CHAPTER I
INTRODUCTION

Problems associated with the administration of free drugs such as limited solubility, poor biodistribution, lack of selectivity between drug and targeted cells, unfavourable pharmacokinetics and healthy tissue damage can be overcome and improved by the use of a targeted drug delivery system. Nanocarriers such as nanoparticles, nanotubes and nanowires, nanospheres, nanocapsules, dendrimers, polymeric micelles, etc. are widely promising vehicle which used in drug delivery system because they present targeted delivery to targeted cells while provide the drug efficiency. Nanocarriers can deliver drugs to specific area within the body. Furthermore, they can overcome resistance from the physicochemical barriers in the body. Therefore, efficient delivery of drugs to various part of the body is successful because it is directly affected by nanoparticles. Drug delivery system can be improved by nanocarriers such as increasing solubility of poorly soluble drugs in order to enhance bioavailability for timed release of drug molecules and precise drug targeting. The surface properties of nanocarriers can be modified in order to reduce drug toxicity and provide more efficient drug distribution.

Among attractive nanomaterials, carbon nanotubes (CNTs), have been studied in a wide variety of scientific research and applications. Because CNTs possess unique properties, CNTs exhibit excellent thermal and chemical stabilities. In addition, they also possess semi- and metallic-conductive properties. For these reasons, CNTs have been widely used in many applications and impacted to the scientific breakthroughs in the present. Integrating CNTs in biomedical applications as a drug carrier is one of major challenge of CNTs research to date for therapeutic molecules in drug delivery system. Due to unique physicochemical properties of CNTs which maintain their structure in any conditions, CNTs are suitable materials to be used as drug carrier. Moreover, CNTs offer some interesting advantages over the spherical nanoparticles for biomedical applications. The large inner volume of CNTs allows the loading of small biomolecules while their outer surface can be modified by covalent and noncovalent surface modification. Since CNTs can hardly be dispersed in any kind of solvent and tend to aggregate due to

van der Waals interaction of intertube, the development of efficient methodologies for surface modification of CNTs is needed to overcome this obstacle. Two main approaches of surface modification of CNTs have been proposed including covalent and non-covalent surface modification to overcome this barrier. Surface modification of CNTs, especially, using modified CNTs as a drug carrier in drug delivery application, dispersion and stability efficiency of CNTs are necessary improved. In term of dispersion, the modified CNTs provide high specific surface area for high adsorption with other molecules while in term of stability, individual CNT after dispersing should be stable in the solution without any precipitation. To apply CNTs in biomedical applications, cytotoxicity of CNT is another concern which was still argued in scientific research until now. However, many different toxicity results of CNTs have been published and proposed where there are five S factors concerned with CNT toxicity including size, source, shape, surface chemistry and surface area.

In this work, CNTs were modified both by noncovalent and covalent modification to improve CNTs dispersion and stability which are having hydrophilic species either positive or negative charge at their surface. Molecular dynamics simulation was carried out for the pristine CNT and non-covalent modified CNT, with 60%DD chitosan, in aqueous solution. This aims to understand and explain their solubility at molecular level and to confirm the result of noncovalent surface modification of CNT with various degree of deacetylation of chitosan in experimental method. For drug loading, modified CNT with multilayers thin film between PDADMAC and PSS were used as a drug reservoir. The coating multilayers on CNT were loaded with model hydrophilic drugs; gentian violet and diclofenac sodium salt. Furthermore, drug loading were quantified by releasing in ethanol. Cytotoxicity of modified CNT and pristine CNT was evaluated with L929 mouse fibroblast cell using MTT assay. In addition, the interference of formazan adsorption on CNT surface was investigated in order to confirm the potential of this assay. The characterization techniques used in this work are UV-Vis spectroscopy, zeta potential measurement, transmission electron microscopy, gel permeation chromatography, fourier transform infrared spectroscopy and raman spectroscopy.

UV-Vis spectroscopy was used to investigate the dispersion efficiency and stability of modified CNTs. In addition, the drug loading and drug release from modified

CNTs in individual tubes and film were detected using UV-Vis spectroscopy. Modified CNTs with polyelectrolyte via layer-by-layer technique was monitored using transmission electron microscopy. To confirm the surface charge of modified CNTs, electrical charge in term zeta potential was investigated using zeta sizer instrument.

The results obtained from this study can be used as a guidance for preparing CNTs by modifying their surface properly to apply as drug carriers in drug delivery application in future.