CHAPTER 1 INTRODUCTION

1.1 Background

Carbon based nanomaterials having lower than 10nm diameter, known as carbon dots (CD), has caught the attention of researchers since its unprecedented discovery in 2004(Xu et al., 2004). Realization of their photoluminescence property upon surface passivation by Sun *et al.*(Sun et al., 2006) unveiled their unlimited applications in different fields. Potential use for bioimaging both in vitro and in vivo have been demonstrated(Cao et al., 2007; Dias et al., 2019; Fahmi et al., 2020; Kwee et al., 2020; Yang et al., 2009). Carbon dots in comparison to their silicon counterparts possess an encouraging photoluminescence nature coupled with added advantage of significantly lower cytotoxicity and excellent biocompatibility thereby making its usage for cellular staining possible. These nanomaterials were subjected for MCF-7 breast cancer cells imaging which resulted in labeling the cell membrane and cytoplasm(Cao et al., 2007). These CDs enter the cell in temperature dependent manner. At about 4°C, poor entrance was observed(Cao et al., 2007). Recently, Fahmi *et al.* (Fahmi et al., 2020) have shown that CDs could also enter cell via endocytosis, as earlier hypothesized(Cao et al., 2007). As such CDs capable of interacting with membrane surface of the cell could enter even at 4°C.

Influence that surface functional groups on CDs has on cellular penetration and interaction as well as its tunability into cellular recognitive(Gao et al., 2017) material have paved way for more detailed study on the future biomedical applications of carbon dots (Kong et al., 2014). In addition to its use for imaging gastric cancer cell lines (MGC-803), CDs modified with Ribonuclease A showed potency as anticancer candidates due the concentration dependent cytotoxic effect shown by these RNase A@CDs. Thus, suggesting its use in cancer therapy(H. Liu et al., 2014). CDs from ginger juice could selectively suppress the growth of human hepatocellular carcinoma cells (HepG2)(Li et al., 2014). These and many other CDs

from different sources have been shown to be useful in cancer therapy(Gao et al., 2017; Li et al., 2016; Xie et al., 2017). Although not thoroughly studied, CDs with potential procoagulant activity have been reported(X. Liu et al., 2018; Zhang et al., 2017). In addition, HIV-1 infection was hindered by employment of CDs based on Aminophenyl Boronic acids(Aung et al., 2020), thus can be potent in HIV treatment. Besides its application for bioimaging and therapy, CDs also have other applications as biosensors.It was demonstrated that CDs from hydroxypropylmethyl cellulose could be used as sensors for ciprofloxacin detection(S. Wang et al., 2017). A highly sensitive and selective molecularly imprinted polymer based CDs (MIP@CDs) was prepared for the detection of Acetylcholinesterase (AChE), an important enzyme in diagnosis of Alzheimer's disease (AD)(Jia et al., 2019). In addition, Fe_3O_4@Carbon dots nanocomposites were used as curcumin carriers for possible AD treatment(Kuang et al., 2020). On the other hand, CDs have been utilized as initiators for low cost, nontoxic and one-step polymerization of pyrrole and its copolymer(Maruthapandi and Gedanken, 2019). CDs also have other applications as metal ion sensors(Meena et al., 2019; Zhan et al., 2019). Campuzano *et al.*(Campuzano et al., 2019) cited wider applications of CDs in biosensing. They were used for the detection of glucose, H_2O_2, dopamine, TNT, among others. These CDs were also involved in the preparation of DNA sensor for detecting single gene mutation(Campuzano et al., 2019). Mostly, CDs used as molecule detectors has enzymes immobilized at the surface of the CDs nanoparticles. For instance, horseradish peroxidase immobilized on the surface of CDs was used in the detection of hydrogen peroxide while glucose oxidase immobilized at the surface CDs could be used to detect glucose. Similar to what was discussed above, surface functionalization of these CDs played vital role in the enzyme immobilization(Ji et al., 2016; Su et al., 2018). Therefore, it is crucial to consider engineering of CDs surfaces for wider and valuable applications.

On the other hand, as cancer cases continue surge, there is a high demand for the development of newer cancer treatments that offer promising therapeutic effect. Besides, these treatments are demanded to be affordable with better cancer targeting ability. Therefore, cancer treatments with fewer side effects and readily available are in high demand.As stated above, CDs with cytotoxic effects against cancer cell lines were reported(Gao et al., 2017; Li et al., 2014; H. Liu et al., 2014; Xie et al., 2017). CDs could be the new means of cancer treatment with the desired qualities because they could be obtained from various sources that are widely available and sustainable.(Chahal et al., 2021; Ghosal et al., 2020; Kumar et al., 2017; Mewada et al., 2013; Wang and Zhou, 2014; Xue et al., 2016). Because of the promising nature of CDs derived from natural products, especially as anticancer agents, we believe exploring their synthesis from medicinal natural products could unleash the kinds of cancer treatments that have been wanting. Therefore, we aimed to carry out study on reported CDs from organic sources with potential ability of cancer treatment.

1.2 Problem Statement

Neoplasm which is commonly known as cancer has remained to be among the most worrying and death causing diseases. It was predicted that global cancer cases would reach over 28 million by 2040(Sung et al., 2021). Such increase in cancer cases could be linked to the challenges faced in treating the disease. For instance, treatment usually costs thousands of dollars(Dolgin, 2018) and the cost continue to increase. Therefore, treatments could not be afforded especially for those living in low-income countries.

As a result, there is a high demand for newer alternative cancer treatments that could be affordable and having better therapeutic nature. A promising alternative towards this might be in the exploration of organic compounds as raw materials for the development of novel carbon-based nanomaterials. Methotrexate is an organic compound commonly used as an anticancer drug. Carbon dots developed from this

methotrexate have shown enhanced anticancer activity (Azizi et al., 2020). Despite the potencies in developing carbon dots from organic molecules, few considerations are given to this promising area. Therefore, it is necessary to study in details the current advances in the Carbon dots development from organic sources for cancer therapy.

1.3 Research Objectives

The objective of this review study is generally to showcase the potential of carbon dots derived from organic sources for cancer treatments.

Moreover, specific objectives include:

- To review the methods employed in the synthesis of carbon dots;
- To discuss carbon dots derived from small and large molecular weight organic compounds;
- To show the relation between the function and sources of carbon dots;
- To summarize previously reported carbon dots with potential anticancer activity.

1.4 Research Benefits

Although CDs have been prepared from diverse sources for numerous applications, in this review we would focus on the synthesis of CDs from wide range of organic compounds/sources. We would also review their synthetic methods and then end with discussion on the potential application of carbon dots derived from organic sources for cancer therapy. As it is the main focus of our research, selectively cytotoxic CDs derived from organic sources could offer a cheaper alternative for cancer therapy due to their ease of preparation and cheap sources. Some CDs with such ability were even derived from used organic source. Therefore thorough studies in this area could offer an avenue of re-using food wastes for the simple development CDs. As a result,

would provide synergistic benefits through environmental pollution reduction as well as affordable cancer treatments.