CHAPTER V

CONCLUSION

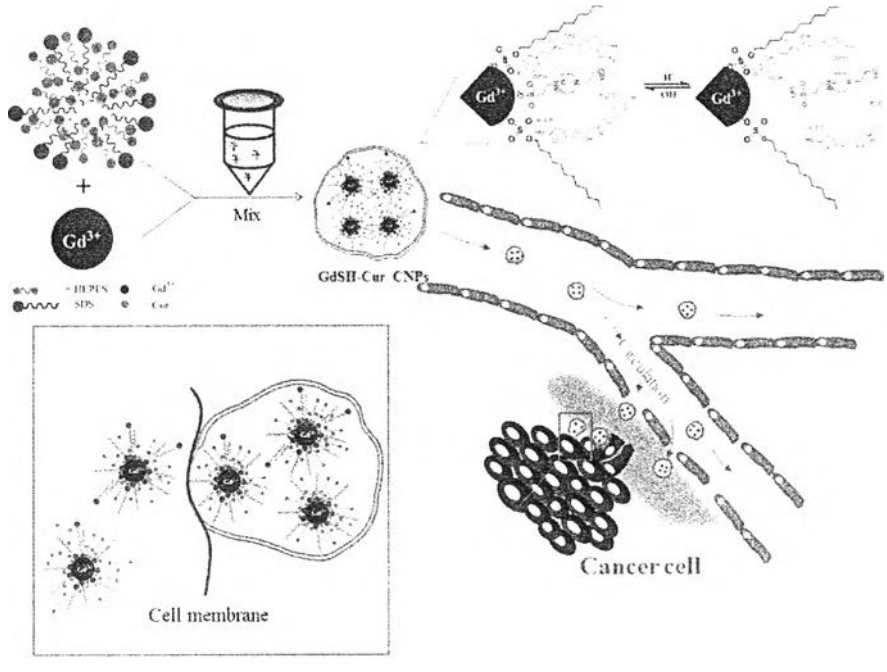
5.1 Conclusion

To study the anti-cancer efficiency of curcumin derivetives, we have investigated the synthesis, stability and anti-cancer efficiency of curcumin derivatives including **Cur**, **$CurBF_2$**, **$CurBF_2OTs$** and **$CurBF_2(OTs)_2$**. From the UV-Vis and fluorescence data, all compounds in 0.1 M HEPES buffer solution pH 7.4 showed a rapid decrease of the fluorescence intensity due to its instability and insolubility in water. Hence, we have demonstrated an easily spontaneous formation of nanoparticles of adaptive self-assembled supramolecular networks from surfactants and lanthanide ions to improve not only the stability but also the fluorescence intensity of curcumin derivatives for used in the further biological tasks.

In the studies of various buffers including HEPES, MOPS, Tris and phosphate and various surfactants including SDS, CTAB and Triton X-100 effects, the morphology and structural properties of the nanoparticles were investigated by SEM, TEM and DLS techniques. They were found that the formation of coordination nanoparticles from Gd^{3+}, SDS and HEPES, namely, **GdSH CNPs** showed excellently uniform spherical nanoparticles with the particles size of 140.65 nm and a possibly suitable candidate for biological tasks. From FT-IR, XAS and XRD techniques, they confirmed the formation of adaptive self-assembled coordination nanoparticles by the interaction of Gd^{3+} and oxygen atom on $-SO_3^-$ group based HEPES buffer and SDS. The linear combination fitting of XANES spectra of Gd^{3+} in **GdSH CNPs** is consistent with Gd^{3+} in $Gd_2(SO_4)_3$ with 90.7 % similarity. Interestingly, the ICP-AES results showed the stoichiometry of the precipitated GdSDS in water of 3:1 ($SDS:Gd^{3+}$), while that of **GdSH CNPs** in HEPES buffer is 2.68:1 ($SDS:Gd^{3+}$). These results suggested that the HEPES buffer could insert between SDS by hydrophobicity and also employed the sulfate anion based HEPES to form the electrostatic interaction with Gd^{3+}. Interestingly, we hypothesized that the hydroxyl group could form hydrophilicity with water inducing the reverse-microemulsion structure dissolved in water.

After the encapsulation of **Cur**, the particle size of **GdSH-Cur CNPs** was increased to 157.57 nm, which was a good candidate for delivery tasks of drug to

target cancer cells via the enhancing permeability and retention effect (EPR) as shown in Scheme 5.1. FT-IR, UV-Vis and fluorescence studies demonstrated that the **GdSH CNPs** can encapsulate the curcumin derivatives in nano-matrix, as well as, they enable to enhance the fluorescence intensity and stability of curcumin derivatives.



Scheme **5.1** Design and preparation of **GdSH-Cur CNPs** containing Gd^{3+}, SDS, HEPES and curcumin and proposed delivery mechanism to cancer cells via the EPR effect then, drug might be released by a destroyed interaction of **CNPs** at low pH

As compared to the corresponding cytotoxicity assay studies of free **Cur** in DMSO and HEPES buffer solution with IC_{50} values of 10 μg/mL and nontoxic, respectively, the **GdSH CNPs** can enhance *in vitro* anti-cancer activity of curcumin to SW620 colon cancer cells with IC_{50} values of 8.0 μg/mL in term of cucumin-equivalent dose. Additionally, **GdSH-CurBF$_2$ CNPs** exhibited higher toxicity to SW620 ($IC_{50\text{-}eq}$ = 0.66 μg/mL) than free **CurBF$_2$** ($IC_{50\text{-}eq}$ = 0.88 μg/mL). In addition, as the results of the confocal fluorescence images, the curcumin immobilized in **GdSH CNPs** could immediately pass through the cancer cells and enhanced the fluorescence brightness. In these approaches, our novel nanoparticles would be beneficial to further development of stability of curcumin for biological tasks.

5.2 Suggestions for future works

Future works will focus on:

i) pH dependent studies of % **curcumin** release from **CNPs** for longer time

ii) cellular uptake studies of others curcumin derivatives with and without **CNPs**

iii) apoptosis assay studies of curcumin derivatives incorporated in **CNPs** by *flow cytometry*.