

P12 SCREENING FOR NATURALLY OCCURRING INHIBITORS OF ARYLAMINE N-ACETYLTRANSFERASE 1 ACTIVITY

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ABSTRACT

Most chemical carcinogens are not active in their original forms but required bioactivation to highly reactive metabolites. The phase I and phase II enzymes play important role in carcinogen activation. Arylamine N-acetyltransferases (NATs) are phase II enzymes existed as two isoforms, NAT1 and NAT2. NAT enzymes catalyse the biotransformation of many primary amines, hydrazines and their N-hydroxylated metabolites, thereby play role in both the detoxification and metabolic activation of numerous xenobiotics. Chemoprotection strategies against cancers usually include the inhibition of various steps in metabolic activation. There were many reports demonstrated that flavonoid had tumor prevention effect. In this study, the chemopreventive agents of interest were focused primarily on some abundant natural products which are found in fruits, vegetables, and teas as part of normal human diets. The chemical classes employed in this study include polyphenol of small molecules i.e. caffeic acid and ferulic acid; flavonoids i.e. quercetin, genistein, silymarin, tea catechin and coumarins. Some nonsteroidal anti-inflammatory drugs which were previously reported possessing NAT1 inhibition activity such as aspirin, paracetamol and diclofenac were also included. This study was aimed to screen the inhibitory action of these compounds *in vitro* on NAT1, since NAT1 enzyme is expressed widely in the body. The sources of enzymes were from human extra-hepatic bile duct carcinoma cell line (KMBC) and surgical liver specimens from cholangiocarcinoma patients. NAT1 activity was determined by using para-aminobenzoic acid (PABA) as a test substrate and was analysed by the high performance liquid chromatography method. This study showed that caffeic acid, (-)epigallocatechin gallate, quercetin and taxifolin showed strong NAT1 inhibition activity, whereas, tyramine and tryptamine, the substrates of alkylarylamine N-acetyltransferase had only slightly inhibitory effects. This study suggest that natural products with potent NAT inhibitory activity may be useful in cancer chemoprevention.

Key words : N-acetyltransferase; polyphenol; flavonoids; chemoprophelaxis

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