



ELSEVIER

Contents lists available at ScienceDirect

Journal of Ethnopharmacology

journal homepage: www.elsevier.com/locate/jep

Review

Chinese herbal medicine-derived compounds for cancer therapy: A focus on hepatocellular carcinoma

Yangyang Hu^{a,1}, Shengpeng Wang^{a,1}, Xu Wu^b, Jinming Zhang^a, Ruie Chen^a,
Meiwan Chen^{a,*}, Yitao Wang^{a,*}

^a State Key Laboratory of Quality Research in Chinese Medicine, Institute of Chinese Medical Sciences, University of Macau, Macau 999078, China

^b Institute of Chinese Materia Medica, China Academy of Chinese Medical Sciences, Beijing 100700, China

ARTICLE INFO

Article history:

Received 5 March 2013

Received in revised form

23 July 2013

Accepted 24 July 2013

Keywords:

Chinese herbal medicine

Cancer therapy

Hepatocellular carcinoma

Curcumin

ABSTRACT

Ethnopharmacological relevance: Hepatocellular carcinoma (HCC) as the major histological subtype of primary liver cancer remains one of the most common malignancies worldwide. Due to the complicated molecular pathogenesis of HCC, the option for effective systemic treatment is quite limited. There exists a critical need to explore and evaluate possible alternative strategies for effective control of HCC. With a long history of clinical use, Chinese herbal medicine (CHM) is emerging as a noticeable choice for its multi-level, multi-target and coordinated intervention effects against HCC. With the aids of phytochemistry and molecular biological approaches, in the past decades many CHM-derived compounds have been carefully studied through both preclinical and clinical researches and have shown great potential in novel anti-HCC natural product development. The present review aimed at providing the most recent developments on anti-HCC compounds derived from CHM, especially their underlying pharmacological mechanisms.

Materials and methods: A systematic search of anti-HCC compounds from CHM was carried out focusing on literatures published both in English (PubMed, Scopus, Web of Science and Medline) and in Chinese academic databases (Wanfang and CNKI database).

Results: In this review, we tried to give a timely and comprehensive update about the anti-HCC effects and targets of several representative CHM-derived compounds, namely curcumin, resveratrol, silibinin, berberine, quercetin, tanshinone II-A and celastrol. Their mechanisms of anti-HCC behaviors, potential side effects or toxicity and future research directions were discussed.

Conclusion: Herbal compounds derived from CHM are of much significance in devising new drugs and providing unique ideas for the war against HCC. We propose that these breakthrough findings may have important implications for targeted-HCC therapy and modernization of CHM.

© 2013 Published by Elsevier Ireland Ltd.

Contents

1. Introduction.....	2
2. The pathogenesis of HCC.....	2
3. Active compounds from CHM with anti-HCC effects.....	3
3.1. Curcumin.....	3
3.2. Resveratrol.....	5

Abbreviations: Akt, protein kinase B; AP-1, activator protein 1; ARNT, aryl hydrocarbon receptor nuclear translocate; ATP5F1, ATP synthase H⁺ transporting mitochondrial Fo complex-subunit B1; CAV1, caveolin-1; CDKs, cyclin dependent protein kinases; CHM, Chinese herbal medicine; COX-2, cyclooxygenase-2; ELAM-1, endothelial leukocyte adhesion molecule; ERK1/2, extracellular regulated protein kinases 1/2; HBV, hepatitis B virus; HCV, hepatitis C virus; HCC, hepatocellular carcinoma; HIF-1 α , hypoxia-inducible factor-alpha; ICAM-1, intracellular adhesion molecule; IL, interleukin; JNK, c-Jun N-terminal kinases; MAPK, mitogen-activated protein kinases; MMP, matrix metalloproteinases; PARP, poly ADP-ribose polymerase; PCNA, proliferating cell nuclear antigen; PTEN, phosphatase and tensin homolog; ROS, reactive oxygen species; STAT, signal transducers and activators of transcription; TCM, traditional Chinese medicine; UGT, UDP-glucuronosyl transferase; VCAM-1, vascular cell adhesion molecule; VEGF, vascular endothelial growth factor.

* Corresponding authors. Tel.: +853 83974691.

E-mail addresses: mwchen@umac.mo (M. Chen), ytwang@umac.mo (Y. Wang).

¹ These authors contributed equally to this work.

3.3. Silibinin	6
3.4. Berberine	6
3.5. Quercetin	7
3.6. Tanshinone II-A	7
3.7. Celastrol	8
4. Conclusion and prospective	8
Acknowledgement	9
References	9

1. Introduction

Liver cancer remains the sixth most frequently diagnosed cancer and the third leading cause of cancer-related mortality globally (Luk et al., 2007; Chan and Yeo, 2012). It is estimated that 748,300 new liver cancer cases and 695,900 cancer deaths occurred in 2008 (Jemal et al., 2011). More seriously, liver cancer incidence rates are still increasing in many parts of the world including the United States and Central Europe, and the incidence range has doubled in Europe over the last 20 years (Belot et al., 2008; Jemal et al., 2011). Hepatocellular carcinoma (HCC) represents the major histological subtype of primary liver cancers, accounting for 70 to 85% of the total liver cancer burden worldwide (Perz et al., 2006). In Asia countries, the situation could be more worrying. Half of the diagnosed liver cancer cases and deaths were estimated to occur in China (Lai and Lau, 2005; Jemal et al., 2011). Both surgery and liver transplant offer limited treatment options for HCC. Although sorafenib as vascular endothelial growth factor (VEGF) receptor and tyrosine kinase inhibitor has been shown to prolong the survival time by almost three months in patients with advanced HCC, its therapeutic potential is limited due to severe adverse effects and unprecedented high cost (Lu, 2010; Darvesh et al., 2012). There exists a critical need to explore and evaluate possible alternative strategies which may be effective in the control of HCC.

It has been a long history for Chinese practitioners to fight against liver cancer since ancient times. Traditional Chinese medicine (TCM) has a wealth of experiences in preventing and treating liver diseases through various treatment modalities such as acupuncture, Chinese herbal medicine (CHM) and Chinese medicated diet. In TCM theory, liver is considered the “the general of an army”, which stores the blood, controls the sinews and maintains a smooth and uninterrupted flow of Qi. Thus a disorder of liver may extraordinarily affect the whole body. In the past decades, phytochemistry and molecular biological approaches have been widely applied to elucidate the

material foundation and pharmacological mechanisms of TCM in fighting HCC. A timely and prospective summary is needed for all researchers who are focusing on this domain. In this review, several representative herbal compounds from CHM (Fig. 1), namely curcumin, resveratrol, silibinin, berberine, quercetin, tanshinone II-A and celastrol, which received relatively more anti-HCC studies were selected for reviewing. We are trying to give a timely and comprehensive update on the anti-HCC actions and targets of these compounds. Reference studies of these herbal compounds were conducted by collecting both English (PubMed, Scopus, Web of Science and Medline) and Chinese (Wanfang and CNKI database) literatures. The aim of this review is to summarize and investigate the latest advances of the functional mechanisms of these compounds and to accelerate the discovery of anti-HCC agents derived from CHM. We propose that these breakthrough findings may have important implications for HCC therapy and modernization of CHM.

2. The pathogenesis of HCC

Advanced researches on liver disease found that HCC is highly associated with multi-gene, multi-factor, and multi-step processes (Kinghorn et al., 2004; Nishida and Kudo, 2013; Padhya et al., 2013). Normal hepatocytes may transform into malignant tumor cells by series of factors, such as viral infection (El-Serag et al., 2003), dietary aflatoxins (Wogan, 1992), alcohol (Yuan et al., 2004a), tobacco (Chen et al., 2003), and specific chemical agents (Chen et al., 1992). Hepatitis virus infection is considered the main reason and the most important risk that induce HCC. Globally, about 80% of HCC cases are attributable to persistent viral infections with either hepatitis B virus (HBV) or hepatitis C virus (HCV) (Thein et al., 2011). It is estimated that about one-third of the world's population has been infected

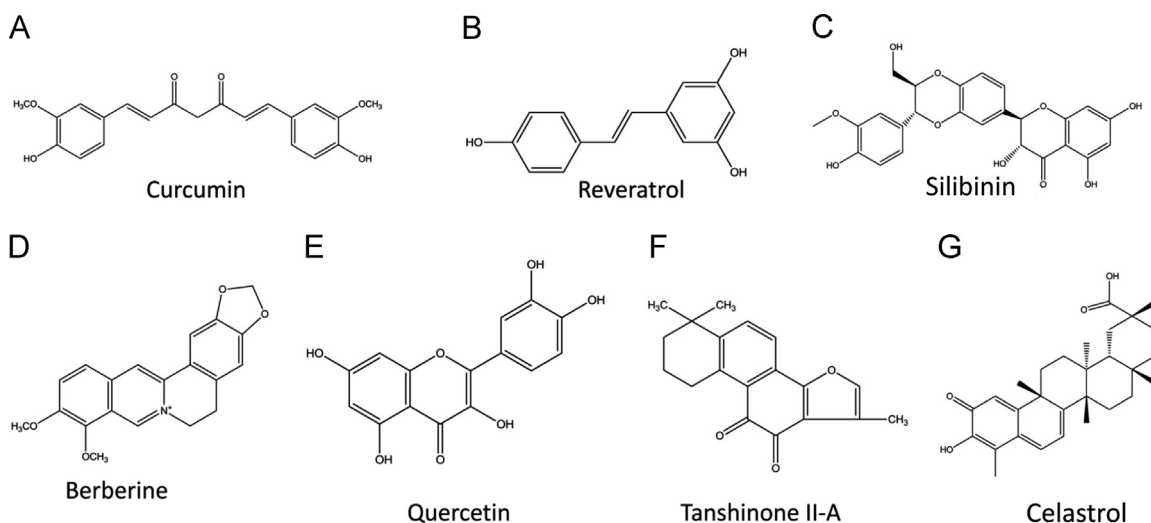


Fig. 1. Chemical structures of some CHM-derived compounds against HCC: curcumin (A), resveratrol (B), silibinin (C), berberine (D), quercetin (E), tanshinone II-A (F), celastrol (G).

Download English Version:

<https://daneshyari.com/en/article/5836985>

Download Persian Version:

<https://daneshyari.com/article/5836985>

[Daneshyari.com](https://daneshyari.com)