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## 1. 0 INTRODUCTION

Cancer is one of the major health problems around the globe. According to National Cancer Institute, cancer is defined as a class of disease in which abnormal cells proliferate in an uncontrolled way and are able to invade other tissues and organs via blood and lymph system in the body. There are 100 different types of cancers exist in this world. Cancer is usually named by the organ or the type of cell where cancerous cell starts to grow, for example, cancerous cell that begins to grow in colon is known as colon cancer. (National Cancer Institute, 2012)In the human body, cells are constantly dividing and growing to form new cells and then old and damaged cells undergo apoptosis and they are constantly replaced by new cells in order to prevent any mutations that may occur in our body. Sometimes, there may be mutation in this controlled process. In other words, there is tremendous amount of new cells formed in an uncontrolled way and the damaged or old cells do not undergo apoptosis properly. Therefore, this causes unregulated accumulation of cells, which leads to the formation of tumor. Hence, cancer may result. (National Cancer Institute, 2012)Image titled Loss of Normal Growth Control. The image shows normal cell division and normal cell suicide or apoptosis of a damaged cell. It also shows cancer cell division, through several mutation stages, ending in uncontrolled growth. Figure 1: Comparison between normal cell division and cancer cell division (National Cancer Institute, 2012)Cancer can be grouped into several categories, which are carcinoma, sarcoma, leukemia, central nervous system (CNS) cancers and also lymphoma and myeloma. Carcinoma is a type of cancer that spreads in the skin or in the tissues that line the internal organs. It can be further divided into a few subgroups, including squamous cell carcinoma, basal cell carcinoma, transitional cell carcinoma and adenocarcinoma. Besides that, sarcoma is regarded as a cancer that spreads in the bone, cartilage, muscle, blood vessel, fat or other connective tissues while leukemia is a type of disease in which cancerous cells are formed in blood-forming tissues, for example, bone marrow. This leads to the mass produced of abnormal blood cells and then circulates in the blood throughout the body. Central nervous system (CNS) cancer is defined as a cancer that spreads throughout the tissues of the brain and spinal cord. Lastly, lymphoma and myeloma result from the cancerous cells that invade immune system. (National Cancer Institute, 2012)In year 2012, American Cancer Society had made an estimation on the amount of cancer patients. They forecast that approximately 1, 638, 910 new cancer cases would be diagnosed. Moreover, about 577, 190 Americans are expected to die because of cancer. The number of patients died of cancer exceeds 1500 people per day. In other words, cancer has been reported for nearly 1 of every 4 deaths in United States of America. (American Cancer Society, 2012) Besides, World Health Organization (WHO) also expected that the number of deaths caused by cancers will keep on increasing, with an estimated 13. 1 million deaths in 2030. (World Health Organization, 2013)Oxidative stress is one of the principal factors that increase the risk of the incidence of cancers. (Rao et al., 2003) The unrepaired oxidative damage changes the cell biology and results in mutation, which can therefore lead to neoplasia, abnormal proliferation of cells. Studies showed that increased intake of vegetables and fruits in daily lives could lead to a lowering risk of cancer. This is because both vegetables and fruits are valuable sources of antioxidants and phytochemicals that act as protective agents which can prevent oxidative damage. Hence, both vegetables and fruits play an important role in combating against cancer. (Key, 2011)Projected Number of Cancer Deaths Worldwide 2008 2030Figure 2: Graph of number of deaths worldwide caused by cancers from 2008- 2030. (American Cancer Society, 2012)Researchers have deduced several risk factors that related to the incidence of cancer. The risk factors that influence the development of cancer are age, family history, dietary factor, lack of physical activity, sunlight and tobacco and alcohol abuse. The chance that a person will be diagnosed with cancer increases with age. Therefore, adults who are middle-aged or older are much easier to be diagnosed with cancer. Most cancer cases usually occur in people of 55 years old or above. (American Cancer Society, 2012)Genetic factor also plays a role in deciding the chances of a person will be diagnosed with cancers. Most cancers are due to the gene mutation. These mutated genes can be passed from parent to their children and therefore increase the risk of getting cancer. Some cancers are usually happened among family members rather than in the rest of the population. For instance, breast, ovary, and prostate cancers often occur around family members. (National Cancer Institute, 2006)Dietary factor and lack of physical activity are other important factors that affect the risk of getting cancer. People who always have a poor diet and lack of physical activity may increase the risk of several types of cancers. Some studies showed that people who always consume red meat or high-fat food products and consume less fruits and vegetables tend to have a higher risk of developing several cancers such as prostate and colon cancers. Besides that, people who have inadequate of physical activity tend to develop cancers of uterus, colon, oesophagus and also kidney. (National Cancer Institute, 2006)The main function of ozone layer is to absorb harmful ultraviolet radiation from sunlight and thus preventing them from entering the Earth's atmosphere. However, the depletion of ozone layer allows these harmful ultraviolet radiations to penetrate into the earth and cause harms to human beings. Ultraviolet radiation not only comes from the sun, but it can also be originated from sunlamps and tanning booths. These harmful ultraviolet radiations result in early skin aging and thus damage our skin that can lead to skin cancer. (National Cancer Institute, 2006)Statistics showed that more than 180, 000 Americans died from cancer every year due to tobacco used. People who are not smoker but often surrounded themselves with tobacco smoke have higher chances to be diagnosed of cancers. Among several types of cancers, smokers are more likely to develop lung, larynx or oesophagus cancer. Other than tobacco, alcohol abuse also increases the risk of getting cancer. Alcoholics tend to have higher chances to develop cancers such as mouth, liver or throat cancer if compared to non-alcoholics. (National Cancer Institute, 2006)In order to combat against cancer, it is important to know the risk factors and also deduce out the effective preventive methods. On recent years, a nutritional approach has been studying for the prevention of cancer. Many studies demonstrated that vegetables and fruits are prevalent sources which can help to reduce the risk of the incidence of the cancer. Carotenoids are one of the most greatly studied among the plant constituents and it is regarded as effective cancer preventive agent. Recently, a tomato carotenoid named lycopene has been gained interest as regards its role in some cancers. Lycopene presents as a red pigment in many vegetables and fruits such as pink grapefruit, pomegranate, watermelon, papaya and so forth. Studies have showed that tomatoes are the predominant source of lycopene among others. Lycopene is a very potent antioxidant that contributes its chemopreventive effect in terms of quenching singlet oxygen. Lycopene is twice as effective as β-carotene and it is also 10-times more active than α.-tocopherol as an antioxidant. (Rao et al., 2003)

## 2. 0 LITERATURE REVIEW

## 2. 1 Characteristics of Lycopene

Lycopene, which is also known as rhodopurpurin, is a carotenoid which presents as a red pigment in tomatoes (Lycopersicon esculentum Mill.) and other vegetables and fruits such as pink grapefruit, pomegranate, watermelon, papaya and so forth. However, tomatoes are found to be the predominant sources of lycopene. Furthermore, it is not an essential nutrient for human beings but it can be easily obtained from our daily dishes such as tomato sauce. With the help of various lipoproteins present in the stomach, it can be easily transported to the liver, testes and adrenal glands via the bloodstream. (Kanwar, 2011)Lycopene is an acyclic isomer of β-carotene. The molecular formula of lycopene is C40H56 and its molar mass is 536. 87gmol-1. Its melting point falls between 172- 175oC. Lycopene is insoluble in water but it is soluble in apolar organic solvents and oil. Lycopene cannot be naturally synthesized by the body of human and animals but it can be produced by the plants and microorganisms. (Ganesan et al., 2012)Lycopene tends to aggregate and appear in crystalline form in aqueous solution. This characteristic is suspected to cause the inhibition of the bioavailability of lycopene in humans. The crystalline form of lycopene that found in fresh tomatoes is thought to give the bright red colour of the ripe fruits. (Shi et al., 2002)Structurally, lycopene is a polyunsaturated hydrocarbon consisting of 11 conjugated and 2 unconjugated double bonds. The two methyl groups are arranged in a 1, 6-position relative to each other while the remaining methyl groups are arranged in a 1, 5-position. Lycopene with its extensively conjugate polyene system has contributed to the biological activity, including its susceptibility to oxidative degradation. (Ganesan et al., 2012)lycopene chemical structureFigure 3: The structural formula of lycopene. (Lycocard, 2006)The most distinctive property of lycopene is that it is always red in colour. This is due to the deposition of greater amount of lycopene in microcrystalline form in chromoplasts of the peel and flesh. Lycopene is the major carotenoid found in tomatoes as it contributes approximately 80% of the total carotenoid content in tomatoes. The remaining 20% carotenoid content including β-carotene, phytoene, phytofluene, lutein, γ-carotene and ζ-carotene. (Goralczyk and Siler, 2004)Lycopene can exist in both trans and cis configuration. This is due to the presence of the double bonds in its structure. Most lycopene in fresh tomatoes are in all-trans configuration, which are the most stable configuration in thermodynamics. In contrast, most lycopene in processed tomato products are in cis form, for instance, 5-Z (cis), 9-Z, 13-Z and 15-Z isomers. This is because heat treatment during processing the tomato products would result in isomerisation, which converting all-trans lycopene to its cis-form. In other words, the amount of cis-form lycopene increasing with increasing temperature and the length of time used to process tomato products. (Goralczyk and Siler, 2004)The critical aspect of the functionality of the lycopene is stability. Due to the highly conjugated nature of lycopene, it can be degraded by isomerisation and oxidation. All-trans isomeric form of lycopene can be isomerised to a less stable mono- or poly-cis- conformation by thermal, light or chemical reactions. (Shi et al., 2002) Chemical and physical factors that cause the degradation of other carotenoids in general also affect lycopene. These factors includes high temperature, light, oxygen, metallic ions such as Cu2+ or Fe3+, pH and active surfaces. Therefore, lycopene can undergo modification during the processing and preparation of tomato-based foods. (Shi et al., 2002)The presence of 11 conjugated double bonds in the backbone structure of the lycopene results in the theoretical arrangement of lycopene in 2048 different geometrical configurations. It is stable at high temperature and can be stored. (Johary et al., 2012) In the contrary, cis isomeric form of lycopene possesses chemical and physical characteristics that are distinctly different from those all-trans isomers of lycopene. normal. img-000. jpgFigure 4: Structures of different isomeric form of lycopene present in processed tomato products. (Goralczyk and Siler, 2004)Lycopene is a potent, natural source of antioxidant that contributes its chemopreventive effect in terms of quenching singlet oxygen. Unlike some other carotenoids, β-ionone ring is absent in the structure of lycopene. As it lacks of β-ionone ring, therefore it cannot be cleaved to produce vitamin A. Thus, there is more availability for the activity of antioxidant. Moreover, the structure of lycopene with extra double bonds and unusual stereochemical properties also devote to its powerful antioxidant effects. Lycopene is twice as effective as β-carotene and also 10-times more active than α.-tocopherol as an antioxidant. (Breemen et al., 2011)

## 2. 2 Lycopene content in fresh tomato versus processed tomato product.

Other than tomatoes, lycopene can also be found in other kinds of fruits and vegetables, for examples, papaya, watermelon, guava, pink grapefruit and etc. However, several studies showed that more than 90% of the lycopene intake comes from tomatoes and processed tomato products like tomato paste and tomato ketchup. (Lycocard, 2006)Fresh tomatoes are the predominant source of lycopene. The availability of lycopene content in fresh tomatoes can be affected by the species and the ripening stages of tomatoes, weather, soil and agricultural practices. (Lycocard, 2006)On the other hand, the availability of lycopene content in processed tomato products depends on the processing and storage conditions. Studies showed that the availability of lycopene in processed tomato products is much higher than that of in fresh tomatoes. This is because food processing increases the lycopene content by disrupting the cell wall and also the tissue matrix of fruits and vegetables, which weakens the bonding force between lycopene and tissue matrix. Hence, it is more available in processed tomato products rather than in fresh tomatoes. (Goralczyk and Siler, 2004)Table 1 Comparison between lycopene in processed tomato products versus lycopene in fresh tomatoes. (Lycocard, 2006)ProductsTotal lycopene content (mg/100g)Tomato paste28. 8Tomato ketchup16. 7Tomato Juice9. 0Canned tomatoes2. 7Raw tomatoes (red)2. 6Pink grapefruit1. 4Embedded image permalinkFigure 5: The physical disruption of the cell structure in processed tomato products (tomato juice, above right) compared to fresh tomatoes (above left) partially explains the difference in the bioavailability of lycopene. (Lycocard, 2006)