54 Smith, T.L., and Hutchins, P.M., Anesthetic effect on hemodynamics of spontaneously hypertensive and Wistar Kyoto rats. Am. J. Physiol. *238* (1980) H539–H544.
55 Timmermans, P.V.B.W.M., Fluitman, P.H.M., Mac Kaay, J.C.J., and Van Zwieten, P.H., Hypotensive and bradycardic effects of classical sympathomimetic drugs upon intravenous administration. Archs int. Pharmacodyn. Ther. *231* (1978) 98–103.
56 Van der Meer, C., Versluys-Broers, J.A.M., Tuynman, H.A.R.E., and Buur, Y.A.Y., The effect of ethylurethane on hematocrit, blood pressure and plasma glucose. Archs int. Pharmacodyn. Ther. *217* (1975) 257–275.
57 Van Meel, J.C.A., De Jonge, A., Kalkman, H.O., Willfert, B., Timmermans, P.B.M.W.M., and Van Zwieten, P.A., Vascular smooth muscle contraction initiated by postsynaptic α_2 adrenoceptor activation is induced by an influx of extracellular calcium. Eur. J. Pharmac. *69* (1981) 205–208.
58 Van Meel, J.C.A., Towart, R., Kazda, S., Timmermans, P.B.M.W.M., and Van Zwieten, P.A., Correlation between the inhibitory activities of calcium entry blockers on vascular smooth muscle contraction in vitro after K^+ depolarization and in vivo after α_2 adrenoceptor stimulation. N.S. Arch Pharmac. *322* (1983) 34–37.
59 Volicer, L., and Loew, C.G., The effect of urethane anesthesia on the cardiovascular action of angiotensin II. Pharmacology *6* (1971) 193–201.

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Short Communications

Protection by iloprost of the myocardial contractility and rhythmicity in frog ventricular strips[1]

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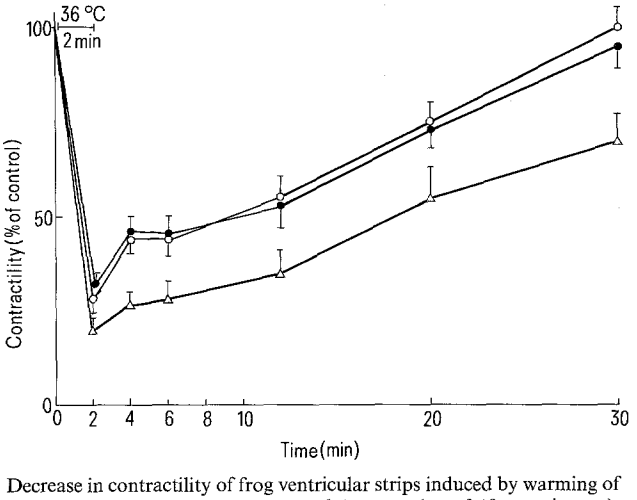
Summary. Incubation of frog ventricular strips with Ringer containing iloprost for 24 h at 4 °C can protect the contractility and rhythmicity from heat stimulation and aconitine when compared with strips incubated in Ringer alone under the same experimental conditions.
Key words. Iloprost; frog ventricular strips; contractility; tissue protection; aconitine; warming.

Iloprost has recently been synthetized as a new stable analog of prostacyclin (PGI_2). This new compound has been shown to have a profile of action similar to natural PGI_2 in various pharmacological preparations[2,3]. Natural PGI_2 has been described to protect myocardium from acute ischemia[4,5]. We have recently described an antiarrhythmic effect of iloprost against digoxin-induced ventricular extrasystoles in anesthetized guinea pigs and isolated Langendorff-perfused hearts from the same species[6]. In ongoing studies we have also shown the antidisrhythmic effect of iloprost in the isolated whole heart, spontaneously beating right atria from rabbit whole heart and spontaneously beating atrial and ventricular strips from frog[7]. The results reported in the present paper show that iloprost, when incubated with the tissue, protects for 24 h the contractility and rhythmicity of the isolated spontaneously frog ventricular strips.

Materials and methods. The experiments were carried out on ventricular strips from frog *(Rana ridibunda)* of either sex weighing 45–65 g, during the winter season (January–February). After decapitation the heart was quickly removed and placed in a frog Ringer solution at room temperature (21 °C). Atrium was carefully separated from ventricle and discarded. Ventricle was spirally cut through the atrioventricular margin to the apex with 4 mm width and 2 cm length. Both tips were carefully tied and suspended in a jacketed bath and superfused with oxygenated (5% CO_2 in O_2) Ringer solution (15 ml/min) at 21 °C. 1.0 g initial tension was applied and the isometric contractions were recorded on a Grass polygraph (Model 79 D) via a force-displacement transducer (Grass FT.03). Arrhythmias were followed from mechanical activity on the recorder and consisted of multifocal single or repetitive premature ventricular beats and the change in interval between contractions. The onset of ectopic beats and fibrillation were determined. Arrhythmias were produced by heating the medium from 21 °C to 36 °C for 2 min by a thermostatically controlled water circulating pump. In another series of experiments aconitine was used as an arrhythmogen. Intact freshly prepared strips were first bathed for 60 min and the contractions were recorded. Strips showing regular rhythmicity and stable contractility during this equilibration period were taken for further experiments. However, strips which were disrhythmic during the equilibration period were discarded. The strips which showed regular rhythmicity and stable contractility during control experiments were then carefully transferred into beakers containing Ringer's solution for cold storage in the refrigerator. Half of the strips were kept in Ringer alone, others in Ringer containing iloprost (10 ng/ml), without supplying exogenous oxygen, at a constant temperature of 4 °C for 24 h. In a preliminary experiment iloprost at the concentration of 1 ng/ml



Decrease in contractility of frog ventricular strips induced by warming of the bathing medium. ●—● control (mean value of 19 experiments). ○—○ preincubated with Ringer containing iloprost (10 ng/ml) (mean value of 10 experiments). △—△ preincubated with Ringer alone (mean value of 9 experiments). Vertical bars show SEM.

was found to be ineffective. Higher concentrations of the drug were not used in this study because of its possible reversible arrhythmogenic action[6].

Results and discussion. Warming of the bathing medium from 21 °C to 36 °C for 2 min produced a decrease in contractility and an increase in the beating rate of ventricular strips. The strips did not show any disrhythmicity during a 30-min investigation period and the contraction amplitude reached the control level within this period. Nine out of 19 strips were then incubated with Ringer alone and 10 strips with Ringer containing iloprost (10 ng/ml) for 24 h at 4 °C. The strips were then superfused with Ringer alone under the same experimental conditions for a 30-min equilibration period and the test was repeated. Eight out of 9 strips which were incubated with Ringer alone showed apparent rhythm disturbances and a decrease in contractility following 2 min exposure to the warming (36 °C) of the bathing medium. The contraction amplitude was significantly less than that of the control during a 30 min investigation period (fig.). However, 10 strips which were incubated with Ringer containing iloprost for 24 h at 4 °C, did not develop rhythm disturbances to the warming stimulation, except one strip which was arrhythmic. The difference between the two groups was statistically significant when evaluated with Fisher's exact test[8] ($p < 0.01$). In this group the contractility did not differ from control measurements but was significantly higher than that observed with the strips incubated in Ringer alone ($p < 0.001$). Aconitine, when added to the superfusion medium at the concentration of 3.2 µg/ml, produced multifocal ectopic beats in strips preincubated in Ringer and Ringer containing iloprost. The contact time of aconitine with the strips was 1 min and was kept constant for all preparations. The onset of ectopic beats and of fibrillation in both conditions is summarized in the table. The calculated results obtained in both groups were significantly different when evaluated using the Mann-Whitney U-test[9] ($p < 0.01$). These results indicate that iloprost has a functional protective effect on the contractility and rhythmicity of frog ventricular strips in anoxic conditions, and support its beneficial effect on functional recovery in the isolated rat heart after 24 h hypothermic arrest[10]. Recent studies have been reported on the protective effects of PGI_2 and its stable analogs[4,5]. It has been suggested that the membrane stabilizing action of PGI_2 is the mechanism underlying its myocardial protective action. This speculation has further been supported by the decrease in 17-(^{131}I)-heptadecanoic acid washout from ischemic myocardium in the presence of iloprost[11], a finding supporting the membrane stabilizing action of the compound. Whether or not the same mechanism is responsible for the functional protective effect of iloprost in frog myocardium remains to be elucidated. In addition, the dose-response relation of iloprost at concentrations ranging between 1 to 10 ng/ml should be studied in the winter season. Higher concentrations of the compound were not tested in the present study because of its reversible arrhythmogenic action observed in the guinea pig heart[6].

Onset of ectopic beats and of fibrillation in spontaneously beating ventricular strips preincubated with Ringer and Ringer containing iloprost (10 ng/ml) for 24 h at 4 °C. Arrhythmias were induced by aconitine added to the superfusion medium at the concentration of 3.2 µg/ml (mean ± SEM of 9 strips)

	Onset of ectopic beats (sec)	Onset of fibrillation (sec)
In Ringer	28.0 ± 4.1	72.0 ± 21.0
In Ringer plus iloprost	159.0 ± 44.0	260.0 ± 35.0

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2 Schrör, K., Darius, H., Matzky, R., and Ohlendorf, R., Naunyn-Schmiedeberg's Arch. Pharmac. *316* (1981) 252.
3 Ercan, Z. S., and Türker, R. K., Pharmacology *31* (1985) 61.
4 Ogletree, M. L., Lefer, A. M., Smith, J. B., and Nicolaou, K. C., Eur. J. Pharmac. *56* (1979) 95.
5 Ohlendorf, R., Perzborn, E., and Schrör, K., Thromb. Res. *19* (1980), 447.
6 Metin, M., Dörtlemez, Ö., Dörtlemez, H., Akar, F., Ercan, Z. S., and Türker, R. K., Eur. J. Pharmac. *98* (1984) 125.
7 Aksulu, H. E., Ercan, Z. S., and Türker, R. K., Archs Int. Pharmacodyn. *277* (1985) 223.
8 Armitage, P., Statistical Methods in Medical Research, p. 135. Blackwell Sci. Publ. London 1973.
9 Snedecor, G. W., and Cochran, W. G., Statistical Methods, 6th edn, p. 130. Iowa State University Press, Ames 1967.
10 Gilst, W. H. van, Boonstra, P. W., Terpstra, J. A., Wildevuur, Ch. R. M., and de Langen, C. D. J., J. molec. cell. Cardiol. *15* (1983) 789.
11 Smith, E. F., Kloster, G., Stöklin, G., and Schrör, K., Biomed. biochim. Acta *43* (1984) 155.

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Telodendrial contacts between foveolar cone pedicles in the human retina

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Summary. The synaptic pedicles of foveolar cones in the human retina contact each other by means of telodendrial processes. Thus direct lateral coupling of photoreceptor terminals exists even in the area of highest acuity function.
Key words. Retina; human fovea; photoreceptors.

Interreceptor contacts have been demonstrated between synaptic terminals of photoreceptors in many vertebrate retinas[2,3]. Most contacts between cones and cones and between cones and rods are considered to be 'gap' junctions that may subserve electrical coupling[4]. Contacts between cones of primate retinas have been found between extrafoveal cones only[5,6] and not between cones of the central fovea. We here report from a light microscopical study the existence of direct contacts between neighboring foveolar cone pedicles of human retinas.

To minimize artifactual influences human foveas were obtained from eyes immediately after enucleation for melanomas. Only specimens in which the tumor was restricted to the anterior segment of the eye, not affecting macular vision, were used (Donors: two females, 72 and 82 years; 1 male, 47 years). 5 min. after enucleation the supramacular sclera was trephined and after short prefixing the underlying retino-choroidal disc was removed and immersed in the fixative (3% glutaraldehyde in a Sørensen phosphate buffer (0.1 M, pH 7.4)). Two specimens