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Antihepatotoxic Principles of *Swertia japonica* Herbs[1)]

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The constituents of *Swertia japonica* herbs have been assessed for antihepatotoxic activity employing carbon tetrachloride- and galactosamine-induced cytotoxicity in primary cultured rat hepatocytes.

Keywords——*Swertia japonica*; Gentianaceae; terpenoids; flavonoids; xanthones; carbon tetrachloride-induced cytotoxicity; galactosamine-induced cytotoxicity; primary cultured rat hepatocytes; antihepatotoxic activity

The crude drug "senburi," the whole plants of *Swertia japonica* Makino (Gentianaceae), is an important bitter stomachic in Japan. In China, a plant of the same genus, *S. mileensis* Hee et Shi (*S. yunnanensis* Burkill), is claimed to be especially efficacious for hepatitis induced by virus.[2,3)] Hence we carried out screening of extracts of *S. japonica* herbs and found that they exhibited intense antihepatotoxic activity in galactosamine (GalN)-induced cytotoxicity utilizing primary cultured rat hepatocytes (Table I).

The main constituents of this drug were thus examined and the results are demonstrated in Table I.

It is worthy to note that out of active constituents tested, the iridoid, amarogentin, the flavonoids, swertiajaponin, swertisin and homoorientin, and the xanthones, bellidifolin, methylbellidifolin and methylswertianin, exerted more prominent antihepatotoxic activity in GalN-induced cytotoxicity, while the triterpenoid, oleanolic acid, mediated more significant antihepatotoxic activity in carbon tetrachloride (CCl_4)-induced cytotoxicity as in the previous report.[4)]

It is interesting to note that although the iridoid, swertiamarin, showed no significant antihepatotoxic activity, its acetylation to swertiamarin acetate remarkably potentiated the activity.

We have previously observed that flavonoid glycosides exhibit stronger antihepatotoxic activity in GalN-induced cytotoxicity than in CCl_4-induced cytotoxicity,[5)] as is the case in the present work.

Oleanolic acid has been shown to have an antihepatotoxic action by *in vivo* experiments and also reported to be effective for the treatment of hepatitis.[3)]

It is concluded that all these constituents contribute to antihepatotoxic activity of the extracts.

Experimental

Materials——The constituents were isolated from the whole plants of *Swertia japonica*.[6)]

Assay for antihepatotoxic activity——The substances were evaluated by means of CCl_4- and GalN-induced cytotoxicity in primary cultured rat hepatocytes.[7,8)]

References and Notes

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TABLE I. Effect of Extracts and Constituents of *Swertia japonica* on Carbon Tetrachloride- and Galactosamine-induced Cytotoxicity in Primary Cultured Rat Hepatocytes

Substance	Dose (mg/ml)	GPT (%)	
		CCl_4	GalN
Control	—	100±2	100±2
Hot water ext.	1.0	76±3*	27±3**
50% EtOH ext.	1.0	74±1**	38±1**
95% EtOH ext.	1.0	89±3	19±1**
Amarogentin	0.01	97±1	101±5
	0.1	96±1	108±1
	1.0	90±2	31±1**
Amaroswerin	0.01	98±1	87±2
	0.1	98±3	95±1
	1.0	83±1*	75±6
Swertiamarin	0.01	94±3	100±1
	0.1	96±2	104±2
	1.0	100±1	93±2
Swertiamarin acetate	0.01	90±3	96±3
	0.1	96±2	76±3*
	1.0	86±2*	65±1**
Homoorientin	0.01	101±1	98±3
	0.1	91±3	76±3*
	1.0	76±3*	77±4*
Swertiajaponin	0.01	97±2	94±2
	0.1	96±2	37±3**
	1.0	70±2**	29±1**
Swertisin	0.01	94±1	97±3
	0.1	78±2*	100±3
	1.0	61±3**	41±3**
Bellidifolin	0.01	97±2	82±1**
	0.1	97±1	41±2**
	1.0	96±2	49±1**
Methylbellidifolin	0.01	94±3	73±3*
	0.1	92±1	41±2**
	1.0	90±3	34±0**
Methylswertianin	0.01	101±3	88±1*
	0.1	99±1	77±4*
	1.0	93±3	67±1**
Oleanolic acid	0.01	91±1	98±3
	0.1	86±1*	76±0**
	1.0	28±2**	115±2†

Control GPT values, CCl_4: 320±7 IU/*l* and GalN: 128±3 IU/*l*.
$n=3$ (dishes). Significantly different from the control, effective $p<0.01$* or $p<0.001$**, toxic $p<0.01$†.

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