Communications to the editors

ANTITUMOR ACTIVITY OF MONOGLYCERIDES AND OTHER ESTERS OF FATTY ACIDS

Sir:

Antitumor active monoglycerides have been isolated from the acetone extracts of the mycelia of *Sepedonium ampullosporum*[1], *Cercospora oryzae*[2] and *Coriolus unicolor*[2]. Fatty acids composition of the monoglycerides was examined and it was found that hexadecanoic, octadecenoic and octadecadienoic acids are the main components[3]. They also contain other fatty acids as the minor components.

In order to determine the active principle in the mixtures of the monoglycerides, antitumor activity *in vivo* of each monoglycerides was studied using EHRLICH ascites tumor in mice. In addition to the monoglycerides, the glycerol esters of fatty acids, other esters were examined for the activity. In this paper we report the antitumor activity of monoglycerides and other esters of fatty acids.

In this study we chose those fatty acids with even carbon numbers between ten and eighteen. For the alcoholic moieties we selected methanol, propylene glycol, sorbitol and sucrose in addition to glycerol.

A part of the monoglycerides and all the sucrose esters were synthesized in this laboratory. Monoglycerides were synthesized according to the method of DAUBERT and BALDWIN[4] except that pyridine was used instead of quinoline in the reaction mixture. For the synthesis of sucrose esters of fatty acids the method of OSIPOW *et al.*[5] was applied. Other materials were commercially available.

To examine purity of the fatty acid component of the esters each sample was subjected to methanolysis and the methyl esters obtained were analyzed with gas-

Table 1. Antitumor activity of monoglycerides

Monoglycerides	Dose (mg/mouse/day)	7 Days after implant: Tumor		7 Days after implant: Body wt. gain (g)		Survival time (days)	
Monostearin	10.0	+++	+++	+4.0	+5.3	13	15
	2.5	−	+++	+2.3	+7.8	29	22
Monoolein	6.0	−	−	+2.4	+2.9	>30	>30
	1.5	+	+++	+7.0	—	22	26
Monolinolein	6.0	+++	+++	—	—	26	24
	1.5	+++	+++	—	—	22	17
Monolinolenin	20.0	−	−	−6.8	−3.6	28	25
	5.0	+	+++	+6.0	+3.1	>30	>30
Monopalmitin	10.0	+	+	+4.7	+5.0	18	21
	2.5	−	−	+2.8	+1.6	>30	>30
Monomyristin	10.0	+	+	+4.2	+2.5	18	24
	2.5	−	+++	+5.3	+7.5	18	15
Monolaurin	10.0	−	−	+2.1	+0.5	28	>30
	2.5	−	−	+3.7	+4.4	27	24
Monocaprin	20.0	—	—	—	—	3	1
	5.0	−	+	+0.6	+1.9	28	22
Monocaproin	10.0	−	+++	+2.0	+5.2	18	11
	2.5	+++	+++	+7.5	+7.3	18	15
Control	0.0	+++	+++	+8.8	+9.2	15	16
		+++	+++	+9.5	+6.4	13	17

The method of the assay is described in the text. Two mice were used for each dose in this experiment. The degree of the tumor growth is as follows: +++ marked growth, ++ moderate growth, + slight growth, − no growth.

liquid chromatography using a poly butanediol succinate column. The results indicated that all of the samples were 70~90 % pure for fatty acid components.

Antitumor activity *in vivo* was assayed using EHRLICH ascites tumor in mice. The ascitic tumor cells of EHRLICH carcinoma (2×10^6 cells) were implanted intraperitoneally in *ddY* mice, 5 weeks old, weighing 18 to 22 g. Saline solution of the samples was administered once daily for 5 successive days and the tumor growth and body weight gain after 7 days and life span were observed.

Antitumor activity of nine monoglycerides is shown in Table 1. When the tumor growth after 7 days was compared with that of the control mice, stearic, linoleic and caproic monoglycerides were thoroughly ineffective, whereas linolenic, oleic, palmitic, myristic and capric glycerides were somewhat effective and monolaurin completely inhibited the tumor growth at two doses tested. Most of the treated animals showed prolongation of the survival periond while control mice were observed to die within 17 days. In the cases of monolinolenin, monoolein and monopalmitin some of the mice survived more than 30 days but their tumor cure was not complete. On the other hand, monomyristin- and monolaurin-treated mice exhibited complete cure though their survival periods were more or less short. Thus, monoglycerides with carbon numbers between 12 and 16 were active against EHRLICH ascites tumors in mice. Moreover some of the unsaturated monoglycerides with 18 carbon atoms in their fatty acids, namely monoolein and monolinolenin, were also active *in vivo*.

When the antitumor activity of sucrose esters of linoleic, palmitic, myristic, lauric and capric acids was examined, palmitic, myristic and lauric esters exerted remarkable inhibition of the tumor growth with prolongation of the survival time. In the case of propylene glycol esters, oleic, palmitic and myristic esters were examined and myristic ester showed a complete cure with prolonged survival time. All of the methyl esters and sorbitol esters tested were inactive against the tumor except methyl laurate which exerted an inhibitory activity against the tumor.

The details of this study will be reported elsewhere.

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