



STRAWBERRY (*Fragaria ananassa* Duch): PHYTOCHEMICALS, NUTRACEUTICALS AND HEALTH BENEFITS. A BRIEF REVIEW

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ABSTRACT

Strawberry is an accessory fruit stimulated by cold weather as a berry, reported to constitute, phenolic acid, ellagic acid and its derivatives EA-4-arabinside, EA-4-acetyl arabinoside, EA-4-acetylxyloside, β -carotenoids (Lutein, β -carotene), omega-3 fatty acids and derivatives. Fruits especially berries/soft fruits have combination of antioxidants and phytochemicals. The phenolic compounds present in strawberries are responsible for antioxidant properties rather than to vitamin C and these dietary antioxidants prevent or limit the potential cancer-inducing oxidative damage. These compounds play a synergistic and cumulative role in health promotion. The risk of persistent diseases and oxidative damage to the cellular system can also be prohibited or lowered by these antioxidant compounds (phytochemicals), such as phenolics and carotenoids. Strawberries enhance the palatableness of a cholesterol-dropping food whereas it maintains the serum lipid reductions of the food consumed. Cognitive and motor functions are age-related declines that are slowed by strawberry intake and it also has cancer fighting constituents, it also has a potential of decreasing the risk of heart diseases, the females with high strawberry ingestion have reduced levels of an inflammatory marker in their blood. Strawberry extract was found to decrease the activity of transcription factors involved in tumor promotion and there is a need to consume sufficient amounts of antioxidants avoid or reduce the oxidative stress stimulated by free radicals.

Key word: Strawberry; nutraceutical; phytochemical; phenolics; ascorbic acid; folate; ellagic acid; quercetin; anthocyanins; kaempferol; flavonoids; antioxidants; urate; tannins; phytoestrogen; hydroxycinnamic acid; health; catechins; anti-aging; vitamin.

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Received: 03 September 2019 Accepted: 04 October 2019

INTRODUCTION

Strawberry is belongs to North America. Its name has derived from farmers mulching practice by using "straw". Strawberry was first discovered by the Europeans in the year 1588. Before Carolus Linneaus strawberry was only used as medicinal plant, he for the first time introduced it as edible fruit. California is the largest producer of strawberry followed by Florida. French were the first who laid the way in strawberry cultivation and the first cross breeding was made in 18th century for the improvement, the first hybrid was developed in USA in 1780 with the name of "Hudson". The increasing spread of chronic diseases among people worldwide has boosted the concern to use natural commodities for the cure rather than depending upon pharmaceuticals. Plant based chemicals such as those obtained from strawberry (*Fragaria ananassa* Duch.) are universally consumed nowadays, as in red berries there is the most familiar dietary source of anthocyanins including strawberries and tomato which have lycopene and β -carotene (Ikram *et al.*, 2012). Soft fruits like strawberries are rich source of nutrients especially vitamin C and bioactive compounds. These are required for maintaining homeostasis, and their intake reduces the incidence of cancer and coronary heart diseases (Steinmetz and Potter, 1996). Colorful fruits contain wide range of photochemicals and are associated with cardiovascular health gain. Strawberry and apple are a good example among all the fruits consumed, these are the major contributors of cellular antioxidants. Strawberry is rich in phytochemical especially (ellagic acid, anthocyanins) vitamins, potassium and fiber, which are anti-inflammatory

and antioxidant (Hannum, 2004) and anti-hyperglycemic agents (Da Silva *et al.*, 2007).

The most renowned portion of daily food with antioxidant activity comprises fat soluble vitamins A (ratinol) and tocopherol vitamin E, ascorbic acid (vitamin C) that is water soluble, β -carotene and lycopene. Most of these components are identified in colorful fruits like strawberries, cranberries and blackberries. Strawberries have a massive amount of cancer fighting constituents, including ascorbic acid, folate, ellagic acid, quercetin, anthocyanins, and kaempferol, the flavonoids present in them may lessen the threat of cardiac disease and the females with more strawberry intake have reduced degrees of an inflammatory marker in their blood. Phytochemicals phenolic substances with antioxidant properties are now regarded as a vital ingredient in the fruit and vegetable industry and are responsible for the positive effects on health. Fruits also contain various known phenolics like hydrolyzable tannins, condensed tannins (proanthocyanidins), hydroxybenzoic derivatives (hydroxycinnamic acid), anthocyanins, and flavanols (Macheix *et al.*, 1990). Humans who eat nutrients loaded in vegetables and fruit were shown, to have a smaller frequency of oxidation linked illnesses like chronic illnesses, cancer, heart cycle - illnesses and diabetes (Panico *et al.*, 2009).

Botany of strawberry: Strawberries are the edible fruits of the belongs to the family Rosaceae genus *Fragaria* (Hancock, 1999). Although commonly referred to as "berries," strawberries are actually the part of the mature fruit known as the receptacle and the seed-like parts of the fruit are known as

achenes (Hancock, 1999). The commercially-grown cultivars within the United States are from the hybrid *Fragaria x ananassa* (Darrow, 1966).

Strawberry is herbaceous plant which is propagated by seed and also by runners and stolons. The leaves are basal, leathery with a petiole ranging 2-20 cm. leaves have three leaflets that are glabrous without hairs above. It has white flower with five petals that are 10-18 mm, with many pistils on a common receptacle and 20-35 stamens. The five bractlets are unlobed. Achenes cover the beautiful red color fleshy fruit (Hancock, 1999).

NUTRACEUTICAL FACTS

Nutraceutical components: Various common and advanced tools have used to evaluate chemical constituents of strawberry. The most frequent tools include Liquid Chromatography/Mass Spectrometry coupled with Ultra Violet detection (Määttä-Riihinen *et al.*, 2004; Seeram *et al.*, 2006; Aaby *et al.*, 2007). In a single run over hundred of compounds can be measured with UPLC and accurate mass measurement with high-resolution mass spectrometers (Fait *et al.*, 2008; Hanhineva *et al.*, 2009). Volatile aromatic compounds of strawberry can be analyzed by GC-MS (Aubert *et al.*, 2005; Zabetakis and Holden, 1997; Aubert *et al.*, 2005). NMR spectroscopy has mainly been employed for unambiguous structure elucidation of strawberry secondary metabolites, coupled with LC-MS analysis (Hirai *et al.*, 2000; Hilt *et al.*, 2003; Hanhineva *et al.*, 2009). Advanced techniques like FTICR-MS (Aharoni *et al.*, 2004) and Colloidal GALDI (Zhang *et al.*, 2007) is also used for strawberry.

One hundred grams of whole strawberries contains approximately 32 kilocalories with vitamin C content of (59 mg), fiber (2.0 g), potassium (153 mg), vitamin A (12 IU), folate (24 µg), low weight sugars (4.8 g), and contains carotenoids (β-carotene, lutein), phytosterols, and polyphenolics (anthocyanins, flavonols, hydroxycinnamic acid derivatives, and ellagitannins) (Aaby *et al.*, 2007). The non-nutritive poly-phenolic compounds found in strawberries are important due to their health-promoting benefits. Aaby *et al.* (2005) determined that strawberry achenes contributed eleven percent of total phenolics and fourteen percent of the antioxidant activity. The total phenolics in strawberries at different maturation stages were studied by Wang and Lin (2000), and were found to be highest in small green strawberries. Wang and Lin (2000) also showed that anthocyanin content, total phenolics, and antioxidant capacity varied significantly in different strawberry cultivars. Strawberry also constitutes ellagic acid and its derivatives EA-4-arabinoside, EA-4-acetyl-arabinoside, EA-4-acetylxyloside (Lei, 2002; Mullen *et al.*, 2003). Table 1 shows the availability of certain phytochemicals of strawberries.

Flavonoids: In the strawberry flavonoids at 3' and/or 4' of the B-ring hydroxylated backbone is present. The main flavonoid metabolites are derivatives of the kaempferol, flavonols and quercetin. The anthocyanidins cyanidin and pelargonidin, and the flavan 3-ols (epi)catechin and (epi)epiafzalechin are also derivatives of the main flavonoid (Määttä-Riihinen *et al.*, 2004; Aaby *et al.*, 2005). Flavonoids are monomeric constituents of condensed tannins typically present in a glycosylated form (Seeram, 2008). Anthocyanins are glycosylated. hydroxyl or

methoxyl. derivatives of 2-phenylbenzopyrylium

Table 1: Availability of phytochemicals per kg of strawberry

Phytochemical	Concentration (Fresh fruit)	Reference
Phenolic acids	85 mg/kg	Aaby <i>et al.</i> (2007)
Total ellagic acid	293 mg/kg	Aaby <i>et al.</i> , (2007)
Carotenoids	260 µg/kg	Marinova and Ribarova (2007)
ω-3 Fatty acids	292 mg/kg	Connor <i>et al.</i> (2002)
Vitamin C	1041 mg/kg	Klopotek <i>et al.</i> (2005)
Flavonoids	13 mg/kg	Aaby <i>et al.</i> , (2007)
Anthocyanin	5256 mg/kg	Aaby <i>et al.</i> , (2007)
Phenolic acids	85 mg/kg	Aaby <i>et al.</i> , (2007)

derivatives of 2-phenylbenzopyrylium (anthocyanidin) or flavylium ions and different from each other with number and positioning of methoxyl and hydroxyl groups on the anthocyanidin backbone, the position, identity, and type of glycoside moiety, and acylation of the glycoside (Wu *et al.*, 2002).

Strawberry anthocyanins mostly include cyaniding-3-glucoside (7%), pelargonidin-3-rutinoside (8%) and pelargonidin-3-glucoside (83 %) (Wu *et al.*, 2002). Flavonols quercetin and kaempferol are typically found in strawberries as kaempferol-glucuronide, quercetin-rutinoside, quercetin-glucuronide, and quercetin-glucoside (Seeram *et al.*, 2006). Anthocyanin content significantly increase as strawberries ripened (Wang and Lin, 2000).

Catechins: Catechin a typical flavanol, was found in strawberries as isomers *p*-coumaroyl ester and *p*-coumaroyl-glucoside (Määttä-Riihinen *et al.*, 2004; Seeram *et al.*, 2006). Catechins are typically found in free forms rather than glycosylated forms (Törrönen and Määttä, 2002). Dimers, oligomers, and polymers of catechin molecules are known as proanthocyanidins, and upon application of heat and acid are hydrolyzed to anthocyanidins (Törrönen and Määttä, 2002).

Hydrolyzable Tannins: Hydrolyzable tannins are found as either ellagitannins or gallotannins, but the latter is not found in strawberries (Seeram *et al.*, 2006). The structure of (glucose or quinic acid) constitutes a polyol center that is esterified with either HHDP or gallic acids and is soluble in water (Seeram *et al.*, 2006). Upon acid hydrolysis of ellagitannins, HHPD is released and ellagic acid is formed by joining two gallic acid molecules (Määttä-Riihinen *et al.*, 2004). The main sources of ellagic acid in the diet are raspberries, strawberries, and blackberries (Wu *et al.*, 2002). Ellagitannins and ellagic acid were found to be the main contributors of antioxidant activity within strawberry achenes (Aaby *et al.*, 2005).

Qualitative analysis of strawberry ellagitannins indicates that strawberry is rich in ellagitannins (Fait *et al.*, 2008; Hanhineva *et al.*, 2009), which includes lambertianin C, sanguin H-6 and galloyl-bis-HHDP-glucose (Seeram *et al.*, 2006; Aaby *et al.*, 2007).

Among natural products it is one of the most intensively studied products, resveratrol has been rarely reported in strawberry fruit and achenes (Ehala *et al.*, 2005). Resveratrol

has never been found in strawberry in profiling studies, as it is most likely present in detectable quantities only after induction or after targeted purification.

Hydroxycinnamic acid derivatives: Glucose and quinic acid esters of hydroxycinnamic acid have been identified in strawberries (Määttä-Riihinen *et al.*, 2004). The hydroxycinnamic acid derivative found in strawberries is *p*-coumaric acid (Määttä-Riihinen *et al.*, 2004).

Vitamin C and folate: Free radical damage in humans is prevented by water soluble anti-oxidants these acts as cofactor of many enzyme activities and also helps to regenerate vitamin E (Jacob *et al.*, 2003). Regular intake of vitamin C reduces risk of strokes and certain cancer. The post-harvest studies showed that increase in temperature decreases ascorbic acid in small fruit like strawberry. Strawberries are rich source of ascorbic acid. RDA of vitamin C can be fulfilled by having a handful of strawberries (Carr and Frei, 1999) and they are also the amplest natural reserves of folate. For instance, 200-250 grams of strawberries may provide sixty two percent of the daily European folic acid intake prescribed (200-300 micro gram/day) (Bailey and Gregory, 1999).

Phytoestrogen: The phytoestrogen has recently been found in small fruits as lignin (Mazur, 1998) it protect against osteoporosis, hormone dependent cancers and cardiovascular diseases (Bingham *et al.*, 1998). Among all small fruits, lignins was mostly consumed from strawberry (Mazur *et al.*, 2000).

Strawberries have the potential to satisfy oxidative stress linked with inflammatory changes that are a result of the consumption of high-fat or carbohydrate diet (Guo *et al.*, 1997). Strawberry significantly satisfy the postprandial inflammatory response subsequent to the intake of (high carbohydrate, moderate fat meal) in an obese populace, enhanced insulin action and increased plasma concentration of anthocyanins (Edirisinghe *et al.*, 2011).

In strawberries the most essential phenolic compound is ellagic acid (Häkkinen *et al.*, 1999). Ellagic acid is of prime importance due to its antibacterial, anti-inflammatory and chemoprotective effect (Vattem *et al.*, 2005). The anthocyanin are swiftly engrossed from the stomach (Passamonti *et al.*, 2003; Talavéra *et al.*, 2003) and in the small intestine (Miyazawa *et al.*, 1999) as methylated, glucuronidated or sulphated compounds (Wu *et al.*, 2002; Felgines *et al.*, 2003; Kay *et al.*, 2004). Strawberries are superb fruit to study the bioavailability of Pel-glc (Palergonidin glucoside) as they contain extensive amount of anthocyanins. The ingestion of sweetened strawberries either alone or in combination with other food (typical breakfast) may raise the bio-availability of Pel-glc (Hollands *et al.*, 2008).

AVAILABILITY OF PHYTOCHEMICALS

Bio-availability of phytochemicals: Strawberries produced in Scotland are rich source of phenolic acids, namely benzoic and cinnamic acids, in free form and in blend with plant elements (Russell *et al.*, 2009). Bio-availability is often described as the ability of a compound to be absorbed and enter the systemic circulation, but the more important issue is whether it reaches the target tissue and site of physiological action. These cinnamic acid derivatives and their metabolites protect against diseases of gastrointestinal tract. Earliest

researches revealed that soft fruits such as strawberries have phenolic compounds with potential health benefits (Seeram, 2008), which have many phenolic compounds (Stöhr and Herrmann, 1975; Seeram *et al.*, 2006; Tulipani *et al.*, 2008).

Phenolic acids consumption from plant based foods will lead to careful absorption and secretion of phenolic acids founded on their structural characteristics, which efficiently influence on the bio-availability and major bioactivity (Russell *et al.*, 2009).

HEALTH BENEFITS OF STRAWBERRY

Nutritional health benefits of strawberry: Anthocyanins are related with an extensive health benefits including lower risk of CVD (Bell and Gochenaur, 2006), less risk of cancer (Rechner and Kroner, 2005), improved neuron function and it also protects brain tissue from hypoxic ischaemic injury (Andres-Lacueva *et al.*, 2005). Improved vision (Rice-evans *et al.*, 1995), memory (Joseph *et al.*, 1999) and as well as suppression of putting on weight (Tsuda, 2008).

Apoptosis induction is the major contribution of berry phenolics, especially anthocyanins. These phenolics also have antimicrobial activities which help to manage the natural spectra of pathogens against antibiotic resistance. The phenolics also possess antioxidant properties that contribute to protect humans from degenerative diseases and their effects on health (Zhao and Moghadasian, 2008).

Phenolics may also cause toxicity because of their pro-oxidant activity, inducing properties, apoptosis and their relations with drug metabolizing enzymes (Dai *et al.*, 2007). These compounds inhibit the enzymes action by making complexes with other elements that catalyze oxidation reactions (Rice-evans *et al.*, 1995; Harborne and Williams, 2000; Heim *et al.*, 2002). Berries are the fruits referred to as natural valuable foods reported by many researchers (Häkkinen and Törrönen, 2000; Wang and Lin, 2000; Connor *et al.*, 2002; Hakala *et al.*, 2003; Skupień and Oszmiański, 2004; Taruscio *et al.*, 2004). The bio-availability of these natural compounds in fruits and vegetables significantly maximize the beneficial health effects as pharmaceutical form of supplements in (Wang *et al.*, 1996; Sellappan *et al.*, 2002).

Strawberry ameliorate lipid profile and lipid oxidation in females: Epidemiological observations also imply that strawberries have valuable effects on cardiovascular activity of women. The Women's health study revealed that strawberry intake has a significant inverse relation with cardiovascular disease mortality among 34,489 obese postmenopausal women (Mink *et al.*, 2007) another study between 26,966 obese postmenopausal women recommended that intake of strawberries two times a week reduces the chance of superior CRP (Sesso *et al.*, 2007). It was also observed that frozen strawberry consumption reduced serum cholesterol levels; this study suggests a need for future studies to verify their beneficial role as a possible nutritional approach that can lower cholesterol in chubby women. Phytosterols, potassium, fiber, vitamin C, folic acid and phytochemicals are known agents in strawberries that are cardio protective and contribute to the anti-inflammatory, antioxidant and hypo-cholesterolemic activities (Carkeet *et al.*, 2008).

Some non-conclusive results showed positive correlations

between shelf life of strawberries their antioxidant capacity and disease susceptibility (Khanizadeh *et al.*, 2008; Tao *et al.*, 2010). Phenolic compounds delays senescence of fresh fruits by inducing oxidative degradation and thus contribute to extend the shelf life and improved fruit quality (Connor *et al.*, 2002).

Strawberry and cholesterol lowering diet: Strawberries maintain serum lipid reduction of daily diet and can improve palatability of cholesterol-lowering food. The risk of cardiovascular attack are reduced by inhibition of LDL-cholesterol oxidation caused by antioxidants present in strawberries, it also promotes sign stability, decreased tendency of thrombosis, better vascular endothelial functions, suppresses regulation and proliferation of tumors and, it also has anti cancerous effects (Hannum, 2004).

Jenkins *et al.*, (2008) suggested that cholesterol level can be lowered by eating freeze-dried strawberry powder supplementation. Phytosterol, fiber and phytochemical content present freeze-dried strawberry powder may be responsible for cholesterol lowering. Clinical studies revealed that the lower cholesterol levels and reduce cholesterol absorption is due to phytosterols (Rudkowska *et al.*, 2008). Cholesterol lowering effects can be due to dietary fiber present in strawberry (Nickel *et al.*, 2009) reversing or slowing the process of atherosclerotic heart problems in overweight females with factors of metabolic risk that may be achieved by long-term intake of antioxidant-rich fruits e.g.: strawberries. Strawberry powder supplementation enhances lipids and lipid peroxidation. Lipid peroxidation in females with metabolic disorder can be achieved by ingesting strawberry as a natural source of phytosterols, polyphenolic flavonoids and fiber present in FSP (Basu *et al.*, 2009).

Anti-cancerous effect of strawberry phytochemicals: The phenolic constituents of the berry's through multi-mechanistic mean of action including the antioxidation protects DNA from damage and also their effects are exerted outside thus leading to anticancerous effects (Seeram *et al.*, 2006). The lignans from plant origin adds to plasma and urinary intensity of mammalian entero lactone are present in ample amount as constituent of berries (Mazur *et al.*, 2000).

The Past auto-oxidation and multiple step mechanisms action, including antioxidant protection of DNA from oxidative damage is a result of strawberry phytochemicals which protects humans from cancer (Seeram *et al.*, 2006). Viral , parasitic infections and Chronic bacteria can be caused by over production of these oxidants, as an imbalance, leads to oxidative stress (Liu and Hotchkiss, 1995), that can cause oxidative damage to bigger biomolecules such as lipids, proteins, and DNA, resulting in an increased risk for cancer and heart disease (Ames and Gold, 1991; Ames *et al.*, 1993; Liu and Hotchkiss, 1995). Apoptotic effects have been shown in human cancer cells by the berry extracts (Heo and Lee, 2005; Meyskens Jr and Szabo, 2005; Ramos *et al.*, 2005).

There is a need to consume sufficient amounts of antioxidants avoid or reduce the oxidative stress stimulated by free radicals. The risk of persistent diseases and oxidative damage to the cellular system can be prohibited or lowered by antioxidant compounds (phytochemicals), such as phenolics and carotenoids present in the natural fresh food (Ames *et al.*,

1993; Adom and Liu, 2002; Chu *et al.*, 2002; Sun *et al.*, 2002). The cell-signaling pathways, the modulation of gene expression and the inhibition of transcription factors caused suppression of cancer cell proliferation, transformation and tumor progression, this have been entailed as major contribution of strawberry phytochemicals (Seeram *et al.*, 2006).

Fruits like strawberry contains dietary antioxidants prevent or limit the potential cancer-inducing oxidative damage. The antiangiogenic and chemopreventive properties of the extracts have been recorded, due to their ability to inhibit mutagenesis caused by several carcinogens. Another mechanism of action of strawberry phenolics hypothesized by inhibitory effects of these compounds on enzymes implicated in cancer development, such as phase-II detoxification enzymes and cyclo-oxygenase enzymes (Seeram *et al.*, 2001). Cyclooxygenase enzymes, converts arachidonic acid to eicosanoids and is linked with the development of inflammation, is considered as part of common pathway of many chronic disease development hypothetically.

The phenol mechanisms and unit of tissue distribution and accumulation after berry intake does not determine the direct effect of these compounds in the health benefits correlated with the whole fruit. Strawberries have great potential as chemo-preventative agents in that their naturally-occurring phytochemical compounds have health-promoting properties that can prevent disease progression, malignancy, and recurrence (Seeram, 2008; Stoner, 2009).

Wang and Stoner (2008) demonstrated the antiproliferative activity of strawberry extracts on human lung epithelial cancer cell lines. Strawberry extract was found to decrease the activity of transcription factors involved in tumor promotion mediators, specifically activator protein-1 (AP-1) and nuclear factor- κ B (NF- κ B), in TPA- or UVB-induced tumor promotion as well as inhibited MAPK signaling (Wang and Stoner, 2008). Seeram *et al.* (2006) reported a dose-dependent anti-proliferative effect in oral cell lines with a phenolic-enriched strawberry extract. Inhibition of proliferation of human oral tumor cell lines with both crude extracts and 32 isolated compounds from strawberries was reported by Zhang *et al.* (2008). Similarly, it was found that strawberry extract was able to stimulate apoptosis in human HT-29 colon cancer cell lines (Seeram *et al.*, 2006) and inhibit angiogenesis in a berry extract blend (Bagchi *et al.*, 2004).

Strawberry consumption and urate level: Nutritional quality of many fruits is now evaluated by using the antioxidant ability (TAC) of fruit extracts; it is also used as a measure of antioxidant concentration in the food matrix. The considerable raise in plasma or serum TAC is always linked with the consumption of flavonoid rich foods. As per observation of the consumption of different types of fruit without uric acid contributes to the increase of the serum concentrations of urate, which is a very important contribution to plasma antioxidant effect. However, recent studies hypothesized that fructose present in fruits like apples may possibly be responsible for the increase in plasma urate (Lotito and Frei, 2004).

Clinical case reports of patients with gout showed that it is cured by the consumption of a daily serving of cherries and

cherry products for up to 3 months as it reduces plasma urate to normal levels. This is further confirmed by the scientists that cherry consumption positively decrease plasma urate supporting the reputed anti-gout efficacy of cherries (Jacob *et al.*, 2003).

Linnaeus further confirmed the role of strawberries as a gout reliever. Adding to it another herbalist message from France encouraged strawberry regime for persons suffering from kidney stones or gout. Many researchers conducted experiments to verify the serum level concentration before and after strawberry consumption, led to non-significant results (Cao *et al.*, 1998; Jacob *et al.*, 2003), due to the difference of the experimental designs and the analytical methods used.

Tulipani *et al.* (2008) reported that high concentration of vitamin C found in strawberry significantly increases the serum concentrations but no variation in the urate levels. However, experimental studies on people revealed that urate concentrations in response to strawberry consumption, ranging from slight modification to 50 % decrease and 20 %, it was measured that the serum urate up to 3 h of strawberries consumption had no change on urate level though it decreased later on; similar results were also observed for cherries.

Antioxidant activity of strawberry: Recent studies have revealed that the phenolic compounds present in strawberries are responsible for antioxidant properties rather than to vitamin C (Eberhardt *et al.*, 2000; Rekika *et al.*, 2005; Tao *et al.*, 2010). The Strawberries can be consumed as a natural antioxidants source (Wang and Lin, 2000; Khanizadeh *et al.*, 2008).

Antioxidants from fruits and vegetables protect humans from oxidative stress and its deleterious consequences (Battino *et al.*, 2009). Strawberry is a beautiful bright berry with excellent visual appearance and delicious flavor is one of the major source of antioxidant, high ascorbic acid and phenolic contents. Phenolic compounds present in strawberries are hydroxycinnamic acids (*p*-cumaric), flavonols (quercetin, kaempferol and myricetin), hydroxybenzoic acids (gallic and ellagic acids), flavan-3-ols (catequins, hydrolysable tannins (epicatechins), (ellagitannins), and anthocyanins, being pelargonidin-3-glycoside, the most chief flavonoid pigment (Seeram *et al.*, 2006; Tulipani *et al.*, 2008).

It is found that strawberry extract increased the activity of antioxidant and oxidative stress repair enzymes (Zhang *et al.*, 2008). Strawberry flavonoids are also able to chelate metal ions and therefore prevent generation of reactive oxygen species. Flavonoids have been shown to inhibit lipid peroxidation within the phospholipid bilayer by localization within the polar and nonpolar phases (Movileanu *et al.*, 2000). Quercetin has been show to increase glutathione S-transferase activity, an enzyme responsible for protecting cells against oxidative stress (Van Zanden *et al.*, 2003).

The World Health Organization signifies the vital role of small colorful fruits for their antioxidant activity of phenolic components that prevents humans from many health problems like diabetes, cancer, cardiovascular diseases and obesity (Stapleton *et al.*, 2008). Three-fold more ellagitannins content are present in berries than walnuts and pecans and about fifteen-fold more than other fruits and nuts (Rommel

and Wrolstad, 1993; Beekwilder *et al.*, 2005). Many biologically significant mechanisms are exhibited by phenolic compounds like detoxification or scavenging of ROS, blocking ROS production, impacting cell cycle, tumors suppression, modulation of signal transduction, detoxifying enzymes, apoptosis, and metabolism (Liu, 2004; Han *et al.*, 2007).

Strawberry as oral disease preventive: Oral health has a significant effect on overall health and quality of life. Conditions such as periodontitis, xerostomia, mucositis, and tooth decay are associated with co-morbidities such as decreased saliva production, difficulty in chewing and swallowing, and loss of taste (Gift and Atchison, 1995). In addition, new diagnoses of oral cancer are estimated to be in excess of 35,000 in 2010 (Centers for Disease Control and Prevention, 2009).

Strawberry phytochemicals could improve oral maladies (Seeram *et al.*, 2006; Hämäläinen *et al.*, 2007; Zafra-Stone *et al.*, 2007; Wang and Stoner, 2008; Palacios *et al.*, 2009). Fruit phenolics have been shown to elicit significant protective effects on oral mucosa when evaluated in numerous pre-clinical animal models (Seeram, 2008; Stoner, 2009) and may be a novel prevention tool instead of costly pharmaceutical agents that may have undesirable side effects.

The association of chronic disease and oral health is possibly due to infection, chronic inflammation, genetic predisposition, and potentially nutrition (Ritchie *et al.*, 2002; Ritchie *et al.*, 2003). Seeram *et al.* (2006) reported a dose-dependent anti-proliferative effect in oral cell lines with a phenolic-enriched strawberry extract. Inhibition of proliferation of human oral tumor cell lines with both crude extracts and 32 isolated compounds from strawberries was reported by Zhang *et al.* (2008).

Anti-aging property of strawberry: There are numerous cognitive (Bartus, 2000) and motor behavioral deficit that occur during aging and are related to the alteration in the striatal dopamine (DA) system (Joseph, 1992) or in the cerebellum. Long term exposure to oxidation (Cantuti-Castelvetri *et al.*, 2000) and inflammation (Hausse-Wegrzyniak *et al.*, 1999) are thought to be the contributing factors to the decrements in cognitive and motor performance that is evident in aging and other neurodegenerative diseases. Strawberry exerts their effects directly by changing cell signaling to improve or increase neuronal communication, calcium buffering ability neuro-protective stress shock, plasticity and stress signaling pathway (Shukitt-Hale *et al.*, 2008).

Strawberries have the potential of slowing and even reverse age-related deficits in behavior and signal transduction in rats (Joseph *et al.*, 1998; Shukitt-Hale *et al.*, 1999). The scientists kept rats on a control diet for 8 weeks prior to being exposed to whole-body irradiation for evaluating the efficacy of berry diets (Shukitt-Hale *et al.*, 2007). It was found that the berry diets protected deficits irradiation impaired performance in the Morriswater maze.

The strawberry consumption show better protection for spatial deficits the studies that have been initiated by the researcher suggest that phytochemicals present in antioxidant-rich foods such as strawberries may have benefits in retarding functional age-related, cognitive behavioral

deficits and central nervous system thus positively impacting neurodegenerative disease in humans also.

Strawberry and leukemia: Strawberries have known anti-cancer benefits like it inhibit the initiation and promotion of the carcinogenic process (Hannum, 2004). The strawberries and other types of berries have methanol extracts, that helps to inhibit the growth of colon, prostate, breast, and oral cancer cells (Seeram, 2008).

The need is to develop alternative dietary and therapeutic approaches that may be more effective for prevention or treatment of this disease. Zunino *et al.* (2009) reported that the patients with high-risk of B-lineage suffer apoptotic cell death in cell lines due to resveratrol, curcumin, carnosol, and quercetin including those that carry the translocation of t (4;11) as well as the other lines without the translocation (Dörrie *et al.*, 2001; Kellner and Zunino, 2004), The bioactive components displaying anti-cancer activities have been shown by strawberries, the purified foam of these constituents induce apoptosis in high-risk t (4;11) cell lines (Dörrie *et al.*, 2001; Kellner and Zunino, 2004).

The quercetin, kaempferol, and ellagic acid are the most effective anti-leukemia phytochemicals (Kellner and Zunino, 2004). The fresh strawberries (w/w) contains 1.1–1.9 mg and 0.5 mg per 100 g of quercetin and kaempferol respectively (Harnly *et al.*, 2006). The in-vitro studies confirm that the components of strawberries kill leukemic cells in a cell culture system.

FUTURE PROSPECTS

Although considerable progress has been made in our understanding of the possibilities of strawberry phytochemicals as an important source of food for a better health and prevention of disease, there are always standstill holes in our knowledge of bio-chemistry about these compounds. Therefore future studies should be planned to boost our knowledge related to these complex compounds and the roles and functions of strawberry phytochemicals at the cellular and molecular level. Future works should also focus on promoting healthy aging, the prevention of chronic diseases in humans and to improve the quality of life through new gene-nutrient interactions and health outcomes in order to achieve better human life.

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