CURCUMIN BENEFITS AS ANTIOXIDANT, ANTIINFLAMMATION AND ANTIAPOTOTIC AMELIORATE PARACETAMOL TOXICITY

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Received: 07 December 2017, Revised and Accepted: 28 August 2018

BACKGROUND

Paracetamol poisoning due to the use of paracetamol overdose is the most prevalent case of poisoning. Toxic metabolites from paracetamol cause glutathione depletion and lead to hepatic cell death. Curcumin, a polyphenol substrate in Curcuma longa, has been known to ameliorate the toxic effects of paracetamol. The mechanisms have been known are curcumin as antioxidant, anti-inflammatory, and anti-apoptotic. The curcumin protection mechanism against paracetamol poisoning will be discussed.

METHODS: The journal’s search for the protective effects of curcumin on paracetamol toxicity is derived from PubMed database using keyword curcumin and acetaminophen. Research on experimental animals is as the limits of the study subjects of the journal search.

RESULT: From a search in PubMed database, there are 15 journal titles discussing the effects of curcumin protection against paracetamol toxicity, and 11 journals selected that correspond to the research topic. Of the 11 journals selected, concluded that curcumin was found to prevent worsening of paracetamol toxicity by increasing antioxidant activity and decreasing inflammation and apoptotic.

Conclusion: Curcumin has the potential benefit to be used as a medical therapeutic for the prevention and treatment of paracetamol toxicity.

Keywords: Curcumin, Paracetamol, Antioxidants, Anti-inflammatory, Anti-apoptotic.

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BACKGROUND

Paracetamol or acetaminophen is also known as N-acetyl p-aminophenol has been used as an antipyretic and analgesic for more than 30 years. Paracetamol poisoning is the largest poisoning case according to the American Association of Poison Control Centers causes 140,000 cases of poisoning and approximately 100 mortalities in the year 2006 [1]. At therapeutic dose, paracetamol will be metabolized in the liver through a process of glucuronidation and sulfation and excreted from the cell, a small part will be metabolized by Cytochrome P450 especially CYP2E1 to N-acetyl-p-benzoquinoneimine (NAPQI) toxic product. NAPQI will be rapidly detoxified by glutathione (GSH) and removed from the cell. An overdose of paracetamol may cause hepatic dysfunction, necrosis of hepatic cells, and hepatic organ injury [2]. GSH depletion due to the NAPQI detoxification process will occur rapidly [2-4], so that the free NAPQI will bind to intracellular proteins and lipids as well as intranuclear deoxyribonucleic acid, through covalent bonding, causing mitochondrial dysfunction, lipid peroxidation, oxidative stress, DNA fragmentation, leading to liver cell death, liver organ damage, and ending with death [2,3].

N-acetyl cysteine has been used as a paracetamol poisoning antidote, has a narrow therapeutic dose range and side effects, so an alternative therapeutic need is sought. Curcumin (1H, 6E) -1,7-bis-(4-hydroxy-3-methoxyphenyl) -1,6-heptadien-3,5-dione), a polyphenol presents in the roots of the Curcuma longa plant has been used as a treatment traditional for liver disorders that are now known to be caused by oxidative stress. Curcumin has properties as antioxidants, anti-inflammatory, and anti-apoptosis that can improve the toxic effects of paracetamol overdose. This is interesting to discuss further. The review paper will gather several journals to discuss curcumin protection mechanisms in improving paracetamol toxicity.

RESEARCH METHODS

Journal searches on the benefits of curcumin as an antioxidant and anti-inflammatory to reduce the toxic effects of paracetamol derived from the PubMed database using curcumin and acetaminophen as the keywords, no years of limitation, and research on experimental animals as the limits of the study subjects.
Administration of curcumin: Amelioratif hepatic histologic damage; decrease of ALT serum, hepatic MDA, IL-12 and IL-18 serum; and increase of hepatic GSH

Research on four groups of male B6C3F1 mice

Li et al., 2013 [3] Research on three groups of Balb-c male mice

Administration of curcumin: Reduce hepatic histologic damage; decreases of ALT serum and hepatic MDA; increases of hepatic SOD, hepatic Bax gene expression; increases of hepatic Bcl-2 gene expression; and prevent hepatic apoptosis

Research on six groups of male CD1 mice

Granados-Castro et al., 2016 [1] Research on six groups of male CD1 mice

Administration of curcumin protecting hepatic histologic damage; decrease of ALT and AST; prevent decrease in mitochondrial activity of respiratory complex I, III, and IV; and prevent decrease in mitochondrial membrane potential, ATP synthesis, and aconitase activity

Research on Wistar mouse hepatocyte culture

Kheradpezhouh et al., 2016 [6] Research on Wistar mouse hepatocyte culture

Administration of curcumin inhibits TRPM2 channel activation by ADPR

Table 1: Several curcumin protection effects research on paracetamol toxicity

| Author | Method | Result |
|--------|--------|--------|
| Bulku et al., 2012 [5] | Research on four groups of male B6C3F1 mice | Administration of curcumin: Mortality decreased; decrease of ALT serum, lipid peroxidation, and DNA fragmentation; increase of GSH, SOD, NO synthase, decrease of DNA fragmentation, Bax gene expression, caspase 3, cytochrome c, and p53; and increase of Bcl-XL |
| Somanawat et al., 2013 [2] | Research on four groups of male mice | Administration of curcumin: Decrease of AST and ALT serum, hepatic MDA, IL-12 and IL-18 serum; and increase of hepatic GSH |
| Li et al., 2013 [3] | Research on three groups of Balb-c male mice | Administration of curcumin: Reduce hepatic histologic damage; decreases of ALT serum and hepatic MDA; increases of hepatic SOD, hepatic Bax gene expression; increases of hepatic Bcl-2 gene expression; and prevent hepatic apoptosis |
| Soliman et al., 2014 [4] | Research on four groups of male rats Wistar strain | Administration of curcumin: Amelioratif hepatic histologic; decrease of ALT, AST, and urea serum; increased level of hepatic catalase antioxidants; decreased of hepatic MDA, hepatic MMP-8 expression in ihc imaging, increase of hepatic hepatic GSH, GPx, SOD, and catalase gene expression; and decrease of hepatic IL-1β, IL-8, and TNFα gene expression |
| Granados-Castro et al., 2016 [1] | Research on six groups of male CD1 mice | Administration of curcumin protecting hepatic histologic damage; decrease of ALT and AST; prevent decrease in mitochondrial activity of respiratory complex I, III, and IV; and prevent decrease in mitochondrial membrane potential, ATP synthesis, and aconitase activity |
| Kheradpezhouh et al., 2016 [6] | Research on Wistar mouse hepatocyte culture | Administration of curcumin inhibits TRPM2 channel activation by ADPR |

ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, MMP: Mitochondrial membrane potential, GSH: Glutathione; SOD: Superoxide dismutase, NO: Nitric oxide, MDA: Malondialdehyde, IL-12, IL-18, IL-8: Interleukin, MMP-8: Matrix metalloproteinase-8, TRPM2: Transient receptor potential melastatin 2, ADPR: Adenosine diphosphate ribose, TNF-α: Tumor necrosis factor-α
CONCLUSION

The toxic effects of paracetamol overdose are better understood now. Oxidative stress mechanisms and NAPQI covalent bonds with intracytosol and intramicrosome proteins play an important role. Curcumin has antioxidant and anti-inflammatory activity, is expected to be one of the natural ingredients selected for the prevention of paracetamol toxicity in patients receiving long-term and high-dose paracetamol therapy.

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