and the pH-value of the incubation medium was obtained (figure 2). It is presumed that, in an acid medium, the diffusion of the protonized hydralazine is more strongly inhibited than the diffusion of the free base present in a neutral medium.

Two metabolites of hydralazine, 3-methyl-s-triazolo-[3,4,a]-phthalazine (MTP) and hydralazine-acetonhydrazone (acetonide), were studied with respect to their effect on the elasticity module. None of the metabolites lowered the blood pressure in spontaneously hypertensive rats, but they caused a significant increase in the elasticity of collagen (table).

Whereas acetonide has a greater effect on the collagen than has a comparable concentration of hydralazine, the effect of MTP is definitely reduced.

The marked reduction in the elasticity module by metabolites which have no blood-pressure lowering effect, raises the question whether the effect of hydralazine on the mechanical features of collagen fibres is only of secondary significance for the overall action of hydralazine.

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Toxicity of Dithane M-45 on *Drosophila melanogaster*

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Summary. The toxicity of different concentrations of Dithane M-45 on *Drosophila melanogaster* was determined. The chemical was administered by larval feeding. It has been estimated that the LC_{50} is 17.5 mg/100 ml food medium. The studies have suggested that Dithane M-45 has a pronounced effect on the rate of development and viability.

Pesticides are being used extensively in the control of crop pests and vector-borne diseases. Adequate mutagenicity testing on pesticides might be useful for the evaluation of their toxicities. Dithane M-45 is a new broadspectrum dithiocarbamate fungicide and a residual pollutant, which requires a continuous monitoring in the ecosystem. It has been shown that Dithane M-45 is toxic for the alga *Stichococcus bacillaris*[2] and least phytotoxic[3]. Studies of Vasudev and Krishnamurthy[4] have revealed that Dithane M-45 has an effect on crossing over in *D. melanogaster*. The knowledge on the toxicological effects of this environmental pollutant on animals and man is very meagre. The authors therefore considered it interesting to report here the findings on the action of Dithane M-45 on the rate of development and viability in *D. melanogaster*.

Materials and methods. *D. melanogaster*, Oregon-K strain, was used in the present investigations. The eggs were collected following the procedure of Delcour[5]. Eggs of the same age (±4 h) and in equal numbers (35 eggs/vial) were placed in normal and Dithane M-45 (Indofil Chemicals Limited, Bombay) supplemented media. Different concentrations of 2, 5, 10, 15, 17.5, 20, 25 and 30 mg of the chemical were thoroughly mixed in 100 ml wheat cream agar medium. 700 eggs were alloted to each group. The normal medium was used as control.

Flies were counted every day from the first day of eclosion to the last day of emergence. Sexes were noted. From this data, mean developmental time of the whole group, as well of sexes, survival value and sex-ratio were calculated. All the experiments were carried out at a constant temperature of 23±1 °C.

Results and discussion. As the rate of development is one of the parameters by which the toxicity of the chemical is measured, the effect of various concentrations of Dithane M-45 on rate of development has been analyzed. The table incorporates the data on the mean developmental time in

Toxicity of Dithane M-45 on *D. melanogaster*

Concentration in food agar	Mean developmental time for group	Number of adults emerged out of 700 eggs laid		Mean number of offspring per vial	Percentage lethality
		M	F		
Control	11.51±0.07	331	324	32.75±0.45	6.43
2 mg/100 ml (20 ppm)	15.29±0.17*	292	283	28.75±1.32	17.86
5 mg/100 ml (50 ppm)	15.98±0.07*	271	257	26.40±1.24	24.58
10 mg/100 ml (100 ppm)	16.49±0.08*	246	229	23.75±2.05***	32.15
15 mg/100 ml (150 ppm)	17.72±0.12*	203	184	19.35±1.05***	44.72
20 mg/100 ml (200 ppm)	18.59±0.23*	168**	130**	14.90±2.86***	57.43
25 mg/100 ml (250 ppm)	21.72±0.24*	68	71	6.95±2.22***	80.15
30 mg/100 ml (300 ppm)	24.44±0.24*	51	44	4.75±1.35***	86.43

* Control versus treatment significant at 5% level. ** Sex-ratio is significant; $p < 0.05$. *** Control versus treatment; by analysis of variance: $p < 0.05$. F = Female, M = male.

different concentrations and control for group. Lengthening of developmental time is a fairly good indication of somatic effects caused by the chemical in test substrate[6]. It is evident that the rate of development is prolonged even at the lowest concentration tested. The highest developmental delay was noticed in 30-mg concentration. Thus the mean developmental time is significantly different when compared to controls ($p < 0.05$, table). However, none of the concentrations had any discernible effect on the mean developmental time in either of the sexes. In most groups, the means for males and females did differ by less than 1 SD. The SD were similar in both sexes. Hence, these results clearly indicate that Dithane M-45 has a pronounced effect on the rate of development in *D. melanogaster*. Such a type of chemical effect on the rate of development was also demonstrated by other workers[6-10]. Bhowmik[11] has shown that Dithane M-45 inhibits the mycelial growth and sporulation in *Alternaria triticina*.

In addition to the rate of development, the other usable parameter for evaluating toxicity is lethality. Comparison between the control and treated series clearly shows that even the lowest concentration used caused about 17.86% lethality (table). The extent of lethality is directly proportional to the concentration. The male and female larvae exhibited the same sensitivity in each concentration, except in 20 mg, to which female larvae were more sensitive than males ($\chi^2 = 4.84$, $p < 0.05$; table). By calculating the analysis of variance, it has been shown that Dithane M-45 induced significant effect on viability in concentrations above 5 mg/100 ml food medium ($p < 0.05$). The present findings have revealed that the LC_{50} for Dithane M-45 on *D. melanogaster* is 17.5 mg/100 ml. Experiments with *Phytophthora* has revealed that Dithane M-45 at 5 ppm killed the zoospores[3].

The authors have observed that mortality occurs mostly during the larval stages and that first instar larvae are the most sensitive to 25- and 30-mg concentrations. This is strong evidence to indicate that concentrations of Dithane M-45 greater than 0.025% are lethal to various larval stages of fruit fly and the greatest fungicidal potency is expressed in the larval stages.

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An adrenergic participation subserving a positive inotropism and chronotropism of prostacyclin on isolated rat atria[1]

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Summary. The effects of prostacyclin (PGI_2) on the contractile frequency and on the isometric developed tension of spontaneously beating or paced isolated rat atria were explored. PGI_2 enhanced frequency and contractile tension, both effects being blocked by the presence of propranolol, or following a pretreatment with 6-OHDopamine.

Prostacyclin (PGI_2) a nobel prostaglandin formed by blood vessel walls, has been recently identified and proved to have powerful inhibitory properties of arachidonic acid and adenosine-diphosphate platelet aggregation[2-4]. PGI_2 has also been found to relax isolated strips of coronary arteries and to be the main prostaglandin released by the rat, rabbit and guinea-pig heart[5,6]. Furthermore other cardiovascular actions, namely lowering of systemic blood pressure, coronary vascular and total peripheral resistance without cardiostimulatory actions or changes in heart rate, have been described in the cat[7]. However, augmentation of heart rate and perfusion pressure in the isolated rat heart, and depression of diastolic blood pressure accompanied by tachycardia in rats and rabbits, were also documented[8,9]. Lefer et al.[7] suggested that the increased cardiac output in response to PGI_2 is an indirect (increased cardiac ejection in the face of increased venous return) rather than a direct cardiostimulatory effect[7]. In view of these contradictory findings, it was decided to explore the direct influences of PGI_2 on the isolated rat atria.

Methods. Male albino rats of the Wistar strain were decapitated; their atria removed and suspended in a modified Krebs-Ringer-Bicarbonate media gassed with 95% O_2–5% CO_2; maintained at a constant pH and temperature of 7.4 and 30 °C, respectively, and composed as reported elsewhere[10]. After 1 h of equilibrium, initial atrial isometric developed tension (IDT) and contractile frequency (CF) were recorded as previously described[11,12]. Forthwith cumulative dose-response curves for PGI_2 were constructed for untreated atrial controls as well as for auricles exposed to propranolol or obtained from chemical sympathectomized animals injected 24 h prior sacrifice with 6-hydroxydopamine (6-OHDA). PGI_2 was kindly provided by Dr John Pike (Upjohn Laboratories, Kalamazoo Michigan, USA). L-Propranolol (for delivery into the tissue bath prior PGI_2 at a final concentration of 10^{-7} M) and 6-OHDA (for i.v. injection with 16.5 mg kg^{-1}) were obtained from standard commercial sources. The effect of PGI_2 on IDT was also tested on atria driven with slightly suprathreshold (+10%) square pulses of 0.5 msec duration and 3.3 Hz of frequency delivered by a conventional stimulator and conveyed to the tissue via 2 platinum electrodes. Experimental records were compared with initial control ones and expressed as percent changes. Differences between mean values were considered significant if $p = 0.05$ or less.

Results. As can be seen in figure 1, A, the IDT of spontaneously beating isolated rat atria exhibited a distinct increasing magnitude following increasing concentrations of PGI_2 within a wide range from of 1×10^{-15} to 1×10^{-9} M. A similar situation, i.e. a significant enhancement, was