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Dandelion polysaccharides exert anticancer effect on Hepatocellular carcinoma by inhibiting PI3K/AKT/mTOR pathway and enhancing immune response

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ABSTRACT

Dandelion polysaccharides (DP) have been reported to possess anticancer activity. In this study, we showed that DP significantly inhibited Hepatocellular carcinoma (HCC) cell proliferation *in vitro* and *in vivo* and induced cell apoptosis and arrested cell cycle at the G0/G1 phase. Moreover, RNA sequencing data revealed that DP dampened PI3K-AKT signaling pathway. Western blot results confirmed that DP treatment negatively regulated the levels of p-PI3K, p-AKT, and p-mTOR in HCC cells, suggesting that DP inhibited PI3K/AKT/mTOR pathway. Furthermore, immunophenotyping experiments showed that DP significantly improved the spleen index, spleen germinal center reaction and modulated T cell activation *in vivo*, which could contribute to the inhibition of tumor growth in animals. In addition, *in vivo* studies demonstrated that 400 mg/kg DP treatment was well-tolerated by mouse without any adverse systemic toxicological changes. In summary, we propose that DP might be a potential drug candidate for the treatment of HCC.

1. Introduction

Hepatocellular carcinoma (HCC) is the sixth most common cancers and the third leading cause of cancer-related death worldwide, which threatens human health seriously (Jemal et al., 2011). Current approaches for HCC therapy include surgical resection, chemotherapy and liver transplantation. At present, surgery is still the first choice for the treatment of HCC, but only for the radical resection of lesions or focal lesions at the early and middle stages of HCC. As HCC patients are often diagnosed at an advanced stage when surgical therapies are no longer feasible, chemotherapy is still one of the essential means in the treatment of HCC (Hiraoka et al., 2015). However chemotherapy exhibits low efficacy, severe toxic side effects, and resistant to traditional chemotherapeutics, which limit the clinical application of the chemotherapy to some extent (Hiraoka et al., 2015; Wong et al., 2014). To this end, finding drugs with therapeutic effects and less toxicities for the prevention and treatment of HCC are urgently needed.

Plants are considered as valuable sources of compounds that can be used to treat various complex diseases, including cancer (Newman & Cragg, 2012). According to the World Health Organization (WHO), 60% of the population around the world is accustomed to the fruits, vegetables, herbs, and vitamins to prevent or treat cancer (Gao et al., 2017; Ren et al., 2018). Dandelion, a common weed, can be found in almost every part of the world and is often consumed as a vegetable. In Asian countries including China, dandelion leaves are commonly consumed as salad greens and cooked greens and its roots and leaves are dried and used to make dandelion tea. In Europe, dandelion can normally be ground into powder and used as a substitute for coffee by those who are allergic to caffeine (Sweeney, Vora, Ulbricht, & Basch, 2005). Dandelion has been listed in the Natural Pharmacopoeia of the People's Republic of China and used as a remedy for disorders of the breast, liver and gallbladder as well as hepatitis and digestive diseases.

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