CHAPTER V

CONCLUSION

Glabridin, an isoflavan which possessed tyrosinase inhibitory activity, was isolated from licorice extract as starting material, in order to modify the structure and study on tyrosinase inhibitory as well as free radical scavenging activities. The newly 3″,4″-dihydroglabridin and a variety of acylated ester derivatives were successfully prepared. The 3″,4″-dihydroglabridin was prepared by catalytic hydrogenation reaction using Parr apparatus. The aliphatic esters with various carbon chain lengths and aromatic esters including benzoyl and substituted benzoyl, were prepared by the reaction of glabridin with the corresponding acid anhydrides and acid chlorides, respectively. The chemical structures of all modified compounds were elucidated by spectroscopic techniques, mainly NMR spectra, mass spectra and elemental analysis.

The structure-activity relationships of these compounds on tyrosinase inhibitory and free radical scavenging activities were explored. The results revealed that, of all the synthetic compounds only 3″,4″-dihydroglabridin showed higher potency than the parent compound on both activities. The 3″,4″-dihydroglabridin exhibited potent tyrosinase activity with the IC_{50} values of 11.40 μM. However it displayed a weak free radical scavenging activity.

The lipophilicity of all aliphatic ester derivatives were evaluated as the partition coefficient (log P), which determined by measuring the concentration of these prodrugs partitioning between *n*-octanol and phosphate buffer. The log P values of all prodrugs ranged from 1.71 to 2.25. The esters **18-20** had higher log P values than the parent compound.

Moreover, the enzymatic hydrolysis of the glabridin diacetate ester was performed using porcine liver esterase as a model of esterase found in the skin. The results showed that the ester was rapidly bioconverted to glabridin by porcine liver esterase and reached the steady-state within 10 min. The half-life of glabridin diacetate in the presence of porcine liver esterase was 2.34 min. In phosphate buffer

solution (pH 5.5 and 7.4), the half-life was more than 15 days, thus the ester showed sufficient chemical stability.

Hence, in this investigation, a potent tyrosinase inhibitor, 3″,4″-dihydroglabridin is prepared from naturally occurring compound, glabridin, and it appears to be a good candidate for development as a skin-whitening agent or an anti-browning agent for vegetable and food. Moreover, the acyl ester of glabridin can be served as a prodrug for skin-whitening in cosmetic or topical products.