Neuroprotective Effects of Five Melatonin Derivatives
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Introduction: Alzheimer disease (AD) is a progressive degenerative disorder characterized by the presence of amyloid deposits, neurofibrillary tangles and neuronal loss. Emerging evidence indicates that antioxidants could be useful either for the prevention or treatment of AD. Several studies showed that melatonin may play an important role in AD as an antioxidant and neuroprotector. Recently, five melatonin derivatives including melatonin, melatonin acetate, nitro-melatonin, naphthoyl melatonin and benzoyl melatonin were developed. Thus, the aim of our study was to investigate the effects of these five melatonin derivatives on neuroprotective activity and on the improvement of cognitive impairment induced by scopomeline in mice. Materials and Method: The five melatonin derivatives were screened for their antioxidant activity through the in vitro ABTS method. The protective effect against hydrogen peroxide- or beta amyloid-induced neuronal cell damage was also investigated by MTT assay in neuroblastoma cell (NG108-15) and astroglialoma cell (C6), respectively. For investigation of their mechanism, western blotting analysis was performed to assess protein expression. Moreover, the effect of melatonin acetate on the improvement of memory deficit in mice was evaluated by 3 behavioral models including Morris water maze, Y-maze and object recognition test. Results: The results exhibited that all five derivatives showed an ability to scavenge ABTS radical with IC50 values ranging from 28.11 to 62.67 μM. Naphthoyl melatonin possessed the highest potency with IC50 value of 28.11 ± 2.61 μM. For the neuroprotection, melatonin, melatonin acetate and nitro-melatonin exhibited protective effect against both hydrogen peroxide- and beta-amyloid-induced cell damage. The result from western blotting analysis indicated that melatonin acetate inhibited beta-amyloid-induced cell death by inhibiting AKT phosphorylation and cleavage of Parp-1 and Caspase-3. Moreover, melatonin acetate, the highest potency for neuroprotection, exhibited an ability to improve both short-term and long-term memory deficit in mice induced by scopomeline. Conclusion: All results indicated that melatonin derivatives could be a promising candidate for treatment of Alzheimer’s disease.

Keywords: Melatonin derivatives, Neuroprotection, Antioxidant, Signaling pathway, Behavioral test, Alzheimer

Effect of Thai sour Fruits on the Expression of Hepatic Cytochrome P450 in Mouse Livers
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Introduction: Hepatic cytochrome P450 enzyme (CYPs) is the superfamily of metabolizing enzyme response to xenobiotics or drug metabolism, leading to more polar metabolites and more excretion. Poly-medicine or receiving several drugs can inhibit or induce some isoform of CYPs and cause drug interactions. Beside drugs and xenobiotics, daily food or supplements might affect the expression of CYPs. In the present study, the effects of eight sour Thai fruits juice namely common lime, star fruit, Burmese grape, Southern langsat, salak, Thanathon orange, special honey orange, and pomell on the activities of hepatic CYPs were determined. Materials and Method: The effects of eight sour Thai fruits juice namely common lime, starfruit, Burmese grape, Southern langsat, salak, Thanathon orange, special honey orange, and pomell on the activities of hepatic CYPs were examined in vitro (in mouse hepaticmicrosomes), in which ethoxyresorufinO-deethylase (EROD), methoxyresorufinO-demethylase (MROD), benzyloxyresorufinO-dealkylase (BROD), pentoxysresorufinO-dealkylase (BROD/PROD), and erythromycin N-demethylase (ENMD) activities are the specific markers for CYP1A1, CYP1A2, CYP2B9/CYP2B10, and CYP3A respectively. Results: The median inhibitory concentrations (IC50) of eight sour Thai fruits juice on CYPs activities were reported. All of eight sour Thai fruits juice inhibited the activities of CYP1A1, CYP1A2, CYP2B9/CYP2B10, and CYP3A enzymes via inhibitions of EROD, MROD, BROD/PROD, and ENMD reactions, respectively. Moreover, Burmese grape possessed the highest potency on inhibition of several CYPs isoforms. Conclusion: The observations suggested that consumptions of these eight sour Thai fruit juice, especially Burmese grape, might be concerned in the term of food-drug interaction, especially consumption for a long time and the large amount.

Keywords: Thai fruit, Burmese grape, cytochrome P450

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