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Editorial

Open, sesame! The gateway to mitigate hepatic injury using sesamin

The magic phrase "Open, sesame!" from the famous Arabian story, *Ali Baba and the Forty Thieves*, is familiar and popular worldwide, and may have originated from the sudden opening of the sesame capsule to spread seeds. Sesame seeds and their oil have been utilized as an important foodstuff for thousands of years. They are regarded as healthy food and widely used for their distinct taste and flavor.[1]

Sesamin is the most abundant lignan in sesame oil. It is well known for its multiple health benefits, including hypocholesterolemic activity, antihypertensive effect, anticarcinogenic potential, antiaging effect, immunoregulatory activity, hypoglycemic action, antithrombotic activity, and hepatoprotective effect. Among its various biological effects, the antioxidant activity of sesamin occupies a central role, and has been well explored in the past few decades.[1]

Sesamin has been reported to protect against alcohol and chemical-induced liver injury.[1] It is speculated that the mechanism underlying hepatoprotection of sesamin is via suppression of the free radical-mediated process triggered by hepatotoxins.[1] In addition to its antioxidant activity, sesamin has also been demonstrated to work synergistically with vitamin E against lipid peroxidation.[1]

Sesamin itself has little antioxidant effect, but it can be metabolized into several catechol forms in the liver.[2] Sesamin is first metabolized to sesamin monocatechol via cytochrome P450 2C9 in human liver. Sesamin monocatechol can be further metabolized to sesamin dicatechol via cytochrome P450 2C9. These catechol metabolites have been shown to have the potent ability to scavenge superoxide radicals.[2]

Many researchers in Taiwan and Japan investigated the role of sesame oil in the attenuation of hepatic injury. A study by Hsu et al[3] revealed that parenteral sesame oil can ameliorate hepatic oxidative stress after endotoxin intoxication in rats. An additional investigation by Chang et al[4] showed that a mixture of sesamin and schisandrin B can exert a hepatoprotective effect by improving the antioxidative capacity in rats under carbon tetrachloride-induced hepatic oxidative stress. Also, Chandrasekaran et al[5,6] further demonstrated that sesame oil can maintain intracellular glutathione levels, reduce reactive oxygen species levels, and inhibit lipid peroxidation in rats with acetaminophen-induced acute liver injury. In a study that may have important implications for drug interaction and drug safety, Lim et al[7] recently disclosed that sesamin can inhibit cytochrome P450 3A4 (CYP3A4) by antagonizing the pregnane X receptor activation. CYP3A4 is the most abundant cytochrome P450 and has clinical importance because it metabolizes many drugs and endogenous substrates. This study suggests a complementary mechanism by which ingestion of this naturally occurring chemical may decrease the occurrence of adverse drug reactions secondary to pregnane X receptor-mediated induction of drug metabolism via CYP3A4.[7]

Recently, a single-blind, placebo-controlled, parallel-group and multiple oral dose study was conducted in 48 healthy Japanese to investigate the pharmacokinetics and safety of multiple oral doses of sesame lignans (sesamin and episesamin).[8] No serious adverse events were observed in this study. Sesamin was absorbed with a peak plasma concentration at 5 hours. The plasma concentration of the main metabolite, SC-1, also peaked at 5 hours. Ultimately, sesamin lignans were confirmed to be safe and tolerable in this study. The results of the pharmacokinetic study demonstrate that no accumulation was observed following multiple 50 mg doses daily of sesame lignans.[8]

Although the aforementioned studies cast a spotlight on the hepatoprotective potential of sesamin, little is known about the detailed pathway of hepatoprotective effect by sesamin. In this issue of the *Journal of Chinese Medical Association*, we are happy to find that Chiang et al[9] have shown that sesamin effectively ameliorated lead and lipopolysaccharide-induced acute liver injury in rats by the inhibition of proinflammatory cytokines and nitric oxide. They further pointed out that the inhibition of liver injury is through the suppression of several signaling pathways, such as c-Jun N-terminal kinase, p38 mitogen-activated protein kinase, cyclooxygenase-2, inducible nitric oxide synthase, and growth arrest DNA damage 45β. It seems that sesamin can mitigate the hepatic injury through these gateways, which echoes the magic phrase "Open, sesame!" The result of this study is crucial in the elucidation of the underlying mechanism of sesamin in hepatoprotection.[9] However, the authors found that the effect of sesamin was through the suppression of several signaling pathways. The interaction and real role of these pathways in relation to the effect of sesamin are unknown. Further studies are warranted to reveal the major pathway and the interaction of these pathways. Of note, the authors used a lead coupled with lipopolysaccharide overload model to induce liver injury in

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this study. This hepatotoxicity model may be different from the previous studies, in which acetaminophen, carbon tetrachloride, or only lipopolysaccharide was used to induce liver injury. Whether sesamin has similar hepatoprotective effect in rats challenged by different hepatotoxins is unknown. Interpretation of the data and exploration of the results of this study should be undertaken prudently.

Healthy and safe utilization of cooking oil is always a challenge worldwide. Sesame seeds and their oil have been used in human diets for thousands of years globally, especially in Asia.[1] There have been an abundance of studies to verify their health benefits.[1,2] Sesamin, as the major lignan of sesame, has a potentially hepatoprotective effect via its antioxidative property. Hepatotoxicity is always a major concern in the premarketing drug development, and postmarketing safety surveillance in drugs and food. Although many efforts have been enforced to ameliorate the hepatic injury by health authorities and members of the pharmacy industries, hepatic injury by drugs, food, and other chemicals have still occurred unrelentingly.[10] Under this circumstance, a hepatoprotectant is urgently needed. The mechanistic exploration of hepatoprotectants, such as the sesamin study in this issue, is welcomed in this field. This kind of approach may help us realize the pathogenesis of liver injury, and consolidate our confidence to utilize sesamin and other hepatoprotectants properly.

Conflicts of interest

The author declares that there are no conflicts of interest related to the subject matter or materials discussed in this article.

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