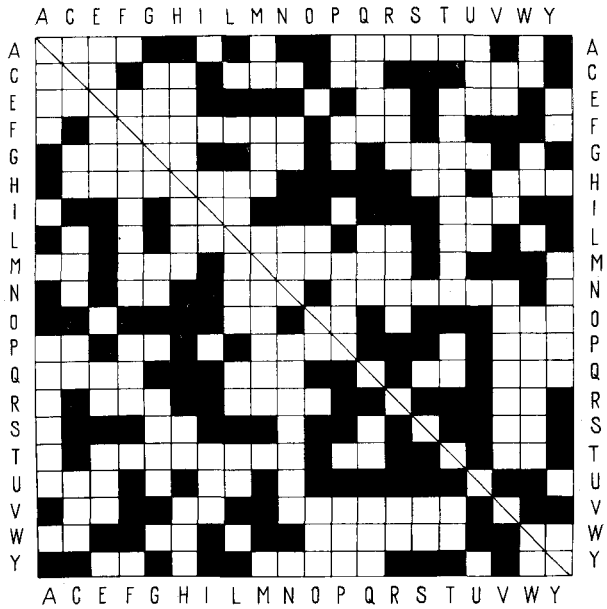

Full squares indicate amino acids which can be interchanged in the structure of proteins, provided only one single base is changed for another base in the triplet codon.

A list of symbols[1] for amino acids

A – asp	G – glu	M – met	Q – gln	U – leu
C – cys	H – his	N – asn	R – arg	V – val
E – thr	I – lys	O – tyr	S – ser	W – ile
F – phe	L – ala	P – pro	T – trp	Y – gly

amino acid on a single line, whereas in a three-dimensional scheme[9] an amino acid must be looked for at different places (e.g.[9] Asn, Leu, Lys, Ser). In consequence of the existence of ApGpU and ApGpC codons[8] for lysine the Table includes also the interchange Arg/Lys which was not permitted by previously accepted codons. If the codon ApGpA introduced by NISHIMURA et al.[10] for arginine were included in the Table this would be a further confirmation of the Arg/Lys interchange, but the Table would then contain new interchange possibilities such as Met/Arg, Thr/Arg, and at the same time the interchanges Arg/Ser, Gly/Ser, Lys/Ser and Met/Ser would disappear.

Zusammenfassung. Auf Grund vorausgegangener Experimente, besonders über degenerierte Triplettcodons, wird ein Verfahren entwickelt, aus dem sich die Austauschmöglichkeiten von Aminosäuren in Eiweißstoffe ergeben, dann nämlich, wenn im Codon nur je eine Base des Tripletts ersetzt wird.

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The Effect of the Venom of the Digger Wasp Philanthus on the Fast and Slow Excitatory and the Inhibitory System in the Locust Muscle[1]

Although many authors[2–11] have described the physiology of the fast and slow excitatory and the inhibitory neuromuscular system in insects, still very little is known about the pharmacology of these systems. A neuromuscular block of the fast system of the locust muscle can be caused by tryptamine and 5-hydroxytryptamine[12], gallamine[13], and the venom of *Philanthus triangulum* F.[13–15]. USHERWOOD and GRUNDFEST[9] showed that γ-aminobutyric acid activates the inhibitory postsynaptic membrane in *Romalea* and *Schistocerca*. Although picrotoxin abolishes the inhibitory postsynaptic potentials and also the effect of γ-aminobutyric acid, it does not affect the excitatory postsynaptic potentials of the fast system[9].

In the present paper some effects of *Philanthus* venom on the fast and slow excitatory and on the inhibitory system of the locust jumping muscle will be described.

The wasps (*Philanthus triangulum* F.) originating from the South of France are reared in our laboratory by Dr. R. T. SIMON THOMAS[16]. The method of extracting the venom as well as the preparation of the locust (*Locusta migratoria migratorioides* R. & F.) has been described in a preceding paper[13].

Intracellular action potentials were recorded from the upper part of the extensor muscle of the tibia of the metathoracic leg, using glass capillary microelectrodes filled with $3\,M$ KCl. The electrodes with a resistance between 20 and $40\,M\Omega$ were connected to the input of a unity gain negative capacity preamplifier.

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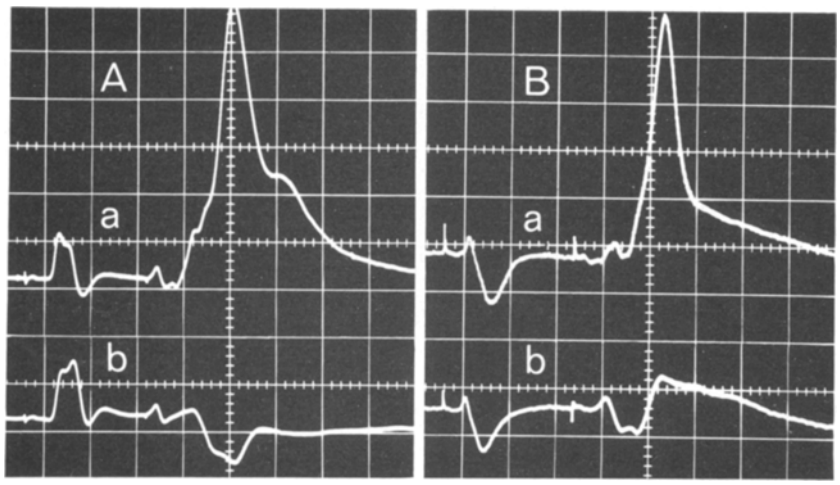

Fig. 1. Effect of 50 µl *Philanthus* venom (equivalent to one sting organ) on the internal action potentials of the extensor muscle of the tibia of the locust, following stimulation of nerve 3 B (first potentials in A and B) and of nerve 5 (second potentials in A and B). Interval between stimulation of 3 B and 5 is about 15 msec. (A) Example of majority of records. (B) Incidental record with an abnormal response following stimulation of nerve 3 B. (a) Before injection, (b) 1 min after injection of *Philanthus* venom. Calibration: 5 mV and 5 msec per major division.

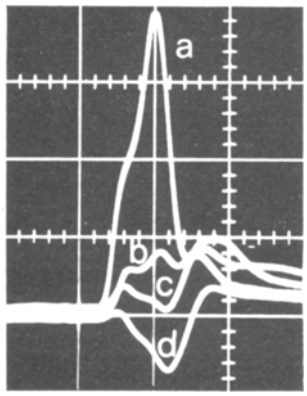

Fig. 2. Internal muscle action potentials of the locust muscle. Stimulation of nerve 5 only. (a) Before injection; (b)–(d) 10, 20 and 30 sec after injection of 50 µl *Philanthus* venom (equivalent to one sting organ). Calibration: 10 mV and 5 msec per major division.

In all experiments nerve 3 B (containing a 'slow' excitatory as well as an inhibitory fibre) was stimulated first. This was followed by a stimulation of nerve 5 (containing a 'fast' excitatory fibre) after an interval of about 15 msec. This sequence of stimulation results in two action potentials (Figure 1A, curve a). The first potential resulting from stimulation of nerve 3 B often shows a notch. It is often followed by a short hyperpolarization. Since nerve 3 B contains a slow and an inhibitory axon[5,6,8,9], this potential may be a superposition of an excitatory response (depolarization) and an inhibitory response (hyperpolarization). The second potential, following stimulation of nerve 5, shows a large depolarization in which a 'junctional' component can be observed (curve a in Figures 1A, 1B and 2).

Separate single stimulation of nerve 5 is followed by a brief contraction of the muscle. After separate stimulation of nerve 3 B with 10–200 c/sec a slow contraction occurs.

The potentials, shown in Figure 1A, have been observed in more than 20 preparations. However, one preparation showed a different reaction to stimulation of nerve 3 B, as shown in Figure 1B. After stimulation of nerve 3 B a short depolarization followed by a marked hyperpolarization could be recorded from several sites in the muscle. Moreover, this particular muscle did not respond mechanically to stimulation of nerve 3 B, but it showed a normal response to stimulation of nerve 5. It seems likely that in this preparation the excitatory fibre in nerve 3 B was damaged and that only the inhibitory fibre remained intact.

The mechanical responses following both fast and slow stimulation are abolished by the venom of *Philanthus*. 1 min after the administration of 50 µl *Philanthus* venom (equivalent to one sting organ) the action potential of the fast system predominantly shows a hyperpolarization instead of a depolarization (Figure 1A, curve b; Figure 1B, curve b; Figure 2, curve d). Figure 2 shows the decrease of the fast muscle potential after 10 sec (curve b) followed by a reversion of the potential after 20 and 30 sec (curves c and d).

Although the dose of *Philanthus* venom used paralyses the muscular contractions following stimulation of the slow system, it does not affect the muscle action potential (Figure 1A, curve b). The action potential shown in Figure 1B, and presumably originating from the inhibitory stimulus, was also not affected (Figure 1B, curve b).

These findings show that *Philanthus* venom affects the fast as well as the slow muscular contractions. It also abolishes the fast electrical responses. Apparently it does not affect the slow electrical responses. There is an indication that hyperpolarizing electrical responses are also not affected by the venom.

Zusammenfassung. Es wird gezeigt, dass das Gift der Wespe *Philanthus triangulum* F. bei der Heuschrecke eine reversible Muskellähmung bewirkt, die auf einer Blockierung der Axon-Muskel-Synapse der «schnellen» Faser beruht. Die Synapse der langsamen und hemmenden Faser wird offenbar nicht beeinflusst.

T. Piek[17]

Pharmacological Laboratory, University of Amsterdam (The Netherlands), February 4, 1966.

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