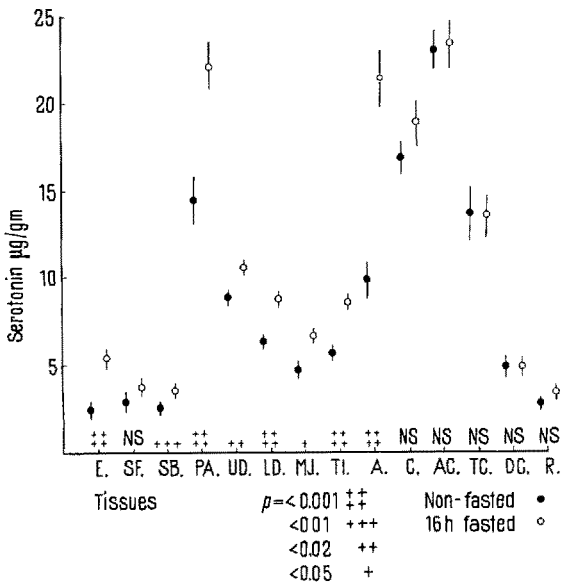
assayed by BOGDANSKI's method[9]. Results were calculated from a graph drawn daily from standard serotonin solutions (prepared in 0.1 *N* HCl) and a reagent blank (0.1 *N* HCl), both of which were carried through the extraction procedure. Values are expressed as μg/g mucosa (wet weight).

The 2 groups of rats are shown in the Figure. Each point represents the mean of 15–20 estimations. Differences between the mean values for each tissue in the fasted and non-fasted rats were determined using the Student *t* test. With the exception of the stomach fundus, all the tissues from the esophagus to the appendix in the fasted rats demonstrate an increase in mucosal serotonin compared to the non-fasted animals. The largest increase is seen in the pyloric antrum and appendix, while the amine levels from the cecum to the rectum are similar in both groups.



Mean values ± 1 S.E. for esophogeal (E), stomach fundus (SF), stomach body (SB), pyloric antrum (PA), upper and lower duodenum (UD, LD), mid-jejunum (MJ), terminal ileum (TI), appendix (A), cecum (C), ascending, transverse and descending colon (AC, TC, DC), and proximal rectum (R), serotonin in fasted and non-fasted rats. Each point is the mean of 15–20 estimations, and the *p* value (determined with the Student *t* test) for each pair is indicated.

The physiological function of bowel serotonin is unknown. However, the most likely role appears to be associated with peristalsis[10,11]. It is interesting therefore, that in the proximal gastrointestinal tract, which is relatively empty after a 16 h fast (the rodent colon being more resistant to depletion of food residues than the small bowel), higher levels of serotonin are evident. These higher mucosal serotonin levels may assume importance when evaluating the in vivo and in vitro effect of drugs[12].

Zusammenfassung. Der Serotoningehalt der Darmmucosa aus 14 Schnittpräparaten von Sprague-Dawley Rattenweibchen nach 16-stündigem Fasten und nach normaler Fütterung wurde bestimmt. Grössere Serotoningehalte wurden im oberen Teil des Verdauungstraktus (ausschliesslich den Magenblindsack) der Hungertiere gefunden.

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Effect of the Mast Cell Disruptor B.W. 48/80 on Dietary Atherosclerosis in the Male Rabbit

It has been claimed that there is a relationship between tissue mast cell population and the incidence of atherosclerosis[1]. Studies have been carried out in our laboratory[2] and in another laboratory[3] to determine the role of the mast cells on the development of atherosclerosis in the rat. The synthetic polymer compound 48/80 (Burroughs Welcome Inc.), a drug having mast cell depletion properties, was used[4]. Rats fed high cholesterol diet and injected with compound 48/80 for 3 months or longer failed to demonstrate atherosclerosis[2,3] and showed an increase in the lipoprotein lipase activity of the arterial wall (aorta)[5].

To test further the hypothesis that compound 48/80 protects against the development of atherosclerosis, experiments were carried out on rabbits – animals in which atheroma is easily produced by dietary means. 32 male rabbits of undetermined strain with an initial body weight of about 1600 g, were distributed in 6 groups: (A) Control animals, receiving common rabbit diet; injected daily with saline solution i.p. (B) Animals receiving 1 g cholesterol daily added to the diet; injected with saline solution i.p. (C) Rabbits receiving common diet; injected with compound 48/80 (1.5 mg/day/kg body weight) i.p. (D) Animals receiving 1 g cholesterol daily added to the diet; injected with compound 48/80 (1.5 mg/day/kg body weight) i.p. (The animals of these four groups were maintained for about 65 days under experimental conditions, then sacrificed by bleeding.) (E) Animals receiving common diet

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Experimental condition	Atherosclerotic area of aortic arch (%)				Serum cholesterol concentration (mg%)			
	No.	Mean ± S.D.	p	(Groups compared)	No.	Mean ± S.D.	p	(Groups compared)
(A) Control	3	0			3	116 ± 4		
(B) High cholesterol diet	7	49.9 ± 7.4			6	584 ± 80		
(C) Compound 48/80	3	0			3	87 ± 11	< 0.05	(A–C)
(D) High cholesterol diet + compound 48/80	9	27.5 ± 4.4	< 0.02	(B–D)	8	474 ± 65	< 0.01	(B–D)
(E) High cholesterol diet discontinued	4	53.9 ± 6.8			4	432 ± 129		
(F) High cholesterol diet discontinued + compound 48/80	5	14.8 ± 7.9	< 0.01	(E–F)	5	138 ± 38	< 0.05 < 0.01	(E–F) (D–F)

plus 1 g cholesterol daily for 62 days; then put on common diet and injected daily with saline solution i.p. (F) Animals feeding on cholesterol-enriched diet (1 g/day) for 62 days; then put on common diet and injected with compound 48/80 i.p. (1.5 mg/day/kg body weight). Following suspension of the cholesterol diet, the treatment in groups E and F was prolonged for about 60 days and the animals then sacrificed by bleeding.

Results showing the % of the area of the aortic arch with atheroma lesions (measured by the planimetric method) and the cholesterol concentration of serum measured[6] at the time of sacrifice are presented in the Table. Compound 48/80 reduces the cholesteraemia in the animals fed with high cholesterol diet and shows less atheromatous involvement of the aortic arch in comparison with those animals fed only high cholesterol diet and injected with saline (group B). When compound 48/80 treatment is started after atheromatous plaques have developed (group F), the serum cholesterol levels are much lower than in group E rabbits in which it remains high and in those injected with compound 48/80 and maintained on high cholesterol (group D). It is thus conceivable that a drop in serum cholesterol induced by compound 48/80 may be responsible for the diminution of atheromatous lesions of the aorta. However, as has already been stated, in the rabbit, once the cholesterol diet has been discontinued and the serum cholesterol level is returning to control values, there is no disappearance of atheroma[7,8]. Sometimes there is instead of a decrease of atheroma an increase in the lipid concentration of the aorta[9]. Thus a drop in cholesterol alone is insufficient to diminish the atherosclerosis process.

The question therefore remains open as to whether compound 48/80 interferes with the atherosclerotic process. The microscopic study[10] of the mast cells of the skin shows modifications in the tissue mast cell population (diminution of the number, degranulation and release of the metachromatic material). This effect is parallel to the protective effect of compound 48/80 on atheromatous development. The results on mast cell survey are clear even though it has been described as being difficult to study the mast cells because of the few cells in the rabbit[11].

The mast cells have been related to glycosaminoglycan metabolism[12]. In a previous paper the alteration of the mucopolysaccharide composition of the arterial wall of rats chronically injected with compound 48/80 was demonstrated[13]. It is possible that the protective action of compound 48/80 may be related to the glycosaminoglycans of the aorta. Preliminary investigations have shown that there is some increase of the acid glycosaminoglycans and sulphated glycosaminoglycans below the atheroma in the cholesterol fed rabbit; the condensation of glycosaminoglycans is more marked in animals treated additionally with compound 48/80[14].

It can be postulated that compound 48/80 treatment induces changes in the distribution, and maybe also in the total amount, of acid glycosaminoglycans in the arterial wall of the rabbit. Because there is a clearance of atheroma from the aorta after the cholesterol-enriched diet has been discontinued in compound 48/80 treated rabbits, it is possible to assume that compound 48/80 can interfere in the removal of cholesterol deposit from the atheromatous plaque rather than in the prevention of lipid deposit in the intima. The decrease of serum cholesterol level produced by compound 48/80 could represent a secondary factor in the effect of the drug on experimental atherosclerosis in the rabbit.

Zusammenfassung. Mit Cholesterin ernährte Kaninchen, denen gleichzeitig Compound 48/80 injiziert wurde, wiesen gegenüber nur mit Cholesterinzusatz gefütterten Tieren geringere Atheromatose des Aortenbogens auf. Compound 48/80 rief auch eine Verminderung des Serumcholesteringehaltes hervor. Unter dem Einfluss von Compound 48/80 schien ein beschleunigter Abbau der atheromatösen Plaques einzusetzen bevor noch eine Verminderung des Serumcholesterins auftrat. Es wird vermutet, dass der Schutz von Compound 48/80 gegen die durch Diät erzeugte Atheromatose des Kaninchens auf einer Veränderung des arteriellen Glykosaminglykans beruht.

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