CHAPTER V
CONCLUSION

Leukemia, one of the most threatening hematological malignant cancers, has been found to be very sensitive to anticancer reagents which either block the process of the cell cycle or cause cell apoptosis. This chemotherapy-sensitive property of leukemia entices researchers to look for more specific and potent drugs against it. As potent new drug candidates, natural compounds have been highlighted because of their low degree of cytotoxicity. Curcuminoids, the major active compounds in the rhizome of tumeric, present various biological activities include antioxidant, anti-inflammation, anti-mutation, antiproliferation, and anticancer activity. Pure curcumin, demethoxycurcumin, and bisdemethoxycurcumin are the major derivatives of curcuminoids. Several studies in recent years have shown that pure curcumin is a potent inhibitor of the initiation and promotion of chemical carcinogen-induced tumor formation.

The *WT1* gene is a tumor suppressor gene that is responsible for Wilms' tumor. However, *WT1* gene is found to express at high level in leukemic blast cells with an increase expression levels at the relapse. Moreover, the *WT1* gene expression level is inversely correlated with a prognosis of this cancer. Thus, *WT1* gene acts as an oncogene in leukemia. This study demonstrated that tumeric curcuminoid derivatives including commercial grade curcuminoids mixture (Sigma-Aldrich), in-house curcuminoid mixture, pure curcumin, demethoxycurcumin, and bisdemethoxycurcumin decreased the *WT1* gene expression in 4 types of leukemic cell lines; K562, U937, HL-60, and Molt4 cell. From this result, it can be concluded that the pure curcumin exhibited the maximum inhibitory effect on WT1 mRNA expression and WT1 protein production. Whereas, bisdemethoxycurcumin and demethoxycurcumin showed moderate and least inhibitory effect respectively on the WT1 mRNA expression and WT1 protein production. It can be explained that the diketone groups and the imbalance between the phenolic methoxyl groups of each type of curcuminoids derivatives may contribute to these effects. Moreover, the treatment with non-cytotoxic concentration of pure curcumin decreased the WT1 mRNA and

WT1 protein in dose and time-dependent manners. The mechanism that the pure curcumin suppresses WT1 mRNA expression and WT1 protein production is now unclear. This finding is important for the search for new treatments for leukemia since pure curcumin can be potentially used as a chemotherapeutic agent. The clinical trial study is currently investigating. In summary, pure curcumin can decrease both transcription and translation of *WT1* gene. This study may be use as a guide line for pure curcumin treatment in clinical leukemic patients in the future.