Invert Neurosci (2017) 17:4
DOI 10.1007/s10158-017-0197-8

REVIEW

The current state of knowledge on the neuroactive compounds that affect the development, mating and reproduction of spiders (Araneae) compared to insects

Marta Sawadro[1] · Agata Bednarek[1] · Agnieszka Babczyńska[1]

Received: 16 January 2017 / Accepted: 3 April 2017 / Published online: 18 April 2017

Abstract The neuroendocrine system of insects, including the presence of the main neuroactive compounds, and their role in ontogenesis are probably best understood of all the arthropods. Development, metamorphosis, the maturation of the gonads, vitellogenesis and egg production are regulated by hormones (juvenile hormones, ecdysteroids) and neuropeptides. However, knowledge about their presence and functions in spiders is fragmentary. In this paper, we present a summary of the current data about the juvenile hormones, ecdysteroids and neuropeptides in selected groups of arthropods, with particular emphasis on spiders. This is the first article that takes into account the occurrence, action and role of hormones and neuropeptides in spiders. In addition, the suggestions for possible ways to study these compounds in Araneomorphae spiders are unique and cannot be found in the arachnological literature.

Keywords Juvenile hormones · Ecdysteroids · Neuropeptides · Spiders

Introduction

Spiders are one of the most important groups of arthropods that play a crucial role in ecosystems because they belong to the most abundant group of terrestrial predators (Turnbull 1973). Analysis of available data indicates that spiders as a bioindicators of environments (e.g., Bednarek et al. 2016), their venom and silk (e.g., Konwarh et al. 2016; Wang and Wang 2016) are top researching aspects of spider life. In contrast, knowledge about the neuroendocrine system of this group of arthropods, which includes the presence of the main hormones (juvenile hormones, ecdysteroids) and neuropeptides, and their role in ontogenesis, is still not well understood and explored (compare with Table 1). On the other hand, the neuroendocrine system of insects is probably the best understood of all of the arthropods (for reviews, see Davey 2000; Roe et al. 2014; Weaver and Audsley 2009).

Every scientist who has tried to investigate the physiology of spiders knows what the reason is for this great divergence in knowledge between groups of arthropods. The fact that spiders do not tolerate any invasive manipulation is the first and most important reason. It should be emphasized that spiders can be divided into two infraorders—Mygalomorphae and Araneomorphae that differ in several aspects. Mygalomorphae spiders are larger in size that can be helpful in micromanipulations. Moreover, it should be noted that the smaller size of spider body is correlated with a decrease in the tolerance for these kinds of procedures. Obviously, injecting and administering active compounds is possible. However, the high mortality rate and the weaker effect of used substances should be expected (personal communications). The efficient detoxification system in spiders may be the reason for this phenomenon (Pourié and Trabalon 2003). Therefore, the use of a higher concentrations of chemical substances than those shown in studies on insects is required (personal communications). However, the using of Mygalomorphae spiders is restricted, because the majority of these spiders is protected by the Washington Convention. Moreover, long-term experiments require spiders with a short period of ontogenesis (to obtain many generations in a brief time) and easy to laboratory breeding. Mygalomorphae spiders

✉ Marta Sawadro
msawadro@us.edu.pl

[1] Department of Animal Physiology and Ecotoxicology, University of Silesia, Bankowa 9, 40007 Katowice, Poland

have a long development cycle that prolongate the time of the experiment to achieve appropriate stages of ontogenesis. Thus, it seems that using of Araneomorphae spiders with a short time of development is more appropriate. However, selecting a suitable species within this infraorder of spider will determine the possibility of carrying out the experiments (doing the appropriate number of replications resulting from the spider size) and their success (the high mortality should be borne in mind). It should be noticed that there are only a few Araneomorphae spiders that can be successfully grown via laboratory breeding (e.g., *Parasteatoda tepidariorum*, *Cupiennius salei*; Mcgregor et al. 2008).

Despite the fact of quite accurate description of the anatomy and morphology of the nervous and neuroendocrine systems of spiders (Gabe 1955; Legendre 1953, 1959), the knowledge about their role in the synthesis of neuroactive compounds is still insufficient and unclear. Therefore, until now, the potential role of the molting organ (MO) in the ecdysteroids synthesis is not proven (Bonaric 1980; Bonaric and De Reggi 1977; Bonaric and Juberthie 1983). Moreover, the analogue organs to insect *corpora cardiaca* (CC) and *corpora allata* (CA) are still not discovered, although the data indicate that Schneider organ 1 and Neurohemal organ 1 can refer to the insect CC, and Schneider organ 2—CA (Bonaric 1980; Bonaric and Juberthie 1983; Bonaric et al. 1984). It should be emphasized that the CA plays an essential role in JH synthesis in insects (Tobe and Stay 1985), whereas an allatotectomy (CA removal) is a method that is widely used to understand the functions of the hormones (compare with Table 2). Thus, studies about the presence and roles of JH in spiders by observing changes in the morphology of the analogs of the CA and allatotectomy are not possible because data about this organ in spiders are not known. Similarly, the removal of any other organ that may be responsible for JH synthesis is not possible because only rudimentary data about the morphology of the central nervous system of spiders are available. In addition, the localization and the protection mechanism of the nervous system prevents the removal of its elements in vivo.

Another very important issue is connected with the differences in the physiology of spiders, compared with insects. For instance, spiders do not have a true phenoloxidase (a component of the immune system), which is in contrast to other arthropods (Decker and Rimke 1998), and their RNA isolation yield is lower than in insects (personal communication). Thus, optimization of all of the available protocols, such as determining the enzyme activity, detecting various proteins, isolating RNA and determining gene expression, is necessary (personal communications; Babczyńska et al. 2011; Bednarek et al. 2016; Posnien et al. 2014). In addition, some methods cannot be used in spider studies (Western blot, ELISA, IHC) because commercially available antibodies that are dedicated to spiders are not present. The antibodies that are dedicated for other animals do not always give a positive response to the material from spiders (personal communication).

Finally, studies about the physiology of spiders at the gene level (detection, expression, knockout) are also limited for several reasons. The sequence of the genome is only available for a few species of spiders (thanks to the Project i5K). Comprehensive genomic or transcriptomic resources are not available. Therefore, previous studies about spiders have relied on cloning the genes that are involved in the process being analyzed in a model organism, such as *Drosophila melanogaster* (Posnien et al. 2014).

To sum up, it seems that the analysis of the role of the neuropeptides, JHs and ecdysteroids in the well-known physiological processes in spiders with short period of development (Araneomorphae) is an appropriately chosen, safe and easy method with which to explore these compounds in this group of arthropods. Furthermore, our experience with spiders indicates that the processes of reproduction and molting are a good starting point to begin the exploration of the neuroendocrine system. Hence, in this paper, we emphasize the influence of selected hormones and neuropeptides in the control of these processes.

This paper is the first article that summarizes the current knowledge about the role of juvenile hormones, ecdysteroids and neuropeptides in the reproduction, molting induction and development in spiders from Araneomorphae infraorder. In addition, the authors suggest possible ways to detect these substances and identify their function in the ontogenesis of spiders what is unique and cannot be found in the arachnological literature.

Juvenile hormones

A juvenile hormone (JH) is a sesquiterpenoid that is synthesized from a farnesoic acid derivative in the classical mevalonate pathway (Riddiford 1994).

Insect JHs are biosynthesized by the CA (Tobe and Stay 1985). This process is regulated by the antagonistic action of neuropeptides—allatostatins (Stay and Tobe 2007) and allatotropins (Elekonich and Horodyski 2003). Six various forms of the JHs have been described in insects, and their occurrence is dependent on the insect order (Riddiford 1994). However, JH III is widely distributed in this group of arthropods (Crone et al. 2007). JHs are secreted into the hemolymph and transported (Hidayat and Goodman 1994) to the target cells by juvenile hormone binding proteins (JHBP). Then, the hormone enters the cell and interacts with the dimer of the nuclear receptor. The two main

Table 1 Current knowledge about role of the neuroactive compounds in molting and reproduction in spiders

Neuroactive compounds	Effect/functions	Confirmed in spiders	Effect/functions	References
Juvenile hormones and/or their analogues	The presence of juvenile hormones or analogues	*Pisaura mirabilis* (Pisauridae)	Lack of data about presence of the insect JHs. Confirmation of the occurrence the substance similar to JHs, but its chemical nature is still undefined	Bonaric (1988)
	Site of the synthesis de novo	Ld	Not determined. The candidate is the Schneider organ 2 that can be the analog of the insects CA	Bonaric (1980), Bonaric and Juberthie (1983), Bonaric et al. (1984)
	Receptors—presence and action	Ld	Ld	Ld
	Role in molting	In females: *Pisaura mirabilis* (Pisauridae)	Prolongation of the intermolting times	Bonaric (1979, 1986)
	Role in reproduction	In females: *Pisaura mirabilis* (Pisauridae)	Probably role in the control of processes connected with reproduction. The proof is the presence of JH analogues during the vitellogenesis	Bonaric (1988)
Ecdysteroids	The presence of ecdysteroids	In females: *Pisaura mirabilis* (Pisauridae), *Tegenaria domestica* (Agelenidae), *Coelotes terrestris* (Agelenidae), *Tegenaria atrica* (Agelenidae), *Brachypelma albopilosum* (Theraphosidae), *Schizocosa avida*, *S. rovneri*, *S. uetzi* (Lycosidae). In males: *B. albopilosum* and *S. uetzi*	Ld	Bonaric and De Reggi (1977), Stubbendieck et al. (2013), Trabalon et al. (1992, 1998), Trabalon and Blais (2012)
	Site of the synthesis de novo	*Pisaura mirabilis* (Pisauridae), *Tegenaria atrica* (Agelenidae), *Stromatopelma calceata* Fabr (Theraphosidae)	Not confirmed. The candidate is the molting organ (MO) that can be the analog of the prothoracic gland. The proof is the correlation between ultrastructural changes in the MO and the release the secret from them during the following stages of ontogenesis	Bonaric and De Reggi (1977), Bonaric and Juberthie (1979), Bonaric and Juberthie (1983), Bonaric (1980), Gabe (1966), Kühne (1959), Legendre (1953, 1958)
	Receptors—presence and action	Only in females; *Agelena silvatica* (Agelenidae)	Detection of their presence and conservative domains	Honda et al. (2009)
	Role in molting	Only in females; *Pisaura mirabilis* (Pisauridae), *Larinioides cornutus* (Araneidae), *Aphonopelma hentzi* (Theraphosidae)	Reduction in the intermolt periods or induction of ecdysis. In addition, the correlation between the ecdysteroid level and the molt appearance	Bonaric (1976, 1977, 1979), Bonaric and De Reggi (1977), Eckert (1967), Krishnakumaran and Schneiderman (1970)
	Role in reproduction	*Tegenaria atrica* (Agelenidae), *Brachypelma albopilosum* (Theraphosidae), *Schizocosa avida*, *Schizocosa rovneri*, *Schizocosa uetzi* (Lycosidae)	Role in ovarian development, pheromone production, sexual cannibalism. Probable involving in the vitellogenesis regulation	Pourié and Trabalon (2003), Stubbendieck et al. (2013), Trabalon et al. (1992, 1998, 2005)
Allatoregulatory neuropeptides	The presence of allatostatin A	*Cupiennius salei* (Ctenidae)	Ld	Loesel et al. (2011)
	In silico detection of allatostatin A, allatostatin B, allatostatin C, allatotropin	*Acanthoscurria geniculata* (Theraphosidae), *Latrodectus hesperus* (Theridiidae), *Latrodectus tredecimguttatus* (Theridiidae), *Stegodyphus lineatus* (Eresidae), *Stegodyphus mimosarum* (Eresidae), *Stegodyphus tentoriicola* (Eresidae)	Ld	Christie (2015b), Christie and Chi (2015)

Ld lack of data

candidates for the JH receptor were selected—*ultraspiracle* (USP) (Riddiford et al. 2000) and Methoprene-tolerant (Met) proteins (Konopova et al. 2011; Konopova and Jindra 2007; Wilson and Fabian 1986). It is generally believed that the Met protein is actually the JH receptor (Miura et al. 2005). The lack of JHs in the cell induces the formation of Met–Met homodimers. However, the appearance of the hormone induces the disintegration of this complex and Met binds with a co-activator (e.g., Taiman, FITC, SRC). The complex of Met-JH-co-activator acts by activating or repressing specific target genes in the regulatory sequences (Riddiford 2012; Zhang et al. 2011). JHs together with ecdysteroids play a crucial role in the regulation of metamorphosis and development. This sesquiterpenoid hormone is responsible, among others, for the "status quo" of larvae (Riddiford 1994). Moreover, JHs are involved in reproduction (for example, vitellogenesis, the development of gonads, egg production) (Davey 2000; Handler and Postlethwait 1977; Kethidi et al. 2005; Venugopal and Kumar 2000) and the regulation of diapause and lifespan (Liu et al. 2008).

It should be emphasized that while knowledge about JHs in insects is quite extensive, data about this sesquiterpenoid hormone in Arachnida are rudimentary and equivocal.

The presence of juvenile hormone or its analogue is still not confirmed in Acari (mites, hard and soft tick) (Neese et al. 2000). However, Zhu et al. (2016) suggested the methyl farnesoate (MF) may play a role of JHs in this group of arthropod. MF is the immediate precursors of JH, which plays a similar role in crustaceans as insects JHs (Laufer et al. 1986; Tobe et al. 1989). Moreover, some evidence about the gonadotrophin from the synganglion–lateral organ complex in the tick (Marzouk et al. 1985), which acts in a similar manner as insect JHs, was found (Aeschlimann 1968). Studies about exogenous JHs (Obenchain and Mango 1980) and the anti-juvenoid (Leahy and Booth 1980) on tick reproduction indicate the occurrence of specific JH receptors and JHBP (Kulcsar et al. 1989) in this group of arthropods. However, the only data about the identification of the JH receptor in Acari resulted from in silico analysis, which indicate the presence of the Met protein only in tick *Ixodes scapularis* (Qu et al. 2015). The role of JH-like substances (e.g., MF, gonadotrophin) in ticks in reproduction (e.g., egg development, the induction of vitellogenesis and oviposition) and in suppressing molting is unclear (see reviews Belozerov 2006; Rees 2004). For instance, vitellogenesis is stimulated by administration of a JH analog, JH I or JH III in virgin female *Ornithodoros moubata* (Connat et al. 1983), while the lack of this effect was observed in other similar experiment on the same species (Chinzei et al. 1991).

Until now the occurrence of juvenile hormones or other similar substances, such a MF is not confirmed in spiders. Despite the fact that Bonaric (1988) confirmed the presence of substances similar to the insect hormones in spider *Pisaura mirabilis* (Pisauridae), until now their chemical nature is still undefined. The site of JHs and/or their analog synthesis is constantly undetermined. Nonetheless, it is emphasized that such hypothetical organ should occur (Bonaric 1995). It is suggested that Schneider organ 2 (part of stomatogastric ganglion; Legendre 1953, 1959) can be a possible homolog of the insects CA, and hence, it can be a structure responsible for juvenile hormone or analogues synthesis (Bonaric 1980; Bonaric et al. 1984; Juberthie 1983; Bonaric and Juberthie 1983). Molecular mechanism of action of this group of hormones is still unknown. Furthermore, no protein receptors are identified. Few studies on the role of JHs and/or their analogues in the physiological processes of spiders indicate that this group of hormones probably plays a similar role in the development and reproduction in spiders. For instance, it was described that application of the insect JH prolonged the intermolting times in *P. mirabilis* (Bonaric 1979, 1986) as like as in insects, (e.g., Konopova and Jindra 2007). Moreover, the presence of JH analogues during the vitellogenesis in female spider *P. mirabilis* was noticed (Bonaric 1988). Thus, it seems that this group of hormones may play a role in the regulation of this process in spiders.

Ecdysteroids

Zooecdysteroids are a group of animal steroid hormones that include ecdysone (α-ecdysone) and 20-hydroxyecdysone (20E, initially named β-ecdysone). In insects and ticks, 20E is the major active hormone (Dees et al. 1984; Lafont 1997; Lafont et al. 2005; Riddiford 1993).

In insects, ecdysone is produced by a prothoracic gland until the metamorphosis, at which time the gland degenerated (Sakurai and Williams 1989). In adults, ecdysteroids are synthesized by the ovaries (Carney and Bender 2000; Hagedorn et al. 1975) and male accessory glands (Hentze et al. 2013). The response of tissues to ecdysteroids is mediated by a heterodimer of the nuclear receptors: the ecdysone receptor (EcR; Koelle et al. 1991) and *ultraspiracle* protein (USP; Yao et al. 1992, 1993)—EcR–USP. Low titer of 20E in cell induces the EcR–USP binding with co-repressors. The EcR–USP-co-repressor complex has the ability to bind to DNA and to repress the transcription of target genes. However, in the case of the elevated 20E titer, the 20E-EcR–USP complex binds to the co-activator and then, by attaching to the specific DNA sequence (*ecdysone response elements*), induces transcription of the gene (King-Jones and Thummel 2005; Riddiford et al. 2000; Thummel 1996). Ecdysteroids coordinate the critical developmental events, including embryonic morphogenesis

Table 2 Examples of possible direction of research about hormones and neuropeptides

Neuroactive compounds	Species	Research direction	Methods	References
Juvenile hormones/ MF	*Dermacentor variabilis* (Arachnida, Ixodidae), *Ornithodors parkeri* (Arachnida, Ixodida)	Detection of the hormone in various tissues in different stages of ontogenesis	Determination of JH or MF level in different tissues (synganglia, salivary glands, midgut, gut, ovaries, hemolymph and muscle) using gas chromatography–mass spectrometry (GC–MS)	Neese et al. (2000)
	Pteromalus puparum (Insecta, Hymenoptera)		JH determination in whole body, fat bodies and ovaries of radioimmunoassay and GC–MS	Dong et al. (2009)
	Lacanobia oleracea (Insecta, Lepidoptera)		Determination the JH level in larvae before and after molting, and pupae using HPLC and GC/MS	Edwards et al. (1995)
	Calliphora vomitoria (Insecta, Diptera)	Detection of the site of the JH synthesis de novo	In vitro culture of the CA and determination of the JH III level using GLC–MS	Trabalon et al. (1987)
	Dermacentor variabilis (Arachnida, Ixodidae), *Ornithodors parkeri* (Arachnida, Ixodida)		Detection of the presence of the elements of metabolic pathway of JH synthesis by in vivo and in vitro radiosynthesis assay in different tissues and radio-HPLC	Neese et al. (2000)
	Bombyx mori (Insecta, Lepidoptera), *Schistocerca gregaria* (Insecta, Orthoptera)		Detection of the JH acid O-methyltransferase (JHAMT) in various tissues (CC–CA complexes, prothoracic glands, fat body, midgut, epidermis, muscle, Malpighian tubule, ilk gland, salivary gland, testis, ovary) using PCR. Determination of the JHAMT expression level and action using qRT-PCR and enzyme assay	Marchal et al. (2011), Shinoda and Itoyama (2003)
	Lacanobia oleracea (Insecta, Lepidoptera)		In vitro *corpota allata* culture and determination of the JH level using RP-HPLC	Audsley et al. (2000a)
	Dermacentor variabilis (Arachnida, Ixodidae)	Detection of the tissues whose physiology is regulated by JHs	Role of different tissues in the JH metabolism by measuring the activity of the JH esterase and JH epoxide hydrolase	Venkatesh et al. (1990)
Juvenile hormones/ MF	*Drosophila melanogaster* (Insecta, Diptera)	Detection of tissues whose physiology is regulated by JHs	Determination of the JH receptor—Met using the DCC (dextran-coated charcoa) assay	Miura et al. (2005)
	Drosophila melanogaster (Insecta, Diptera)		Detection of the potential JH receptor—Gce and its action with the Met protein by the overexpression and knockdown of the *Gce* gene and observation of the oviposition, the Met eye-defect phenotype and male courtship	Baumann et al. (2010)
	Aedes aegypti (Insecta, Diptera)		Identification of juvenile hormone target genes by the determination of the mRNA level various genes in different stages and after the topical application of JH, methoprene and pyriproxyfen	Zhu et al. (2010)
	Dermacentor variabilis (Arachnida, Ixodidae), *Galleria mellonella* (Insecta, Lepidoptera)	Investigation of the role of the hormone in metamorphosis in both sexes in different stages of ontogenesis and in various tissues	The *Galleria* cuticle wax assay (topical application of JH III or homogenate from different tissues of *D. variabilis* to *Galleria mellonella* L.) and observation of the ecdysis	Neese et al. (2000)

Table 2 continued

Neuroactive compounds	Species	Research direction	Methods	References
Juvenile hormones/ MF	*Spodoptera exigua* (Insecta, Lepidoptera)		JH I, II and III application and observation of the morphological changes after eclosion	Kim et al. (2000)
	Bombyx mori (Insecta, Lepidoptera)		Topical application of fenoxycarb (juvenile hormone analog) and observation of the duration of the larval stages	Cappellozza et al. (1990), Kamimura (1995)
	Rhodnius prolixus (Insecta, Hemiptera)	Investigation of the role of the hormone in metamorphosis in both sexes in different stages of ontogenesis and in various tissues	Injection with methoprene and juvenile hormones and observation of the morphology after molting and during the molt	Nakamura et al. (2007)
	Tribolium castaneum (Insecta, Coleoptera), *Pyrrhocoris apterus* (Insecta, Hemiptera)		Knockout of the *Met* gene and observation of the duration of metamorphosis	Konopova and Jindra (2007), Konopova et al. (2011)
Juvenile hormones/ MF	*Drosophila melanogaster* (Insecta, Diptera), *Calliphora vomitoria* (Insecta, Diptera)	Role of the hormone in reproduction (vitellogenesis induction and control, ovary development, characteristics of the eggs and their number, fecundity of males)	Correlation between JH level and vitellogenesis by observation	Bownes (1989), Trabalon et al. (1987)
	Pteromalus puparum (Insecta, Hymenoptera)		Detection of the correlation between the JH level and Vg mRNA in the whole body, fat body, ovaries and hemolymph	Dong et al. (2009)
	Pteromalus puparum (Insecta, Hymenoptera)		Decapitation and observation of the Vg mRNA level	Dong et al. (2009)
	Ornithodoros moubata (Arachnida, Ixodida), *Drosophila melanogaster* (Insecta, Diptera)		Topical application of JH I, JH III and observation of oviposition and oogenesis	Grutenko et al. (2010), Obenchain and Mango (1980)
	Apis melifera (Insecta, Hymenoptera)		Pyriproxyfen (juvenile hormone analog) application and detection of Vg subunits using SDS–PAGE electrophoresis in the hemolymph; TEM analysis of fat body slices	Pinot et al. (2000)
	Drosophila melanogaster (Insecta, Diptera)	Role of the hormone in reproduction (vitellogenesis induction and control, ovary development, characteristics of the eggs and their number, fecundity of males)	Precocene I and II (anti-juvenoids) application and observation of the number of oocytes in different stages	Wilson et al. (1983)
	Ornithodors parkeri (Arachnida, Ixodida)		Topical application of precocene II and observation of oviposition, egg development and the ultrastructure of ovaries	Pound and Oliver (1979)
	Drosophila melanogaster (Insecta, Diptera), *Spodoptera frugiperda* (Insecta, Lepidoptera)		20E and JHA injections and detection of the Vg subunits in the hemolymph using SDS–PAGE electrophoretic gels and determination of the concentration of Vgs using autofluorographic method	Postlethwait and Handler (1979), Sorge et al. (2000)
	Drosophila melanogaster (Insecta, Diptera)		*Met* null mutant and observation of egg maturation and fecundity	Wilson and Ashok (1988)

Table 2 continued

Neuroactive compounds	Species	Research direction	Methods	References
Juvenile hormones/ MF	*Plautia stali* (Insecta, Hemiptera)	Role of the hormone in reproduction (vitellogenesis induction and control, ovary development, characteristics of the eggs and their number, fecundity of males)	Determination of the diameter of the terminal oocyte in female adults and the width of the ectadene (ectodermal accessory gland) in male adults by removing and measuring the *corpus cardiacum–corpus allatum* complex	Kotaki et al. (2011)
Ecdysteroids	*Ornithodoros parkeri* (Arachnida, Ixodida)	Detection of the hormone in various tissues in different stages of ontogenesis	Determination of the concentration of ecdysone in the epicuticle, salivary glands, coxal glands, synganglion, testis, midgut and fat body using high-pressure liquid chromatography and radioimmunoassay (HPLC-RIA method)	Zhu et al. (1991)
	Blattella germanica (Insecta, Blattodea)		Determination of the 20E level in ovaries using enzyme immunoassays (EIA) and HPLC method	Pascual et al. (1992)
	Pteromalus puparum (Insecta, Hymenoptera)		Determination of the level of ecdysteroids in whole bodies using RIA and GC–MS	Dong et al. (2009)
	Ornithodoros parkeri (Arachnida, Ixodida)	Detection of the site of ecdysteroids synthesis de novo	Incubation in vitro of epicuticle, salivary glands, coxal glands, synganglion, testis, midgut, fat body and determination of the concentration of ecdysone using HPLC-RIA method	Zhu et al. (1991)
	Aedes aegypti (Insecta, Diptera), *Drosophila melanogaster* (Insecta, Diptera)		Culture of ovaries in vitro and determination of the presence and concentration of the hormone using the RIA method	Bownes (1989), Hagedorn et al. (1975)
	Bombyx mori (Insecta, Lepidoptera), *Drosophila melanogaster* (Insecta, Diptera)		Detection of the *spook* (and its paralogs), *phantom*, *disembodied* and *shadow* genes using standard molecular methods or in silico	Ono et al. (2006), Mitchell and Smith (1986), Rewitz et al. (2006), Warren et al. (2002, 2004)
	Ornithodoros parkeri (Arachnida, Ixodida)	Detection of tissues whose physiology is regulated by ecdysteroids	Determination of the concentration of ecdysone in various tissues (epicuticle, salivary glands, coxal glands, synganglion, testis, midgut, fat body) and in different stages of ontogenesis hormone HPLC-RIA method	Zhu et al. (1991)
	Drosophila melanogaster (Insecta, Diptera)		Detection of the *shade* gene hormone standard molecular methods or in silico	Petryk et al. (2003)

Table 2 continued

Neuroactive compounds	Species	Research direction	Methods	References
Ecdysteroids	*Drosophila melanogaster* (Insecta, Diptera), *Liocheles australasiae* (Arachnida, Scorpiones),	Detection of tissues whose physiology is regulated by ecdysteroids	Detection of the ecdysteroid receptors—*EcR* and *USP* genes using standard molecular methods or in silico	Koelle et al. (1991), Nakagawa et al. (2007), Palmer et al. (1999), Yao et al. (1993)
	Cell culture		Detection of the EcR using ligand-binding assay	Tremmel et al. (2011)
	Liocheles australasiae (Arachnida, Scorpiones)		Gel mobility shift assay of the EcR and USP protein	Nakagawa et al. (2007)
	Drosophila melanogaster (Insecta, Diptera), *Manduca sexta* (Insecta, Lepidoptera)	Investigation of the role of the hormone in molting induction and metamorphosis in both sexes in different stages of ontogenesis and in various tissues	Expression level of genes: *spook* (and its paralogs), *phantom*, *disembodied* and *shadow*, *shade*, *EcR* and *USP* genes in different stages of ontogenesis and in various tissues using quantitative real-time PCR	Talbot et al. (1993), Truman et al. (1994)
	Apis mellifera (Insecta, Hymenoptera), *Drosophila melanogaster* (Insecta, Diptera), *Laodelphax striatellus* (Insecta, Hemiptera), *Manduca sexta* (Insecta, Lepidoptera), *Sogatella furcifera* (Insecta, Hemiptera)		Knockout of genes: *spook* (and its paralogs), *EcR*, *shade*, *disembodied* and observation of the possibility of molting	Jia et al. (2013), Mello et al. (2014), Ono et al. (2006), Wan et al. (2014a, b)
	Apis mellifera (Insecta, Hymenoptera)		Gene *spook* (and its paralogs) silencing and rescuing by 20E application and observation of the possibility of molting	Ono et al. (2006)
	Aedes aegypti (Insecta, Diptera)		Finding the correlation between the hormone level in whole body and ovaries and the stage of development (before and after blood meal) using the RIA method and observation	Hagedorn et al. (1975)
Ecdysteroids	*Drosophila melanogaster* (Insecta, Diptera), *Spodoptera frugiperda* (Insecta, Lepidoptera)	Investigation of the role of the hormone in reproduction (vitellogenesis induction and control, ovary development, characteristics of the eggs and their number, fecundity of males)	20E and JHA injections and detection of the Vg subunits in the hemolymph using SDS–PAGE electrophoretic gels and Vgs concentration determination using the autofluorographic method	Postlethwait and Handler (1979), Sorge et al. (2000)
	Aedes aegypti (Insecta, Diptera)		Finding the correlation between the hormone level in the whole body and ovaries and reproduction processes (ovary development and egg production) before and after blood meal using the RIA method and observation	Hagedorn et al. (1975)
	Blattella germanica (Insecta, Blattodea)		Finding the correlation between the parameters of the oocyte and follicle cells (size, age, specific surface, presence of chorion) and 20E level. Observation of slides from dissected ovaries during the seven-day cycle of oocyte maturation to search for the yolk protein in oocytes	Pascual et al. (1992)

Table 2 continued

Neuroactive compounds	Species	Research direction	Methods	References
	Drosophila melanogaster (Insecta, Diptera)	Ecdysteroids	Indirect method—detection and expression level of the *Broad-Complex* (*BR–C*), *E74* and *E75* genes in ovaries using in situ hybridizations, RNAse protection assay in the wild line and in recombinants without *EcR* gene	Buszczak et al. (1999)
	Drosophila melanogaster (Insecta, Diptera)		Expression of the EcR in ovaries using the Western blot method and immunolocalization of the EcR protein in slices from dissected ovaries in different stages; observation of ovary development and physiology (egg numbers, fecundity of males, counting the defective egg chambers) in the *EcR* mutants that were created	Carney and Bender (2000)
	Ixodes scapularis (Arachnida, Ixodida)		Finding the correlation between the levels of ecdysteroids and Vgs in the fat body, two days before and after detachment from the host using HPLC method	James et al. (1997)
Ecdysteroids	*Drosophila melanogaster* (Insecta, Diptera)	Investigation of the role of the hormone in reproduction (vitellogenesis induction and control, ovary development, characteristics of the eggs and their number, fecundity of males)	Immunodetection of EcR protein in the central nervous system, seminal vesicles, ejaculatory duct, testes, ejaculatory bulb, developing egg, midgut, Malpighian tubules in both sexes of adult flies	Schwedes et al. (2011)
	Drosophila melanogaster (Insecta, Diptera)		Determining the expression level of the *USP* gene in the central nervous system, abdominal cuticle tissue (contains the epidermis, muscle, fat body and oenocytes), gut and Malpighian tubules, male reproductive tract tissues (testes, seminal vesicles, accessory glands, ejaculatory duct, ejaculatory bulb) in both sexes of 0-, 5- and 10-day-old flies using qPCR	Schwedes et al. (2011)
	Drosophila melanogaster (Insecta, Diptera)		Determining the expression level of the *EcR*/*USP* dimer in line with LacZ in the brain, fat body, cuticle, oenocytes, follicle cells, developing and mature eggs in 0-day-old and 10-day-old flies by observation of the blue color of tissues	Schwedes et al. (2011)
	Pteromalus puparum (Insecta, Hymenoptera)		20E treatment and Vg level determination using ELISA and Vg mRNA level measurement using qPCR in the fat bodies, hemolymph, ovaries; finding the correlation between Vg mRNA, 20E and JH III levels	Dong et al. (2009)
Allatostatin A	*Diploptera punctata* (Insecta, Blattodea)	Detection, characterization and isolation of the allatostatin A in various tissues in different stages of ontogenesis	Determination of the expression level of A-type *Ast* 120 and *Ast R* genes using quantitative real-time PCR (RT-PCR)	Garside et al. (2002)
	Blattella germanica (Insecta, Blattodea), *Diploptera punctata* (Insecta, Blattodea), *Periplaneta americana* (Insecta, Blattodea)		Determination and isolation of *AST* using the polymerase chain reaction (PCR)	Ding et al. (1995), Garside et al. (2002), Maestro and Bellés (2006)

Table 2 continued

Neuroactive compounds	Species	Research direction	Methods	References
	Diploptera punctata (Insecta, Blattodea)		Determination of the allatostatin content of oviducts using ELISA methods with a monoclonal antibody to Dippu-AST 7. Oviducts were dissected on day 7 before ovulation, immediately after ovulation and one day post-ovulation	Woodhead et al. (2003)
	Blattella germanica (Insecta, Blattodea), *Diploptera punctata* (Insecta, Blattodea), *Popillia japonica* (Insecta, Coleoptera), *Tenebrio molitor* (Insecta, Coleoptera)		Determination of the allatostatin content of the brain extract using ELISA methods with a monoclonal antibody to Dippu-AST 7	Elliott et al. (2010), Maestro and Bellés (2006)
	Carausius morosus (Insecta, Phasmatodea), *Diploptera punctata* (Insecta, Blattodea)		Determination of the allatostatin level in the ovaries and brain extract using the HPLC method	Lorenz et al. (2000), Woodhead et al. (2003)
	Diploptera punctata (Insecta, Blattodea) and *Periplaneta americana* (Insecta, Blattodea)		Organization of allatostatin genes by DNA blot hybridization	Ding et al. (1995)
Allatostatin A	*Popillia japonica* (Insecta, Coleoptera),*Tenebrio molitor* (Insecta, Coleoptera)	Localization in the wholemounts, the central nervous system, the ovaries, oviducts and in early embryos	Localization using histochemistry methods with a monoclonal antibody to Dippu-AST 7 (5F10) or a rabbit polyclonal antiserum Dippu-AST 7	Elliott et al. (2010), Garside et al. (2002), Woodhead et al. (2003)
	Diploptera punctata (Insecta, Blattodea)	Investigation of the role of allatostatin A in the biosynthesis of JHs	Injection of dsDippu-AstR RNA and JH production determined using the radiochemical assay	Lungchukiet et al. (2008a, b)
	Diploptera punctata (Insecta, Blattodea), *Popillia japonica* (Insecta, Coleoptera), *Tenebrio molitor* (Insecta, Coleoptera)		Effect of *P. japonica* and *T. molitor* brain extract with anti-Dippu-AST-5 on the percent of the inhibition of JH synthesis by cockroach CA. Determination of the difference between preincubated and not incubated brains. JH biosynthesis by CA in vitro was quantified using a radiochemical assay	Elliott et al. (2010)
	Diploptera punctata (Insecta, Blattodea)		JH biosynthesis by the CA in vitro was quantified using a radiochemical assay	Elliott et al. (2010), Holbrook et al. (1996), Maestro and Bellés (2006), Tobe et al. (2000), Woodhead et al. (2003)
	Diploptera punctata (Insecta, Blattodea)		Rates of JH biosynthesis by *treated* CA exposed to the test substances was compared directly to the rates of JH biosynthesis by untreated glands	Pratt et al. (1991)
	Diploptera punctata (Insecta, Blattodea)		Injection of the synthetic neuropeptides Dip-AST 7 and Dip-AST 5 or their analogs [AST(b)φ2, Dip-AST analogs 397-2, 396-1, 419]. JH biosynthesis by the CA was measured in vitro using the radiochemical assay	Garside et al. (2000)

Table 2 continued

Neuroactive compounds	Species	Research direction	Methods	References
Allatostatin A	*Diploptera punctata* (Insecta, Blattodea)	Investigation of the role of the allatostatin in reproduction (vitellogenesis induction and control, ovary development, characteristics of the eggs and their number, fecundity of males)	Measured the oocyte length after the injection of Dip-allatostatin using an ocular micrometer	Garside et al. (2000)
	Blattella germanica (Insecta, Blattodea)		Incubation of tissues with neuropeptide solution to check the level and release of vitellogenins the ELISA or Western blot methods	Martin et al. (1996)
	Diploptera punctata (Insecta, Blattodea), *Drosophila melanogaster* (Insecta, Diptera)	Effect on the allatostatin level and activation of their receptors	Determination of the expression level of *DAR-1* and *DAR-2* receptor genes using by RT-PCR after injection of allatostatin	Larsen et al. (2001)
	Blattella germanica (Insecta, Blattodea)		Knockdown of *BgAST* genes using dsRNA. The brains and midguts were dissected on days 1, 4, and 7 after treatment. Tissues were then processed for RT-PCR and ELISA analysis	Maestro and Bellés (2006)
Allatostatin B	*Drosophila melanogaster* (Insecta, Diptera), *Gryllus bimaculatus* (Insecta, Orthoptera)	Detection, characterization and isolation of the allatostatin B in various tissues in different stages of ontogenesis	Determination of the expression level of *DAP-B* genes RT-PCR	Wang (2004), Williamson et al. (2001a)
	Carausius morosus (Insecta, Phasmatodea)		Determination of the allatostatin level using the high-performance liquid chromatography (HPLC) method	Lorenz et al. (2000)
	Gryllus bimaculatus (Insecta, Orthoptera),		Determination and isolation of *Grybi-AS B* gene by the polymerase chain reaction (PCR)	Wang (2004)
	Gryllus bimaculatus (Insecta, Orthoptera),		Determination of the number of *Grybi-AS B* genes within the *G. bimaculatus* genome by southern blot analysis	Wang (2004)
	Gryllus bimaculatus (Insecta, Orthoptera)	Localization in the wholemounts, the central nervous system, the ovaries, oviducts and early embryos	Localization using histochemistry methods with a monoclonal antibody to Dippu-AST 7 (5F10), in situ hybridizations and RT in situ PCR	Wang (2004)
	Drosophila melanogaster (Insecta, Diptera)		Wholemount in situ hybridizations of the brain and gut from third-instar larvae	Williamson et al. (2001a)
	Acheta domesticus (Insecta, Orthoptera), *Blaptica dubia* (Insecta, Blattodea), *Carausius morosus* (Insecta, Phasmatodea), *Gryllus bimaculatus* (Insecta, Orthoptera), *Leptinotarsa decemlineata* (Insecta, Coleoptera)	Effects on the biosynthesis of juvenile hormones and ecdysteroids	JH biosynthesis by the CA in vitro was quantified using a rapid partition assay	Lorenz et al. (1995, 2000, 2004), Meng et al. (2015)

Table 2 continued

Neuroactive compounds	Species	Research direction	Methods	References
Allatostatin C	*Aedes aegypti* (Insecta, Diptera)	Detection, characterization and isolation of allatostatin C in various tissues in different stages of ontogenesis	Expression of receptor genes by three different cell lines used, HEK293 cells, HEK293 cells stably expressing Ga15 and HEK293T cells expressing Ga16gust44	Mayoral et al. (2010)
	Aedes aegypti (Insecta, Diptera)		Determination of the expression level of *AedesAS-C*, *AeAS-CrA* and *AeAS-CrB* genes using quantitative real-time PCR (RT-PCR)	Mayoral et al. (2010)
	Drosophila melanogaster (Insecta, Diptera)		Determination of the expression level of genes using the Northern plot in different developmental stages	Williamson et al. (2001b)
	Aedes aegypti (Insecta, Diptera)	Effects on JH biosynthesis	Incubation of tissues with neuropeptide solution. Check the effect using HPLC-FD	Nouzova and Rivera-Perez (2015)
	Spodoptera frugiperda (Insecta, Lepidoptera)		Injection of the Spofr/Manse-AS dsRNA. Concentration was measured using liquid chromatography–mass spectrometry (LC–MS) method	Griebler et al. (2008), Hassanien et al. (2014)
	Spodoptera frugiperda (Insecta, Lepidoptera), *Heliothis virescens* (Insecta, Lepidoptera), *Lacanobia oleracea* (Insecta, Lepidoptera), *Manduca sexta* (Insecta, Lepidoptera), *Pseudaletia unipuncta* (Insecta, Lepidoptera), *Samia cynthia* (Insecta, Lepidoptera)		JH biosynthesis by the CA in vitro was quantified using a radiochemical assay	Audsley et al. (1999a, b, 2000a, b), Duve et al. (2003), Kramer et al. (1991), Li et al. (2004), Oeh et al. (2000), Teal (2002)
Allatotropin	*Spodoptera frugiperda* (Insecta, Lepidoptera)	Detection of the action site	Determination of the expression level of genes (*Spofr-AT*) using RT-PCR	Abdel-Latief et al. (2004)
	Aedes aegypti (Insecta, Diptera)		Identification of allatotropin receptor (AeATr) using the bioinformatic approach	Nouzova et al. (2012)
	Spodoptera frugiperda (Insecta, Lepidoptera)	Effects on the At level	Knockdown of *Manse/Spofr-AT* genes using dsRNA	Hassanien et al. (2014)
	Spodoptera frugiperda (Insecta, Lepidoptera)	Effect on development, egg production and oviposition	Injection of the Spofr-AT/Spofr-AT 2 dsRNA	Griebler et al. (2008), Hassanien et al. (2014)
	Spodoptera frugiperda (Insecta, Lepidoptera)	Effects on JH and free ecdysteroids biosynthesis	Injection of the Spofr-AT/Spofr-AT 2 dsRNA. Concentration was measured using liquid chromatography–mass spectrometry (LC–MS) method	Griebler et al. (2008), Hassanien et al. (2014)

Table 2 continued

Neuroactive compounds	Species	Research direction	Methods	References
	Romalea microptera (Insecta, Orthoptera), *Galleria mellonella* (Insecta, Lepidoptera), *Heliothis virescens* (Insecta, Lepidoptera), *Lacanobia oleracea* (Insecta, Lepidoptera), *Manduca sexta* (Insecta, Lepidoptera), *Samia cynthia* (Insecta, Lepidoptera), *Spodoptera frugiperda* (Insecta, Lepidoptera)		JH biosynthesis by the CA in vitro was quantified using a radiochemical assay	Audsley et al. (1999b, 2000a), Bogus and Scheller (1996), Hebda et al. (1994), Kataoka et al. (1989), Li et al. (2005), Oeh et al. (2000, 2001), Rachinsky et al. (2003)
	Galleria mellonella (Insecta, Lepidoptera)	Identification of neurosecretory cells	Localization using histochemistry methods with a monoclonal antibody	Bogus and Scheller (1996)

(Kozlova and Thummel 2003), larval molting and metamorphosis (Riddiford 1993). Additionally, in adults, ecdysone signaling is essential for particular aspects of oogenesis such as vitellogenesis and follicle development (Carney and Bender 2000; Hodin and Riddiford 1998), as well as for courtship (Ganter et al. 2012).

Compared to knowledge about juvenile hormones, data about ecdysteroids in arachnids are more extensively explored. The site of ecdysteroids synthesis is prothoracic glands in larvae and in the nymphal integument in adult ticks (Lomas et al. 1997; Zhu et al. 1991). Similar to insects, these steroid hormones act by EcR and USP receptors (Palmer et al. 1999). The results of various experiments indicate that the function of ecdysteroids in ticks is quite similar to that in insects (the induction of molting—Solomon et al. 1982, sperm maturation—Oliver and Dotson 1993). Data about the role of these steroid hormones in the regulation of oogenesis and oviposition are ambiguous (stimulatory effect—Sankhon et al. 1999; inhibition effect—Diehl et al. 1986).

Similar to Acari, data about ecdysteroids in spiders are also described in detail than about juvenile hormones and/or their analogues (see Table 1.). Until now, the presence of ecdysteroids has been documented in the females of eight arachnid species: *P. mirabilis* (Pisauridae) (Bonaric and De Reggi 1977), *Tegenaria domestica* (Agelenidae), *Coelotes terrestris* (Agelenidae) (Trabalon et al. 1992), *T. atrica* (Agelenidae) (Trabalon et al. 1998), *Brachypelma albopilosum* (Theraphosidae) (Trabalon and Blais 2012), *Schizocosa avida*, *S. rovneri*, *S. uetzi* (Lycosidae) (Stubbendieck et al. 2013). Data about the occurrence of ecdysteroids in spider males exclusively come from research Trabalon and Blais (2012), and Stubbendieck et al. (2013) about *B. albopilosum* and *S. uetzi*. The site of ecdysteroid synthesis in this group of arthropods is still not confirmed. However, the presence of the molting organ (MO) was shown. The MO can be responsible for ecdysteroids synthesis, because the correlation between ultrastructural changes in these cells of the organ and the following molting was observed (Bonaric and Juberthie 1983). Moreover, the relationships between the release of the secret from the MO and the highest titer of ecdysone in *P. mirabilis* were noticed (Bonaric 1980; Bonaric and De Reggi 1977). The structure of this gland was described for the first time in spider *P. mirabilis* (Bonaric 1980; Bonaric and Juberthie 1979; Gabe 1966; Kühne 1959; Legendre 1958, 1959). The MO consists of groups of cells, mainly located in the lower part of the prosoma, and it is an endocrine tissue in the meaning of Millot (1930). The localization and volume of this organ are dependent on sex, stage of ontogenesis and age of the animal. The hypothetical model of regulation of the molting process was put forward by Bonaric (1995) based on changes in

ecdysteroids titer fluctuation and ultrastructural alternation in the MO cells in *P. mirabilis*. The cyclic MO activity is controlled by the neuroendocrine system via the retrocerebral system. Neurosecretory cells from the brain, mainly from protocerebrum, produce the neurosecret under stimuli (e.g., proprioceptors or climatic factors). It was transported to the Neurohemal organ 1 by Schneider organ 1, where is the release to hemolymph. Neurosecret contains molting hormone activation, which is responsible for the MO activation. Moreover, the neurosecretory components can stimulate the hypothetical organ to synthesize juvenile hormones. However, it should be emphasized that the role of MO in the synthesis of ecdysteroids has not yet been confirmed. Mechanism of molecular action on the gene transcription level is still not known. Nevertheless, research about the EcR and USP receptors are restricted to only short communications about the spider *Agelena silvatica* (Agelenidae) (Honda et al. 2009). It seems that ecdysteroids play a similar role in the regulation of the molting process, as like as in insects. It was observed the correlation between the ecdysteroid level and the molt appearance in *P. mirabilis* (Eckert 1967; Bonaric and De Reggi 1977). Moreover, the application of ecdysone and 20E reduced a shortening of intermolting time and induced a molting in *P. mirabilis*, *Larinioides cornutus* (Araneidae), *Aphonopelma hentzi* (Theraphosidae) (Bonaric 1976, 1977; Krishnakumaran and Schneiderman 1970). Ecdysteroids can be responsible for the spider ovaries development (Trabalon et al. 1992), pheromone production, sexual cannibalism (Stubbendieck et al. 2013; Trabalon et al. 1998, 2005) and regulation of metabolism (Trabalon and Blais 2012). It seems that ecdysteroids are involved in the control of vitellogenesis. However, contradictory data are present. On the one hand, the correlation between the ecdysteroids titer and the start of vitellogenesis and the probable induction of this process are observed in *C. terrestris*, *T. domestica* and *T. atrica* (Pourié and Trabalon 2003; Trabalon et al. 1992, 1998). On the other hand, observation of the ecdysteroids titers in different stages of ontogenesis in spiders from genus *Schizocosa* indicates the lack of role of these groups of hormone in the induction of the vitellogenesis (Stubbendieck et al. 2013).

Neuropeptides

The neuroendocrine system of insects regulates most critical metabolic, behavioral, homeostatic, developmental and reproductive processes. The *corpora cardiaca* (CC) glands, which store and release the neurohormones that are synthesized in neuroendocrine cells of the brain, are one of the most important structures of the neuroendocrine system. CC glands can also produce their own peptides due to the presence of specific secretory cells (De Loof and Hoffmann 2001; Marciniak et al. 2011).

One group of proteins that are secreted by the neuroendocrine system in insects is neuropeptides. They belong to neurosecret together with steroids and sesquiterpenoids. Neuropeptides represent the largest single class of signal compounds. They are diversified chemical messengers that can act as neuromodulators, neurotransmitters and neurohormones. They are produced in the central nervous system of insects by the neurosecretory cells and interneurons (Duve et al. 1999; Bendena 2010; Harshini et al. 2002; Marciniak and Rosinski 2007; Sarkar et al. 2003).

Insect neuropeptides are grouped into families that are based on the structural similarity of the amino acid sequence of each substance and their main physiological functions. After the first successful attempt of sequencing the genome of the insect *D. melanogaster*, a classification system that was based on the peptide precursor genes that encode them was added. The main assumption of the categorization is the fact that the neuropeptides that belong to the same family are encoded by a single precursor gene. It is supposed that peptides encoded by ortholog genes in other species of insects are members of the same family of neuropeptides (Marciniak and Rosiński 2007; Marciniak et al. 2011; Nassel 2002).

Among the previously identified neuropeptides are the peptides that regulate the majority of physiological and behavioral processes in insects, the most well known of which is their impact on growth and reproduction and the control of JH synthesis by the CA.

Allatoregulating neuropeptides

Allatoregulating neuropeptides are multifunctional peptides. One of their main functions is to regulate the biosynthesis of JHs. Allatostatins have an inhibitory effect, whereas allatotropins stimulate biosynthesis and are released by the CA (Bendena 2010; Gade and Hoffmann 2005; Harshini et al. 2002; Marciniak and Rosiński 2007; Sarkar et al. 2003).

Allatostatin

Allatostatins (ASTs) are a superfamily of invertebrate neuropeptides that were originally defined by their action as inhibitors of JH biosynthesis in vivo. ASTs act on the G-protein-coupled receptors (GPCRs) in the cells of the CA to inhibit JH biosynthesis in insects. To date, more than 60 allatostatins have been isolated and characterized from a variety of insect species. Structurally similar neuropeptides have also been identified in crustaceans and ticks (Stay and Tobe 2007; Zhu and Oliver 2001). These peptides can be

classified into three groups: the FGL—allatostatin superfamily (A type), the W(X)6W allatostatins (B type) and the lepidopteran (*M. sexta*) allatostatin (C type) (Bendena 2010).

FGL-allatostatin superfamily (A type) Allatostatins of the FGLamide (phenylalanine–glycine–leucine) type were originally identified and isolated from brain extracts of the cockroach *Diploptera punctata*. Subsequently, the members of this peptide family were isolated from other insect orders, for example from the cricket *Gryllus bimaculatus*, the locust *Schistocerca gregaria* and the blowfly *Calliphora vomitoria*. The A-type allatostatins are 5–18 amino acids long, which is the minimum required for biological activity, and are characterized by a common C-terminal pentapeptide (F/YXFGLamide) (Marciniak et al. 2011; Tobe et al. 2000). The rapid and reversible inhibition of JH synthesis after the application of the synthetic or isolated allatostatin A has only been observed in cockroaches, crickets and, most recently, in termites (Belles et al. 1994; Lorenz et al. 1995; Pratt et al. 1991; Woodhead et al. 1989). To date, the A-type allatostatin has not been reported to have any significant effect of JH synthesis by the CA in any lepidopteran (Audsley et al. 2008).

The W(X)6W-allatostatins (B type) The second family of allatostatins was isolated from the brains of the cricket *G. bimaculatus* and has the general sequence W(X)6Wamide. These C-terminal nonapeptides contain the amino acid tryptophan at positions 2 and 9 and have a high sequence similarity to the myoinhibiting peptides that were previously isolated from *Locusta migratoria* (Locmi-MIP) and *Manduca sexta*. Neuropeptides with a similar structure were also isolated from the stick insect *Carausius morosus* and the silkworm *Bombyx mori* (Audsley et al. 2008; Wang 2004). They are active in JH biosynthesis in crickets but are less potent than the A-type neuropeptides. They have also not been investigated as precisely as the FGLamide type (Stay et al. 2002).

Lepidopteran (M. sexta) allatostatin (C type) The first peptide of this group Manse-AST (pEVRFRQCYFNPISCF) was purified from the brains of the moth *M. sexta*. The C-type allatostatin is a non-amidated, N-terminally blocked, 15-residue peptide that contains a disulfide bridge between the C residues at positions 7 and 14. It strongly inhibited JH biosynthesis in vitro by the CA of fifth-instar larvae and adult females of the moth. It also had an inhibitory effect on the activity of the CA from adult females of other lepidopterans but was ineffective in other orders of insects (Abdel-Latief and Hoffmann 2014; Stay et al. 2002; Tobe et al. 2000).

Among arachnids, allatostatins have also been identified in ticks. A-type allatostatins were detected by immunocytochemistry methods in the synganglion of *Dermacentor variabilis* by Zhu and Oliver (2001) and *I. scapularis* (Simo and Park 2014). The immunoreactive cells were detected in the different regions of the synganglion: protocerebral, cheliceral, palpal, stomodeal, postesophageal and opisthosomal. The stronger positive reaction in the preesophageal part of the synganglion was observed. Therefore, authors suggest that this may be a part of neuroendocrine system where allatostatins are released. Another type of allatostatin (Manse-AST) in the central nervous system of *I. scapularis* was also described (Neupert et al. 2009). Despite the presence of these peptides in ticks, their role is still unknown. As mentioned, Zhu et al. (2016) suggested that the methyl farnesoate may act as JHs in ticks and allatoregulatory neuropeptides may stimulate or inhibit the mevalonate–farnesol pathway in *I. scapularis*.

Allatotropin

The allatotropin (AT) peptide was first isolated from *M. sexta* (Manse-AT). Its sequence (GFKNVEMMTARGF-NH2) was confirmed based on cDNA. Allatotropin exhibits stimulating activity for biosynthesis in vivo and release of juvenile hormone by *corpora allata* (Dyker et al. 2001). This effect was only confirmed in adult members of *M. sexta*, whereas the stimulation in larval stages and in pupae was not observed (Kataoka et al. 1989). Allatotropin compared to other allatoregulatory neuropeptides are characterized by high species specificity. Therefore, Bogus and Scheller (1996) reported that allatotropin caused increased secretion of juvenile hormone II from *corpora allata* in larvae in stage 6 (L6) in the *Galleria mellonella*. Allatotropins have a number of other physiological functions, although their exact role is still not fully understood (Dyker et al. 2001).

Allatoregulating neuropeptides in spiders

The current knowledge about this family of neuropeptides comes from studies that were carried out on insects. There are only a few publications (Table 1) that are based on the immunohistochemical distribution and localization of allatostatins in the model spider species *C. salei*. These studies have shown the presence of allatostatins in the arcuate body, which is a principal part of the central nervous system of spiders (Loesel et al. 2011). Recent studies have also indicated the presence of allatoregulating neuropeptides in spiders. Christie (2015a) identified peptides that belong to allatostatin A, allatostatin B, allatostatin C and allatotropin in *Latrodectus hesperus* based on an in silico

characterization of the neuropeptidome. Subsequently, he performed a similarity analysis using *L. hesperus* as the reference. He detected the same allatoregulating neuropeptides in *Latrodectus tredecimguttatus*, *Stegodyphus mimosarum*, *Stegodyphus lineatus*, *Stegodyphus tentoriicola* and *Acanthoscurria geniculata* (Christie and Chi 2015). The available results of the study of allatoregulating neuropeptides in spiders are presented in Table 1. Until now, there are no data about potential functions of allatostatins and allatotropin and/or their analogues on the development, reproduction and molting induction in spiders.

Future prospects

We believe that future research should be directed toward the confirmation of the presence of JHs and/or their analogues in spiders. The knowledge about ecdysteroids and neuropeptides requires revision and needs more details. The evolutionary relationship between spiders and the other arthropods described (e.g., ticks, mites) suggests the possibility of the presence of JHs and/or their analogues in spiders and indicates that neuroactive compounds may play a similar role in all arthropods. Analysis of the studies about JHs and their analogues, ecdysteroids and neuropeptides in other arthropods (see Table 2) indicates several possible directions for the research of these compounds.

Determining the concentration of hormones and neuropeptides in various tissues during the different stages of ontogenesis seems to be the first appropriate method to study these compounds (Abdel-Latief et al. 2004; Dong et al. 2009; Edwards et al. 1995; Elliott et al. 2010; Maestro and Bellés 2006; Neese et al. 2000; Pascual et al. 1992; Wang 2004; Williamson et al. 2001b; Zhu et al. 1991). Identifying the relationship between the concentration of these substances and the age of the animal is a good starting point for analyzing the functions of these compounds in ontogenesis of spiders. However, it should be noted that the studies on the concentration of JHs and its presence in various tissues are difficult due to the fact that the molecules of these hormones adhere to various surfaces, including glass, in a non-selective manner. Thus, not only is the determination of the level of JHs difficult to implement, but also the identification of its receptors (Konopova and Jindra 2007).

In recent years, a number of researches about the neuroactive compounds that are based on an analysis of the presence of various genes and their expression level have been undertaken. Detecting the genes that encode the enzymes of the biosynthesis pathway of these substances is the most accurate way of determining the tissues and organs that are responsible for the synthesis of hormones and neuropeptides de novo. Analysis of the available data about the determination of the presence of genes: *spook* (and its paralogs), *phantom*, *disembodied*, *shadow* (for pathway of ecdysteroids; Ono et al. 2006; Mitchell and Smith 1986; Rewitz et al. 2006; Warren et al. 2002, 2004), *jhamt* (*JH acid o-methyltransferase* gene) (for JH synthesis; Marchal et al. 2011; Shinoda and Itoyama 2003), and the gene that encodes the AST and At preprohormone (for neuropeptides pathway, Maestro and Bellés 2006) indicates that this approach is very appropriate for this purpose. Determining the tissues whose physiology is regulated by hormones and neuropeptides can be carried out by detecting the genes that encode the receptors (or potential candidates for JH and/or their analogues) or enzymes from the last step of the biosynthesis pathway (in the case of ecdysteroids, 20E is synthesized by ecdysone conversion by 20-hydroxylase, Petryk et al. 2003). Moreover, this approach is widely used in the literature. Studies about the genes that encode the ecdysteroid receptors EcR and (Bortolin et al. 2011; Koelle et al. 1991; Nakagawa et al. 2007; Palmer et al. 1999; Yao et al. 1993), enzyme 20-hydrolase, potential JH and its analogues receptor candidates Met, USP, Gce (Baumann et al. 2010; Gong et al. 2016) and the neuropeptide receptors for allatostatin A (*AlstR/DAR-1* and *DAR-2* receptor genes) (Larsen et al. 2001; Lungchukiet et al. 2008a), allatostatin C (*AeAS-CrA* and *AeAS-CrB*) (Mayoral et al. 2010) and the allatotropin receptor (*AeATr*) (Nouzova et al. 2012) have been observed (compared with Table 2). It should be emphasized that studies at the gene level allow the correlation between the expression level of the genes in the various tissues and the stages of ontogenesis be identified. This enables the identification of the critical organ of the synthesis and action of neuroactive compounds. Hence, determining the crucial physiological processes that are controlled by JHs and/or their analogues, ecdysteroids or neuropeptides is possible (Buszczak et al. 1999; Hassanien et al. 2014; Larsen et al. 2001; Schwedes et al. 2011; Williamson et al. 2001b, compared with Table 2). It seems that the silencing of the genes that encode the receptors or the enzymes of the biosynthesis pathway of JHs and/or their analogues, ecdysteroids and neuropeptides and then identifying the occurrence and course of various physiological processes (e.g., vitellogenin levels or the time between moltings) is the best way to study the role of these compounds (Griebler et al. 2008; Hassanien et al. 2014; Jia et al. 2013; Konopova et al. 2011; Konopova and Jindra 2007; Maestro and Bellés 2006; Mello et al. 2014; Wan et al. 2014a, b).

However, the problems that are associated with the studies of the genomes of spiders (see Sect. 1) have not been solved. Therefore, another possible method should be used to test neuroactive compounds. The synthetic hormones and neuropeptides and (in the case of JHs and/or

their analogues) chemical analogs and anti-juvenoids (which are commercially available) can be provided to an organism. This would allow the differentiated roles of these compounds to be detected in several physiological processes. The duration of their action and the point at which they are deactivated in various tissues, depending on sex and age, can be determined by applying various concentrations of synthetic neuroactive compounds for different periods of incubation (for the treatment of spiders with the appropriate concentration of substances—see Sect. 1).

We would like to emphasize once again that choosing the appropriate physiological processes to investigate is the key stage of any study about JHs and/or their analogues, ecdysteroids and neuropeptides. It seems that the site of the synthesis of these compounds de novo, as well as the site and mechanisms of their action in the context of the reproduction and molting induction and regulation of Araneomorphae spiders, is the best approach in the initial stages of the discovery of these hormones and neuropeptides. We believe that these preliminary studies are necessary as starting points for further studies, which could lead to the rapid development of research about the neuroendocrine system in spiders.

Compliance with ethical standards

Conflict of interest None.

References

Abdel-Latief M, Hoffmann KH (2014) Functional activity of allatotropin and allatostatin in the pupal stage of a holometablous insect, Tribolium castaneum (Coleoptera, Tenebrionidae). Peptides 53:172–184

Abdel-Latief M, Meyering-Vos M, Hoffmann KH (2004) Expression and localization of the *Spodoptera frugiperda* allatotropin (Spofr-AT) and allatostatin (Spofr-AS) genes. Arch Insect Biochem Physiol 55:188–199

Aeschlimann AA (1968) La ponte chez *Ornithodoros moubata* Murray (Ixodoidea: Argasidae). Rev Suisse Zool 75:1033–1039

Audsley N, Weaver RJ, Edwards JP (1999a) Juvenile hormone biosynthesis by the *corpora allata* of the Tomato moth *Lacanobia oleracea*, and regulation by a lepidopteran allatostatin. Eur J Entomol 96:287–293

Audsley N, Weaver RJ, Edwards JP (1999b) Significance of *Manduca sexta* allatostatin in the tomato moth *Lacanobia oleracea*. Ann N Y Acad Sci 897:330–341

Audsley N, Duve H, Thorpe A, Weaver RJ (2000a) Morphological and physiological comparisons of two types of allatostatin in the brain and retrocerebral complex of the tomato moth, *Lacanobia oleracea*, (Lepidoptera: Noctuidae). J Comp Neurol 424:37–46

Audsley N, Weaver RJ, Edwards JP (2000b) Juvenile hormone biosynthesis by *corpora allata* of larval tomato moth, *Lacanobia oleracea*, and regulation by *Manduca sexta* allatostatin and allatotropin. Insect Biochem Mol Biol 30:681–689

Audsley N, Matthews HJ, Price NR, Weaver RJ (2008) Allatoregulatory peptides in Lepidoptera, structures, distribution and functions. J Insect Physiol 54:969–980

Baumann A, Barry J, Wang S, Fujiwara Y, Wilson TG (2010) Paralogous genes involved in juvenile hormone action in *Drosophila melanogaster*. Genetics 185:1327–1336

Bednarek A, Sawadro M, Babczyńska A (2016) Modulation of the response to stress factors of *Xerolycosa nemoralis* (Lycosidae) spiders living in contaminated environments. Ecotoxicol Environ Saf 131:1–6

Belles X, Maestro JL, Piulachs MD, Johnsen AH, Duve H, Thorpe A (1994) Allatostatic neuropeptides from the cockroach Blattella germanica (L.) (Dictyoptera, Blattellidae). Identification, immunolocalization and activity. Regul Pept 53:237–247

Belozerov VN (2006) Juvenile hormones in development of Ixodoid tick a short review of current controversial situation in tick endocrynology. Acarina 14:113–121

Bendena WG (2010) Neuropeptide physiology in Insects. In: Geary TG, Maule A (eds) Neuropeptide systems as targets for parasite and pest control. Advances in experimental medicine and biology. Springer, Berlin, pp 166–191

Bogus M, Scheller K (1996) Allatotropin released by the brain controls larval molting in *Galleria mellonella* by affecting juvenile hormone synthesis. Int J Dev Biol 40:205–210

Bonaric JC (1976) Effects of ecdysterone on the molting mechanisms and duration of the intermoult period in *Pisaura mirabilis* Cl. Gen Comp Endocrinol 30(3):267–272

Bonaric JC (1977) Action de l'ecdystérone sur la réduction de durée de la période d'intermue chez *Pisaura mirabilis* Cl. (Araneae, Pisauridae): détermination de l'effet optimal par inoculation de concentratons croissantes. Arch Zool Exp Genet 118:43–51

Bonaric JC (1979) Effets des ecdysones et de l'hormone juvénile sur ladurée du cycle de mue chez l'araignée *Pisaura mirabilis* (Araneae, Pisauridae). Rev Arachnol 2:205–207

Bonaric JC (1980) Contribution aI'.itude de fa biofogie du devefoppement chez f'Araignee *Pisaura mirabilis* (Cferck, 1758). Approche physiofogique des phenomenes de mue et de diapause hivemale. These Doctoral Science of nature, Montpellier

Bonaric JC (1986) Moulting hormones. In: Nentwig W (ed) Ecophysiology of spiders. Springer, Berlin, pp 111–118

Bonaric JC (1988) Presence de composes apparentes aux Hormones Juveniles (lH.) d'lnsectes chez les Arachnides: detection et difficultes d'interpretation. Bull Buffalo Soc Nat Sci 59:27–36

Bonaric JC (1995) Le systeme neuroendocrine retrocerebral des Araignees: structure et function. In: Ruzicka V (ed) Proceedings of the 15th european colloquium of arachnology. Institute of Entomology, Ceske Budejovice, pp 27–34

Bonaric JC, De Reggi M (1977) Changes in ecdysone levels in the spider *Pisaura mirabilis* nymphs (Araneae pisauridae). Experientia 33:1664–1665

Bonaric JC, Juberthie C (1979) La glande de mue des Araignees. Etude structurale et ultrastructurale de cette formation chez *Pisaura mirabilis* Cl. (Araneae, Pisauridae). C.R. Vè. Colloque Arachnology IX, Barcelone, pp 99–109

Bonaric JC, Juberthie C (1983) Ultrastructure of the retrocerebral neuroendocrine complex in *Pisaura mirabilis* Cl. (Araneae, Pisauridae). Zool Jahrb Histol 87:55–64

Bonaric JC, Emerit M, Legendre R (1984) Le complexe neuroendocrine rétrocérébral et la «glande de mue» de Filistata insidiatrix Forskôl (Araneae, Filistatidae). Revue Arachnol 5:301–310

Bortolin F, Piulachs MD, Congiu L, Fusc G (2011) Cloning and expression pattern of the ecdysone receptor and retinoid X receptor from the centipede Lithobius peregrinus (Chilopoda, Lithobiomorpha). Gen Comp Endocrinol 174:60–69

Bownes M (1989) The role of juvenile hormone, ecdysone and the ovary in the control of Drosophila vitellogenesis. J Insect Physiol 35:409–413

Buszczak M, Freeman MR, Carlson JR, Bender M, Cooley L, Segraves WA (1999) Ecdysone response genes govern egg chamber development during mid-oogenesis in *Drosophila*. Development 126:4581–4589

Cappellozza L, Miotto F, Moretto E (1990) Effeti del fenoxycarb a basse concentrazioni sulle larve di, *Bombyx mario*. Redia 73:517–529

Carney GE, Bender M (2000) The *Drosophila* ecdysone receptor (EcR) gene is required maternally for normal oogenesis. Genetics 154:1203–1211

Chinzei Y, Taylor D, Ando K (1991) Effects of juvenile hormone and its analogs on vitellogenin synthesis and ovarian development in *Ornithodoros moubata* (Acari: Argasidae). J Med Entomol 28:506–513

Christie AE (2015a) In silico characterization of the neuropeptidome of the Western black widow spider *Latrodectus hesperus*. Gen Comp Endocrinol 210:63–80

Christie AE (2015b) Neuropeptide discovery in *Eucyclops serrulatus* (Crustacea, Copepoda): in silico prediction of the first peptidome for a member of the Cyclopoida. Gen Comp Endocrinol 211:92–105

Christie AE, Chi M (2015) Neuropeptide discovery in the Araneae (Arthropoda, Chelicerata, Arachnida): elucidation of true spider peptidomes using that of the Western black widow as a reference. Gen Comp Endocrinol 213:90–109

Connat J-L, Ducommun J, Diehl P-A (1983) Juvenile hormone-like substances can induce vitellogenesis in the tick *Ornithodoros moubata* (Acarina: Argasidae). Int J Invertebr Reprod 6:285–294

Crone EJ, Sutherland TD, Campbell PM, Coppin CW, Russell RJ, Oakeshott JH (2007) Only one esterase of *Drosophila melanogaster* is likely to degrade juvenile hormone in vivo. Insect Biochem Mol Biol 37:540–549

Davey KG (2000) The modes of action of juvenile hormones: some questions we ought to ask. Insect Biochem Mol Biol 30:663–669

De Loof A, Hoffmann KH (2001) Neuropeptides in insect development and reproduction. Arch Insect Biochem Physiol 47:127–128

Decker H, Rimke T (1998) Tarantula hemocyanin shows phenoloxidase activity. J Biol Chem 273:25889–25892

Dees WH, Sonenshine DE, Breidling E (1984) Ecdysteroids in the American dog tick, *Dermacentor variabilis* (Acari: Ixodidae), during different periods of tick development. J Med Entomol 21:514–523

Diehl PA, Connat JL, Dotson EM (1986) Chemistry, function, and metabolism of tick ecdysteroids. In: Sauer JR, Hair JH (eds) Morphology, physiology and behavioral biology of ticks. Ellis Horwood, Chichester, pp 165–193

Ding Q, Donly BC, Tobe SS, Bendena WG (1995) Comparison of the allatostatin neuropeptide precursors in the distantly related cockroaches *Periplaneta americana* and *Diploptera punctata*. Eur J Biochem 234:737–746

Dong SZ, Ye GY, Guo JY, Hu C (2009) Roles of ecdysteroid and juvenile hormone in vitellogenesis in an endoparasitic wasp, *Pteromalus puparum* (Hymenoptera: Pteromalidae). Gen Comp Endocrinol 160:102–108

Duve H, East PD, Thorpe A (1999) Regulation of lepidopteran foregut movement by allatostatins and allatotropin from the frontal ganglion. J Comp Neurol 413:405–416

Duve H, Audsley N, Weaver RJ, Thorpe A (2003) Allatostatins and allatotropin in the *corpus cardiacum/corpus allatum* complex of larval and adult lepidopterans studied by confocal laser scanning microscopy: correlation to juvenile hormone biosynthesis. Cell Tissue Res 314:281–295

Dyker H, Lösel P, Hoffmann KH (2001) In vivo effects of *Manduca sexta* allatotropin and allatostatin on development and reproduction in the fall armyworm, *Spodoptera frugiperda* (Lepidoptera, Noctuidae). Int J Invertebr Reprod Dev 39:239–247

Eckert M (1967) Experimentelle Untersuchungen zur Hautungsphysiologie bei Spinnen. Zool Jahrb Physiol 73:49–101

Edwards JP, Corbitt TS, McArdle HF, Short JE, Weaver RJ (1995) Endogenous levels of insect juvenile hormones in larval, pupal and adult stages of the Tomato moth, *Lacanobia oleracea*. J Insect Physiol 41:641–651

Elekonich MM, Horodyski FM (2003) Insect allatotropins belong to a family of structurally myoactive peptides present in several invertebrate phyla. Peptides 24:1623–1632

Elliott KL, Chan KK, Stay B (2010) Evidence for a Phe–Gly–Leu-amide-like allatostatin in the beetle *Tenebrio molitor*. Peptides 31:402–407

Gabe M (1955) Données histologiques sur la neurosecretion chez les Arachnides. Arch Anat Microsc Morphol Exp 44:351–383

Gabe M (1966) Neurosecretion. Pergamon Press, Oxford, p 1091

Gade G, Hoffmann KH (2005) Neuropeptides regulating development and reproduction in insects. Physiol Entomol 30:103–121

Ganter GK, Desilets JB, Davis-Knowlton JA, Panaitiu AE, Sweezy M, Sungail J, Tan LCH, Adams AM, Fisher EA, O'Brien JRM, Kincaid KM, Heinrich R (2012) *Drosophila* female precopulatory behavior is modulated by ecdysteroids. J Insect Physiol 58:413–419

Garside CS, Nachman RJ, Tobe SS (2000) Injection of Dip-allatostatin or Dip-allatostatin pseudopeptides into mated female *Diploptera punctata* inhibits endogenous rates of JH biosynthesis and basal oocyte growth. Insect Biochem Mol Biol 30:703–710

Garside CS, Koladich PM, Bendena WG, Tobe SS (2002) Expression of allatostatin in the oviducts of the cockroach *Diploptera punctata*. Insect Biochem Mol Biol 32:1089–1099

Gong J, Huang C, Shu L, Bai C, Huang H, Ye H, Zeng C, Li S (2016) The retinoid X receptor from mud crab: new insights into its roles in ovarian development and related signaling pathway. Sci Rep 6:1–12

Griebler M, Westerlund SA, Hoffmann KH, Meyering-Vos M (2008) RNA interference with the allatoregulating neuropeptide genes from the fall armyworm *Spodoptera frugiperda* and its effects on the JH titer in the hemolymph. J Insect Physiol 54:997–1007

Gruntenko NE, Wen D, Karpova EK, Adonyeva NV, Liu Y, He Q, Faddeeva NV, Fomin AS, Li S, Rauschenbach IY (2010) Altered juvenile hormone metabolism, reproduction and stress response in Drosophila adults with genetic ablation of the corpus allatum cells. Insect Biochem Mol Biol 40:891–897

Hagedorn HH, O'Connort D, Fuchs MS, Safe B, Schlaeger DM, Bohm MK (1975) The ovary as a source of α-ecdysone in an adult mosquito. Proc Natl Acad Sci 72:3255–3259

Handler AM, Postlethwait JH (1977) Endocrine control of vitellogenesis in *Drosophila melanogaster* effects of the brain and *corpus allatum*. J Exp Zool 202:389–402

Harshini S, Nachman RJ, Sreekumar S (2002) Inhibition of digestive enzyme release by neuropeptides in larvae of *Opisina arenosella* (Lepidoptera: Cryptophasidae). Comp Biochem Physiol B 132:353–358

Hassanien ITE, Grötzner M, Meyering-Vos M, Hoffmann KH (2014) Neuropeptides affecting the transfer of juvenile hormones from males to females during mating in *Spodoptera frugiperda*. J Insect Physiol 66:45–52

Hebda C, Yu JH, Bhaskaran G, Dahm KH (1994) Reactivation of *corpora allata* in pharate adult *Manduca sexta*. J Insect Physiol 40:849–858

Hentze JL, Moeller ME, Jørgensen AF, Bengtsson MS, Bordoy AM, Warren JT, Gilbert LI, Andersen O, Rewitz KF (2013) Accessory gland as a site for prothoracicotropic hormone controlled ecdysone synthesis in adult male insects. PLoS ONE 8(2):e55131

Hidayat P, Goodman WG (1994) Juvenile hormone and hemolymph juvenile hormone binding protein titers and their interaction in

the hemolymph of fourth stadium *Manduca sexta*. Insect Biochem Mol Biol 24:709–715

Hodin J, Riddiford LM (1998) The ecdysone receptor and ultraspiracle regulate the timing and progression of ovarian metamorphosis during *Drosophila* metamorphosis. Dev Genes Evol 208:304–317

Holbrook GL, Chiang AS, Schal C (1996) Allatostatin inhibition and garnesol stimulation of *corpus allatum* activity in embryos of the viviparous cockroach, *Diploptera punctata*. Arch Insect Biochem Physiol 32:341–352

Honda Y, Horigane M, Taylor D (2009) Isolation of the ecdysone receptor and retinoid X receptor from the araneomorph funnelweb spider *Agelena silvatica* (Araneae: Agelenidae). Annual Meeting of Entomological Society of America

James AM, Zhu XX, Oliver JH (1997) Vitellogenin and ecdysteroid titers in *Ixodes scapularis* during vitellogenesis. J Parasitol 83:559–563

Jia S, Wan PJ, Zhou LT, Mu LL, Li GQ (2013) Knockdown of a putative Halloween gene *Shade* reveals its role in ecdysteroidogenesis in the small brown planthopper *Laodelphax striatellus*. Genes 531:168–174

Juberthie C (1983) Neurosecretory systems and neurohemal organs of terrestrial Chelicerata (Arachnida). In: Gupta AP (ed) Neurohemal organs of arthropods. CC Thomas, Springfield, pp 149–203

Kamimura M (1995) Effects of a juvenile hormone analogue, fenoxycarb, on larval growth of the silkworm, *Bombyx mario*. Appl Entomol Zool 30:487–489

Kataoka H, Toschi A, Li JP, Carney L, Schooley A, Kramer SJ (1989) Identification of an allatotropin from adult *Manduca sexta*. Science 243:1481–1483

Kethidi DR, Xi Z, Palli SR (2005) Developmental and hormonal regulation of juvenile hormone esterase gene in *Drosophila melanogaster*. J Insect Physiol 51:393–400

Kim Y, Kim D, Lee J (2000) Disturbance of adult eclosion by fenoxycarb, a juvenile hormone mimic, in the beet armyworm, *Spodoptera exigua*. J Asia Pac Entomol 3:103–111

King-Jones K, Thummel CS (2005) Nuclear receptors—a perspective from *Drosophila*. Nat Rev Genet 6:311–323

Koelle MR, Talbot WS, Segraves WA, Bender MT, Cherbas P, Hogness DS (1991) The *Drosophila EcR* gene encodes an ecdysone receptor, a new member of the steroid receptor superfamily. Cell 67:59–77

Konopova B, Jindra M (2007) Juvenile hormone resistance gene Methoprene tolerant controls entry into metamorphosis in the beetle *Tribolium castaneum*. Proc Natl Acad Sci 104:10488–10493

Konopova B, Smykal V, Jindra M (2011) Common and distinct roles of juvenile hormone signaling genes in metamorphosis of holometabolous and hemimetabolous insects. PLoS ONE 6(12):e28728

Konwarh R, Gupta P, Mandal BB (2016) Silk-microfluidics for advanced biotechnological applications: a progressive review. Biotechnol Adv 34(5):845–858

Kotaki T, Shinada T, Kaihara K, Ohfune Y, Numata H (2011) Biological activities of juvenile hormone III skipped bisepoxide in last instar nymphs and adults of a stink bug, *Plautia stali*. J Insect Physiol 57:147–152

Kozlova T, Thummel CS (2003) Essential roles for ecdysone signalling during *Drosophila* mid-embryonic development. Science 301:1911–1914

Kramer SJ, Toschi A, Miller CA, Kataoka H, Quistad GB, Li JP, Carney L, Schooley DA (1991) Identification of an allatostatin from the tobacco hornworm *Manduca sexta*. Proc Natl Acad Sci 88:9458–9462

Krishnakumaran A, Schneiderman HA (1970) Control of molting in mandibulate and chelicerate arthropods by ecdysones. Biol Bull 139:520–538

Kühne H (1959) Die neurosekretorischen Zellen und der retro cerebrale neuro- endocrine Komplex von Spinnen (Araneae, Labidognatha) unter Berücksichtigung einiger histologisch erkennbaren Yeranderungen wahrend des postembryonalen Lebensablaufes. Zool Jahrb 77:527–600

Kulcsar P, Prestwich GG, Sonenshine DE (1989) Detection binding proteins for juvenile hormone-like substances in ticks by photoaffinity labelling. In: Borovsky D, Spielman A (eds) Host regulated developmental mechanisms in vector arthropods. IFAS, University of Florida Press, Vero Beach, pp 18–23

Lafont R (1997) Ecdysteroids and related molecules in animals and plants. Arch Insect Biochem Physiol 35:3–20

Lafont R, Dauphin-Villemant C, Warren JT, Rees H (2005) Ecdysteroid chemistry and biochemistry. In: Gilbert LI, Iatrou K, Gill S (eds) Comprehensive molecular insect science. Elsevier, Oxford, pp 125–195

Larsen MJ, Burton KJ, Zantello MR, Smith VG, Lowery DL, Kubiak TM (2001) Type A allatostatins from *Drosophila melanogaster* and *Diplotera puncata* activate two *Drosophila* allatostatin receptors, DAR-1 and DAR-2, expressed in CHO cells. Biochem Biophys Res Commun 286:895–901

Laufer H, Landau M, Borst D, Homola E (1986) The synthesis and regulation of methyl farnesoate, a new juvenile hormone for crustacean reproduction. Invertebr Reprod Dev 4:135–143

Leahy MG, Booth KS (1980) Precocene induction of tick sterility and ecdysis failure. J Med Entomol 17:18–21

Legendre R (1953) Le systeme sympathique stomatogastrique (organe de Schneider) des araignees du genre *Tegenaria*. C R Acad Sci 237:1283–1285

Legendre R (1958) Contributions a l'étude du systeme nerveux des Araneides. Annee Biol 34:193–223

Legendre R (1959) Contribution it I'etude du systeme nerveux des Araneides. Ann Sci Nat Zool 1:339–473

Li YP, Hernandez–Martinez S, Noriega FG (2004) Inhibition of juvenile hormone biosynthesis in mosquitoes: effect of allatostatic head factors, PISCF– and YXFGL–amide–allatostatins. Regul Pept 118:175–182

Li S, Ouyang YC, Ostrowski E, Borst DW (2005) Allatotropin regulation of juvenile hormone synthesis by the corpora allata from the lubber grasshopper, Romalea microptera. Peptides 26:63–72

Liu Z, Li X, Prasifka JR, Jurenka R, Bonning BC (2008) Overexpression of *Drosophila* juvenile hormone esterase binding protein results in anti-JH effects and reduced pheromone abundance. Gen Comp Endocrinol 156:164–172

Loesel R, Seyfarth EA, Bräunig P, Agricola HJ (2011) Neuroarchitecture of the arcuate body in the brain of the spider *Cupiennius salei* (Araneae, Chelicerata) revealed by allatostatin-, proctolin-, and CCAP-immunocytochemistry and its evolutionary implications. Arthropod Struct Dev 40:210–220

Lomas LO, Turner PC, Rees HH (1997) A novel neuropeptide-endocrine interaction controlling ecdysteroid production in ixodid ticks. Proc R Soc Lond B 264:589–596

Lorenz MW, Kellner R, Hoffmann KH (1995) A family of neuropeptides that inhibit juvenile hormone biosynthesis in the cricket, *Gryllus bimaculatus*. J Biol Chem 270:21103–21108

Lorenz MW, Kellner R, Hoffmann KH, Gade G (2000) Identification of multiple peptide homologous to cockroach and cricket allatostatins in the stick insect, *Carausius morosus*. Insect Biochem Mol Biol 30:711–718

Lorenz JI, Lorenz MW, Hoffmann KH (2004) Regulators of ovarian ecdysteroid release display opposite effects in the cricket *Gryllus bimaculatus* and the cockroach *Blaptica dubia*. Mitt Dtsch Ges Allg Angew Entomol 14:447–450

Lungchukiet P, Donly BC, Zhang J, Tobe SS, Bendena WG (2008a) Molecular cloning and characterization of an allatostatin-like

receptor in the cockroach *Diploptera punctata*. Peptides 29:276–285
Lungchukiet P, Zhang J, Tobe SS, Bendena WG (2008b) Quantification of allatostatin receptor mRNA levels in the cockroach, *Diploptera punctata*, using real-time PCR. J Insect Physiol 54:981–987
Maestro JL, Bellés X (2006) Silencing allatostatin expression using double-stranded RNA targeted to preproallatostatin mRNA in the German cockroach. Arch Insect Biochem Physiol 62:73–79
Marchal E, Zhang J, Badisco L, Verlinden H, Hult EF, Van Wielendaele P, Yagi KJ, Tobe SS, Vanden-Broeck J (2011) Final steps in juvenile hormone biosynthesis in the desert locust, *Schistocerca gregaria*. Insect Biochem Mol Biol 41:219–227
Marciniak P, Rosiński G (2007) Aktualny stan badań nad neuropeptydami miotropowymi owadów: tachykininy, sulfakininy i FMRFapokrewne peptydy. Postępy Biologii Komórki 34:241–249
Marciniak P, Szymczak M, Rosiński G (2011) Hormony peptydowe owadów—przegląd najważniejszych rodzin. Postępy Biologii Komórki 38:43–63
Martin D, Piulachs MD, Belles X (1996) Inhibition of vitellogenin production by allatostatin in the German cockroach. Mol Cell Endocrinol 121:191–196
Marzouk AS, Mohamed FSA, Khalil GM (1985) Neurohemalendocrine organs in the camel tick, *Hyalomma dromedarii* (Acari: Ixodoidea: Ixodidae). J Med Entomol 22:385–391
Mayoral JG, Nouzova M, Brockhoff A, Goodwin M, Hernandez-Martinez S, Richter-Meyerhof DW, Noriega FG (2010) Allatostatin-C receptors in mosquitoes. Peptides 31:442–450
McGregor AP, Hilbrant M, Pechmann M, Schager EE, Prpic N-M, Damen WGM (2008) *Cupiennius salei* and *Achaearanea tepidariorum*: spider models for investigating evolution and development. BioEssays 30:487–498
Mello TRP, Aixo AC, Pinheiro DG, Nunes FMF, Bitondi MMG, Hartfelder K, Barchuk AR, Simoes ZLP (2014) Developmental regulation of ecdysone receptor (EcR) and EcR–controlled gene expression during pharate-adult development of honeybees (*Apis mellifera*). Front Genet 5:1–19
Meng QW, Liu XP, Lü FG, Fu KY, Guo WC, Li GQ (2015) Involvement of a putative allatostatin in regulation of juvenile hormone titer and the larval development in *Leptinotarsa decemlineata* (Say). Gene 554:105–113
Millot J (1930) Le tissu réticulé du céphalothorax des Aranéides et des dérivés: néphrocytes et cellules endocrines. Arch Anat Microanat 26:43–81
Mitchell MJ, Smith SL (1986) Characterization of ecdysone 20-monooxygenase activity in wandering stage larvae of *Drosophila melanogaster*. Insect Biochem 16:525–537
Miura K, Oda M, Makita S, Chinzei Y (2005) Characterization of the *Drosophila* Methoprene-tolerant gene product. FEBS J 272:1169–1178
Nakagawa Y, Sakai A, Magata F, Ofura T, Miyashita M, Miyagawa H (2007) Molecular cloning of the ecdysone receptor and the retinoid X receptor from the scorpion *Liocheles australasiae*. FEBS J 274:6191–6203
Nakamura A, Stiebler R, Fantappié MR, Fialho E, Masuda H, Oliveira MF (2007) Effects of retinoids and juvenoids on moult and on phenoloxidase activity in the blood-sucking insect *Rhodnius prolixus*. Acta Trop 103:222–230
Nassel DR (2002) Neuropeptides in the nervous system of Drosophila and other insects: multiple roles as neuromodulators and neurohormones. Prog Neurobiol 68(1):1–84
Neese PA, Sonenshine D, Kallapur VL, Apperson CS, Roe RM (2000) Absence of insect juvenile hormones in the American do *Dermacentor variabilis* (Say) (Acari: Ixodidae), and *Ornithodoros parkeri* Cooley (Acari: Argasidae). J Insect Physiol 46:477–490
Neupert S, Russell WK, Predel R, Russell DH, Strey OF, Teel PD, Nachman RJ (2009) The neuropeptidomics of *Ixodes scapularis* synganglion. J Proteome Res 72:1040–1045
Nouzova M, Rivera-Perez C (2015) Allatostatin-C reversibly blocks the transport of citrate out of the mitochondria and inhibits juvenile hormone synthesis in mosquitoes. Insect Biochem Mol Biol 57:20–26
Nouzova M, Brockhoff A, Mayoral JG, Goodwin M, Meyerhof W, Noriega FG (2012) Functional characterization of an allatotropin receptor expressed in the *corpora allata* of mosquitoes. Peptides 34:201–208
Obenchain FD, Mango CKA (1980) Effects of exogenous ecdysteroids and juvenile hormones on female reproductive development in *Ornithodoros p. porcinus*. Am Zool 20:1192
Oeh U, Lorenz MW, Dyker H, Loesel P, Hoffmann KH (2000) Interaction between *Manduca sexta* allatotropin and *Manduca sexta* allatostatin in the fall armyworm *Spodoptera frugiperda*. Insect Biochem Mol Biol 30:719–727
Oeh U, Dyker H, Losel P, Hoffmann KH (2001) In vivo effects of *Manduca sexta* allatotropin and allatostatin on development and reproduction in the fall armyworm, *Spodoptera frugiperda* (Lepidoptera, Noctuidae). Invertebr Reprod Dev 39:239–247
Oliver JHJ, Dotson EM (1993) Hormonal control of molting and reproduction in ticks. Am Zool 33:384–396
Ono H, Rewitz KF, Shinoda T, Itoyama K, Petryk A, Rybczynski R, Jarcho M, Warren JT, Marqués G, Shimell MJ, Gilbert LI, O'Connor MB (2006) *Spook* and *Spookier* code for stage-specific components of the ecdysone biosynthetic pathway in Diptera. Dev Biol 298:555–570
Palmer MJ, Harmon MA, Laudet V (1999) Characterization of EcR and RXR homologues in the Ixodid tick, *Amblyomma americanum* (L.). Am Zool 39:747–757
Pascual N, Cerda X, Benito B, Tom J, Pwlachs MD, Bell X (1992) Ovarian ecdysteroid levels and basal oocyte development during maturation in the cockroach *Blattella germanica* (L.). J Insect Physiol 38:339–348
Petryk A, Warren JT, Marqués G, Jarcho MP, Gilbert LI, Kahler J, Parvy JP, Li Y, Dauphin-Villemant C, O'Connor MB (2003) Shade is the Drosophila P450 enzyme that mediates the hydroxylation of ecdysone to the steroid insect molting hormone 20-hydroxyecdysone. Proc Natl Acad Sci 100:13773–13778
Pinot LZ, Bitondi MMG, Simoes ZLP (2000) Inhibition of vitellogenin synthesis in *Apis mellifera* workers by a juvenile hormone analogue, pyriproxyfen. J Insect Physiol 46:153–160
Pound JM, Oliver JH Jr (1979) Juvenile hormone: evidence of its role in the reproduction of ticks. Science 206:355–357
Posnien N, Zeng V, Schwager EE, Pechmann M, Hilbrant M, Keefe JD, Damen WG, Prpic NM, McGregor AP, Extavour CG (2014) A comprehensive reference transcriptome resource for the common house spider *Parasteatoda tepidariorum*. PLoS ONE 9(8):e104885
Postlethwait JH, Handler AM (1979) The roles of juvenile hormone and 20-hydroxyecdysone during vitellogenesis in isolated abdomens of *Drosophila melanohaster*. J Insect Physiol 25:455–460
Pourié G, Trabalon M (2003) The role of 20-hydroxyecdysone on the control of spider vitellogenesis. Gen Comp Endocrinol 131:250–257
Pratt GE, Farnsworth DE, Siegel NR, Fok KF, Feyereisen R (1991) Two types of allatostatic peptides from brains of the cockroach *Diploptera punctata*. In: Menn JJ, Kelly TJ, Masler EP (eds) Insect neuropeptides: chemistry, biology and action. Journal of the American Chemical Society, Washington, pp 177–192
Project iK5, https://www.hgsc.bcm.edu/arthropods/i5k-pilot-project-summary. Accessed 25 June 2016
Qu Z, Kenny JN, Lam HM, Chan TF, Chu KH, Bendena WG, Tobe SS, Hiu JHL (2015) How did arthropod sesquiterpenoids and

ecdysteroids arise? Comparison of hormonal pathway genes in noninsect arthropod genomes. Genome Biol Evol 7:1951–1959
Rachinsky A, Srinivasan A, Ramaswamy SB (2003) Regulation of juvenile hormone biosynthesis in *Heliothis virescens* by *Manduca sexta* allatotropin. Arch Insect Biochem Physiol 54:121–133
Rees HH (2004) Hormonal control of tick development and reproduction. Parasithology 29:127–143
Rewitz KF, Rybczynski R, Warren JT, Gilbert LI (2006) The Halloween genes code for cytochrome P450 enzymes mediating synthesis of the insect molting hormone. Biochem Soc Trans 34:1256–1260
Riddiford LM (1993) Hormones and *Drosophila* development. In: Bate M, Arias AM (eds) The development of *Drosophila melanogaster*. Cold Spring Harbor Press, New York, pp 899–939
Riddiford LM (1994) Cellular and molecular actions of juvenile hormone. I. General considerations and premetamorphic actions. Adv Insect Physiol 24:213–227
Riddiford LM (2012) How does juvenile hormone control insect metamorphosis and reproduction? Gen Comp Endocrinol 179:477–484
Riddiford LM, Cherbas P, Truman JW (2000) Ecdysone receptors and their biological actions. In: Harris RS (ed) Anonymous vitamins and hormones. Academic Press, New York, pp 1–73
Roe RM, Donohue KV, Khalil SMS, Bissinger BW, Zhu J, Sonenshine DE (2014) Hormonal regulation of metamorphosis and reproduction in ticks. In: Sonenshine DE, Roe RM (eds) Biology of Ticks. Oxford University Press, New York, pp 434–437
Sakurai S, Williams CM (1989) Short–loop negative and positive feedback on ecdysone secretion by prothoracic gland in the tobacco hornworm *Manduca sexta*. Gen Comp Endocrinol 75:204–216
Sankhon N, Lockey T, Rosell RC, Rothschild M, Coons L (1999) Effect of methoprene and 20-hydroxyecdysone on vitellogenin production in cultured fat bodies and backless explants from unfed female *Dermacentor variabilis*. J Insect Physiol 45:755–761
Sarkar NRS, Tobe SS, Orchard I (2003) The distribution and effects of Dippu-allatostatin-like peptides in the blood-feeding bug, *Rhodnius prolixus*. Peptides 24:1553–1563
Schwedes C, Tulsiani S, Carney GE (2011) Ecdysone receptor expression and activity in adult *Drosophila melanogaster*. J Insect Physiol 57:899–907
Shinoda T, Itoyama K (2003) Juvenile hormone acid methyltransferase: a key regulatory enzyme for insect metamorphosis. Proc Natl Acad Sci 100:11986–11991
Simo L, Park Y (2014) Neuropeptidergic control of the hindgut in the black-legged tick *Ixodes scapularis*. Int J Parasitol 44:819–826
Solomon KR, Mango CKA, Obenchain FD (1982) Endocrine mechanisms in ticks: effects of insect hormones and their mimics on development and reproduction. In: Obenchain FD, Galun R (eds) Physiology of ticks. Pergamon, Oxford, pp 399–438
Sorge D, Nauen R, Range S, Hoffmann KH (2000) Regulation of vitellogenesis in the fall armyworm, *Spodoptera frugiperda* (Lepidoptera: Noctuidae). J Insect Physiol 46:969–976
Stay B, Tobe SS (2007) The role of allatostatins in juvenile hormone synthesis in insects and crustaceans. Annu Rev Entomol 52:277–299
Stay B, Zhang JR, Tobe SS (2002) Methyl farnesoate and juvenile hormone production in embryos of *Diploptera punctata* in relation to innervation of *corpora allata* and their sensitivity to allatostatin. Peptides 23:1981–1990
Stubbendieck RM, Zera AJ, Hebets EA (2013) No evidence for a relationship between hemolymph ecdysteroid levels and female reproductive behavior in *Schizocosa* wolf spiders. J Arachnol 41:349–355
Talbot WS, Swyryd EA, Hogness DS (1993) Drosophila tissues with different metamorphic responses to ecdysone express different ecdysone receptor isoforms. Cell Press 73:1323–1337
Teal PEA (2002) Effects of allatotropin and allatostatin on in vitro production of juvenile hormones by the *corpora allata* of virgin females of the moths of *Heliothis virescens* and *Manduca sexta*. Peptides 23:663–669
Thummel CS (1996) Flies on steroids—*Drosophila* metamorphosis and the mechanisms of steroid hormone action. Trends Genet 12:306–310
Tobe SS, Stay B (1985) Structure and regulation of the *corpus allatum*. Adv Insect Physiol 18:305–432
Tobe SS, Young DA, Khoo HW, Baker FC (1989) Farnesoic acid as a major product of release from crustacean mandibular organ in vitro. J Exp Zool 249:165–171
Tobe SS, Zhang JR, Bowser PRF, Donly BC, Bendena WG (2000) Biological activities of the allatostatin family of peptides in the cockroach, *Diploptera punctata*, and potential interactions with receptors. J Insect Physiol 46:231–242
Trabalon M, Blais C (2012) Juvenile development, ecdysteroids and hemolymph level of metabolites in the spider *Brachypelma albopilosum* (Theraphosidae). J Exp Zool A Ecol Genet Physiol 317:236–247
Trabalon M, Campan M, Baehr JC, Mauchamp B (1987) In vitro biosynthesis of juvenile hormone III by the *corpora allata* of *Calliphora vomitoria* and its role in ovarian maturation and sexual receptivity. Experientia 43:1113–1115
Trabalon M, Bautz AM, Morini M, Porcheron P (1992) Ovarian development and correlated changes in hemolymphatic ecdysteroid levels in two spiders, *Coelotes terrestris* and *Tegenaria domestica* (Araneae, Agelenidae). Gen Comp Endocrinol 88:128–136
Trabalon M, Pourié G, Hartmann N (1998) Relationships among cannibalism, contact signals, ovarian development and ecdysteroid levels in *Tegenaria atrica* (Araneae, Agelenidae). Insect Biochem Mol Biol 28:751–758
Tremmel C, Schaefer M, Azoitet A, Ruff H, Spindler-Barth M (2011) Interaction of the N-terminus of ecdysone receptor isoforms with the ligand-binding domain. Mol Cell Endocrinol 332:293–300
Truman JW, Talbot WS, Fahrbach SE, Hogness DS (1994) Ecdysone receptor expression in the CNS correlates with stage-specific responses to ecdysteroids during *Drosophila* and *Manduca* development. Development 120:219–234
Turnbull AL (1973) Ecology of the true spiders (Araneomorphae). Annu Rev Entomol 18:305–348
Venkatesh K, Roe RM, Apperson CS, Sonenshine DE, Schriefer ME, Boland LM (1990) Metabolism of juvenile hormone during adult development of *Dermacentor variabilis* (Acari: Ixodidae). J Med Entomol 27:36–42
Venugopal KJ, Kumar D (2000) Role of juvenile hormone in the synthesis and sequestration of vitellogenins in the red cotton stainer, *Dysdercus koenigii* (Heteroptera: Pyrrhocoridae). Comp Biochem Physiol C 127:153–163
Wan PJ, Jia S, Li N, Fan JM, Li GQ (2014a) RNA interference depletion of the halloween gene disembodied implies its potential application for management of planthopper *Sogatella furcifera* and *Laodelphax striatellus*. PLoS ONE 9(1):e86675
Wan PJ, Jia S, Li N, Fan JM, Li GQ (2014b) The putative Halloween gene phantom involved in ecdysteroidogenesis in the white-backed planthopper *Sogatella furcifera*. Gene 548:112–118
Wang J (2004) Isolation and characterization of the B-type allatostatin gene of *Gryllus bimaculatus* de Geer (Ensifera, Gryllidae). Ph.D

Wang X, Wang G (2016) Insights into antimicrobial peptides from spiders and scorpions. Protein Peptide Lett 23(8):707–721

Warren JT, Petryk A, Marqués G, Jarcho M, Parvy JP, Dauphin-Villemant C, O'Connor MB, Gilbert LI (2002) Molecular and biochemical characterization of two P450 enzymes in the ecdysteroidogenic pathway of *Drosophila melanogaster*. Proc Natl Acad Sci 99:11043–11048

Warren JT, Petryk A, Marqués G, Parvy JP, Shinoda T, Itoyama K, Kobayaski J, Jarcho M, Li Y, O'Connor MB, Dauphin-Villemant C, Gilbert LI (2004) Phantom encodes the 25-hydroxylase of *Drosophila melanogaster* and *Bombyx mori*: P450 enzyme critical in ecdysone biosynthesis. Insect Biochem Mol Biol 34:991–1010

Weaver RJ, Audsley N (2009) Neuropeptide regulators of juvenile hormone synthesis. Structures, functions, distribution and unanswered questions. Ann N Y Acad Sci 1163:316–329

Williamson M, Lenz C, Winther AME, Nassel DR, Grimmelikhuijzen CJP (2001a) Molecular cloning, genomic organization, and expression of a C-type (*Manduca sexta*-type) allatostatin preprohormone from *Drosophila melanogaster*. Biochem Biophys Res Commun 282:124–130

Williamson M, Lenz C, Winther AME, Nassel DR, Grimmelikhuijzen CJP (2001b) Molecular cloning, genomic organization, and expression of a B-type (cricket-type) allatostatin preprohormone from *Drosophila melanogaster*. Biochem Biophys Res Commun 281:544–550

Wilson TG, Ashok M (1988) Insecticide resistance resulting from an absence of target-site gene product. Proc Natl Acad Sci 95:14040–14044

Wilson TG, Fabian J (1986) A *Drosophila melanogaster* mutant resistant to a chemical analog of juvenile hormone. Dev Biol 118:190–201

Wilson TG, Landers MH, Happ GM (1983) Precocene I and II inhibition of vitellogenic oocyte development in *Drosophila melanogaster*. J Insect Physiol 29:249–254

Woodhead AP, Stay B, Seidel SL, Khan MA, Tobe SS (1989) Primary structure of four allatostatins: neuropeptide inhibitors of juvenile hormone synthesis. Proc Natl Acad Sci 86:5997–6001

Woodhead AP, Thompson ME, Chan KK, Stay B (2003) Allatostatin in ovaries, oviducts, and young embryos in the cockroach *Diploptera punctata*. J Insect Physiol 49:1103–1114

Yao TP, Segraves WA, Oro AE, McKeown M, Evans RM (1992) *Drosophila* ultraspiracle modulates ecdysone receptor function via heterodimer formation. Cell 71:54–63

Yao TP, Forman BM, Jiang Z, Cherbas L, Chen JD, McKeown M, Cherbas P, Evans RM (1993) Functional ecdysone receptor is the product of EcR and Ultraspiracle genes. Nature 366:476–479

Zhang Z, Xu J, Sheng Z, Sui Y, Palli SR (2011) Steroid receptor co-activator isrequired for juvenile hormone signal transduction through a bHLH-PAS transcription factor, Methoprene tolerant. J Biol Chem 286:8437–8447

Zhu XX, Oliver JH (2001) Cockroach allatostatin–like immunoreactivity in the synganglion of the American dog tick *Dermacentor variabilis* (Acari: Ixodidae). Exp Appl Acarol 25:1005–1013

Zhu XX, Oliver JH, Dotson EM (1991) Epidermis as the source of ecdysone in an argasid tick. Proc Natl Acad Sci USA 88:3744–3747

Zhu J, Busche JM, Zhang X (2010) Identification of juvenile hormone target genes in the adult female mosquitoes. Insect Biochem Mol Biol 40:23–29

Zhu J, Khalil SM, Mitchell RD, Bissinger BW, Egekwu N, Sonenshine DE, Roe RM (2016) Mevalonate-farnesal biosynthesis in ticks: Comparative synganglion transcriptomics. PLoS ONE 11:e0141084