アズレンエステルの合成とその薬理活性

(城西大学[1]・明海大学[2]) ○古市 飛雄人[1]・三浦 航[1]・坂上 宏[2]・若林 英嗣[1]
Synthesis of Azulene Ester Derivatives and Their Pharmacological Activities ([1]*Josai University*, [2]*Meikai University*) ○ Hiyuto Furuichi,[1] Wataru Miura,[1] Hiroshi Sakagami,[2] Hidetugu Wakabayashi[1]

Our recent work is on azulene, a structural isomer of naphthalene. Azulene is very interesting because of its unique structure. We are conducting basic research on the synthesis of azulene and its applications.[1)] I have synthesized azulene ester derivatives, which are novel compounds with an ester bond at the 1-position of azulene. Furthermore, I observed the antitumor activity of azulene ester derivatives against oral cancer cells and normal oral cells. As a result, we found azulene ester derivatives that exhibit certain antitumor activity. However, a comparison of the anti-tumor activity of azulene ester derivatives with anti-cancer drugs used in actual medical practice showed that azulene ester derivatives do not show such excellent values.

Keywords : Non-benzenoid aromatic compounds; Synthesis of azulene ester derivatives; Pharmacological activity of azulenes; Antitumor activity **【4 words】**

当研究室では近年、ナフタレンの構造異性体であるアズレンの構造の特異性に着目し、基礎研究の一端としてアズレンの合成法やその応用研究[1)]を行っている。本実験ではアズレンの 1 位にエステル結合を介した全 16 種類の新規化合物であるアズレンエステル誘導体の合成を行い、口腔癌細胞と口腔正常細胞に対する抗腫瘍活性を評価した。アズレンエステル誘導体は一定の抗腫瘍活性を示したものもあったが、実際の抗がん剤と比較した結果それほど強い値は出ていないことが分かった。

	CC_{50} (μM)											
	Oral squamous carcinoma			Normal oral cells			Neuronal cells			TS	NT	TS/NT
	Ca9-22	HSC-2	mean (A)	HGF	HPC	mean (B)	PC-12	SH-SY5Y	mean (C)	(B/A)	(B/C)	(C/A)
1	>1600	427.1	>1014	1506.7	>1600	>1553	360.8	354.0	357	><1.53	>4.35	0.35
2	357.8	478.4	418	1592.1	1444.5	1518	295.9	441.2	369	3.63	4.12	0.88
3	260.5	224.9	243	1163.2	1144.9	1154	241.4	288.5	265	4.75	4.36	**1.09**
4	243.5	198.0	221	1506.0	1552.9	1529	233.0	291.1	262	**6.93**	5.84	**1.19**
5	304.3	276.1	290	>1600	>1600	>1600	196.8	337.0	267	**>5.51**	>5.99	0.92
6	667.3	614.5	641	>1600	1285.7	>1443	553.9	661.5	608	>2.25	>2.37	0.95
7	621.7	662.1	642	1245.6	1411.6	1329	592.5	589.4	591	2.07	2.25	0.92
8	389.5	513.1	451	1263.9	1332.0	1298	351.7	554.2	453	2.88	2.87	**1.00**
9	275.2	320.0	298	>1600	>1600	>1600	162.2	215.9	189	**>5.38**	>8.46	0.64
10	47.1	103.9	75	298.9	300.7	300	10.1	31.1	21	3.97	14.54	0.27
11	45.8	104.3	75	371.0	196.1	284	55.6	42.8	49	3.78	5.76	0.66
12	125.1	171.9	148	647.8	384.4	516	86.0	143.6	115	3.48	4.49	0.77
13	107.4	109.7	109	570.9	342.7	457	24.8	55.9	40	4.21	11.33	0.37
14	98.2	132.3	115	570.0	365.1	468	16.1	108.2	62	4.06	7.52	0.54
15	16.1	71.3	44	>400	201.3	>301	40.5	4.7	23	**>6.88**	>13.3	0.52
16	29.6	58.5	44	79.5	127.8	104	27.2	6.3	17	2.35	6.19	0.38
DOX	44.1	14.0	29	>1600	>1601	>1600	<12.5	<12.5	<12.5	>55.0	>128	0.43
5-FU	12.4	44.1	28	>400	>400	>400	3.1	4.4	3.79	>14.1	>105.7	0.13
CDDP	326.9	>1600	>963	>400	>400	>400	60.8	118.8	89.79	><0.4	>4.45	0.09

1) T. Wada, R. Maruyama, Y. Irie, M. Hashimoto, H. Wakabayashi *et al*. *in vivo*. **2018**, 32, 479-486.