

EFFECTS OF DIETARY *MICROMELUM MINUTUM* LEAVES ON THE METABOLIZING ENZYMES AND *IN VITRO* METABOLIC ACTIVATION OF CHEMICAL CARCINOGENS IN RATS

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The susceptibility of biological systems to chemical carcinogenesis is partly controlled by the balance between phase I enzyme systems (cytochrome P450[P450]-dependent mono-oxygenases) and phase II enzymes (i.e. glutathione-S-transferase [GST], UDP-glucuronyltransferase(UGT) and NAD(P)H:quinone reductase [QR]. Various kinds of fruits and green and yellow vegetables, particularly cruciferous vegetables, have been shown to decrease the risk of various types of cancers in humans as well as in experimental animals exposed to some chemical carcinogens. These vegetables also induced phase II detoxification enzymes such as GST and QR. Thus, it is suggested that the protective effects elicited by those vegetables and chemical compounds may be a result of the modulation of carcinogen metabolism especially the induction of phase II detoxification enzymes.

In this report we have evaluated the effect of dietary *Micromelum minutum* leaves that are commonly eaten among Southern Thai people, on the activities of metabolizing enzymes in rat liver. Male Wistar rats were fed AIN-76 semipurified diet or diet containing 5% ground lyophilized *Micromelum minutum* leaves for 2 weeks before sacrifice. Hepatic S9 fractions were prepared and assayed for the level of cytochrome P450 (CYP), i.e. total CYP, erythromycin N-demethylase (ED), p- nitrophenol hydroxylase (NH) as well as the capacity to metabolically activate the mutagenicities of aflatoxin B1 (AFB1), benzo(a)pyrene (B(a)P) and 2-Amino-3-methylimidazo[4,5-f]quinoline (IQ). In addition, the activities of detoxifying enzymes such as glutathione-S-transferase(GST), UDP-glucuronyltransferase(UGT) and NADPH-quinone reductase (QR) were also determined.

It was found that feeding of *Micromelum minutum* leaves significantly induced the activities of hepatic ED as well as the capacity to activate the mutagenicity of BP and IQ towards *Salmonella typhimurium* TA100 and TA98, being 124, 203 and 183 per cent of control group, respectively. It did not change the capacity to activate the mutagenicity of AFB1 towards a *S. typhimurium* TA100. On the other hand, however, the activities of phase II detoxification enzymes, GST, UGT and QR were markedly

Table 3. Effects of dietary Siamese cassia leaves on the activities of phase I and phase II metabolizing enzymes in the rat liver

Hepatic Enzyme	Diet group			P value
	Control	5% Mui	fold control	
Phase I enzymes				
1. Total CYP (nmol/mg protein)	0.065 ± 0.007	0.039 ± 0.005*	0.60	0.015
2. CYP 3A4 (nmol p-aminophenol formed/min/mg protein)	1.008 ± 0.076	1.246 ± 0.082*	1.24	0.019
3. CYP 2E1 (nmol formaldehyde formed/min/mg protein)	0.030 ± 0.003	0.028 ± 0.003	0.93	0.912
4. Capacity of S9 fraction to activate the mutagenicity of				
4.1 AFB ₁ (0.03 mg) ^a	837.16 ± 123.07	724.35 ± 93.44	0.87	0.644
4.2 BP (25 mg) ^a	129.80 ± 24.91	263.82 ± 20.64*	2.03	<0.001
4.3 IQ (10 ng) ^b	96.56 ± 8.28	825.68 ± 86.05*	8.55	<0.001
4.4 IQ (1.5 ng) ^b	34.61 ± 3.54	63.23 ± 3.76*	1.83	<0.001
Phase II enzymes				
1. GST (nmol CDNB-glutathione conjugated formed/min/mg protein)	0.378 ± 0.052	0.724 ± 0.046*	1.92	<0.001
2. UGT (nmol p-nitrophenol disappeared/min/mg protein)	0.030 ± 0.002	0.057 ± 0.004*	1.94	<0.001
3. QR (umol/min/mg protein)	0.365 ± 0.033	0.883 ± 0.057*	2.42	<0.001
Values are means ± SE from 10 animals in each group				
^a No. of his ⁺ TA100 revertants/plate				
^b No. of his ⁺ TA98 revertants/plate				
[*] Significantly different from control group				

increased in those animals, being 192, 194 and 220 per cent of control animals.

The results in the present study therefore demonstrated that *Micromelum minutum* leaves possess phase II enzyme inducing property as well as the ability to reduce some phase I enzyme activities in rat liver. Although this Thai vegetable capable of preventing cancer potential by inducing phase II detoxification enzymes, however, its activity to activate chemical carcinogenesis should be concerned.