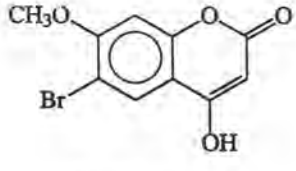
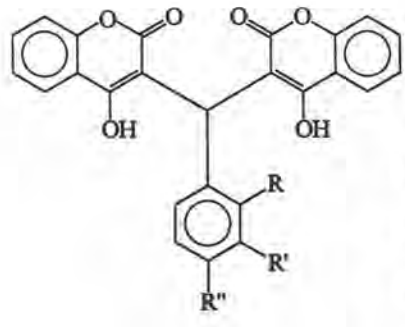
CHAPTER 4

CONCLUSION

During the course of this work, the synthesis of 4-hydroxycoumarins, dicoumarols and related compounds was carried out with the aim to comprehend the structure - activity relationship (SAR) of this analogue of compounds and its biological activities as insect antifeedant against *Galleria mellonela* Linn. and weed growth inhibition against *Mimosa pigra* Linn. The desired products were attained in medium yield utilizing the condensation of phenols with malonic acid in the presence of phosphorus oxychloride and zinc chloride. However, the better result could be achieved by employing the condensation of 2-hydroxyacetophenone and diethyl carbonate with an alkali metal, especially when NaH was used. Most dicoumarols were obtained in very good yield (85-99 %) by condensation of 2 mol equivalent of 4-hydroxycoumarin with interested aromatic aldehyde. All synthesized compounds were well-confirmed their identities by their physical properties and spectroscopic evidences such as IR, ^{1}H-NMR and ^{13}C-NMR, and elemental analysis. To our best knowledge, there have not been any reports concerning with five compounds synthesized, *i.e.*, **8**, **D7**, **D11**, **D13** and **D18**. The structures of new compounds are showed as the following:



Compound **8**



Cpd	R	R′	R″
D7	Cl	H	Cl
D11	H	H	CF_3
D13	H	H	*i*-Pr
D18	H	OH	OH

Even though 4-hydroxycoumarins and dicoumarols have been well-recognized to possess their biological activity such as anticoagulant, HIV protease inhibition, antimicrobial action, enzyme inhibition, *etc.*,[6,8,19] the application of this class of compounds has never been discerned in the field of agriculture. In this research, both studied 4-hydroxycoumarins and dicoumarols were subjected to examine for antifeedant activity against greater wax moth larvae, *G. mellonella* larvae, and weed growth inhibition against giant mimosa, *M. pigra* L.

4-Hydroxycoumarin derivatives with a methoxy group at C-5 and various substituents at C-6 displayed a good trend to exhibit high % antifeedant. Whereas, the methoxy substituent at C-7 showed lower activity than a parent molecule. The smaller substituents at C-6 showed better activity than the bigger ones. The halogen was found to be the best substituent for this activity, whereas a methoxy group substituted at C-7 decreased activity. For dicoumarols, it could obviously be seen that dicoumarols with a substituent on a benzylidene ring at *para-* position always showed the highest activity, *meta-* showed the middle and *ortho-* revealed the lowest activity. This observed activity was excluded for *o*-nitro substituent which revealed the highest activity among the nitro series. Dicoumarols with a methoxy group showed the highest activity, followed by nitro and halogen, alkyl and hydroxy groups, respectively, as a substituent in the molecule.

Considering in the case of weed growing inhibition against *M. pigra,* almost 4-hydroxycoumarins did not show any noticeably eminent activity, except for **2** and **4**. Both compounds displayed the activity comparable with selected commercial herbicides. Among interested twenty three dicoumarols, it was found that molecules with a hydroxy and/or methoxy groups on a benzopyran ring displayed inhibition activity as good as commercially available herbicides. The SAR study of this part was clearly shown that dicoumarols with hydroxy and methoxy substituents showed high activity, next is alkyl. Halogen substituents do not show any influence on this activity, whereas nitro group decreased this biological activity. In addition, the dicoumarol isomers showed a range of inhibition from the highest to the lowest as *ortho*, *meta* and *para*, respectively.

The intent of this research is not only try to find out the new chemicals to use as insecticides or herbicides, but also to look for the relationship between the structures of 4-hydroxycoumarins and their agricultural activities. This derived outcome as one of worth ingredients provides many possibilities to carry on for further investigation. The insect antifeedant against the greater wax moth and weed growth inhibition with giant mimosa testing with 4-hydroxycoumarins were the preliminary work; nevertheless, this research was the pioneer work for adaptation of this information in agriculture. Awareness of their potentials, together with additional research on structural activity relationship studies may facilitate the development of more effective and promising agrochemicals for the future.

Proposal for the Future Work

From this study, the results of insect antifeedant with greater wax moth and weed growth inhibition with giant mimosa of 4-hydroxycoumarins disclosed the relationship of these studied biological activities and 4-hydroxycoumarin structures. The quantum calculation and interaction of substrate and enzyme testing as key-lock might be needed for investigating of deeply actual enzyme role in these beings. The possibly further work related to this research would be finding out the role of 4-hydroxycoumarins in these activities for the truth being revealed. An account of interesting biological activities of them, the further research would be the study of 4-hydroxycoumarin structure and other biological activity (*e.g.*, antimicrobial testement) relationship.

Moreover, the structure - activity relationship study of other types of molecules synthesized by effective and simple methodologies (high product yield and various derivative structures) should be explored. The attractive SAR study of other natural molecules such as cinnamic acids, quinones or *etc.* might interest the next generation-researchers.