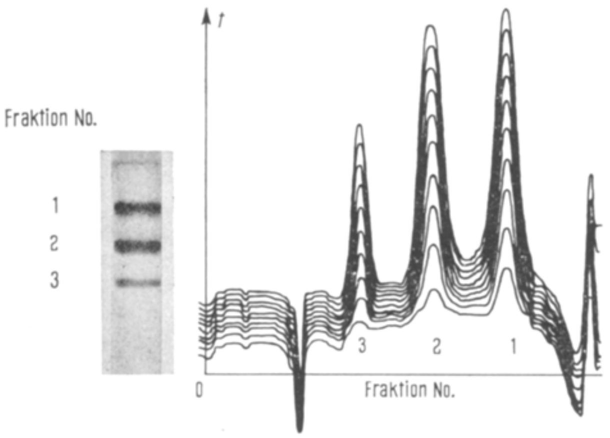

Fig. 1. LDH-Isoenzyme aus menschlichen Fibroblasten (Kontrolle). Acrylamidgelelektrophorese Densitometrie

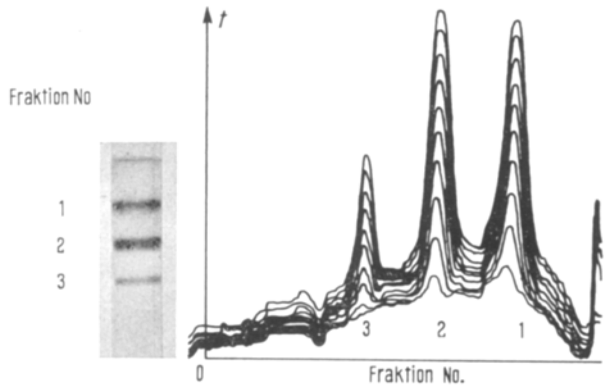

Fig. 2. LDH-Isoenzyme aus menschlichen Fibroblasten (DMBA-behandelt, 0,1 μg/ml).
Acrylamidgelelektrophorese Densitometrie

nolischer oder chinoider Natur; in ihrer Wirkung sind sie jedoch meist geringer als ihr Ausgangsprodukt[9].

In unseren Versuchen wurde das LDH-Isoenzymmuster durch DMBA nicht verändert, doch traten Enzymaktivitätsverminderungen in den einzelnen Banden unterschiedlich auf. Parallel dazu war auch die Proteinsynthese innerhalb der LDH-Isoenzymbande vermindert. Ob eine spezifische Regulationsstörung durch kanzerogene Substanzen auftritt, soll in weiteren Untersuchungen an anderen Enzymsystemen geprüft werden[10].

Summary. The effect of 7,12-Dimethylbenz(a)anthracene (DMBA) on the activity of lactate dehydrogenase (LDH)-isoenzymes was studied in human fibroblast cultures. 3 isoenzyme components were separated by discelectrophoresis. A clear reduction in the enzyme-activity of the first and third component was observed, while the other fraction was little or not affected. The incorporation of radioactive amino acids in proteins of the LDH-isoenzyme bands shows the same trend.

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Influence of Diuretics on Renal Calcium Excretion

Since under conditions of osmotic diuresis renal Ca clearance is a function of Na clearance (Walser[1]), it may be expected that diuretics also influence calcium excretion. A number of publications show evidence of changes in Ca excretion after administration of various diuretics (Lamberg and Kuhlbäck[2], Schirmeister and Willmann[3], Hänze and Seyberth[4], Duarte[5]). Diuretics may affect Ca excretion by acting on Na excretion or by affecting directly the tubular Ca transport. In our paper we are trying to answer the question to what extent the elevated Ca excretion found after a single dose of various diuretics is conditioned by their natriuretic effect.

The investigations were made in 50 healthy subjects under the conditions of maintained water diuresis. The initial water load was 20 ml/kg body weight. The urine was collected by spontaneous micturition after 10–15 min intervals. After stabilization of the diuresis during the control period, the diuretic was administered. The following diuretics were tested: acetazolamide (i.v. 250 mg), aminophylline (i.v. 0.24 g or orally 0.3 g), ethacrynic acid (i.v. 1–10 mg), furosemide (i.v. 1–20 mg) and chlorothiazide (i.v. 250 mg).

In addition, in another group of 10 healthy subjects, the Ca and Na excretion was investigated after a single water load and after infusion of a 10% mannitol solution.

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Diuretic	Period	V ml/min	C_{Cr} ml/min	$U_{Ca}\cdot V$ µEq/min per 100 ml C_{Cr}	$U_{Na}\cdot V$ µEq/min per 100 ml C_{Cr}	C_{H_2O} ml/min per 100 ml C_{Cr}	r
Acetazolamide	C	13.1 (± 1.8)	128.2 (± 32.5)	3.4 (± 1.5)	113.9 (± 48.3)	8.0 (± 2.3)	0.7013
	D	18.4 (± 2.8)	131.5 (± 30.2)	5.0 (± 2.8)	334.6 (± 92.0)	9.8 (± 2.4)	
Aminophylline	C	12.7 (± 2.1)	114.0 (± 31.0)	4.7 (± 2.2)	128.9 (± 57.1)	8.9 (± 2.4)	0.7296
	D	17.7 (± 4.0)	108.7 (± 32.6)	11.4 (± 6.7)	328.1 (± 160.4)	12.4 (± 4.1)	
Ethacrynic acid	C	10.0 (± 2.6)	119.3 (± 33.7)	3.4 (± 2.8)	102.5 (± 50.6)	6.7 (± 3.0)	0.8914
	D	14.3 (± 4.4)	121.7 (± 35.4)	14.0 (± 8.5)	654.8 (± 301.1)	6.3 (± 2.2)	
Furosemide	C	12.0 (± 3.3)	132.0 (± 37.0)	3.3 (± 1.5)	115.0 (± 58.3)	7.2 (± 2.7)	0.8911
	D	17.4 (± 7.0)	131.8 (± 44.8)	21.0 (± 16.0)	725.5 (± 516.2)	6.8 (± 3.3)	
Chlorothiazide	C	12.6 (± 3.5)	119.6 (± 28.7)	4.1 (± 1.1)	121.6 (± 43.1)	7.7 (± 1.7)	0.6258
	D	17.3 (± 4.0)	107.0 (± 24.9)	6.3 (± 2.1)	632.6 (± 177.5)	9.2 (± 2.2)	
Mannitol[a]		8.2 (6.0–12.0)	129.0 (95.4–156.0)	6.9 (3.0–12.9)	321.0 (144.6–468.9)	–	0.7695

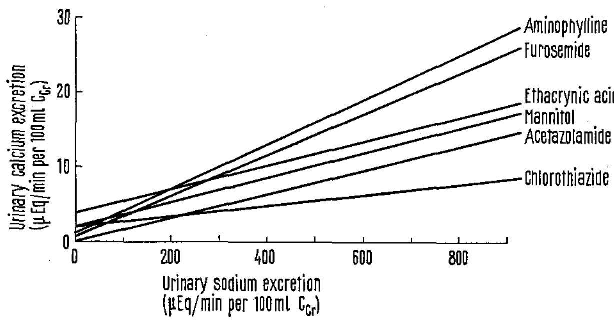
C, control period; D, period after the administration of diuretic; r, correlation coefficient $U_{Ca}\cdot V$ vs $U_{Na}\cdot V$. [a] Average values at maximum urinary flow, the range of variation is quoted in brackets.

The examination was made in the morning fasting, the diet on previous days contained a normal amount of NaCl and protein. In urine and plasma samples the Ca concentration (PŘIBIL[6]) as well as the Na (on a flame photometer) and endogenous creatinine concentration (BONSNES and TAUSSKY[7]) were assessed.

We found that all tested diuretics produced an increase in the Ca excretion in a linear relation with the Na excretion (see the Table; the regression lines are illustrated in the Figure). The increment of Ca excretion in relation to the increment of Na excretion was not the same for all diuretics. It was significantly higher for aminophylline and furosemide ($p < 0.001$) than for the remaining diuretics. It was also found that this increment was significantly smaller after the administration of chlorothiazide ($p < 0.01$) than after the remaining diuretics. With regard to the changes assessed during infusion of a hypertonic mannitol solution, it was found that Ca excretion for a given level of Na excretion was significantly higher after the administration of aminophylline and furosemide ($p < 0.05$); it did not differ significantly after the administration of ethacrynic acid and acetazolamide and was significantly smaller after the administration of chlorothiazide ($p < 0.005$).

The increased Ca excretion is not merely a function of diuresis, as is apparent from the fact that under conditions of high water diuresis (during the control period) the Ca excretion is not significantly raised. The different relationship between Ca and Na excretion after administration of different diuretics is not connected with their mode of action on the clearance of osmotically free water (C_{H_2O}).

Based on these findings we may conclude that the increased Ca excretion after administration of the investigated diuretics is in all instances a function of the raised Na excretion; however, obviously this is not the only factor in all instances. The different way in which the diuretic influences the Ca excretion, does not depend on the part of the nephron, where it influences Na absorption. If we adopt the idea that changes in Ca excretion after the mannitol infusion are merely a function of Na excretion (WALSER[1], SCHÜCK and CORT[8]), we may assume that changes in the Ca excretion after ethacrynic acid and acetazolamide are merely a function of Na excretion while furosemide and aminophylline reduce the Ca reabsorption by yet another mechanism, and chlorothiazide stimulates this process (it reduces the effect of natriuresis on Ca excretion).



Regression lines indicating relation between Na and Ca urinary excretions after the administration of diuretics and during mannitol infusion.

Zusammenfassung. Die renale Kalziumausscheidung wird bei einmaliger i.v. Zufuhr von Aminophyllin, Furosemid, Etacrynsäure, Azetazolamid und Chlorothiazid erhöht. Dies kann nicht nur durch die erhöhte Natriumausscheidung erklärt werden, sondern muss mit dem direkten tubulären Kalziumtransport im Zusammenhang stehen.

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