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# Letter to the Editor

## Mediation of inflammation, obesity and fatty liver disease by advanced glycation endoproducts

*Dear Editor,*

We read with great interest the article by Xiong et al[1] regarding the critical role of advanced glycosylation end products (AGEs) in liver diseases. It is known that hepatic steatosis is one of the most important risk factors for liver diseases. The oxidative hepatocellular damaging, the inflammation fat accumulation, and the non-alcoholic steatohepatitis are circumstances that may progress towards liver cirrhosis and HCC[2]. Moreover, in patients with these conditions, frequent co-morbidity, as cardio-renal-metabolic conditions, may increase hepatic/extrahepatic cancer risk[3].

In their study, Xiong et al[1] examined sixty Sprague Dawley rats, randomly divided into 3 groups including control, obesity fatty liver model and AGESs inhibitor groups (n=20 each). They found in model rats higher levels of AGEs, higher total cholesterol, triglyceride, low-density lipoprotein, and high-density lipoprotein. Hematoxylin-eosin (HE) detected the pathological changes of liver; Real-time PCR and enzyme-linked immunosorbent assay (ELISA) showed how inflammatory cytokine levels, including tumor necrosis factor (TNF)-$\alpha$ and interleukin (IL)-6 were increased in model group. The application of AGEs inhibitor amino-guanidine significantly improved liver functions and lower TNF-$\alpha$ or IL-6 levels. Moreover, other studies evaluated the concentrations of the major AGEs in cirrhotic patients. *In vivo* and *in vitro*, some researchers found increased AGEs values, and alteration gene expression that caused adverse effects in hepatocytes[4,5].

Other authors also studied the important effects of antioxidant agents and complementary and alternative medicines (CAM)(2) in patients with non-alcoholic fatty liver disease, HCC and HIV[6], in HCV- HBV-positive patients[7,8]. In some pilot studies, patients treated with Sylimarin plus vitamin E, N-acetyl cysteine and selenium, in association with hypo-caloric diet and exercise for three months, showed ameliorated hepatic functions. These studies also marked the importance of a genetic testing for the detection of individual metabolic profile, to prevent fibrosis-related grade ≥ 3 toxicity and to preserve treatment compliance[9].

In the last years, the identification of cellular pathways playing a key role in the pathogenesis of HCC, primarily neo-angiogenesis with the overexpression of VEGFR and FGFR, has led to development of new targeted drugs to be used in association with standard therapies[10].

Accumulation of AGEs also promotes triple negative breast cancer cells. AGEs enhanced the proliferation, tumorigenicity, invasion and migration of primary breast cancer cells. They directly promote primary breast cancer cells via ERK and NF-KB pathway, which may lead to advanced therapies[11].

### Conclusions

We believe that the AGEs inhibition could improve the obesity fatty liver, but many other complex mechanisms are involved in the pathogenesis of the fatty liver disease.

**Abbreviations**

AGEs = Advanced glycosylation end products; ELISA = Enzyme-linked immunosorbent assay; TNF = Tumor necrosis factor; IL = Interleukin; CAM = Complementary and alternative medicines.



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**Conflict of Interest**
The Authors declare that they have no conflict of interests.

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