Hepatocellular carcinoma (HCC) is a major health problem, with more than 500,000 cases diagnosed annually. It is also an important cause of human mortality in the world. The incidence of HCC is rising due to the widespread of hepatitis and alcoholism, which may be caused by infection, injury, exposure to drugs or toxic compounds, autoimmunity, or genetic defect that leads to the deposition of harmful substances.[1]

In the broadest sense, natural products (NPs) are chemical compounds or substances produced by a living organism found in nature.[2,3] Consequently, NPs can be extracted from animals, plants, microbes, and marine organisms.[4,5] NPs can be considered as a coin with two sides, which have to be considered in the application in modern or alternative medicine. Some NPs have beneficial effects while some others have toxic effects. For example, mycotoxins and some other microbial toxins are carcinogenic, and the International Agency for Research on Cancer classified several mycotoxins as hepatocarcinogenic.[6] Exposure to some mycotoxins resulted in liver cancer,[7-10] especially aflatoxin B₁, which is a mutagenic natural compound that contaminates many food sources in some parts of Africa and Asia and is recognized as hepatocarcinogens in humans and many animal species.[7,11]

The use of herbal medicines can be traced back several thousand years ago in ancient China, ancient Egypt and ancient Roma. Recent research pointed out an increasing interest concerning the health benefits of a diet rich in NPs.[12] NPs can act as chemoprotective agents against common liver diseases, such as hepatitis, cirrhosis, liver cancer, fatty liver diseases, and gallstones.[1]

In general, NPs play a key role in drug discovery and are also a prolific source of novel lead compounds or pharmacophores for medicinal chemistry. Although naturally active substances are usually good lead compounds, most of them can hardly satisfy the demands for druggability. Hence, these structural phenotypes have to be modified and optimized to overcome existing deficiencies and shortcomings.[13]

Although HCC is always hard to treat, this special issue aims to gather updated progress in this important area and shed the light on the possibility to introduce a new drug based on the benefit of NPs.

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**REFERENCES**