subcellular fractions 2 h after [^{35}S]-DADS injection is shown in the table. The results show that the cytosol has over 70% of the total radioactivity. The distribution of the radioactivity in the other subcellular fractions is in the order mitochondria > nuclei > microsomes. Further analysis of the cytosol shows that the trichloroacetic acid (TCA) soluble fraction (supernatant) contains nearly 90% of the [^{35}S] radioactivity (table). The TCA insoluble constituent (protein) accounts for approximately 10% of the radioactivity with only traces of [^{35}S] associated with the lipids. Of the radioactivity present in the cytosol, over 80% is found as sulphates and only 8% as [^{35}S]-DADS. Sulphur-containing compounds are liable to be oxidized to sulphates by the hepatic mixed-function oxidases[17]. It is interesting to note that we have recently observed substantial increases in hepatic microsomal mixed-function oxidases within 2 h following administration of diallyl disulphide (unpublished results). It appears that the bulk of DADS is converted to sulphates before it is transferred to the cytosol fraction preparatory to elimination from the system.

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Chelate treatment in acute cadmium poisoning

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Summary. Treatment of cadmium-poisoned rats with mixed ligand chelates does not decrease the lethality of cadmium more than treatment with one chelate alone.

Cadmium (Cd) is one of the most poisonous metals in our environment. Until now, no effective treatment against intoxication with this metal has been discovered. The report by Schubert and Derr[1], which described successful therapy for acute Cd-poisoning in mice, was therefore of great interest. The work reported here was performed to determine whether such favourable results using a similar therapeutic regimen could be achieved with another animal species, namely the rat.

All experiments were carried out with male albino rats of the Heiligenberg strain (age: 7 weeks, b.wt: 180–200 g). In the 1st experiment 0.03 mmoles/kg $CdCl_2$ (= 5.5 mg/kg) were injected i.v. and the chelants administered i.p. 60 min later. In the 2nd experiment $CdCl_2$ was given i.p. at a higher dose of 0.1 mmoles/kg. The LD 50/24 h for injection i.p. had been determined previously by the staircase-method[2] to be 0.0444 ± 0.001 mmoles/kg. The chelants were also injected i.p. but this time 5 min after the Cd, according to the corrections given recently by Schubert[3]. When 2 chelants were given simultaneously they were mixed before administration. All the injected solutions were between pH 6.5 and 7.2.

In the control of the animals in the 1st experiment in addition to the liver and kidneys the Cd concentration was determined in the spleen, testes, blood, femur and muscle. The figures were at the lower limit of our detection method (< 1 to ~ 3 ppm) and we therefore did not include these values in our further determinations.

Table 1 shows that there is an equal enhancement of urinary Cd-excretion after treatment with Na-dimercaptopropanesulfonate (Dimaval, DMPS – a gift from Heyl and Co., Berlin), $CaNa_2$-EDTA (EDTA), or the combination of

Table 1. Cd content (µg per organ) in liver and kidney 24 h after i.v. injection of rats with 5.5 mg (i.e. 0.03 mmoles)/kg $CdCl_2$ and in the 24 h urine without or with chelate treatment 1 h after Cd

Chelant Primary 0.5 mmoles/kg	Secondary 2.0 mmoles/kg	Urine	Liver	Kidneys
–	–	4.69 ± 4.61	260.1 ± 1.15	16.2 ± 0.41
–	SA 1 animal only	–	214.5	12.4
–	DMPS	72.6 ± 23.2*	170.2 ± 9.5*	17.0 ± 1.1
EDTA	–	97.4 ± 24.4*	177.7 ± 7.3*	17.7 ± 1.8
EDTA	SA	No survival		
EDTA	DMPS	71.9 ± 10.1*	184.1 ± 8.9*	19.2 ± 1.5

3 (control) or 6 animals. Mean values ± SE. * Statistically significant difference from the control ($p < 0.05$).

both 60 min after Cd. This corresponds to a reduction of the Cd-content of the liver whereas that of the kidneys remains unchanged. It is doubtful whether the removal of Cd from the liver has any beneficial effect as it does not lead to reduced mortality following EDTA treatment. This can be seen from table 2 which summarizes the mortality observed in both experiments. Table 2 also shows that treatment with Na-salicylate (SA) alone exacerbates the effect of $CdCl_2$. Administration of the chelant combinations does not improve the effect achieved with one chelator alone. The results appear to depend very much on the Cd-dose and/or the time interval between chelant and metal injection, the effects being different for the different substances tested. This is corroborated to some extent by the results of Jones and Basinger[4]. It is very unfortunate, however, that these authors do not give any control figures for the mortality-rate for animals receiving $CdCl_2$ only. The reason for the apparently contrary effects of the chelators in the 2 experiments are not known. However, the results in table 2 suggest that EDTA and DMPS may act by different mechanisms.

In the meantime Schubert[3] has withdrawn the results on which our first experiment (chelate treatment 1 h after Cd) was based. In a personal communication he later suggested that a combination of DMPS and $CaNa_3$-DTPA (DTPA) instead of EDTA showed a greater effectiveness and recommended intraperitoneal treatment with 0.04 mmoles/kg DTPA and 0.2 mmoles/kg DMPS at 5 and 95 min after Cd administration. However, in our animals this treatment also proved ineffective, the mortality being 80%, as in the Cd-controls. Our results, therefore, do not confirm the results of Schubert and Derr and suggest that the mixed ligand chelate theory of Schubert[3,5] in the present form does not apply in vivo to rats. Further careful studies, especially in vivo, are needed to show why neither our experiments nor those of others[6] correspond to Schubert's potentiometric titration studies which appear to suggest superior stability of at least some mixed ligand chelates over single ligand chelates.

Table 2. Mortality of rats after $CdCl_2$ with or without subsequent treatment with single or mixed ligand chelants

$CdCl_2$	Primary chelant 0.5 mmoles/kg	Secondary chelant 2.0 mmoles/kg	Mortality 0.03 mmoles/kg $CdCl_2$ i.v. Chelant(s) after 1 h	0.1 mmoles/kg $CdCl_2$ i.p. Chelant(s) after 5 min
+	-	-	16/27= 59%	37/43= 86%
−	-	SA	0/10= 0%	0/15= 0%
+	-	SA	9/10= 90%	15/15=100%
+	-	DMPS	1/9 = 11%	14/16= 88%
+	EDTA	-	9/16= 56%	14/30= 47%
+	EDTA	SA	11/11=100%	7/15= 47%
+	EDTA	DMPS	3/10= 30%	12/15= 80%

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Anti-oxidative effect of coenzyme Q_{10}

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Summary. Coenzyme Q_{10} is effective as an anti-oxidant like α-tocopherol, especially in the heart.

The peroxidation of lipids is closely related to several pathological disorders[1-3]. To prevent lipid peroxidation in the living body, α-tocopherol has been widely used. However, a ubiquinone was also reported to have anti-oxidative activity[4] in vitro. In this experiment, we studied the anti-oxidative activity of coenzyme Q_{10} (Co Q_{10}), one of the ubiquinones, both in vivo and in vitro, comparing its activity with that of α-tocopherol.

Materials and methods. In vivo study: Female rats of the Wistar strain, weighing 200 ± 10 g, were injected i.p. with 0.2 ml of isotonic saline including Co Q_{10} (2 mg/kg, 2.5 mg/ml) or α-tocopherol (10 mg/kg, 12.5 mg/ml) for 5 successive days. On the last day, hearts and livers were isolated and their mitochondria were prepared by Hatefi's method[5]. Each mitochondrial suspension was made to contain 3.0 mg of mitochondrial protein per ml of the mannitol - sucrose mixture. Mitochondrial lipoperoxides were measured by Packer's method[6].

In vitro study: To elucidate the inhibitory action of Co Q_{10} or α-tocopherol on peroxidation of mitochondrial fatty

Table 1. Lipoperoxides in mitochondria isolated from liver or from heart of rats given CoQ_{10} or α-tocopherol in vivo

Administration		Lipoperoxides in mitochondria (nmoles/mg protein) Liver	Heart
None		16.7 ± 1.7	11.2 ± 1.5
CoQ_{10}	2 mg/kg/day, 5 days	10.9 ± 1.8	8.5 ± 0.6
α-tocopherol	10 mg/kg/day, 5 days	7.2 ± 0.8	8.0 ± 1.4

Values are mean ± SD.

Table 2. Lipoperoxides in mitochondria with or without anti-oxidants in vitro

Additions in vitro	Lipoperoxides (nmoles/mg protein)
None	16.7 ± 1.7
CoQ_{10}, 0.2 mg	12.7 ± 1.4
CoQ_{10}, 0.4 mg	11.1 ± 1.5
CoQ_{10}, 0.8 mg	9.4 ± 1.0
α-tocopherol, 0.1 mg	13.2 ± 1.3