# BIOSYNTHESIS OF UBIQUINONE-9 IN THE REGENERATING ALBINO RAT LIVER

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The uptake of radioactivity from acetate-1-$C^{14}$ into ubiquinone-9 in thin slices of regenerating albino rat liver was investigated on the 1st, 2nd, 3rd, 6th, 9th, 12th, and 15th day after partial hepatectomy. Marked acceleration of ubiquinone-9 biosynthesis was found during the first 3 days after removal of two-thirds of the liver. The maximal increase in biosynthesis (almost eightfold) was found 24 h after hepatectomy. This increase in the rate of ubiquinone-9 biosynthesis coincides with the time of increased mitotic activity and accelerated biogenesis of the mitochondria. A very small increase in the biosynthesis of ubiquinone-9 was found on the 12th and 15th days of regeneration.

KEY WORDS: ubiquinone-9; hepatectomy; regeneration of the liver.

During regeneration of the liver after partial hepatectomy a rapid increase in the mass of the residual part of the organ is observed [1, 4]. This period is characterized by intensified biogenesis of the mitochondria [7]. The ubiquinone concentration in the regenerating liver, expressed per gram protein, despite the rapid increase in weight of the organ remains practically unchanged, and the relative concentration of ubiquinone in the mitochondria remains constant [3, 5]. However, the rate of formation of ubiquinone in the normal liver is low [13] and, for that reason, ubiquinone biosynthesis is evidently intensified during regeneration.

The investigation described below was carried out to study the rate of biosynthesis of ubiquinone-9 by slices of regenerating albino rat liver.

## EXPERIMENTAL METHOD

Noninbred male albino rats weighing 140-160 g were used. Two-thirds of the liver was removed by the method of Higgins and Anderson [10]. The lobes of the liver, removed at operation or taken from animals decapitated on the 1st, 2nd, 3rd, 6th, 9th, 12th, and 15th days after the operation were used for preparing slices 0.3-0.5 mm thick [11]. The slices were incubated for 6 h in Krebs–Ringer–phosphate buffer [9] in the presence of sodium acetate-1-$C^{14}$ (20 $\mu$Ci isotope/g of liver slices). A current of oxygen was passed through the buffer [9]. The unsaponified lipids were then extracted from the sections [6] and chromatographed on an alumina column [5] to obtain the fraction of ubiquinone. Ubiquinone-9 was separated from the other homologs on a thin layer of LCL-254 silica gel, soaked with a 3% solution of mineral oil in petroleum ether, and 95% aqueous acetone was used as the solvent [5]. The stain of ubiquinone-9 was rechromatographed on a thin layer of silica gel in benzene. Ubiquinone-9 was eluted from the silica gel with diethyl ether; some was used for quantitative determination [6] and the rest was applied to an aluminum foil target. The radioactivity was determined with a gas-flow counter attached to an instrument of the "Protok" type. The working space of the counter was 2 liters. The working gas was a mixture of methane and propane. The results were subjected to statistical analysis [2].

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TABLE 1. Content and Biosynthesis of Ubiquinone-9 in Thin Slices of Regenerating Albino Rat Liver (M±m)

| Days after hepatectomy | No. of animals investigated | Ubiquinone concn. (μg/g wet weight of slices) | Ubiquinone biosynthesis: incorporation of $C^{14}$ into ubiquinone of slices (pulses/min/g slices) | Ubiquinone biosynthesis: specific radioactivity of ubiquinone (pulses/min/mg) |
|---|---|---|---|---|
| 0 | 35 | 60,1±4,8 | 96±6 | 2 148±270 |
| 1 | 12 | 47,0±1,1 | 790±193 | 16 023±3 652 |
| *P* | | 0,28 | <0,001 | 0,001 |
| 2 | 9 | 48,6±4,7 | 325±13 | 10 049±2 892 |
| *P* | | 0,09 | 0,001 | 0,01 |
| 3 | 6 | 48,9±2,9 | 311±31 | 6 262±597 |
| *P* | | 0,05 | <0,001 | 0,001 |
| 6 | 8 | 60,9±10,0 | 104±25 | 2 089±594 |
| *P* | | 0,84 | 0,92 | 0,84 |
| 9 | 6 | 58,8±5,6 | 133±33 | 2 551±726 |
| *P* | | 0,69 | 0,28 | 0,62 |
| 12 | 6 | 48,3±2,2 | 204±59 | 4 076±10 358 |
| *P* | | 0,04 | 0,08 | 0,84 |
| 15 | 6 | 63,7±10,4 | 250±38 | 4 218±6 487 |
| *P* | | 0,84 | <0,001 | 0,76 |

## EXPERIMENTAL RESULTS

It will be clear from Table 1 that the ubiquinone concentration, expressed per gram of liver slices, was lowered on the 2nd and, in particular, on the 3rd-4th days after hepatectomy. These results agree with those published by the writers previously [5].

The fact will be noted that both the specific radioactivity and the incorporation of radioactivity into ubiquinone in the slices rose considerably on the 1st, 2nd, and 3rd days after the operation; this was clear evidence of the more rapid biosynthesis of ubiquinone at this period. On the 6th and 9th days of regeneration the rate of ubiquinone biosynthesis was slowed and was almost indistinguishable from that in the normal liver. On the 12th and 15th days a very small increase in the intensity of ubiquinone biosynthesis was observed. These changes in the rate of ubiquinone biosynthesis coincided with the fluctuating character of the increase in weight of the regenerating part of the liver [1]. During the first days after the operation, when a marked increase in the mass of the residual lobes of the liver was observed on account of increased mitotic activity, the rate of ubiquinone biosynthesis was increased, but when mitotic activity was lowered, the rate of ubiquinone biosynthesis was reduced.

It must be emphasized that the intensification of ubiquinone biosynthesis in the regenerating liver takes place at a time of more rapid biogenesis of the mitochondria. The greatest increase in mitochondrial protein is observed during the first 3-4 days after hepatectomy [3, 7].

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