CHAPTER V

CONCLUSION

The quality of any medicine product and its useful shelf life is strongly dependent on its temperature exposure history. In this study, glibenclamide and aspirin were selected as a model drug. As in the preliminary study, amorphous glibenclamide presented partial transformation and significantly decreased solubility after stored at temperature 60°C for 2 week. Aspirin was degraded to salicylic acid over the limit signified in the pharmacopoeia after storage at temperature 60°C/75%RH for 18 days. The temperature and time were used to design the thin film system as indicator.

In this experiment, red cabbage extract was used as a source of pH indicators (anthocyanin) on the color change when contacted with alkaline. The red cabbage extract film and alkaline film were separated by thin film composed of temperature sensitive PNIAAm polymer in HPMC, that when exposed to high temperatures will produce microporous structure on HPMC. The thin films showed a response to change in temperature.

The increasing amount of PNIAAm caused faster release of red cabbage through thin films than film without PNIAAm at temperatures higher than LCST. The specific temperatures of thin films as degradation indicator were studied between temperatures of 25°C and 60°C. At temperature 25°C the thin films remained unchanged while at 60°C the red color parameter a*value decreased as a function of time. This was due to the higher extent of contraction in this PNIAAm network at 60 °C and porous structure was formed. The red cabbage color was released as the pores where generated. The reactions of red cabbage extract and alkaline was detected by using image editing software, Photoshop®. The parameter a* value was used to compare the color change profile of each film formulations.

The results indicated that this approach can be used to produce thin films as drug degradation indicator. The thermosensitive polymer concentrations could be controlled to produce a film with end point detection at specific time. The rates of color change in thin films showed difference in each films formulation. As a result, the thin film formulation F7 matched the critical change for amorphous glibenclamide tablets and formulation F6 matched the degradation rate of aspirin tablets.

However, the indicator surface area was very important. The thin films as indicator were reduced size to be able to attached on the surface of the tablets. As results, the rates of color change were not exactly similar to the thin films used during the evaluation process and thin films as indicator on surface of tablets. It could be conclude that the permeability rate depended on the surface attachment of each film layer and uniformity of polymer content in each film layer.

As a result, the moisture of the environment was shown to have only small affect on the rate of color change in the indicator. It might be that the indicator color change was due mainly to the levels of temperatures which induced the PNIAAm polymer shrinkage and contraction.

It could be concluded that this experiment was intended to be a proof of concept and to demonstrated to be an independent indicator which detects the degradation where only the temperature factor plays a key role. The degraded substance was not directly affected the indicator. The conditions to induce solid state transformation or degradation of each model drug and the level of indicator color change under the same condition were correlated. This independent indicator could be applied to various model drugs or compounds which degradation was induced by the effect of temperature only.

There have been known that many environmental variables can induce drug degradation such as temperature, moisture and light. The changes in the environment can have huge effects on the solid state transformation and degradation. One should design an indicator which the degraded substances from the formulation directly

interact with the substance in the indicator and results in different color detection. This kind of indicator is called a dependent indicator. The experiment should be conducted in various temperatures, moistures and the experiment should be repeated several times. The percentage of chemical degradation and the color value will be evaluated concurrently. The dependent indicator is more specific on the model drug than independent indicator and can directly approximate the quantity of degraded substance from the color value of indicator.

For the next stage of experiment, the thin films should be evaluated at various temperatures and humidities. The thin films can be modified to change within a specific temperature by copolymerization or incorporation of the cross-linking PNIAAm in other polymers such as poly (L-lactic acid) or polycarbonate. In addition, the rate of the color change could be modified to exhibit slower color change by variation of the thickness of the middle PNIAAm layer.