ABSTRACT

Thesis Title : Synthesis and Biological Activity of Some Ecdysteroids and Their Analogues

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In order to study moulting hormone activity of ecdysteroids and ecdysteroid analogues with different number, location and stereochemistry of oxygen functions at the C24-C27 side chain, the ecdysteroids ponasterone A (**4**), stachysterone C (**20**), abutasterone (**14**), 24-epi-abutasterone (**100**) and two epimers of 20,26-dihydroxyecdysone, i.e., 20,26-dihydroxyecdysone, epimer 1 (**101**) and 20,26-dihydroxyecdysone, epimer 2 (**102**) have been synthesized. In the *Musca* assay, ponasterone A (**4**) was slightly less active than 20-hydroxyecdysone (**1**), the standard ecdysteroid, but was more active than 20,26-dihydroxyecdysone, epimer 1 (**101**). The latter ecdysteroid was more active than abutasterone (**14**) and 24-epi-abutasterone (**100**). The latter two epimers exhibited similar activity in the assay and were more active than 20,26-dihydroxyecdysone, epimer 2 (**102**). Stachysterone C (**20**) was the least active

ecdysteroid. Its weak moulting hormone activity was in contrast to the reported high activity in the *Chilo* and *Sarcophaga* assays.

Shidasterone (**110**), a minor phytoecdysteroid, has been synthesized from 20-hydroxyecdysone (**1**) and the stereochemistry at C22 has been shown to be in R configuration. The moulting hormone activity of this ecdysteroid in the *Musca* assay was low, thus indicating that free 22-hydroxyl group is required for high activity.

A number of naturally occurring 2-deoxyecdysteroids, i.e., 2-deoxy-20-hydroxyecdysone(2-D-20-ECD, **6**), 2-D-20-ECD 3-acetate (**126**), 2-D-20-ECD 22-acetate (**49**), 2-D-20-ECD 22-benzoate (**130**) and 3-epi-2-D-20-ECD (**28**), including some of their analogues, i.e., 3-dehydro-2-D-20-ECD (**123**), 3-dehydro-2-D-5α-20-ECD (**114**) and 2-D-5α-20-ECD (**121**) have been synthesized from 20-hydroxyecdysone (**1**). The moulting hormone activity of 2-D-20-ECD (**6**) was lower than that of 20-hydroxyecdysone (**1**). The activity of 2-D-20-ECD (**6**) was about the same magnitude as that of 2-D-20-ECD 3-acetate (**126**), but was higher than that of 3-epi-2-D-20-ECD (**28**), the latter of which was more active than 2-D-20-ECD 22-acetate (**49**). 2-D-20-ECD 22-benzoate (**130**) exhibited very low activity and was the least active ecdysteroid in the member. The results suggested that *in vivo* deacetylation at the 3-hydroxyl group occurred more readily than the 22-hydroxyl group, and that debenzoylation took place even less readily. In the non-naturally occurring ecdysteroid analogues, 3-dehydro-2-D-20-ECD (**123**) exhibited moderate

activity, while its C5 epimer, 3-dehydro-2-D-5α-20-ECD (**114**) was much less active. The relatively high activity of the former suggested that *in vivo* transformation of this compound to 2-D-20-ECD (**6**) was possible. The activity of 2-D-5α-20-hydroxyecdysone (**121**) was relatively low, it was nevertheless significantly high for a 5α-ecdysteroid. It was therefore likely that C5 epimerization also occurred *in vivo*.