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Quantitative Comparison of Renal and Hepatic Corticosterone Metabolism in vitro

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Recently it has been demonstrated that renal tissue metabolizes corticosteroids. In rats corticosterone (B) is converted by oxidoreductases into various metabolites which have been identified (Pflügers Arch 400 (1984)). In order to compare the renal metabolic activity with that of the well documented activity of liver tissue, renal and hepatic tissue slices were incubated with ^{3}H-labelled B and metabolites formed were identified by HPLC after extraction of lipid and water soluble labelled compounds. - Renal cortical tissue slices gave rise to 5α-H-4.5-dihydro-B (III), 11-dehydro-20ß-dihydro-B (I), 20ß-dihydro-B (II) and (main metabolite:) 11-dehydro-B (IV). Additional water soluble metabolites were not observed. Liver tissue produced all of the above metabolites and in addition further lipid and water soluble products (X). In both tissues metabolism of B was sex dependent:

Kidney ♂	IV ≫ I ≅ II ≫ III ≅ X^O
Liver ♂	I > IV > X" ≅ II ≅ X' > X''' > III > (X^O)
Kidney ♀	IV ≫ X^O > III > I > II
Liver ♀	III ≫ IV ≅ I ≅ II > X" ≅ X' ≫ X^O

In vitro rate of conversion of B was 3 nmol/60' · g wet tissue (renal) and 4.5 nmol/60' · g (hepatic). On the basis of total organ weight in vitro conversion of B was 4 x higher in liver than in renal cortex (male rats). - We conclude that renal B metabolism is of quantitative importance.

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ACTIVE NaCl TRANSPORT INTO THE DESCENDING LIMBS OF HENLE'S LOOPS (DLH) ENHANCES THE NaCl CONCENTRATION GRADIENT IN THE RENAL INNER MEDULLA

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Based on morphological observations and assuming salt secretion into the DLH in some species, it has been hypothesized (1) that this active transmural NaCl transport in certain portions of the long DLH might enhance the NaCl concentration at the papillary tip.
In order to model this hypothesis, a new multinephron model of the renal countercurrent system was established (differential equation model). It includes short loops of Henle, 8 types of long loops differing in length and in the location of the active transport according to (1), distal tubule, collecting duct, central core(CC), and pelvis.
Computed NaCl concentrations (mmol/l) in the CC for differing rates (10-6 mmol cm^{-2} s^{-1}) of active NaCl transport (V_m) into the DLH were:

	V_m 0.0	3.3	6.6	9.9
0.0 (cortico-med. jct.)	140	140	140	140
4.5 (outer-innerm.jct.)	661	653	632	599
8.25	575	598	601	584
10.5 (papillary tip)	664	758	805	813

Active NaCl transport out of the thick asc. limb: V_m =17.6

Conclusion: The hypothesis as advanced on a morphological basis indeed leads to an increase of the NaCl concentration in the inner medullary central core, especially at the papillary tip.

(1) Kriz,W. Federat.Proc. 42: 2379-2385, 1983

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ATRIAL NATRIURETIC PEPTIDE (AP II) INHIBITS RENIN RELEASE FROM JUXTAGLOMERULAR CELLS

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Atrial natriuretic peptide (AP II) has been found to impair renin release (RR) from the kidney and to lower plasma renin activity. Since the intrarenal mechanism by which AP II could inhibit RR is as yet unknown, we tested whether or not AP II affects RR by a direct action on juxtaglomerular cells (JGC). Using cell cultures containing 50%-60% JGC, as described previously (Kurtz et al., B.B.R.C. 124, 359, 1984) we found that AP II (10^{-13}M - 10^{-9}M) strongly inhibited RR from the cells to about 10% of control in a dose dependent fashion ($K_I \sim 10^{-11}$M). Inhibition of RR by AP II was paralleled by a rise in cellular cGMP levels. In presence of the cGMP-phosphodiesterase specific inhibitor M&B 22948 (1mM) tenfold lower concentrations of AP II were required to obtain the same effects on RR and cGMP levels as in absence of M&B 22948. The guanylate cyclase inhibitor methylene blue (10 µM) on the other hand led to a shift of the dose response curves for AP II on RR and cGMP to hundredfold higher concentrations of AP II.
From the entirety of the results we conclude that:
- AP II inhibits RR by a direct action on JGC
- the inhibitory effect of AP II is mediated by cGMP

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KINETIC ANALYSIS OF ELECTROLYTE CONCENTRATION CHANGES IN PORTAL VEIN AND ARTERIAL BLOOD DURING THE ABSORPTION OF WATER IN THE ALERT RAT

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Intraduodenal injections of water (0.5 and 1% BW) were applied during continuous and sumultaneous registrations of total electrolyte concentration in ultrafiltrates of portal vein and arterial blood of alert rats. The ensuing curves were analysed in a computer program using a 3- or 4-compartment model suggested by DOST. The compartments represent in series: 1. gut lumen, 2. unstirred layer, 3. dead space of measuring system, 4. ultrafiltrate as representant of intravascular space. The corresponding rate constants for transport from 1 to 4 are k1-k3, k4 being the elimination constant. k1 and k2 could be evaluated experimentally. C, the parameter denoting initial condition and k3 and k4 were varied until a best fit (<=5%) to 5 actual values was achieved. This was done for arterial concentrations and for course of arteriovenous difference (AVD). Extreme examples for AVD were:

C mmol	k3 min^{-1}	k4 min^{-1}	Δmax mmol	Free H_2O in blood, % of dose	Initial distribution space
15.1	.82	.26	8.8	164	33.6
2.1	.31	.15	1.0	54	83.3

Neither differences of portal flow rate nor of unstirred layer thickness could explain this variability. It was concluded that retardation of osmotic equilibration between blood and gut was due to tight intercellular junctions leading to water accumulation in the tissues, whereas wide junctions cause accumulation of back-diffusing electrolytes.

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