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Bioactive Ingredients from Orange Fruits Extract

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ABSTRACT

Orange fruit extracts have active components like flavonoids and limonene which acts as antioxidant, anti obesity as well as anti carcinogenic agents and also show a tendency to inhibit tumor growth. In this paper an attempt has been made to summarize the various applications of bioactive components extracted from different parts of the orange fruits.

Keywords: *Anticarcinogenic, Antiobesity, Antioxidant, Flavonoid, Limonoid, Orange Fruits.*

INTRODUCTION

Citrus limon and *Citrus aurantifolia* (Christm.) Swingle (family: Rutaceae). Conversely, in the Tanaka system, they are divided into several species characterized by botanical variability (Anon. 1992). Until recently, citrus health promoting properties have always been associated with their content of vitamin C. Only in the last decade studies have focused on several bioactive compounds, specifically limonoids and flavonoids which play a major role in preventing chronic diseases (Tian et. al. 2001). Certain citrus fruits are not bitter when freshly squeezed, but they become bitter after a few hours at room temperature or when refrigerated overnight. The bitterness comes from certain limonoids, which are characteristic of plants in Rutaceae family (Emerson, 1948). Limonoids are compounds in citrus fruits, generally found in the peel, which produce the familiar bitter taste and zesty aroma. Citrus limonoids appear in large amounts in citrus juices and citrus tissues as water-soluble limonoid glucosides or in seeds as water-insoluble limonoid aglycones.

Bioactive ingredients:

In addition to vitamin-C, carotenoids, flavonoids, limonoids, phenolic acids when consumed in appropriate quantities are beneficial to human health (Gray et.al. 1978; Macheix et. al. 1990; McHale et. al. 1989; Tatum et. al. 1977, Kane et. al. 2000; Poulose et. al. 2005; Tian et. al. 2001, and Wang et. al. 2007).

Growing body of evidence seems to suggest that limonoids and flavonoids have different biological functions, including antioxidative, anti-inflammatory, antiallergic, antiviral, antiproliferative, antimutagenic, and anticarcinogenic activities (Hasegawa et. al. 1996; Poulose et. al.2006; Vanamala et. al. 2006, Haaz et. al. 2006 and Jayaprakasha et. al. 2008). Therefore, new Citrus cultivars have been developed for fresh consumption. Furthermore, the particular characteristics of these bioactive compounds have the potential to be used in the pharmacological and food technology area (Del et. al. 1997; Ortuno et. al. 1997).

Consumption of food rich in flavonoids prevents several degenerative pathologies, including cardiovascular diseases, atherosclerosis, cataract and several forms of cancer (Federica et. al. 2005). Apart from antioxidant activity, hesperidin is known to act as anticancer agent through chemical carcinogens inhibition (Kupfer et. al. 1987). The other major flavonoid reported in lemon fruits is rutin, also known as quercetin-3-rutinoside. Furthermore, it has shown antiallergic, anti-inflammatory and antitumor, antibacterial, antiviral and anti-protozoal properties (Deschner et. al. 1991).

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Citrus phytochemicals have shown to inhibit colon (Jayaprakasha et. al. 2008), breast (Sergeev et. al. 2006) and prostate cancer cells (Gao et. al. 2006). Recently, citrus compounds are known to inhibit the colon cancer cells proliferation in both cell culture and animal studies (Poulose et. al. 2006, Vanamala et. al. 2006). Apart from anticancer property of citrus fruits, several antioxidant compounds have been identified in the peels of citrus (Gorinstein et. al. 2004; Jayaprakasha et. al. 2007). These compounds include flavonoids, which can scavenge free radicals and also chelate metal ions, and hence they are potential antioxidant. Hesperidin is a type of flavonoid present in several vegetables and fruits, but mainly in citrus (Cserhati, 1995). Hesperidin is known to posses certain biological activities including antioxidant property, and inhibition of prostaglandin biosynthesis, and also known to inhibit chemical carcinogenesis (Kupfer et. al. 1987).

Pancreatic cancer is one of the most devastating of all malignancies with the highest mortality compared to other cancers (Li et. al. 2004), and is the fourth leading cause of cancer death in the USA (Jemal et. al. 2008). Late diagnosis of cancer is the main cause for limited option for successful treatment and also development of resistance to most of chemotherapy and radiotherapy (Lowenfels et. al. 2005). Hence, prevention seems to be the most promising strategy to reduce the mortality rates of pancreatic cancer (Bobe et. al. 2008). Based on the success rate and complications from currently available synthetic drugs for pancreatic cancer, treatments using natural compounds have gained considerable attention due to their safety and efficacy in overcoming tumor cell resistance to apoptosis (Bharti et. al. 2002). Current research information available suggest that few natural compounds have demonstrated potential benefits in pancreatic cancer prevention including, curcumin (Aggarwal et. al. 2008), flavonoids (Zhang et. al. 2008) and isoflavones (Awale et. al. 2008). Hence, screening of naturally derived compounds may be one of the promising approaches in prevention of pancreatic cancer.

Colon cancer is another prevalent cancer throughout the world and especially in western countries. This is continuously increasing worldwide due to rapid changes in dietary pattern and preferences. Many epidemiological studies indicated that western-style diet, primarily, the consumption of red meat is positively associated with a high colon cancer incidence (Abeysinghe et. al. 2007). Continuous efforts are being made for search of novel source of bioactive compounds to prevent colon carcinoma. In this direction, bioactive compounds of natural origin, particularly from dietary source are gaining significance. In recent years, citrus has gained importance due to their ability to provide multitude health benefits not only from vitamin-C but also from other bioactive compounds.

1. Ingredients from orange peel extracts:

The composition of phytochemicals in citrus fruits are extensively studied, apart from ascorbic acid, some of the major class of compounds includes, flavonoids, limonoids, coumarins and phytosterols (Wang et. al. 2007). Until recently, citrus health

promoting properties have always been associated with their content of vitamin C; only in the last decade studies have focused on several bioactive compounds, specifically limonoids and flavonoids which play a major role in preventing chronic diseases (Tian et. al. 2000).

Citrus limonoids are capable of inducing cytotoxicity in both, cultured human cancer cells and animal models (Poulose et. al. 2006; Tian et. al. 2001; Vanamala et. al. 2006). The antiproliferative effects of limonoids have been reported in various cancer cells such as, MCF- 7 (breast cancer) (Tian et. al. 2001), HT-29 (colon cancer) (Alexandra et. al. 1998; Jayaprakasha et .al. 2008), and SHSY5Y (neuroblastoma) (Poulose et. al. 2005). Further, antiproliferative activity of limonoids through caspase mediated apoptosis has been demonstrated (Poulose et. al. 2005). Further, bioactive compounds in citrus are carotenoids, limonoids, flavonoids, pectin, vitamin C, furocoumarins, and coumarins, when consumed in appropriate quantities are beneficial to human health (Kane et. al 2000; Poulose et. al. 2005; Tian et. al. 2001).

2. Flavonoids and other phytochemicals:

Citrus as source of flavonoids are a large class of low molecular weight polyphenolic compounds that occur ubiquitously in plants. Citrus fruits contain multiple bioactive agents. Flavionoids have antioxidant properties and their involvement in antiproliferation processes, cell cycle arrest and apoptosis, antioxidation, induction of detoxification enzymes, regulation of host immune functions. Consumption of foods rich in flavonoids are known to prevent several degenerative pathologies, including cardiovascular diseases, atherosclerosis, cataract and several forms of cancer (Federica et.al. 2005). Among the flavonoids, hesperidin was found to be the most abundant in citrus fruits (Kawaii et. al. 1999). Apart from antioxidant activity, hesperidin is known to act as anticancer agent through prostaglandin and inhibitor of chemical carcinogens (Kupfer et.al. 1987). The other major flavonoid reported in lime fruits is rutin, which is also known as quercetin-3-rutinoside. Rutin has shown significant scavenging properties on oxidizing species, such as hydroxyl radical, superoxide radical, and peroxyl radical. Furthermore, it has shown antiallergic, anti-inflammatory and antitumor, antibacterial, antiviral and anti-protozoal properties (Deschner et. al. 1991).

3. Antioxidant activities of bioactive compounds:

Antioxidants activity of citrus fraction was also described to their hydrogen donating ability (Girennavar et. al. 2007; Jayaprakasha et. al. 2007), and may be due to the presence of flavonoids, carotenoids and ascorbic acid (Halliwell, 2001). The mechanisms of antioxidant action can include inhibition of reactive oxygen species formation by suppressing enzymes involved in free radical production; scavenging reactive oxygen species; and protecting antioxidant defenses (Halliwell et.al. 2000). Flavonoids inhibit the enzymes responsible for superoxide anion production, such as xanthine oxidase and protein kinase C (Hanasaki et. al. 1994). Besides scavenging, flavonoids may stabilize free radicals involved in oxidative processes by complexing with them. (Shahidi et. al. 1992).

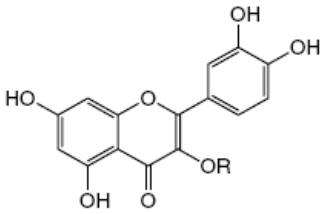

Fig. 1: Structure of flavonoids

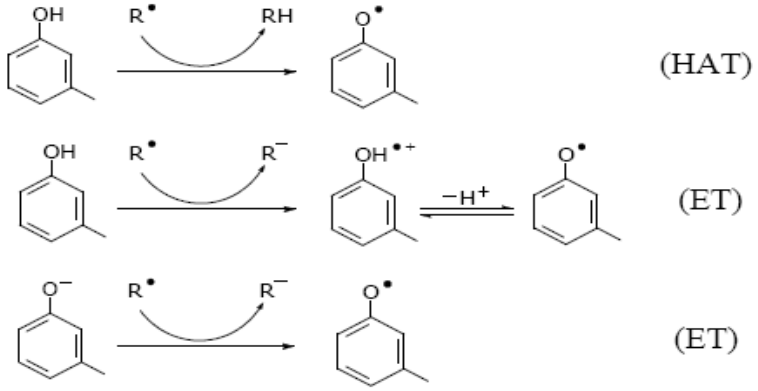

Fig. 2: Reaction mechanism for antioxidant activity

The antioxidant capacity of flavonoids is directly related to their structure (Cos et. al. 1998), and in the case of hesperidin, the presence of a hydroxyl group at position 3 of ring B is responsible for the capacity of hesperidin to scavenge the hydroxyl radicals generated from hydrogen peroxide. It is already known that the ability to scavenge superoxide is due to a hydroxyl group at position C-4 of ring B (Acker et. al. 1996; Cos et. al. 1998). It has previously been shown that the C-4 methyl substitution at C-4 and hydroxyl at C-3 of hesperidin at ring B can activate, making hesperidin as more active scavenger to the superoxide radical (Van Acker et. al. 1998).

4. Antioxidant activity of orange peels extract:

Phenolic are aromatic secondary plant metabolites, which play a significant role in color, sensory and nutritional qualities and antioxidant properties of food (Robbins, 2003). Citrus fruits are known for their rich sources of bioactive compounds, including vitamin C, phenolics and flavonoids, with potential health-promoting properties (Gorinstein et. al. 2001). These bioactive compounds are known to act as free radical-scavengers, to modulate enzymatic activities and to protect against a variety of diseases, particularly cardiovascular diseases and some types of cancer (Kurowska et. al. 2000).

Free radical scavenging is one of the known mechanisms of inhibition of lipid oxidation. In DPPH (1, 1,- diphenyl-2-picryl hydrazine) free radical scavenging assay, antiradical power of an antioxidant is measured as color changes from purple to yellow. This is used to evaluate hydrogen donating ability of the compound. It is a rapid method and most widely employed to characterize antioxidant activity of plant material (Arnao, 2000). Furthermore, mechanisms of antioxidant action can include inhibition of reactive oxygen species formation by suppressing of enzymes involved in free radical production; scavenging reactive oxygen species; and protecting antioxidant defenses (Halliwell et. al. 2000

5. Prevention of colon cancer by citrus peel compounds:

In spite of understanding the exact sequence of genetic mutation of the adenoma to carcinoma in colorectal cancer, it continues to be the main cause of death. Every year about 78 lakhs of new cases are diagnosed worldwide. Colorectal cancer is common in industrialized countries and is a public health priority because of the high incidence and mortality associated with it. Further,

colorectal cancer is the third most commonly diagnosed cancer in the United States and the third most common cause of cancer death among men and women put together. In 2008, 1.49 lakh people were diagnosed with colorectal cancer and 49,960 deaths were expected from the disease. The colon cancer accounted for 72 per cent of total colorectal cancer and cases of rectum cancer was 28 per cent (Jemal et. al. 2008).

A number of studies have shown that certain citrus fruits contain photochemicals which induce proliferation inhibition of some cancer cell (Arias et. al. 2005) and the cause of cell death may be due to apoptosis in case of human colon cancer cells (Kim et. al. 2005). Citrus species are known to accumulate significant amounts of limonoids and flavonoids during the process of plant development and growth (Castillo et.al. 1992). Recent studies indicate the presence of potential dietary bioactive compounds in citrus fruits which possess cancer prevention properties (Poulose et. al. 2006; Vanamala et. al. 2006).

6. Prevention of pancreatic cancer by citrus peel extracts:

Hesperidin is known to possess certain biological activities including antioxidant property, and inhibition of prostaglandin biosynthesis, and also known to inhibit chemical carcinogenesis (Kupfer et. al. 1987). In addition, these naturally-occurring antioxidants can be formulated to give neutraceuticals that can help to prevent oxidative damage from occurring in the body (Moller et. al. 1999).

CONCLUSIONS

The above studies concluded that orange fruits have anticancer effects, including reducing the proliferation of some cancer cells and the induction of apoptosis in human gastric and colon cancer cells. Further, recent research has shown that orange contains several possible anti-cancer agents such as flavonoids and limonoids in different ratios.

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