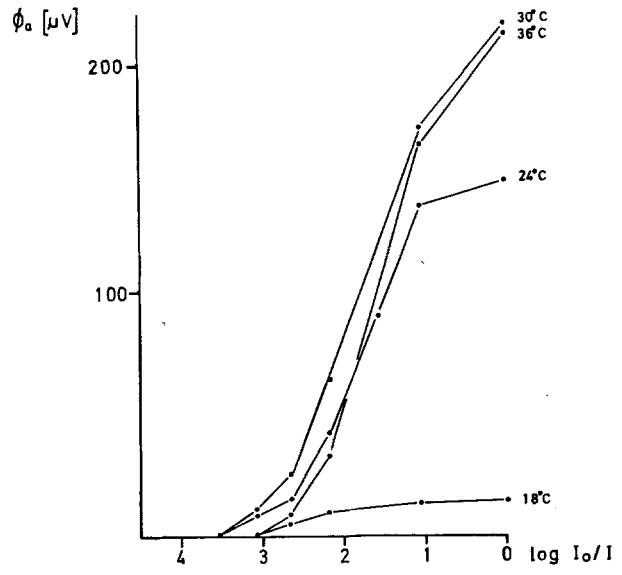

Fig. 3. Dependence on temperature of the function $\phi_a = f(I)$. The maximum light intensity was $I_0 = 40$ lux.

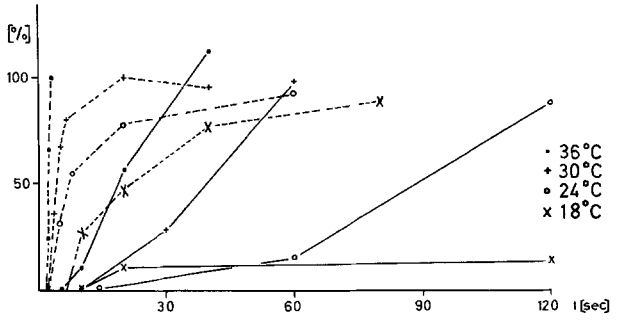

Fig. 4. Influence of temperature on the latency of restoration, measured by means of double stimuli at different intervals. Ordinate: Second potential as percentage of the first; dashed line: late RP (ϕ_a); continuous line: b-wave (ϕ_b). Abscissa: Interval between first and second light stimulus. Intensity of illumination 40 lux, duration 1 sec.

the dog ERG might be attributed to the activity of rods. The influence of temperature on the off-effect is different from that on the b-wave (cf. Figure 2). Below 24 °C, ϕ_a is extinguished while ϕ_b still exists. Therefore the 2 waves seem to originate in different retinal elements. The investigation of early positive components of the rabbit ERG by LÜTZOW[11] showed that a b-wave could only be registered above 28 °C. Our experiments were carried out without adding plasma to the perfusion medium, which seems to play an important role for the isolated rabbit retina[2,3].

The isolated retina of the poikilothermic frog shows maximum potential values at temperatures from 17 to 20 °C, while below 6 °C a b-wave can no longer be registered[1,5]. CORNU and CLOTTES[12] calculated Q_{10}-values between 1.6 and 1.7 for the a-wave of the frog ERG at temperatures from 10 to 30 °C. If one compares the gross activation energies for the b-wave of the frog ERG[5] and the late RP of the dog ERG, their equal size demonstrates that the processes which lead to the formation of both potentials may be ascribed to analogous physicochemical mechanisms. The size of the corresponding Q_{10}-values agrees with the observation that the formation of the potentials is mainly triggered by diffusion processes[13]. The difference between the retina of the homoiothermal dog and the poikilothermal frog is that the first appearance of a potential at low temperatures as well as the range of temperature for the validity of the linear ϕ — log I-relation for the dog retina are shifted by 9 °C to higher temperatures. Comparing the morphology of frog and dog retina, it is striking that the frog retina has a broad inner and small outer nuclear layer, whereas the situation for the dog retina is the reverse. Comparing the corresponding potentials, the frog ERG is characterized mainly by the b-wave and the dog ERG by the late RP.

Zusammenfassung. Grösse und Form des Belichtungspotentials der isolierten Hunderetina stimmen mit den Ergebnissen in vivo überein und lassen sich vorwiegend der Stäbchenaktivität zuschreiben. Ein Vergleich zwischen dem späten Rezeptorpotential des homoiothermen Hundes und der b-Wellenamplitude des poikilothermen Frosches ergibt, dass die Bildung beider Potentiale analogen thermodynamischen Gesetzmässigkeiten folgt, wobei der Temperaturbereich bei der Hunderetina um 9 °C zu höheren Temperaturen verschoben ist.

U. BORCHARD

Pharmakologisches Institut der Universität Köln, Gleueler Strasse 24, D–5 Köln 41 (German Federal Republic, BRD), 5 December 1974.

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The Use of Crocetin in Experimental Atherosclerosis

Several past studies[1–3] have indicated that atherosclerosis may be initiated by hypoxia at the vascular wall. However, atherosclerosis is a very common disease[4], and how can hypoxia by so universal? Some investigators have suggested that it may be induced by increased levels of carbon monoxide in the blood[5]. We have previously suggested that such hypoxia may instead be due to a decreased rate of diffusion of oxygen from the red blood cells to the vascular wall[6].

A decreased rate of oxygen diffusion could be due to several factors. We have found, in vitro, that increases in plasma protein levels[6] or of serum glucose levels[7] cause large decreases in the diffusion rate of oxygen through

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blood plasma. Although there is a significant correlation between the diseases of diabetes and atherosclerosis[4], the effect of increases of plasma protein levels has not been studied extensively. However, we have shown that increased plasma protein levels do result in more severe atherosclerosis in rabbits[6,8]. In addition, we have reported a general increase in certain plasma protein levels with age[9], thus possibly accounting for the general correlation of atherosclerosis with ageing.

A way to counteract such diffusion decreases would be to use a drug which increases oxygen diffusion in plasma. Very few compounds appear to do this; however, the carotenoid crocetin has been found to bring about an 80% increase in the oxygen diffusivity in plasma[10]. We have also found that crocetin reduces atherosclerotic damage and serum cholesterol levels in rabbits, even in the presence of increased plasma protein levels[10]. Since those results were so striking, we decided to further test its effects. Thus, in this study we have investigated the effect of crocetin on experimental atherosclerosis in rabbits with normal protein levels.

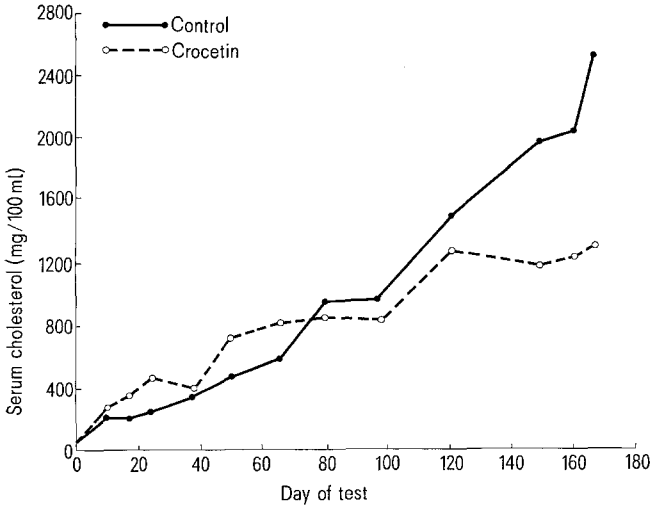

Fig. 1. Serum cholesterol.

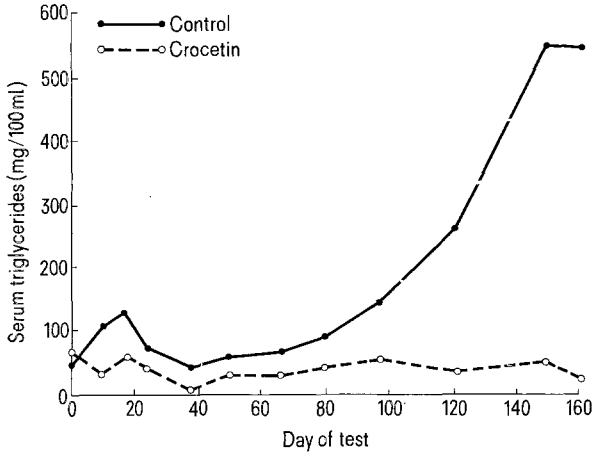

Fig. 2. Serum triglycerides.

Group	Average aorta thickness (mm)	Average lesion coverage (%)		
		Arch	Thoracic	Abdominal
Control	0.592	73	46	37
Crocetin-treated	0.365	57	10	11

Materials and methods. 10 Dutch-belted rabbits, each weighing approximately 2 kg, were divided into 2 equal groups. All rabbits were fed a normal rabbit lab chow diet mixed with 1% cholesterol and pelleted (ICN Pharmaceuticals, Cleveland, Ohio), and were allowed to eat and drink water ad libitum. One group was designated as the control group and the other group was injected i.m. every $2^1/_2$ days with 3 ml of an isotonic saline solution containing approximately 30 µg/ml of crocetin. Blood samples were taken every other week from the ear vein, and standard clinical analyses were used to determine the serum cholesterol and triglyceride contents.

After $5^1/_2$ months, the animals were sacrificed. The aortae were excised and transferred immediately to formalin solutions for storage. Following fixation, a 1 cm length of the lower thoracic aorta (above the upper abdominal bifurcation) was removed and prepared in the usual manner for light microscopy. The remainder of the aortae were opened longitudinally and prepared for gross evaluation of lipid deposits by staining with Sudan IV dye.

Results and discussion. The results of the serum cholesterol and triglyceride analyses are shown in Figure 1 and 2. At the beginning of the test, the crocetin-treated animals maintained higher levels of serum cholesterol. However, as seen in Figure 1, after about 3 months the levels of the controls began to exceed those of the crocetin-treated group, and at the end of the test period the levels of the crocetin-treated groups were 50% lower than those of the control group. The standard deviations were 10–20% of the average values.

The serum triglyceride levels shown in Figure 2 differed even more markedly between the 2 groups. The triglyceride levels of the crocetin-treated group remained in the normal range throughout the test period, while the controls increased by 2000%. The standard deviations here were 30–35% of the average values. The mechanism for the effect of the crocetin on cholesterol and triglyceride levels is not understood at this time, but it may be due somehow to an enhancement of the rabbits' abilities to metabolize lipids.

The results of the visual examinations of the aortae are given in the Table. The standard deviations in the data were small, about 10% of the mean values. It is obvious from these results that the vascular damage is much less severe in rabbits which received crocetin. Whether this effect is due to the influence of crocetin on the permeability of the vascular wall (through the prevention of hypoxia) or is a result of the decreased lipid levels is difficult to ascertain. That point, though, appears to be of much less importance than the fact that crocetin appears to greatly aid in the prevention of atherosclerosis in rabbits.

Résumé. L'action préventive de la crocetine de l'apparition de l'artério-sclerose sur l'aorte du lapin soumis à un régime hypercholestérolémiant est démontrée. Par contre le mécanisme d'action de cette substance n'est pas élucidé par les expériences relatées.

J. L. Gainer and J. R. Jones

Department of Chemical Engineering, University of Virginia, Thornton Hall, Charlottesville (Virginia 22901, USA), 10 January 1975.

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