1.0 INTRODUCTION

Cancer is the main cause of death after cardiovascular diseases. It is also known that, breast cancer is the most common cancer that affects women. Despite early detection and improved adjuvant therapies, breast cancer incidence was 109.7 cases per 100,000 women between 1990 and 1997 (Ries *et al.,* 2000). Meanwhile, on a worldwide basis, cervical cancer ranks second after breast cancer in women, and it will remain as the top three commonest cancers among women for many years to come (Women's Health Report, 2007; Cuzick, 1999). On the other hand, colorectal cancer is one of the most frequent malignancies in Western countries (Leow, 2006). It was reported to be the second leading cancer death with almost 100,000 new cases and 50, 000 deaths each year in the United States of America (USA) (Reinacher-Schick *et al.,* 2003; Van den Branck *et al.,* 2003).

As the etiologic agent of genital warts, as well as precancerous lesions and carcinomas of the cervix, vagina and vulva, human papillomavirus (HPV) infections continue to cause great morbidity and mortality (Huh *et al.,* 2008). In the USA, it is estimated that 24.9 million women, between the ages of 14 and 59 years are currently infected with HPV (Dunne *et al.,* 2008). In Malaysia, cervical cancer ranks third of all cancers with an incidence rate of 11.6 per 100,000 (Nor Hayati, 2003). Based on Women's Health Report (2007), it is estimated that, more than 80% of women will acquire a genital HPV infection by 50 years of age. Out of the 15 oncogenic HPV types, HPV16 and HPV18 account for approximately 52% of cervical intraepithelial neoplasia (CIN) 2+ cases and 70% of cervical cancers cases worldwide (Smith *et al.,* 2007). At the same time, the similar HPV16 and HPV18 oncogenic types account for 54% of CIN 2+ cases and 77% of all cervical cancer causes in the USA (Smith *et al.,* 2007).

E6 oncoprotein is the protein encoded by the oncogenic human papillomavirus types 16 and 18. It is one of two viral products expressed in HPV-associated cancers. E6 oncoprotein incorporates with E7 to immortalize primary human keratinocytes. E6 promotes the degradation of protein p53, which has the gene for tumor suppressor properties, and is a target for several of the oncoproteins encoded by DNA tumor viruses (Scheffner *et al.,* 1990; O'Brian and Compo, 2003).

It is known that, diseases such as cancer are mainly induced by the uncontrolled production of oxygen-derived free radicals, also known as reactive oxygen species (ROS) (Elmastas *et al.,* 2007). These oxygen-derived free radicals are produced by exogenous chemical and endogenous metabolic processes in the body or in the food system such as coffee and tea (Santosh *et al.,* 1998). These free radicals oxidize biomolecules, resulting in cell death and tissue damage (Halliwell and Gutteridge, 2003). However, naturally the organisms are well protected against free radical damage by antioxidants such as superoxide dismutase (SOD), catalase (CAT), or chemical compound such as α-tocopherol, ascorbic acid, carotenoides, polyphenol compounds and glutathione (Niki *et al.,* 1994). At the same time, the mechanism of antioxidant protection becomes unbalanced due to the ageing process and deterioration of physiological functions, which can lead to diseases. However, antioxidant supplements or antioxidant containing foods may be used to help the human body to reduce this oxidative damages (Halliwell and Gutteridge, 2003; Mau *et al.,* 2001; Gulcin *et al.,* 2002a,b).

Antioxidants are compounds, which can scavenge free radicals and increase the life span by retarding the process of lipid peroxidation, which caused deterioration of food products during processing and storage (Halliwell, 1997). Epidemiological data as well as *in vitro* studies strongly suggest that foods containing phytochemicals with antioxidation potential have strong protective effects against risks of major diseases, such as cancer and

cardiovascular diseases (Steinberg, 1991; Block *et al.,* 1992; Ames *et al.,* 1993; Hertog *et al.,* 1993; Byers & Guerrero, 1995; Knekt *et al.,* 1997; Eliot, 1999; Kaur *et al.,* 2001). Recently, many species of mushrooms, white cabbage, cauliflower (Gazzini *et al.,* 1998) garlic, broccoli, kidney and pinto beans (Vinson *et al.,* 1998) have been reported to have high antioxidant activity.

Mushrooms have been used as food and food flavouring material in soups and sauces for centuries, due to their unique and subtle flavour. In studies, mushrooms reported to have therapeutic functions such as preventing hypertension hypercholesterolemia and cancer (Miller *et al.,* 1990; Hong *et al.,* 1997; Sporn *et al.,* 1991). Edible mushrooms have also been found to possess antioxidant activity. Mushrooms have been known to scavenge free radicals and prevent various kinds of degenerative diseases. These functional characteristics possessed by mushrooms are mainly due to their chemical composition (Manzi *et al.,* 2001). For example, species of *Agrocybe, Auricularia, Dictyophora, Grifola, Hericium, Lentinus, Morchella, Pleurotus, Termitomyces,* and *Volvariella* contain antioxidant bioactive compounds in their fruit bodies and mycelium (Mau *et al.,* 2001; Cheung *et al.,* 2003; Mau *et al.,* 2004). Besides being strong antioxidant supplements, mushrooms have become a very popular functional food in treating the cancer. For example, *Ganoderma lucidium, Lentinula edodes,* and *Hericium erinaceus* are some of the mushrooms, which have anticancer properties (Liu *et al.,* 1993).

Recently, considerable attention has been drawn to the medicinal activities, exhibited by edible mushroom, *Auricularia auricula-judae*. The antitumor activities were exhibited by non starch polysaccharides components (ß-glucans) of *A. auricula-judae* which were grown in Japan (Misaki *et al.,* 1993). Besides that, *A. auricula-judae* also possess high dietary fiber content which have potential hypocholesterolemic effect similar to the other high fiber foods (Anderson *et al.,* 1990; Cheung *et al.,* 1996). However, there is

a paucity of literature focused on the cytotoxicity and antitumor (anti HPV) activity towards *A. auricula-judae* grown in Malaysia. The present study was carried out to investigate cytotoxicity, antioxidant and anti–human papillomavirus E6 activities with various solvent extracts from *A. auricula-judae* fresh fruitbodies grown in Malaysia. Therefore, the objectives of the present work were as follows:-

1. To determine cytotoxic activity of ethanol, methanol, dichloromethane, hot aqueous and polysaccharides extracts of *A. auricula-judae* fresh fruitbodies by an *in vitro* growth inhibition assay system against, human ovary carcinoma cells (SKOV), human cervical cancer cells (CaSki), human colon cancer cells (HCT119), human mouth epidermal carcinoma cells (KB), human intestinal colon cancer cells (HT29), human breast cancer cells (MCF 7) compared to the normal cell line, human fetal lung epithelium cells (MRC 5).
2. To screen for anti-human papillomavirus 16E6 activity of ethanol, methanol, dichloromethane, hot aqueous and polysaccharides of *A. auricula-judae* fresh fruitbodies in human cervical cancer cells (CaSki).
3. To determine the antioxidant property of the ethanol, methanol, dichloromethane, hot aqueous and polysaccharides of *A. auricula-judae* fresh fruitbodies using the DPPH radical scavenging assay and ferric reducing ability power (FRAP) assay.
4. To determine the total phenolic content of ethanol, methanol, dichloromethane, hot aqueous and polysaccharides extracts of *A. auricula- judae* fresh fruitbodies.