inhibition of microtubule polymerization or production of special aggregation of microtubules[19,20]. The associations of PA-Ca^{++} activable PDE activity and protein kinase activities with microtubules[5], and of PA with mitotic apparatus[21] are also reported. Together, these data seem to suggest the interactions between microtubule, and PDE, PA-Ca^{++} complex or possibly cyclic nucleotides. Although the characteristics and functions of these interactions are not well understood, recent reports showed the participations of PA and cyclic AMP in the regulation of microtubule polymerization[22-24].

Since the concentration of PA was found to modulate the inhibitory effect of VB, varying effectiveness of VB as an antineoplastic agent[25] may partly depend upon the level of PA, PA-Ca^{++} activable PDE or cyclic nucleotides in tumor cells. Changes in these parameters are known to occur in tumor cells[26-28].

1 Our thanks to Drs A.R. Rhoads, C.B. Klee and R.A. Fergusson for analyzing PA preparations by gel electrophoresis and gel electrofocusing, and to Drs A.A. Suran and D. Soifer for their valuable critiques to this work. This work was partly supported by Biochemical Research Support Grant No. 5SO7RRO5361 to K.W. and Graduate Training Grant No. 5TO2GMO500002 to W.L.W. from NIH.

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Effect of para-methoxyphenylethylamine on chronic stress-induced hypertension in the rat[1]

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Summary. This report presents data showing that para-methoxyphenylethylamine is effective in both preventing and reversing chronic stress-induced hypertension in the rat.

In 1932, Epstein et al.[2] showed that the phenylethylamine derivative para-methoxyphenylethylamine (PMPEA) produced a marked pressor response when acutely injected into the decerebrate cat preparation. These authors also showed PMPEA to be acutely pressor in the vagotomized rabbit preparation. It was not until 1970 that Walker et al.[3] reported that the action of PMPEA on blood pressure was independent of its stimulant action on spinal monosynaptic reflex transmission. During that long interim period, much interest was paid to the derivatives of phenylethylamine with their implication in the basic mechanism(s) of action of several groups of centrally active compounds[4-6], being specifically referred to as a class of compounds known collectively as microamines[7], and finally, the evolvement of a theory of their role in the pathogenesis of affective behavior[8], or more specifically, modulation of synaptic transmission[9].

Recent work in our laboratories has shown PMPEA to have sexual stimulant properties in both the male[10] and female[11] rat and, although hypertensive when acutely administered to the cat[12], corroborating the earlier work of Epstein et al.[2], it was shown to be antihypertensive when fed chronically to rats made hypertensive by successive injections of DOCA-saline[12]. There thus appeared to be a discrepancy in the results produced by PMPEA on blood pressure when administered chronically[12] as opposed to being injected acutely[2,3]. In order to resolve this discrepancy, a protocol was designed to study the potential effectiveness of daily administered PMPEA (in the food) in preventing and/or reversing chronic stress-induced hypertension.

Method. The method for inducing hypertension was that of Perach et al.[13], as modified by Segal et al.[14]. In summary, the method and experimental design was as follows.

30 adult male Sabra rats with an initial b.w of slightly less than 200 g, at the beginning of the experiment, were used in this study. The rats were divided into 3 groups of 10 (with no more than 4 rats being placed together in a cage) immediately upon their arrival in the laboratory, placed in the stress chamber and allowed to acclimatize for 11 days. Standard rat chow and water were allowed ad libitum.

After the acclimatization period, blood pressures were determined at weekly intervals, for 2 weeks by a modification of the tail-cuff method (as also previously reported[14]), and this signified the control period. At the end of the control period, which was 2 weeks following the period of acclimatization, the rats in group 2 were administered PMPEA (0.02%) in their daily food. Groups 1 and 3 remained as controls. Blood pressure determinations were now continued for another 2 weeks - this period being designated the drug pre-treatment period. After 2 weeks of drug pretreatment, the stress schedule was started (alternating 5-min periods of flashing light and buzzing sound for 4 h per day and 3 days per week, selected on a random schedule) and continued for a period of 12 weeks, blood pressure determinations being continued at weekly intervals. At exactly 7 weeks into the stress period, the rats in group 3, which until now were treated the same as the controls, were administered PMPEA (0.02%) in the daily food. At the 11th week of the stress period, i.e., just 1 week before termination of stress, all drug administrations were stopped. The rats were monitored until one week following the termination of stress.

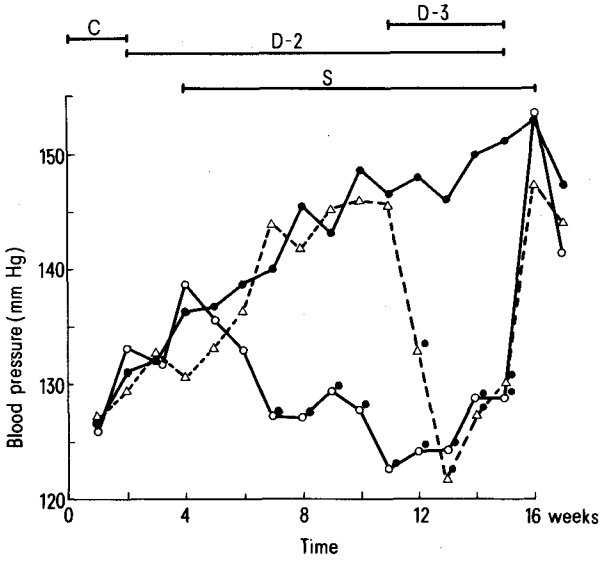

Fig. 1. Blood pressures during each phase of the experimental protocol. ●—● Group 1, controls; ○—○ group 2, PMPEA (0.02%) in the food from week 2-15; △—△ group 3, PMPEA (0.02%) in the food from week 11-15; C, control period; D-2, drug treatment period for group 2; D-3, drug treatment period for group 3; S, stress schedule duration. All values with small black dots at the upper right hand corner are statistically significantly lower than the control group for that time period.

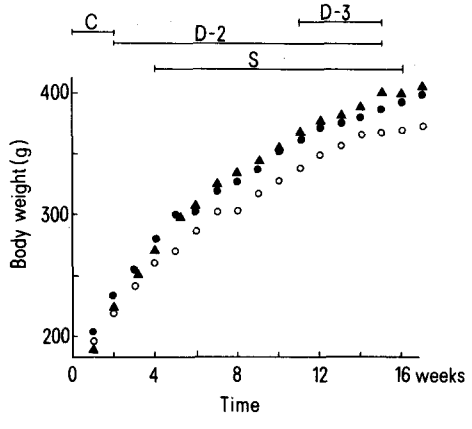

Fig. 2. Body weights during each phase of the experimental protocol. ●—●, Group 1, controls; ○—○, group 2, PMPEA (0.02%) in the food from week 2-15; ▲—▲, group 3, PMPEA (0.02%) in the food from week 11-15; C, control period; D-2, drug treatment period for group 2; D-3, drug treatment period for group 3; S, stress duration.

All drug administrations, based upon daily food intake, were as previously reported[14]. Significance determinations were calculated using Student's t-test. PMPEA was obtained from Sigma.

Results and discussion. The results are outlined in figures 1 and 2. As can be clearly seen, the control blood pressures average 125 mm Hg at the beginning of the design and rise to over 150 mm Hg at the 12th week of stress. On the other hand, after the initial stabilization period (control period and drug pre-treatment period, i.e., 4 weeks into the design), the PMPEA treated group's blood pressure is seen to be significantly lower than the controls, starting 3 weeks into the stress schedule and remaining so until the administration of PMPEA was stopped, with blood pressure values of less than 130 mm Hg during this period (i.e., from the 3rd to the 11th week of stress). All values on the blood pressure curve with a small dot at the right top hand corner are statistically significantly lower than the respective control values for that particular period.

The administration of PMPEA (to group 3, which up to now were treated as controls) in hypertensive stress (146 mm Hg, 7 weeks into the stress schedule) resulted in a decrease in blood pressure to 133 mm Hg within 1 week, a further decrease to 122 mm Hg within 2 weeks of drug administration and a maintainance at less than 130 mm Hg until the 11th week of stress, when PMPEA administration was stopped.

At the 11th week of stress, 1 week before the end of the stress period, all drug administration was stopped, and it can be seen (figure 1) that the blood pressure levels all rose to hypertensive stress levels by the 12th stress week (143 mm Hg and above). Within 1 week of terminating the stress schedule, all 3 groups' blood pressures started to decrease. The body weights of all 3 groups (control and experimental) increased progressively throughout the complete experimental design, with no significant differences appearing between any of the groups.

It is, therefore, clearly seen that PMPEA can both effectively prevent and decrease chronic stress-induced hypertension. These data were shown to be independent of any action that PMPEA may have upon the natural growth pattern of the experimental animal.

Although difficult to speculate upon PMPEA's potential mechanism of action under these stress-induced conditions, it is of interest to note that both saline and DOCA, which induce hypertension when injected into the rat, cause an increase in tyrosine hydroxylase activity[15,16], and that tyrosine hydroxylase activity has also been reported to increase under conditions of chronic stress[17]. If, as reported by Shalita and Dikstein[18], hypertension is due to decreased levels of central tyramine, this might be the case under chronic stress conditions due to increased tyrosine hydroxylase activity. It would be interesting, therefore, to speculate about PMPEA's potential to decrease tyrosine hydroxylase activity, allowing the tyramine levels to remain at their normal levels during chronic stress.

1 Partly supported by a grant from the Israel Center for Psychobiology.

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Effect of reserpine on the larval-pupal moult of the wax moth *Galleria mellonella* L. (Lepidoptera)[1]

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Summary. Significant retardation of *G. mellonella* development was induced by reserpine injected to the last instar larvae in doses having a long-lasting effect on the neurosecretory system.

Reserpine, one of the neuroleptic drugs (a tranquillizer), affects many physiological processes in the insect organism. Among other things, it restricts the reproduction of insects. Several investigators described the influence of reserpine on the development and function of female gonads in different species of insects[3-8]. Some authors[3,6] suggested that reserpine acts through the neurosecretory system. This hypothesis was confirmed at the light microscope level in *Tenebrio molitor* and *Tribolium confusum* by Masner[9], and in *Galleria mellonella* by Cymborowski[10], who noted an increased accumulation of neurosecretory material in the neurosecretory cells of pars intercerebralis, induced by reserpine. The drug doses were very low in both cases.

Recent electron microscope studies[11] in *G. mellonella* brain revealed that, after administration of such a low dose of the drug, accumulation of the neurosecretory granules in the perikarya of neurosecretory cells of pars intercerebralis was short-lived. At 24 h after drug administration, the distribution of granules was quite normal. A very pronounced and long-lasting accumulation of neurosecretory material was evoked by a much higher (100×) dose of reserpine (125 µg/g b.w).

The present study was undertaken to see what would be the effect on development of this high dose of the drug. Besides, we wanted to establish the most sensitive age for the drug recipient-insects.

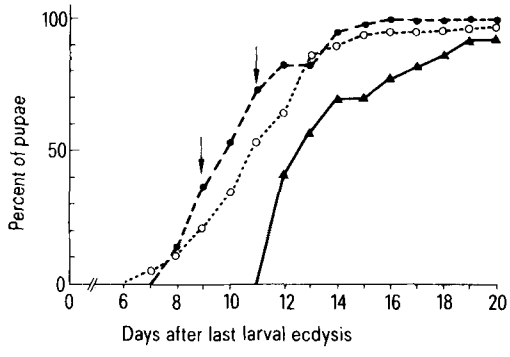
Material and methods. The last (7) instar larvae of *G. mellonella* L. taken from a stock colony cultivated in laboratory conditions (at 30± 1 °C in constant darkness and fed with bee comb) were used in our experiments.

The drug (Serpasil®, Ciba Ltd. in clinical injection vehicle) was injected once, twice or 3 times at 48-h intervals in the high dose of 125 µg/g b.wt into the body cavity of larvae of exactly known age, in a volume of 5 µl. The 1st control group received the same volume (5 µl) of 0.9% NaCl solution (presumed clinical injection vehicle) per specimen. The 2nd control group consisted of uninjected larvae. In our experiments, 24 tranquillized larvae, and 41 injected with saline were analyzed in 5 tests (n = 5) for each group, and 76 untreated larvae in 10 tests (n = 10). The small number of insects in the tranquillized group was due to the lethal properties of this dose of reserpine.

All the larvae were observed daily at 10.00 h for counting the percentage of newly-formed pupae. For comparison, another experimental group was treated as above, but with low doses (1.5 and 3.0 µg/g b.wt) of reserpine. In both cases, the results obtained were evaluated statistically in relation to the control groups. Statistical evaluations were analysed by Smirnov's bilateral test. The homogenity of each group was also tested.

Result and discussion. Injection of small reserpine doses into the body cavity of larvae of the last larval instar of *G. mellonella* produced no effect on the appearance of larval-pupal moult. Neither did a single drug dose of 1.5 µg/g b.wt administered to insects twice (on the 1st and 3rd day of 7th stage) or 3-fold (on the 1st, 3rd and 5th day), nor a single dose of 3.0 µg/g injected once (on the 1st day) cause any apparent differences as compared with control groups.

A high dose (125 µg/g b.wt) of reserpine injected once (on the 1st or 3rd or 5th day of 7th larval instar) caused minimal disturbances in the duration of the last larval stage. Application of this dose on the 3rd day caused a



Percentage of pupae in the group of 3 times tranquillized insects and the control groups in relation to the total number of larvae taken for the experiments. ▲——▲, Tranquillized (n = 5), ●– – –●, control injected with saline (n = 5), and ○·····○, normal (n = 10) insects. Arrows indicate statistically significant differences: ↓, $p < 0.05$, and ↓, $p < 0.001$.