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Short Communication

A taurine phenolic compound (TPC) protect from AAP hepatotoxicity through involvement of Nrf2/ARE pathway

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Oxidative stress is a main contributor to the hepatotoxic effects of acetaminophen, the Nrf2/ARE pathway has been characterized as an important endogenous mechanism for combating oxidative stress. Taurine plays various important roles in a large number of physiological and pathological conditions in human body, such as the antioxidant, anti-inflammatory effects. It proves that phenol compound has antioxidant effect through involvement of Nrf2/ARE pathway. The taurine phenolic compound (TPC) we synthesized belongs to phenolic compounds and we have reported that a TPC protect from AAP hepatotoxicity. We thus hypothesize the protective effects of TPC in an acute chemical model of acetaminophen-induced hepatotoxicity through involvement of Nrf2/ARE pathway.

Key words: TPC, AAp, hepatotoxicity, Nrf2/ARE and hypothesis.

INTRODUCTION

Acetaminophen (AAP) is a widely used analgesic and antipyretic, which is safely employed in the therapeutic range in man and animals. However, an overdose of AAP can induce severe hepatotoxicity. Oxidative stress is a main contributor to the hepatotoxic effects of acetaminophen (Knight et al., 2001). Nuclear factor-erythroid 2-related factor 2 (Nrf2) is a transcription factor that induces the expression of various cytoprotective enzymes possessing an antioxidant response element (ARE) in the promoter region (Scott et al., 2008). Taurine (2-aminoethane sulfonic acid), an essential non protein amino acid, is found in almost all tissues in mammals. Taurine plays various important physiological and pathological roles in each organ, Such as membrane stabilisation, osmoregulation, eliminating the negative effects of oxygen free radicals, anti-lipid peroxide and anti-apoptosis activities. Taurine exhibits an antioxidative effect and is also known to have effects on cell proliferation, inflammation and collagenogenesis. It proves that phenolic compound has antioxidant effect through involvement of Nrf2/ARE pathway (Tanigawa et al., 2007; Chandra Mohan et al., 2005; Chen et al., 2000) The TPC we synthesized belongs to phenol compounds and we have reported that a TPC can protect from AAP hepatotoxicity (Diao et al., 2009; Yun et al., 2009; kun et al., 2010).

Despite both taurine and phenolic compounds have antioxidative effect, but the reports on the effect of TPC are very sparse.

THE HYPOTHESIS

We thus hypothesize that TPC would be a new therapeutic candidate for hepatotoxicity through involvement of Nrf2/ARE pathway just like phenolic compounds. We name the new organic compound taurine phenolic compound (TPC).

SYNTHESIS METHOD OF TAURINE PHENOLIC COMPOUND

The phenolic compound such as Salicylaldehyde was added to a

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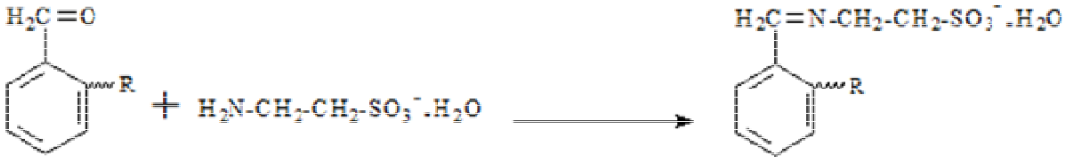

Figure 1. Synthetic schemes of taurine phenolic compound (TPC).

mixture of taurine and KOH in a mixed solvent of methanol and water. The mixture was stirred for 5 h at 40°C. The resulting yellow solution was filtered and the yellow single crystals of this compound were obtained by slow evaporation at room temperature (Figure 1).

DISCUSSION

Over the past decade, AAP hepatotoxicity is related to excessive oxidative stress mainly caused by the electrophile and highly reactive metabolite of N-acetyl-p-benzoquinone imine (NAPQI). The oxidative stress produced by high doses of NAPQI has also been demonstrated to affect the antioxidant system (Bessems, et al., 2001). Recent reports have indicated that the Nrf2/ARE pathway has been characterized as an important endogenous mechanism for combating oxidative stress. Nrf2 activation and subsequent cytoprotective gene induction promotes the restoration of the balance between oxidants and antioxidants after oxidative insult (Aleksunes et al., 2008). It proves that phenolic compound has antioxidant effect through involvement of Nrf2/ARE pathway and the TPC we synthesized belongs to phenolic compounds and we have reported that a TPC protect from AAP hepatotoxicity. As a result, we calculate the AAP hepatotoxicity of TPC connects with involvement of Nrf2/ARE pathway.

RESULTS

The above evidence suggests that TPC may have a potent therapeutic effect to protect from AAP hepatotoxicity through anti-oxidative effect of involvement of Nrf2/ARE pathway. In other words, TPC facilitated Nrf2 translocation to the nucleus, which correlated with increased Nrf2 binding to consensus ARE, and strongly suggesting the induction of cytoprotective genes and subsequent hepatoprotective effects of TPC are Nrf2 dependent. In a word, appropriate use of TPC could be an effective and favorable treatment candidate for AAP hepatotoxicity (Dinkova et al., 2002; Zhang et al., 2003).

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