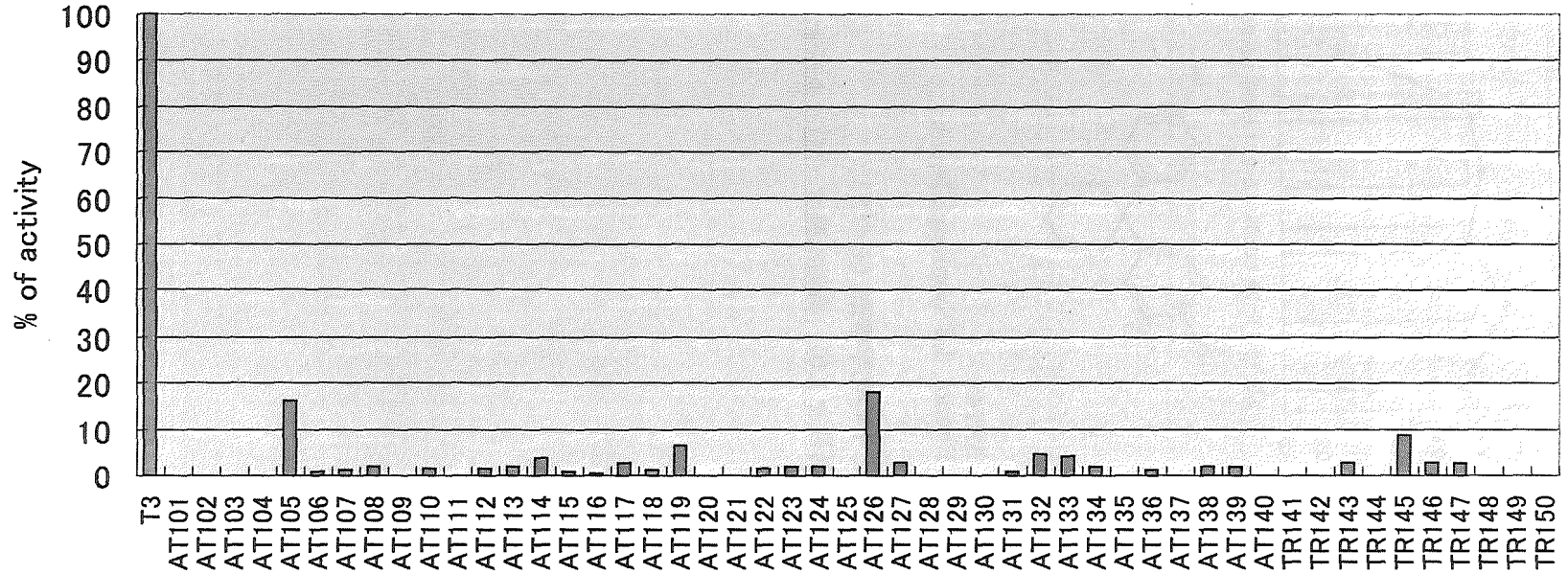


図３　本年度５０化合物のTRアゴニスト測定の結果

$1x10^{-7}$ M のT3活性を100として、それに対するそれぞれの化合物の $1x10^{-5}$ M のLuc活性をグラフにした。

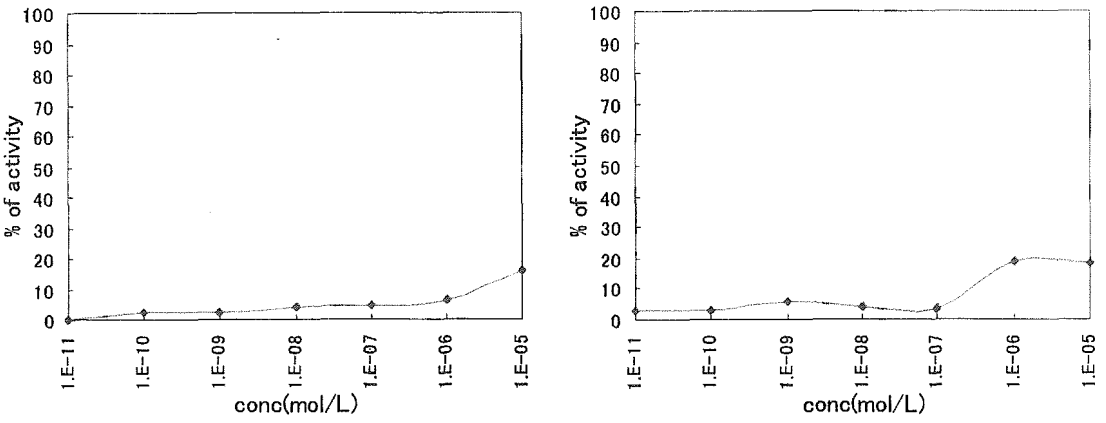


図 4　AT105、AT126 の TR アゴニストアッセイにおける濃度反応曲線

縦軸は $1x10^{-7}$ M の T3 活性を 100 とした相対値、横軸は濃度（M）を示す。

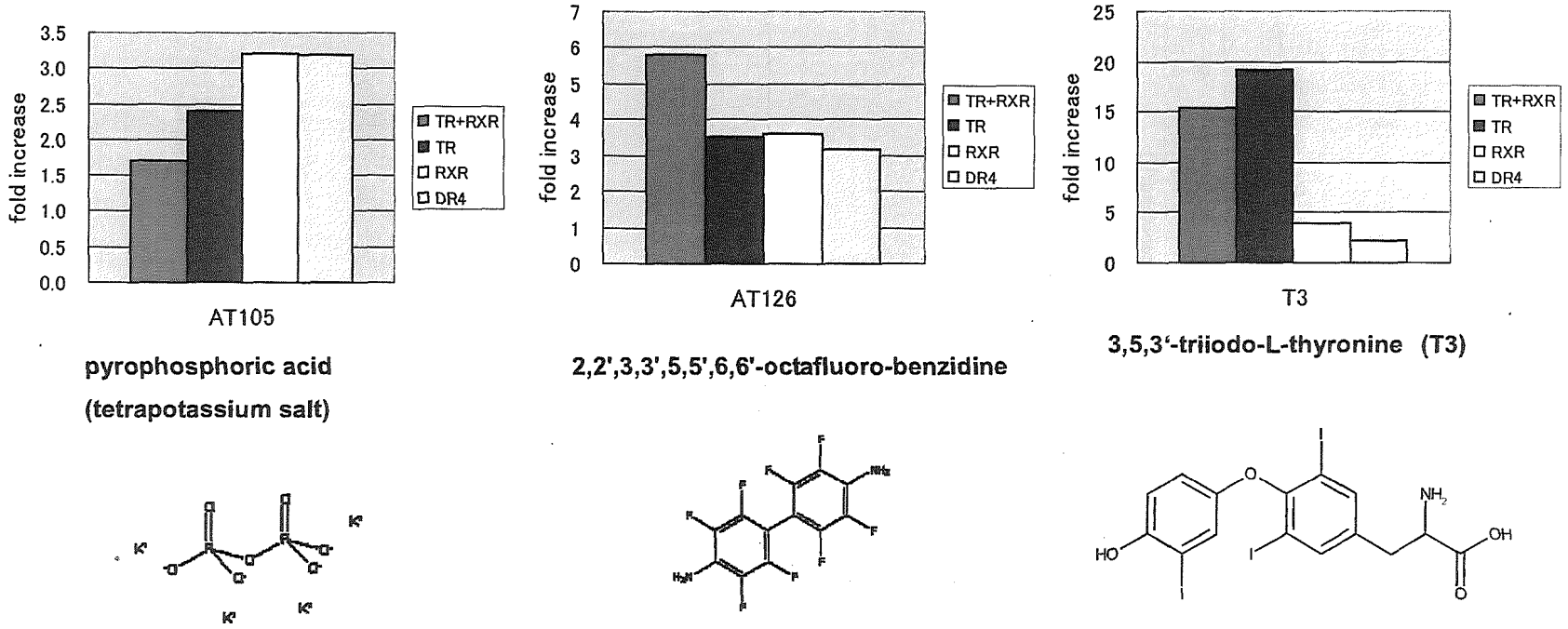


図5　TR-RXR ヘテロダイマー、TR ホモダイマー、RXR ホモダイマー、その他の細胞内在性因子への反応性を調べた実験

各化合物の反応性は、ベースラインからの Fold increase で表してある。

各グラフの下には、それぞれの化合物の名称および化学構造を示した。

付録　物質一覧（その１）

Assay ID	CAS_s	Name	MW
AT101	5421-66-9	1,3-Benzenediamine, 4,4'-_(4-methyl-1,3-phenylene)	461.398
AT102	2444-46-4	NONANAMIDE, N-((4-HYDROXY-3-METHOXYPHENYL)METHY*	293.404
AT103	79-96-9	3,3'-DI-TERT-BUTYLDIAN	340.504
AT104	8003-34-7	Pyrethrins	
AT105	7320-34-5	Pyrophosphoric acid, tetrapotassium salt	330.333
AT106	120-51-4	Benzyl benzoate	212.247
AT107	644-08-6	Biphenyl, 4-methyl-	168.2378
AT108	5331-91-9	5-Chloro-2-benzothiazolethiol	201.6883
AT109	719-03-9	Hydroquinone, (1,1,3,3-tetramethylbutyl)-	222.326
AT110	531-59-9	Herniarin	176.1714
AT111	56-72-4	O,O-Diethyl O-(3-chloro-4-methyl-2-oxo-2H-1-benzop	362.768
AT112	60-56-0	Imidazole-2-thiol, 1-methyl-	114.1648
AT113	51-52-5	Uracil, 6-propyl-2-thio-	170.2288
AT114	61-82-5	3-Amino-s-triazole	84.0804
AT115	106-02-5	Pentadecanoic acid, 15-hydroxy-, .xi.-lactone	240.385
AT116	103-34-4	Morpholine, 4,4'-dithiodi-	236.3466
AT117	298-81-7	7H-Furo(3,2-g)(1)benzopyran-7-one, 9-methoxy-	216.1928
AT118	51630-58-1	Fenvalerate	419.9067
AT119	81-64-1	Anthraquinone, 1,4-dihydroxy-	240.2148
AT120	8	Phenol, 4,4'-(1-(4-(1-(4-hydroxyphenyl)-1-methylethyl)phenyl)ethylidene)bis-	424.53
AT121	96-69-5	4,4'-THIOBIS(6-TERT-BUTYL-M-CRESOL)	358.5378
AT122	603-35-0	TRIPHENYLPHOSPHINE	262.2903
AT123	96-29-7	2-BUTANONE OXIME	87.1212
AT124	81-11-8	2,2'-Stilbenedisulfonic acid, 4,4'-diamino-	370.3944
AT125	4191-73-5	Isopropyl 4-hydroxybenzoate	180.202
AT126	1038-66-0	Benzidine, 2,2',3,3',5,5',6,6'-octafluoro-	328.1642
AT127	84-19-5	Phenol, 4,4'-(diethylideneethylene)di-, diacetate	350.4134
AT128	119-93-7	Benzidine, 3,3'-dimethyl-	212.2938
AT129	3194-55-6	1,2,5,6,9,10-Hexabromocyclododecane	641.698
AT130	25637-99-4	Cyclododecane, hexabromo-	641.6982

Assay ID のATはAR、TR共に測定、またARはARのみ、TRはTRのみ測定

付録　物質一覧（その２）

Assay ID	CAS_s	Name	MW
AT131	3001-15-8	Biphenyl, 4,4'-diiodo-	405.995
AT132	2236-52-4	2,2'-Diiodobiphenyl	405.995
AT133	10605-21-7	Methyl 2-benzimidazolecarbamate	191.189
AT134	77-06-5	Gibberellic acid	348.395
AT135	2032-65-7	4-(Methylthio)-3,5-xylyl methylcarbamate	225.305
AT136	67747-09-5	PROCHLORAZ	376.6693
AT137	97-39-2	N,N'-BIS(2-METHYLPHENYL)GUANIDINE	239.3194
AT138	464-49-3	Camphor, (1R,4R)-(+)-	152.2358
AT139	92-52-4	1,1'-BIPHENYL	154.211
AT140	133-07-3	N-((Trichloromethyl)thio)phthalimide	296.5551
AR141	404-86-4	Capsaicin	305.415
AR142	42436-07-7	Benzeneacetic acid, 3-hexenyl ester, (Z)-	218.295
AR143	124-10-7	METHYL MYRISTATE	242.4008
AR144	934-34-9	2(3H)-Benzothiazolone	151.1826
AR145	13110-37-7	BENZOIC ACID, 4-AMINO-,PENTY ESTER	207.2718
AR146	1980/5/7	Phenol, 4,4'-isopropylidenedi-	228.2902
AR147	56-53-1	4,4'-Stilbenediol, alpha,alpha'-diethyl-	268.3548
AR148	843-55-0	4,4'-Cyclohexylidenebisphenol	268.354
AR149	1003-04-9	3(2H)-Thiophenone, dihydro-	102.1508
AR150	122-40-7	2-Pentylcinnamaldehyde	202.295
TR141	2664-63-3	Phenol, 4,4'-thiodi-	218.2698
TR142	1141-59-9	Resorcinol, 4-(2-pyridylazo)-	215.211
TR143	119-61-9	Benzophenone	182.2214
TR144	611-99-4	Benzophenone, 4,4'-dihydroxy-	214.219
TR145	131-56-6	BENZORESORCINOL	214.2202
TR146	98-54-4	Phenol, p-tert-butyl-	150.22
TR147	140-66-9	P-(1,1,3,3-TETRAMETHYLBUTYL)PHENOL	206.3272
TR148	92-69-3	4-PHENYLPHENOL	170.2104
TR149	1131-60-8	Phenol, p-cyclohexyl-	176.2578
TR150	603-45-2	ROSOLIC ACID	290.3178

Assay ID のATはAR、TR共に測定、またARはARのみ、TRはTRのみ測定

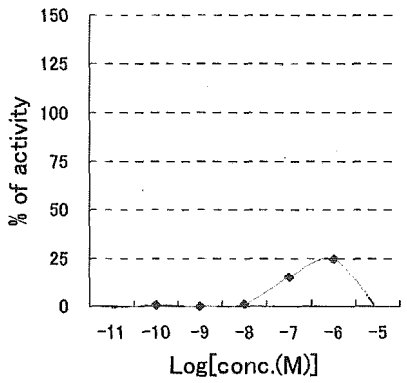
測定結果　一覧

AR レポータージーンアッセイ
TR レポータージーンアッセイ
40 物質
(AT101～AT140)

sample No. AT101
chemical name 1,3-Benzenediamine, 4,4'-(4-methyl-1,3-phenylene)
CAS. 5421-66-9

AR agonist assay

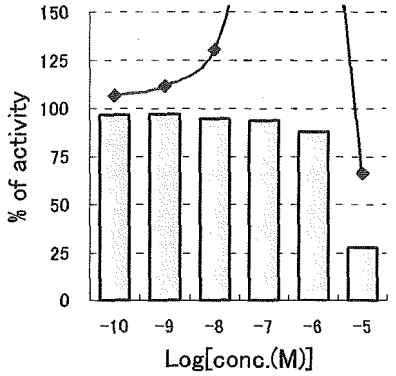
LOG[conc.(M)]	luc
-5	-1.0
-6	24.6
-7	15.2
-8	1.3
-9	0.0
-10	0.5
-11	-0.5



AR antagonist assay

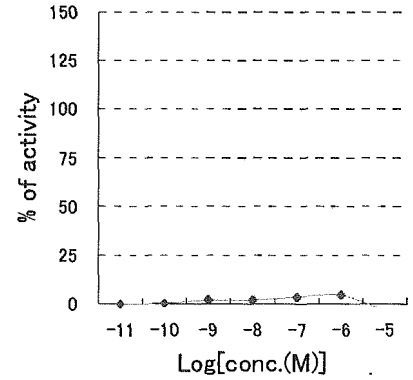
LOG[conc.(M)]	luc	ren
-5	66	28
-6	275	88
-7	222	94
-8	131	95
-9	112	97
-10	106	97

Cell viability



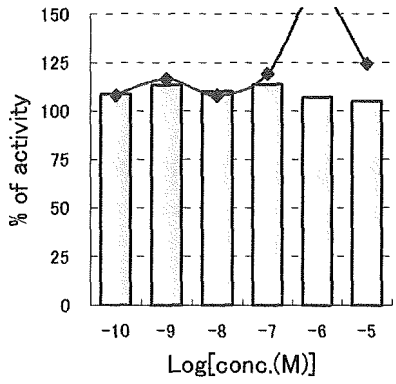
TRβ-RXR agonist assay

LOG[conc.(M)]	luc
-5	-3.6
-6	4.7
-7	3.6
-8	2.1
-9	2.2
-10	0.2
-11	0.0



TRβ-RXR antagonist assay

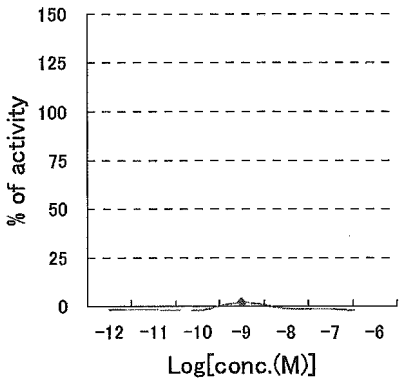
LOG[conc.(M)]	luc	ren
-5	125	105
-6	161	107
-7	119	113
-8	108	110
-9	116	113
-10	108	109



sample No. AT102
chemical name NONANAMIDE, N-((4-HYDROXY-3-METHOXYPHENYL)METHY*
CAS. 2444-46-4

AR agonist assay

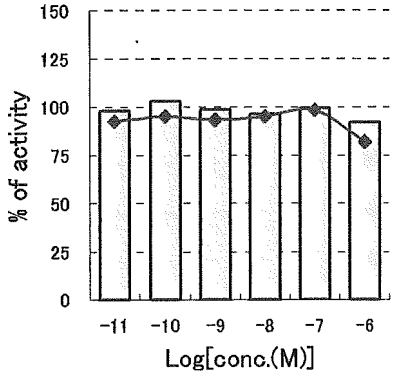
LOG[conc.(M)]	luc
-6	-3.1
-7	-1.1
-8	-0.9
-9	2.1
-10	-2.1
-11	-1.4
-12	-1.5



AR antagonist assay

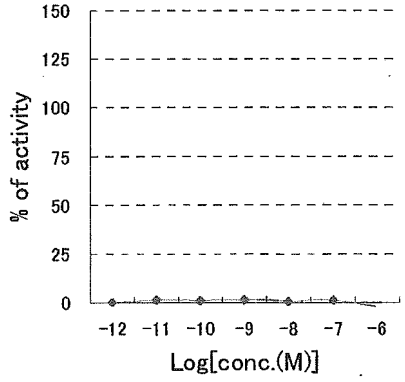
LOG[conc.(M)]	luc	ren
-6	82	92
-7	98	99
-8	95	96
-9	93	99
-10	95	103
-11	93	98

Cell viability



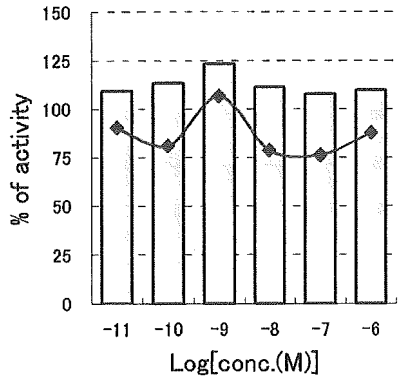
TRβ-RXR agonist assay

LOG[conc.(M)]	luc
-6	-2.0
-7	1.4
-8	0.7
-9	1.9
-10	1.1
-11	1.4
-12	0.2



TRβ-RXR antagonist assay

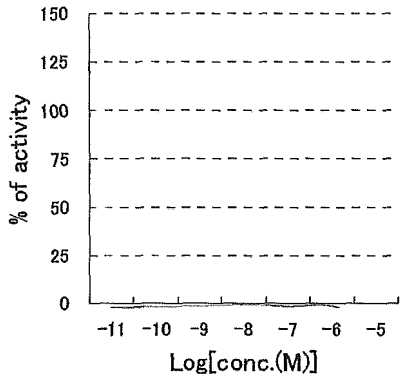
LOG[conc.(M)]	luc	ren
-6	88	109
-7	76	107
-8	79	111
-9	107	123
-10	81	113
-11	91	109



sample No.	AT103
chemical name	3,3'-DI-TERT-BUTYLDIAN
CAS.	79-96-9

AR agonist assay

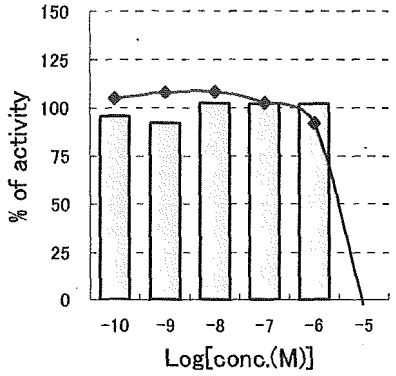
LOG[conc.(M)]	luc
-5	-10.1
-6	-1.1
-7	-1.4
-8	-0.6
-9	-1.1
-10	-1.5
-11	-2.1



AR antagonist assay

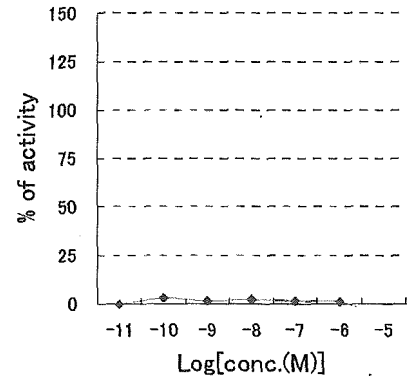
LOG[conc.(M)]	luc	ren
-5	-5	-17
-6	92	102
-7	103	102
-8	108	102
-9	108	92
-10	105	95

Cell viability



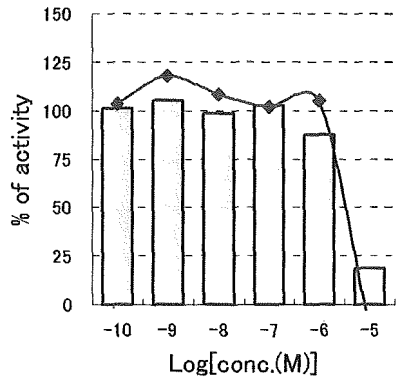
TRβ-RXR agonist assay

LOG[conc.(M)]	luc
-5	-7.6
-6	1.3
-7	1.5
-8	2.2
-9	1.7
-10	3.3
-11	0.0



TRβ-RXR antagonist assay

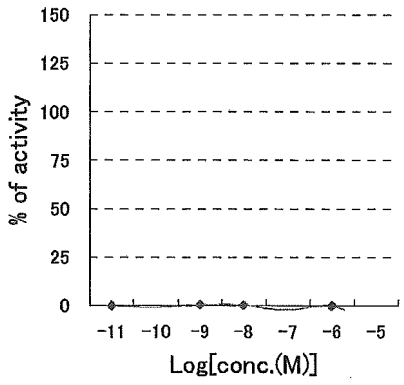
LOG[conc.(M)]	luc	ren
-5	-14	18
-6	105	87
-7	102	103
-8	109	98
-9	118	105
-10	104	101



sample No. AT104
chemical name Pyrethrins
CAS. 8003-34-7

AR agonist assay

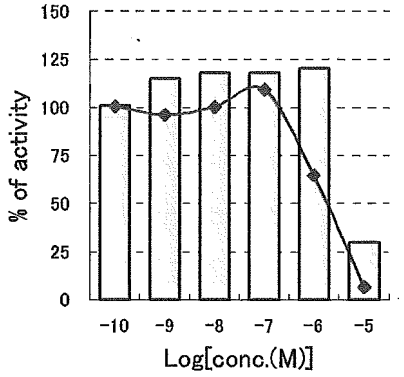
LOG[conc.(M)]	luc
-5	-8.8
-6	0.0
-7	-2.1
-8	0.2
-9	0.7
-10	-0.8
-11	0.1



AR antagonist assay

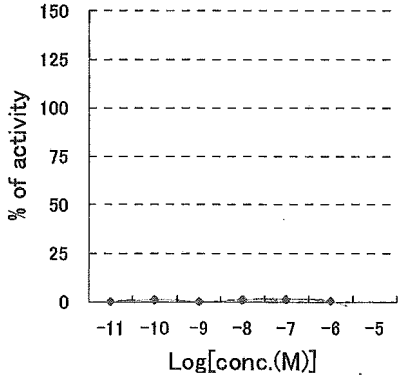
LOG[conc.(M)]	luc	ren
-5	7	30
-6	65	120
-7	109	118
-8	100	118
-9	96	115
-10	101	101

Cell viability



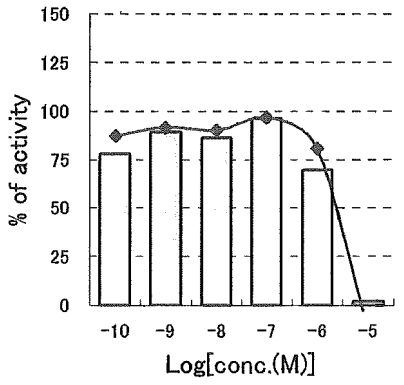
TRβ-RXR agonist assay

LOG[conc.(M)]	luc
-5	-6.9
-6	0.6
-7	1.5
-8	1.2
-9	0.4
-10	1.2
-11	0.4



TRβ-RXR antagonist assay

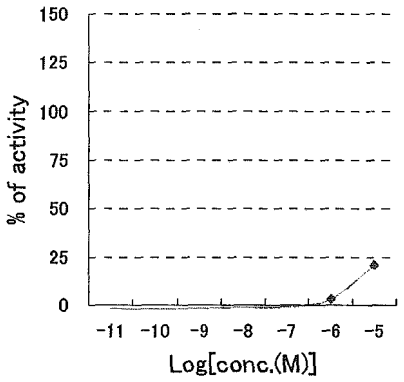
LOG[conc.(M)]	luc	ren
-5	-13	2
-6	81	69
-7	97	96
-8	90	86
-9	92	89
-10	87	78



sample No.	AT105
chemical name	Pyrophosphoric acid, tetrapotassium salt
CAS.	7320-34-5

AR agonist assay

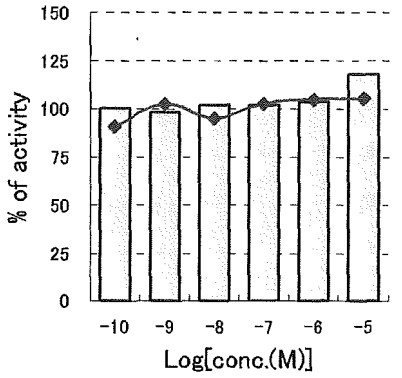
LOG[conc.(M)]	luc
-5	21.0
-6	3.4
-7	-0.7
-8	-0.9
-9	-1.5
-10	-1.9
-11	-1.5



AR antagonist assay

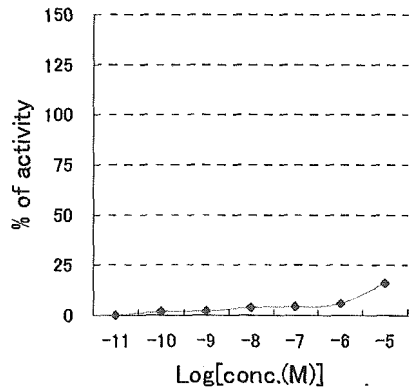
LOG[conc.(M)]	luc	ren
-5	106	118
-6	105	104
-7	103	102
-8	95	102
-9	103	98
-10	91	100

Cell viability



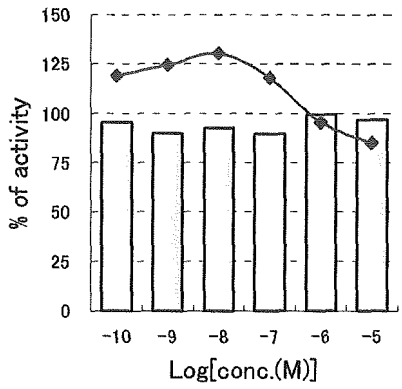
TRβ-RXR agonist assay

LOG[conc.(M)]	luc
-5	16.2
-6	6.1
-7	4.8
-8	3.9
-9	2.3
-10	2.0
-11	0.1



TRβ-RXR antagonist assay

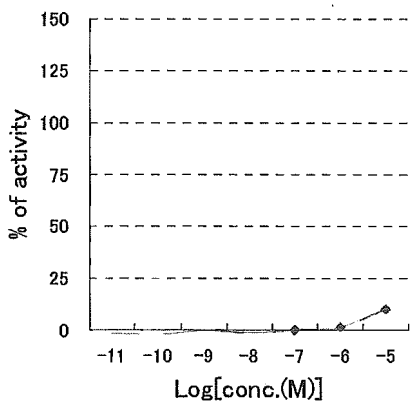
LOG[conc.(M)]	luc	ren
-5	85	97
-6	96	99
-7	118	89
-8	131	93
-9	125	90
-10	119	95



sample No. AT106
chemical name Benzyl benzoate
CAS. 120-51-4

AR agonist assay

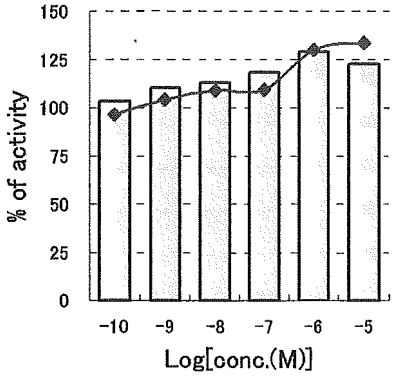
LOG[conc.(M)]	luc
-5	9.9
-6	1.5
-7	-0.1
-8	-1.2
-9	-0.4
-10	-1.8
-11	-1.5



AR antagonist assay

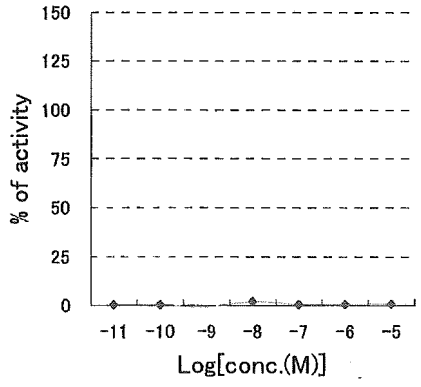
LOG[conc.(M)]	luc	ren
-5	134	123
-6	130	129
-7	109	118
-8	109	113
-9	104	110
-10	96	103

Cell viability



TRβ-RXR agonist assay

LOG[conc.(M)]	luc
-5	0.8
-6	0.5
-7	0.6
-8	2.2
-9	-0.7
-10	0.6
-11	0.6



TRβ-RXR antagonist assay

LOG[conc.(M)]	luc	ren
-5	119	102
-6	111	110
-7	114	116
-8	118	113
-9	108	114
-10	98	108