

Review Article

Anticancer properties of Malaysian herbs: a review

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Abstract Discovery of drugs from medicinal plants continues to provide major leads against various pharmacological targets, particularly in cancer diseases. Hence, there are increasing demands to discover more therapeutic agents from various species of medicinal plants. Chemical compounds in plants are important for human beings due to their therapeutic properties. *Goniothalamus umbrosus*, *Typhonium flagelliforme*, *Myrmecodia pendens*, *Strobilanthes crispus* and *Clinacanthus nutans*, are among the herbal species, which are consumed by cancer patients in order to combat against the growth of cancer cells. The present review aims to highlight on the anti-cancer properties of the listed Malaysian herbs.

Keywords: anticancer, antioxidant, cancer cells, herbs, medicinal compounds, phytochemicals.

Introduction

Cancer is one of the vital causes of morbidity and mortality cases in the world. 8.2 million deaths and approximately 14 million new cases of cancer were reported in 2012 (Stewart and Wild, 2014). The different types of cancer which are commonly found include breast, skin, colon, lung, lymphoma and prostate cancers (Schulz, 2005; Wirotasangthong and Rattanakit, 2006). Deregulating events in cancer progression are mainly associated with changes in genome copy numbers and/or structures (Kallioniemi *et al.*, 1994; Tirkkonen *et al.*, 1998; Roylance *et al.*, 1999; Hyman *et al.*, 2002; Pollack *et al.*, 2002; Loo *et al.*, 2004; Jeffrey *et al.*, 2005). In fact, a number of important oncogenes and tumor suppressor genes were discovered by studying recurrent copy number aberrations in human cancers (Neve *et al.*, 2004).

Chemotherapy remains as the primary mode of therapy in treatment of

various types of cancers (Fisher *et al.*, 2005). However, the emerging of chemotherapeutic drug resistance has inhibited the destruction process of cancer cells and resulted in tumor recurrence. In addition, patients also experience side effects from chemotherapy like mucositis, bone marrow toxicity, cardiotoxicity, pulmonary, renal and neurotoxicity (Plenderleith, 1990; Gaurav *et al.*, 2012). Cardiotoxicity would lead to an increase in left ventricular dysfunction and heart failure symptoms (Beer and Bubalo, 2001; Leonard *et al.*, 2009; Wonders and Reigle, 2009). Historically, natural products play an important role in providing new leads for pharmaceutical development (McChesney *et al.*, 2007), with promising results in oncology practices (Bailey, 2009). The alterations of a normal, finite-life-span somatic epithelial cells into immortalized metastatic cells involve multiple cellular processes, such as proliferation, genomic stability, motility, angiogenesis and apoptosis (Hanahan

and Weinberg, 2000; Albertson *et al.*, 2003). Thus, the progression of cancer diseases comprises various factors, which include environmental, physical, metabolic, genetic and chemical changes, which directly or indirectly affect the cancer events. Epidemiological studies indicated that a diet high in antioxidants might significantly reduce the risk of cancers, as certain dietary antioxidants are an effective agent in preventing cancer. The consumption of antioxidants from diet has now gained further attention due to the universal acceptability, safety and low toxicity (Fresco *et al.*, 2006; Dai and Mumper, 2010).

Plant-derived polyphenolic compounds consist of flavonoids, curcuminoids, tannins, stilbenes and gallo catechins; such as anthocyanidins, resveratrol and delphinidin, which demonstrated anti-oxidative mechanisms and pharmacological properties, making these compounds a subject of great interest. Besides, these compounds have also been identified to possess antiviral and antitumor properties (Mukhtar *et al.*, 1988; Hanasaki *et al.*, 1994). In fact, more than 60% of anticancer agents used nowadays are derived from natural resources, which include plant kingdom, marine organisms and micro-organisms (Cragg and Newman, 2005; Siddiq and Dembitsky, 2008). The therapeutic properties possessed by these medicinal plants are highly associated with the known high capacity of polyphenolic elements. Unfortunately, the exact mechanisms of how those therapeutic events take place in the body have not been fully understood (Jantan, 2006). Hence, it is important to gather more information on plant metabolites derived from food, with focus on the potential effect on human health (Oliveira *et al.*, 2006).

Goniothalamus umbrosus

Kenerak is a local name for *Goniothalamus umbrosus* (*G. umbrosus*) J. Sinclair that is widely utilized by locals in Malaysia for general well-being, inducer of abortion and postpartum healthcare (Mat-Salleh and Latiff, 2002). Water extracts from this plant

were used in the preparation of traditional medication, adopted by the indigenous folks in certain parts of Southeast Asia (Ahmad *et al.*, 1991). Different types of *G. umbrosus* species contain series of styryl-lactones and acetogenins, which are cytotoxic against a broad array of cancer cells including colon, breast, pancreas and kidney (Yang *et al.*, 2000; Wiart, 2007).

As of now, only 22 (13.7%) out of 160 species in the genus of *G. umbrosus* have been studied, particularly to investigate the presence of the phytochemicals such as acetogenins and styryl-lactones (Wiart, 2007). This genus is believed to have various effects on biological activities which include anticancer (Hawariah and Stanslas, 1997; Lee *et al.*, 2003; Umar-Tsafe *et al.*, 2004; de Fátima *et al.*, 2005; Noor Rain *et al.*, 2007), anti-inflammatory and immunosuppressive (Tanaka *et al.*, 2001), anti-malarial (Najila *et al.*, 2002; Ichino *et al.*, 2006; Noor Rain *et al.*, 2007), antioxidant (Likhitwitayawuid *et al.*, 2006), larvicidal activity (Kabir *et al.*, 2003) and inhibitory effects on platelet-activating factor properties (Jantan *et al.*, 2005). Apart from that, styryl-lactones from *G. umbrosus* species are known to activate apoptosis in mammalian and cancer cells (Inayat-Hussain *et al.*, 2003; Lee *et al.*, 2003). In fact, only the ethyl acetate extract of *G. umbrosus* exhibit potential anticancer activities towards breast cancer cells (MCF-7) as cell death was reported after treatment with the plant extract. This exciting discovery could form the basis to develop a new anticancer treatment for breast cancer using the plant extracts (Abdel-Wahab *et al.*, 2009).

Typhonium flagelliforme

One of the herbs that is commonly being used in Malaysia for different types of cancer treatment is Keladi Tikus or scientifically known as *Typhonium flagelliforme* (Lodd.) Blume (Araceae) (Teo and Ch'ng, 1999; C. Lee and Wong, 2004). This herbal plant can grow up to 30cm in height and has triangular leaves, oblong whitish tuber and a spathe (Albre *et al.*, 2003). Juice from *Typhonium flagelliforme* is taken orally after the remedy is prepared by crushing *Typhonium flagelliforme* in a

mortar (Teo and Ch'ng, 1999). *In vitro* studies demonstrated that the non-polar extract of the plant has a significant activity towards NCI-H23 human lung carcinoma, T-47D human breast carcinoma cell lines (Chan *et al.*, 2005) and P388 murine leukemia cells (Choo *et al.*, 2001a).

Malaysian communities also used *Typhonium flagelliforme* as complementary treatment towards many malignancies. Few studies have reported in the past concerning the potential anticancer properties of this plant. Nevertheless, the phytochemical components of the plant have not been fully investigated by using guided systematic bioassay analysis (Lai *et al.*, 2010). Choo *et al.*, (2001b) claimed that both the stem/leaf and tuber chloroform extracts were significantly more active against cancer cells.

Myrmecodia pendens

Myrmecodia pendens or known as Sarang semut in Indonesia is one of the medicinal plants that is currently being used by the natives in Papua Island, Eastern Indonesia as conventional remedy (Soeksmanto *et al.*, 2010). This herbaceous plant has recently been identified to provide cancer-healing properties, especially the *Myrmecodia* species (Hamsar and Mizaton, 2012). Sarang semut is an epiphytic plant that comes from Rubiaceae family. They are *Hypnophytum* (26 species), and *Myrmecodia* (45 species), but only *Myrmecodia pendens* (*M. pendens*) and *Myrmecodia tuberosa* possess therapeutic properties (Soeksmanto *et al.*, 2010). Lately, *M. pendens* is reported to be a promising therapeutic agent because of its immunomodulatory activities (Hertiani *et al.*, 2010). The existence of a few phytochemical compounds like phenolics and flavonoids in the extract of *M. pendens* may be accountable for the exerted activities (Zuas *et al.*, 2014).

Further assessment of *M. pendens* extract on human cervix (HeLa) and canine mammary tumor (MCM) cell lines showed that the extract impeded the growth of MCM-B2 and HeLa cells (Soeksmanto *et al.*, 2010; Hamsar and Mizaton, 2012). Another study reported that the terpenoid

active compound from *M. pendens*, isolated from Papua ant nest has a durable antioxidant activity (Rifayani *et al.*, 2015).

Strobilanthes crispus

Another important herb, which offers potential benefit in regards to healing properties is the *Strobilanthes crispus* (Acanthaceae). These plants are found distributed from Madagascar to the Malay Archipelago regions (Burkill, 1935). By tradition, it is known as 'pecah beling' in Jakarta, 'pecah kaca' or 'jin batu' in Malaysia, 'enyoh kilo', 'kecibeling' or 'kejibeling' in Java (Sunarto, 1977). Traditionally, the leaves from this plant were directly consumed after boiling in water for the anticancer, antidiabetic, diuretic and blood pressure lowering properties (Sunarto, 1977; Goh, 2004). However, the evaluation of efficacy of this plant in treating health problems is still limited.

Recent studies on *Strobilanthes crispus* (*S. crispus*) indicated that the tea contains significant amounts of phenolic and mineral contents, which demonstrated high antioxidant activity particularly the unfermented tea derived from old or matured leaves (Bakar *et al.*, 2005). *S. crispus* comprises catechins, polyphenols, caffeine, alkaloids, vitamins and tannins and also has high mineral content (Ismail *et al.*, 2000). Besides, it also contains bioactive components such as β -sitosterol and stigmasterol (Rahmat *et al.*, 2006). Their water extract was claimed to have compounds with a very high binding affinity to protein molecules, which inhibits the proliferation of retrovirus (Kusumoto *et al.*, 1992). *In vitro* studies revealed that the crude methanol extract of *S. crispus* was cytotoxic against HepG2 (liver), MDA-MB-321 (breast) and Caco-2 (colon) cancer cell lines, whereas, the chloroform extract was proven to be cytotoxic to HepG2 and Caco-2 cells (Rahmat *et al.*, 2006).

Clinacanthus nutans

Clinacanthus nutans (Burm. f) Lindau or known as Sabah snake grass in Malaysia, comes from the family of Acanthaceae and is a native herb in tropical Asia. In Malaysia, China and Thailand, it is

considered as an important conventional medicine (Sakdarat *et al.*, 2009). Primarily in Malaysia and Thailand, this herb has been used in treatment of wide range of health problems, which includes insect and snake bites, skin rashes, *Herpes simplex* virus (HSV) and varicella-zoster lesions, diabetes, mental tension and rheumatoid arthritis (Satayavivad *et al.*, 1996; Kunsorn *et al.*, 2013; Tu *et al.*, 2014). Former reports showed that chloroform extracts from *Clinacanthus nutans* (*C. nutans*) exhibited significant anti-proliferative effects on cancer cells *in vitro* like HepG2, IMR32, NCL-H23, SNU-1, HeLa, LS-174T, K562 and Raji cells (Yong *et al.*, 2013).

C. nutans leaves are also known to possess antiviral properties (Thawaranantha *et al.*, 1992; Jayavasud *et al.*, 2013) and anti-inflammatory properties by inhibiting neutrophil responsiveness and oedema formation (Wanikiat *et al.*, 2008). Pannangpetch *et al.*, in 2007 postulated that the ethanolic extract of *C. nutans* leaves showed antioxidant activity and protective effects against oxidative hemolysis (Pannangpetch *et al.*, 2007). Regardless of all the previously known biological activities, emerging evidences have now proposed that *C. nutans* retains anti-tumorigenic effect and works effectively against numerous cancer cell growth (Huang *et al.*, 2015). Chloroform extract of *C. nutans* leaves comprises the most potent components that are capable of scavenging free radical and inhibiting the growth of cultured cancer cell lines. The research further proposed that the identified phytochemical components available in the chloroform extract to be used in the replacement of adjunctive or chemo-preventive regimen for patients at risk of cancers (Yong *et al.*, 2013). Thus, there is a need for further research to be carried out on *C. nutans* to be used as natural nutraceuticals for the treatment and prevention of cancers (Yong *et al.*, 2013).

Conclusions

Herbs contain high amount of polyphenolic compounds, which are commonly associated with the healing properties. Nevertheless, the potential use and efficacy of herbal plants and its by-

products have not been well documented in treating many of the diseases, particularly malignancies. Such dearth of specific research necessitates initiation of scientific and streamlined exploratory work aimed at identifying and exploiting the key compounds in the potential herbs and their molecular and biochemical pathways to formulate an effective therapeutic strategy towards fighting cancer. However, sufficient preliminary experiments and completion of clinical phase trials are extremely needed, prior to application of the identified natural products in conventional medicine.

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