CHAPTER I

INTRODUCTION

Curcumin is widely used in pharmaceutical, food and cosmetics. Several studies found that curcumin exhibited the immense biological properties such as antioxidant properties, anti-inflammatory effect, anti-cancer and effective in preventing Alzheimer's disease [1-3]. *In vitro* studies, curcumin was reported a toxicity to various cancer cells including DU145 prostate carcinoma, A549 lung carcinoma and HT29 colon carcinoma [4,5]. However, in *vivo* studies showed that curcumin was inactive in clinical trials due to its instability and insolubility in water and phosphate buffered saline (PBS) [6]. Hence many research groups have paid attention to improve the solubility and stability of curcumin by conjugated polymer, chitosan or nanoparticles [7-9].

Nanoparticles were applied in many disciplines, particularly in medical or biological systems as drug delivery into the target cells. Self-assembly of supramolecular structures prepared by using transition metal ions and synthetic ligands has been tremendous growth in the case of increasing the encapsulated ability of target molecules and nanoscale materials in supramolecular networks. The ability of encapsulated molecules of nanomaterials could improve their functions for technologically important applications [10-14].

It is well-known that macromolecule, nanoparticles and colloid drug carrier with 10-200 nm can pass through leaky tumor blood vassels by enhancing permeability and retention effect (EPR) [15-17]. Therefore, this method would be able to improve the selectivity of drug to the target tumor cells.

The research of Nishiyabu and co-workers [19] utilized the nanoparticles of adaptive supramolecular networks self-assembly in HEPES buffer solution pH 7.4 from nucleotides and lanthanide ions for increasing the intensity of fluorescent dyes and for applying to biomedical materials. The report showed that the gadolinium ion could attach on phosphate unit and N_7 based 5'-AMP. Moreover, the binding of dyes referred to the coordination of their carboxyl and hydroxyl groups to Gd^{3+} ions. Likewise, Kulchat et al [20] also used those coordination nanoparticles to stabilize the boronic acid/ fluorescein sensors for detection of cyanide ions in HEPES buffer solution.

In this research, our attempts were to improve the stability of curcumin derivatives by novel self-assembled coordination nanoparticles from gadolinium ion (Gd^{3+}) and surfactants to stabilize curcumin in buffer solution pH 7.4 for drug delivery tasks into cancer cells [21]. This method showed an easier and inexpensive preparation.

In this study, Gadolinium ion was selected as components because it was biocompatible and showed a large coordination numbers and high coordination flexibility [19]. Their properties were suitable for making networks that flexibly adapt the size and shape of guest materials. Moreover the Gadolinium ion was one of the non-fluorescence lanthanide ions, which led to undisturb the intensity of fluorescence interested dye molecule [22]. The SDS surfactant was selected as partners because they widely used for preparing the emulsion, microemulsion and Ag nanoparticles [23-25]. Furthermore, the SDS had been reported about the epidermal cell proliferation study. The SDS concentration of approximated 0.2% did not affect to the histomorphology [26]. Last of all, the HEPES buffer solution was selected in particular preparation because it was a green chemical substance, which widespread used in chemistry laboratory and tissue culture [27,28]. Incidentally, HEPES were used as both reducing gold ions ($AuCl_4^-$) and shape-direction agent for synthesis of the gold nanopartlicle via a nitrogen-centered free radical in the piperazine ring of HEPES buffer [21, 29]. It was also used as the solution for synthesis of the lanthanide nanopartlicle. Moreover, another report showed the surfactant ability of HEPES to bind copper (II) when concentration of HEPES is > 10 mM [30].

1.1 Research objectives

1. To synthesize and characterize the novel self-assembled coordination nanoparticles from surfactants and gadolinium ion to stabilize curcumin derivatives in buffered solution.
2. To study cytotoxicity of curcumin derivatives encapsulated in nanopariticles.

1.2 Scope of this research

In this research, the novel self-assembled coordination nanoparticles from surfactants and gadolinium ion (Gd^{3+}) to stabilize curcumin derivatives in buffered solution were prepared in facile and inexpensive method. First of all, various surfactants and various buffers solution were examined for the optimized condition of preparation of coordination nanoparticles by using various techniques including TEM, SEM, DLS, FT-IR, UV-Vis, XANES, ICP-ASE and XRD. Then, the **GdSH CNPs** (the coordination nanoparticles prepared from gadolinium and SDS in HEPES buffer solution) were excellent candidate to increase the stability of curcumin derivatives, which were monitored by fluorescence spectroscopy. Then, the cytotoxicity and cellular uptake to the cancer cells by the curcumin derivatives encapsulated in **CNPs** were studied by using the MTT assay and confocal fluorescence microscopy.

1.3 Benefits of this research

We expect to obtain the simply novel self-assembled coordination nanoparticles, which could increase the stability of curcumin derivatives in buffered solution and give a high potential for biological and medicinal tasks in the future.