1.0. Introduction

Cancer is basically a form of uncontrolled cell growth and is one of the public problems all over the world. There are many genes in our cells that can cause cancer, if they show deregulated expression in a spatiotemporal manner. These include the genes responsible for encouraging cell growth and preventing cell death.

Hepatocellular carcinoma (HCC) is a major health problem with more than 500,000 new cases being diagnosed each year (Parkin et al., 2001). It is the fifth most common cancer in the world and is responsible for an estimated one million deaths annually (Llovet, 2003; McGlynn et al., 2001). Epidemiological studies have indicated that chronic infection with hepatitis B or hepatitis C viruses are two major etiological risk factors for the development of HCC (Bruix et al., 2004; Bosch et al., 2005). Vaccination programs against viral hepatitis and screening of blood and blood products hold hope for the eventual reduction of HCC incidence (Bosch et al., 2005). Up to now the prognosis of HCC is extremely poor despite remarkable progress in medical sciences. This is largely because of the lack of early diagnostic markers, information on the phenotypic changes and gene expression profile during the genesis of HCC.

The exact pathogenic and molecular mechanisms and sequential alterations in hepatocyte leading to malignant transformation has remained subjects of intense investigation. So far over 20 cellular genes down or up regulated, mutated in HCC such as ras (Kim et al., 2001), c-myc, c-fos and c-jun (Kawate et al., 1999; Yuen et al., 2001), rho (Genda et al., 1999), TGFα (Chung et al., 2000), HGF and c-met (Ueki et al., 1997), c-erbB-2 (Collier et al., 1992), IGF-II (Tkeda et al., 1996), u-PA (De petro et al., 1998), MXR-7 (Hsu et al., 1997), MDM2 (Endo et al., 2000), MAGE (Tahara et al., 1999), matrix metalloproteinase (Musso et al., 1997), Smads (Yakicier et al., 1999), p53
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(Rashid et al., 1999), pRB (Hui et al., 1999), p27^Kip1 (Tannapfel et al., 2000), PTEN (Yao et al., 1999), E-cadherin (Huang et al., 1999), β-catenin (De La Coste et al., 1998), cyclin D1 (Nishida et al., 1994), VEGF (Berse et al., 1992) and several growth factors have been described in human and mice. Many of these molecules are involved in deregulation of intracellular signal transduction and cell cycle, leading eventually to an uncontrolled proliferation of cancerous cells. However, these findings are, in most cases, also observed in many other types of cancers. New biomarker signatures specific to HCC, which will be more informative, remain to be elucidated. This question can be best answered by identifying the genes that are differentially regulated (expressed or silenced) during the process of HCC.

Medical treatments involving surgical resection, liver transplantation and cryosurgery are considered best curative options for HCC to achieve a high rate of complete response, as nearly one-third of patients show early recurrence (Qian et al., 2003). As a reason, regional interventional therapies with transarterial chemoembolization, ultrasound-guided percutaneous ethanol injection, radiofrequency ablation, microwave coagulation therapy, laser-induced thermotherapy etc. are now being used either as palliative treatments or adjunct therapies to surgery (Qian et al., 2003; Beaugrand et al., 2005). Chemotherapy, radiotherapy, hormone therapy or interferon therapy regimens in clinical trials have provided limited success (Lopez et al., 2006; Nowak et al., 2004). Besides, systemic chemotherapy of HCC using drugs like flurouracil, cisplatin and doxorubicin has been of limited value in clinical practice because of their limited benefits and high toxicity (Aguayo et al., 2001). Nevertheless, for majority of the patients, non-surgical treatment is the only alternative (Palmer et al., 2004).

In view of the side effects of drugs used in the chemotherapy of cancers, traditional herbal medicine and complementary and alternative medicine (CAM) are becoming increasingly popular among cancer patients in the developed
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countries (Molassiotis et al., 2005; Yates et al., 2005). In the traditional medicinal systems, about 150 phytoconstituents isolated from 101 plants have been reported to possess liver protective activities and are being sold all over the world as a number of herbal formulations (Subramoniam and Pushpangadan, 1999). The commonly used herbal preparations in the treatment of liver diseases are - Silymarin (a lipophilic extract from the seeds of milk thistle) (Mayer et al., 2005), Glycyrrhizin (an aqueous extract of the licorice root) (Kumada, 2002), Phyllanthus (aqueous plant extract) (Liu et al., 2001), Sho-saiko-to or TJ-9 (a mixture of seven herbs) (Oka et al, 1995) and LIV-52 (a polyherbal Ayurvedic formulation) (Huseini et al., 2005). Curcumin is another plant-derived nontoxic polyphenol with strong anticancer effects in cell culture and animal model systems (Aggarwal et al., 2003; Campbell and Collett, 2005). Curcumin has been quite effective against angiogenesis and metastasis in HCC (Yoysungnoen et al., 2005; Ohashi et al., 2003). More recently, the extracts of root and latex of Calotropis procera have been shown to have a potent anticancer activity in cell culture as well as in animal models (Choedon et al., 2006; Van Quaquebeke et al., 2005). Similarly, the flavonoid-rich alcoholic extracts of the aerial parts of weed Vicia calcarata and flowers of bastard teak Butea monosperma containing isobutrin and butrin are reported to protect the rat liver from chemically-induced hepatic damage (Singab et al., 2005; Wanger et al., 1986). However, the anticancer property of B. monosperma has not been investigated. In view of above findings, it was thought desirable to evaluate the antiproliferative, antitumorogenic and antiangiogenic properties of B. monosperma employing X-15 myc transgenic mouse model of HCC.