CHAPTER V
CONCLUSION

Human keratinocytes expressed 5 isoenzymes of PKC, -α,δ,ε,ζ and η. Several investigators reported that PKCs activation was associated with translocation from cytosol to membrane (69,87,98). This study is revealed that PKC-α and ε, not δ isoenzymes are translocated from the cytosol to the membrane and then downregulated upon TPA activation. PKC- ε isoenzyme is the PKC-isoenzyme in human keratinocyte that involves with proliferation program (99). This study has proposed that TPA activation involves with the translocation from the cytosol to the membrane of existence PKC- ε isoenzyme.

Curcumin, a food phytochemical exhibits anticancer properties in animal model, did not affect the total content of the PKC- ε isoenzyme but inhibit its translocation to the membrane. The inhibitory effect of curcumin on TPA-induced PKC- ε translocation for the cytosol to the membrane was observed only when keratinocytes were pretreated with curcumin. Co-treatment and post-treatment of the cells with TPA were not observed. Therefore, this study suggests that curcumin is the potent inhibitor of PKC- ε isoenzyme activation and may propose its molecular inhibition model, curcumin might enter the cell and then bind to C1 domain of the PKC molecule that is TPA binding site instead TPA. However, this proposal needs to be further investigated.

Accordingly, it has been reported that PKC -α and δ isoenzymes also play a crucial role in the regulation of in human keratinocytes. PKC-α involved with differentiation program within the epidermis (100) Whereas PKC-δ isoenzyme activation is involved in the UV induced death effector pathway of keratinocytes undergoing apoptosis (100,101). Therefore it could be concluded that PKCs are enzymes which play a crucial role in epidermal homeostasis.

The disruption of the differentiation /proliferation homeostasis by phorbol ester may contribute to its carcinogenic effects. This study shows that curcumin may be a potent candidate for modulation of carcinogenic activity of chemical -carcinogens.