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Review

Steroid plant hormones: Effects outside plant kingdom

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ABSTRACT

Brassinosteroids (BS) are the first group of steroid-hormonal compounds isolated from and acting in plants. Among numerous physiological effects of BS growth stimulation and adaptogenic activities are especially remarkable. In this review, we provide evidence that BS possess similar types of activity also beyond plant kingdom at concentrations comparable with those for plants. This finding allows looking at steroids from a new point of view: how common are the mechanisms of steroid bioregulation in different types of organisms from protozoa to higher animals.

Contents

1. Introduction

Steroids have been recognized as the hormones of higher vertebrates for quite a long time, more than half a century [1]. In the middle of the sixties it became evident that steroids play a hormonal role in invertebrates also, in particular in the moulting functions of insects and other arthropods [2]. At about the same time steroid hormones of fungi were found [3]. Isolation of brassinolide and a number of related compounds (named as brassinosteroids), having hormonal functions in plants [4], showed that steroids are versatile hormonal regulators, characteristic to most organisms inhabiting the earth.

A rapid progress in the study of steroidal plant hormones resulted in establishing many intimate details of their action in plants and led to their use in agriculture as crop increasing and

Abbreviations: BS, brassinosteroids; CC_{50}, 50% cytotoxic concentration; EBl, 24-epibrassinolide; EC_{50}, half maximal effective concentration; HSV, herpes simplex virus; HBl, 28-homobrassinolide; MPP^+, 1-methyl-4-phenylpyridinium; TNF-α, tumor necrosis factor α.

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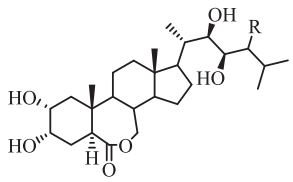
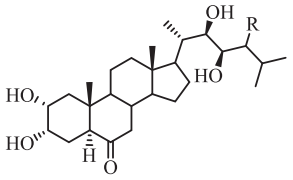
plant-protecting agents [5]. The development of such agents implied detailed toxicological studies of BS, including their influence on bees, aqueous organisms and animals. As was expected, BS proved to be non-toxic compounds [6–9]. However, it was not the only result of these studies. Many experiments revealed a pronounced adaptogenic effect of BS to non-plant test organisms. This offered an incentive to investigate thoroughly brassinosteroid effects outside plant kingdom. Their knowledge will contribute to a solution of a more general problem, namely "How steroidal hormones, typical of certain organisms, relate to the functioning of organisms that belong to other classes or kingdoms?".

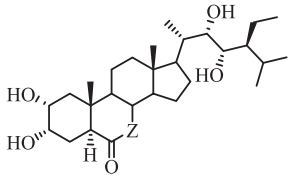
One has to be aware that no complete answer can be given to this question at the present stage of research. The obtained data are still fragmentary and subject to criticisms. One among them is that many studies have been conducted using synthetic BS analogues of unnatural structure. It creates some limitations for their use and generalization in respect to real steroidal plant hormones where brassinolide **1** (Fig. 1) is recognized to play a central role [10,11]. Brassinolide itself has practically never been used for biological experiments on non-plant organisms, although a number of more available natural BS (e.g., epibrassinolide **2**, homobrassinolide **3** and corresponding 6-ketones **4** and **5**) were investigated quite extensively. Among many BS analogues those containing a (22*S*,23*S*)-diol function (e.g., **6** and **7**) should be mentioned as being of a considerable interest in these studies. Although plant growth promoting activity of (22*S*,23*S*)-analogues is very low [12–14], in some tests on non-plant organisms these easily available compounds revealed remarkable effects [15–21].



1: R=Me (24S): brassinolide
2: R=Me (24R): 24-epibrassinolide (EBl)
3: R=Et (24S): 28-homobrassinolide (HBl)



4: R=Me (24R): 24-epicastasterone
5: R=Et (24S): 28-homocastasterone



6: Z=-CH_2: (22S,23S)-28-homocastasterone
7: Z=-OCH_2: (22S,23S)-28-homobrassinolide

Fig. 1. Structures of compounds **1**–**8**.

2. Effects on insects

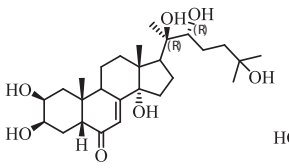
Structural considerations were probably the main reason why studies of BS action outside the plant kingdom were started on insects, moulting hormones of which (e.g., ecdysterone **8**, Fig. 2) are very close structurally to BS. The first experiments showed that steroidal phytohormones could affect normal growth and development of insects. A number of BS effects were revealed at different levels [22], including intact animals [15,23,24], isolated tissues [23,25,26], cultured cells [27,28], particular insect neurons [29], and protein molecules (ecdysteroid receptors) [23,28,30,31]. However, the results of these experiments are not always consistent with each other.

Thus, a number of BS were tested in *in vitro* experiments on imaginal discs isolated from fly species *Phormia terrae-novae* and *Calliphora vicina* and exhibited only a slight (if any) agonistic ecdysteroid activity and a significant antagonistic dose dependent effect when concomitantly applied with ecdysterone **8** [22]. Other studies showed BS acting as either agonists [27] or antagonists [25,30], and none of BS tested in the *Drosophila melanogaster* B_{II} cell bioassay revealed either agonist or antagonist activity [32].

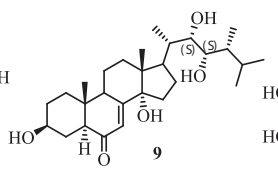
Feeding the cockroach *Periplaneta americana* with artificial diet containing (22*S*,23*S*)-homobrassinolide **3** resulted in a lengthening the larval stage by moulting delay [15], although closely related (22*S*,23*S*)-homocastasterone **5** proved to be inactive in this assay. BS were toxic to the larvae of the cotton leafworm *Spodoptera littoralis* when applied by injection in high doses at the end of the last instar [23]. The observed result could not be attributed to interference of BS in the moulting process since the effects from BS application differed from those of ecdysterone **8** or its non-steroidal agonist.

The investigation in *Phormia terrae-novae* [25] showed that BS could compete with ecdycteroids for the invertebrate nuclear steroid hormone receptor EcR, and this was later confirmed by other studies [22–24,29,30,33]. However, the affinity in most experiments was 10- to 1000 fold lower than that observed for binding to radiolabeled ponasterone A, and no competition at all was observed for EcR in intact Se4 cells even at relatively high (100 μM) concentration of EBl [28]. A number of synthetic hybrids of BS and ecdysteroids were prepared and assessed for their activities in the *Drosophila melanogaster* B_{II} cell bioassay [33]. Nearly all tested compounds displayed no ecdysteroid agonist activity demonstrating the high specificity for the EcR receptor. A distinct activity was noticed only for the hybrid **9** (Fig. 2), however, it was still 2000-fold less active than ecdysterone **8**. Similar studies were performed with two castasterone/ponasterone A hybrid compounds [34]. The (22*R*)-isomer **10** was more potent than the corresponding (22*S*)-isomer for the competitive inhibition of [^{3}H]ponasterone incorporation (about 100 times with K_c cells and about 35 times with Sf-9 cells).

In general, to date, experimental evidence confirming cross reactivity between steroidal insect and plant hormones is lacking.



8: ecdysterone



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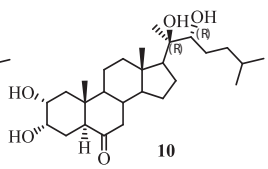

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Fig. 2. Structures of compounds **8**–**10**.