

論文の要約

報告番号	甲 乙 栄第223号	氏名	Bandaruk Yauhen
		Evaluation of the Inhibitory Effects of Quercetin-Related Flavonoids and Tea Catechins on the Monoamine Oxidase-A Reaction in Mouse Brain Mitochondria (マウス脳ミトコンドリアにおけるモノアミンオキシダーゼA反応へのケルセチン関連フラボノイドと茶カテキンの阻害作用の評価)	
<p>Monoamine oxidase-A (MAO-A) plays a crucial role in the metabolism of neurotransmitter serotonin (5-hydroxytryptamine, 5-HT) in the brain. Elevated activity of MAO-A leads to depletion of serotonin in the brain, therefore it is considered to contribute to the pathogenesis of depression.</p> <p>Antidepressant-like activity was shown for many naturally occurring polyphenolic compounds such as flavonol quercetin. Although exact mechanisms of antidepressant-like activity of flavonoids remain unclear, MAO-A is considered as a possible target of their action. Metabolites of flavonoids may penetrate the blood brain barrier and accumulate in the brain. Therefore, it is possible the direct interaction with MAO-A. Inhibitory activity of flavonoids including quercetin on MAO-A was shown.</p> <p>This study aimed to clarify the relationship between structure of some groups of food flavonoids and their MAO-A's inhibitory activity, that could promote the understanding of the contribution of inhibition of MAO-A to antidepressant-like action of flavonoids.</p> <p>MAO-A inhibitory activity of flavonol quercetin and its methylated derivative isorhamnetin (3'-O-methyl quercetin) and tamarixetin (4'-O-methyl quercetin), flavone luteolin, green tea catechins (-)-epicatechin, (-)-epicatechin gallate, (-)-epigallocatechin and (-)-epigallocatechin gallate was evaluated by measuring of 5-hydroxyindole acetaldehyde (5-HIAL) formation during reaction of oxidative deamination of serotonin by MAO-A in isolated mitochondrial fraction obtained from mouse brain. Luteolin and quercetin showed the highest MAO-A inhibitory activity with calculated IC₅₀ (half maximal inhibitory concentration) about 2 μM and 42 μM respectively, whereas their O-methylated derivatives isorhamnetin, tamarixetin and group of catechins exerted weak or didn't exert any inhibitory action on MAO-A activity. Flavone which possesses flat structure of three rings was a strong MAO-A's inhibitor while flavanone which does not possess the flat structure showed very weak activity. Therefore flat structure of three rings, lack of 3-OH-group in the ring C and nonmethylated catechol group in the ring B in the structure of flavonoids seems to be required for exerting the inhibitory effect on MAO-reaction.</p> <p>Analysis of Lineweaver-Burk plot indicated that the inhibition of MAO-A by flavonoids is noncompetitive. Therefore we concluded that flavonoids are bound to MAO-A enzyme molecule at the site different from active center.</p> <p>Quercetin showed a strong inhibitory effect on MAO-A in mitochondrial fraction obtained from mouse brain in contrast to that of small intestine, while MAO-A inhibitor clorgyline showed stronger effect in small intestine. MAO-A in small intestine plays an important role in the detoxification of potentially toxic amines and its inhibition by strong therapeutic inhibitors may cause undesirable side effects. On the other hand, quercetin is a mild MAO-A inhibitor preferably affecting MAO-A in the brain. In other words, quercetin has a potential as mild safe antidepressant compound.</p>			