Available online at www.sciencedirect.com

Insect Biochemistry and Molecular Biology 35 (2005) 1209–1223

Insect Biochemistry and Molecular Biology

www.elsevier.com/locate/ibmb

Minireview

Advances and prospects on biosynthesis, structures and functions of venom proteins from parasitic wasps

S.J.M. Moreau*, S. Guillot

UMR CNRS 6035, Institut de Recherche sur la Biologie de l'Insecte, Université François Rabelais, Avenue Monge, Parc Grandmont, 37200 Tours, France

Received 3 January 2005; received in revised form 13 July 2005; accepted 15 July 2005

Abstract

Molecular and biochemical properties of parasitoid Hymenoptera's venom proteins are currently receiving an increasing interest. In this review, we will highlight the progress that has been made over the past 10 years in fundamental research on this field. Main knowledge acquired on the structural features of parasitoid venom peptides, proteins and enzymes will be summarized and discussed and several examples showing the diversity of their biological functions will be given with respect to future prospects and applications.

Keywords: Insects; Parasitoids; Hymenoptera; Venoms; Proteins; Peptides; Enzymes

1. Introduction

Hymenopteran parasitoids use a diversified range of virulence factors to insure the successful development of their offspring in the hemocoel or at the external surface of host insects. Polydnaviruses (PDVs), virus-like particles (VLPs), ovarian fluids, teratocytes and venoms figure among the parasitic factors of which effects on host physiology were best characterized (Coudron, 1991; Strand and Pech, 1995; Vass and Nappi, 2000; Schmidt et al., 2001; Moreau, 2003). Parasitoid venoms are notably known to induce paralysis, to disrupt the host's development or to interfere with its immune response, alone or in combination with other factors (Coudron, 1991; Beard, 1963, 1978; Schmidt, 1982; Visser et al., 1983; Tanaka, 1987; Quistad et al., 1994; Strand et al., 1994; Weaver et al., 2001; Moreau et al., 2002). The functional diversity of parasitoid venoms reflects the heterogeneity of this group of insects in terms of phylogeny, parasitic habits and host ranges. Despite more than 40 years of a continued interest, few studies investigated the molecular basis of these physiological effects and more generally, our knowledge of the parasitoid venom content has long remained very fragmentary. Nevertheless, the fruitful development of new tools for genomic and proteomic approaches has recently revived the interest of numerous investigators towards the study of parasitoid venoms and has offered the opportunity to analyse their proteinic components in detail.

These last years, an increasing number of original peptides, proteins, and enzymes have been reported from the venoms of ichneumonid, braconid or eucoilid wasps (Digilio et al., 2000; Parkinson et al., 2001, 2002a–c, 2003, 2004; Asgari et al., 2003a, b; Dani et al., 2003; Moreau et al., 2004; Zhang et al., 2004; Labrosse et al., 2005b). These findings may constitute a new step in the investigation of several fundamental topics such as parasitoid–host physiological relationships, phylogeny of parasitoid Hymenoptera or biosynthesis and functional evolution of insect proteins. Venom proteins from parasitoids may also represent an under-estimated source of new molecules with promising

---

*Corresponding author. Tel.: +33 247 367 397; fax. +33 247 366 966.

E-mail address: sebastien.moreau@univ-tours.fr (S.J.M. Moreau).

0965-1748/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.ibmb.2005.07.003

applied potentials in the agronomic and biomedical sectors.

By summarizing the literature related to the biosynthesis, the biochemical properties and the main biological functions of parasitoid venom proteins, the present paper aims at giving an insight on the advances made to date in this area and at highlighting the scientific benefits expected from the study of these proteins.

2. Biochemical properties and functions of venom proteins from parasitoids: hypothesis and certainties

Venoms of parasitoid Hymenoptera contain complex mixtures of proteins and polypeptides. Given the specific physiological context of host–parasitoid relationships, this complexity offers several advantages to the parasitic organism (Parkinson et al., 2002a; Libersat, 2003). A multicomponent venom may notably enable: (1) an avoidance of variations in the susceptibility of different hosts to a single component, (2) a gain of effectiveness by combined effects on a same physiological target or (3) at the opposite a targeting of several host functions with a unique mixture. Complex venom could also allow for adaptation for new or widened host ranges and could increase the difficulty for a resistance to emerge considering that a multimodal tolerance might be set up by the host to insure its survival. This review being dedicated to venom proteins, we will restrict our analysis to enzymes, proteins and peptides reported from venomous secretions. However, non-proteinic components revealed to be the main bioactive factors in some cases, as for the dopamine agonist presented in the venom of the parasitoid wasp *Ampulex compressa* and causing behavioural modulations in the cockroach *Periplaneta americana* (Weisel-Eichler and Libersat, 2002; Haspel et al., 2003; Libersat, 2003).

2.1. Molecular masses

Synthesis of venom proteins in the secreting glands begins during the pupal development of parasitoid females and intensifies within the first 24 h after their emergence (Jones and Wozniak, 1991; Gnatzy and Volknandt, 2000).[1] It has been suggested that unlike venoms from bees and social wasps, parasitoid venoms lacked proteins of low molecular masses (Leluk et al., 1989). Venoms of the Braconids *Chelonus* sp. near *curvimaculatus*, *Bracon hebetor* and *Apanteles glomeratus* did not contain proteins with molecular masses lesser than 30, 20 and 18 kDa, respectively (Quistad et al., 1994; Leluk et al., 1989) while the venom of the Eulophid *Euplectrus* sp. near *plathypenae* contained nine proteins between 45 and 90 kDa (Nakamatsu and Tanaka, 2003). The point is of importance given that, in venoms of other organisms, small peptides often have cytolytic or neurotoxic properties (Piek, 1986; Rappuoli and Montecucco, 1997). However, small polypeptides ($<$10–15 kDa) were since observed in the venom of the parasitoids *Eupelmus orientalis* (Doury et al., 1997), *Pimpla hypochondriaca* (Parkinson et al., 2002b; Dani et al., 2003), *Asobara tabida* (Moreau et al., 2004) and *Cotesia rubecula* (Asgari et al., 2003a; Zhang et al., 2004). These latter examples suggest that at least some parasitoid venoms could exhibit small peptides. More certainly, the presence of proteins of high molecular masses ($>$100 kDa), reported from almost all the parasitoid venoms analysed to date, singularizes these secretions with respect to venoms of aculeate Hymenoptera which lack such large components (Piek, 1986; Leluk et al., 1989; Jones and Wozniak, 1991; Quistad et al., 1994; Doury et al., 1997; Rappuoli and Montecucco, 1997; Gnatzy and Volknandt, 2000; Parkinson et al., 2002a, b, 2003; Asgari et al., 2003b; Dani et al., 2003; Nakamatsu and Tanaka, 2003).

2.2. Acidic nature and post-translational modifications

Few data are available on the acidic or basic nature of the venom proteins of parasitoids. In the Ichneumonoidea superfamily, it is admitted that venom proteins are mostly acidic, which contrasts with the neutral or basic nature of venom proteins from social Hymenoptera (Leluk et al., 1989). For example, venom proteins from *A. tabida* have acidic isoelectric points ranking from 5.1 to 6.5 (Fig. 1), a 52 kDa protein isolated from the venom of *C.* sp. near *curvimaculatus* has been shown to have a *p*I between 4.8 and 5.0 (Krishnan et al., 1994) while the Vn4.6 protein from *C. rubecula*'s venom had an estimated isoelectric point of 3.99 (Asgari et al., 2003a). However, the venom of the latter species also contained another peptide, Vn1.5, whose estimated isoelectric point was 10.01 (Zhang et al., 2004). Although rare, basic proteins may thus also be found in parasitoid venoms.

Data on post-translational modifications of these proteins are still fragmentary: some venom proteins were found heavily glycosylated (Leluk et al., 1989; Gnatzy and Volknandt, 2000; Asgari et al., 2003b) or found to contain potential glycosylation sites (Parkinson et al., 2002a) but the exact nature of their polysaccharidic residues are still unknown. In another hand, the lack of glycosylation of two major proteins isolated from the venom of *Aphidius ervi* (Digilio et al., 2000) suggests that this modification is not an obligatory feature. Although the occurrence of phosphorylation sites has not been investigated in detail, seven potential sites were

---

[1] *Liris niger* is considered here as a parasitoid wasp in agreement with Gnatzy and Volknandt (2000).