ADRENAL BIOSYNTHESIS OF DEHYDROISOANDROSTERONE SULFATE

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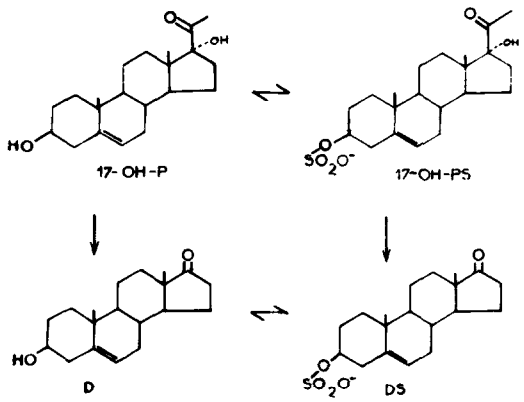
The "direct" metabolism of steroid sulfates (Baulieu et al,1963,1964) has been demonstrated after injection of H^3-3β-hydroxy 5-androstene precursor S^{35}-sulfates to humans and isolation of urinary H^3-3β-hydroxy 5-androstene metabolite S^{35}-sulfates. A problem arising from the recently demonstrated (Baulieu 1960) adrenal biosynthesis of dehydroisoandrosterone (3β-hydroxy 5-androstene 17-one, D) sulfate is to determine if D is formed as a free compound, more specifically from 3β, 17-dihydroxy-5-pregnene-20-one (17P) (Lieberman and Teich, 1955) and then sulfated, or if it derives "directly" from another 3β-hydroxy-Δ^5-steroid sulfate. D, 17P, 3β-hydroxy-5-pregnene-20-one (P) have been demonstrated as easily sulfatable by adrenal tissue in this and other laboratories. Using S^{35}-sulfates, Lieberman and colleagues (Calvin 1963, 1964, Roberts 1964) showed that adrenal enzymes can transform P sulfate directly to 17P sulfate and P sulfate and cholesterol sulfate to D sulfate. Taking into consideration that 1) cholesterol sulfate, still not isolated from the blood, was not obtained by liver (Nose and Lipman 1958) and adrenal (Lebeau, unpublished) preparations; 2) the relative efficiency for making D sulfate from free or sulfate precursors is unknown; 3) the final step of the direct sulfate pathway (probably 17P sulfate to D



sulfate) has not been readily demonstrated, the problem, then, is to assign its physiological significance to the "direct" sulfate pathway in biosynthesis of D sulfate.

7α-H^3-17P and S^{35}-SO_4H_2 were used for making the doubly labeled sulfate (S.A.: H^3 14 mc/μm, S^{35} 1.2 mc/μm) with an adrenal sulfokinase preparation (Lebeau

experiments n°	I	II	III
compounds incubated :	H^3-17P S^{35}-sulfate	H^3-17P	C^{14}_3-D H^3-D sulfate
H3-D	0.1	10	15
C14-D	-	-	30
H3-17P	≤ 2.5	30	-
H3-D sulfate	5	50	70
D S35-sulfate	3	-	-
C14-D sulfate	-	-	60
H3-17P sulfate	15	10	-
17P S35-sulfate	15	-	-

STEROIDS ISOLATED AFTER ADRENAL INCUBATION

(percent yield from the starting material)

and Baulieu 1963). Two incubation experiments, with H^3-17P S^{35}-sulfate (I) and H^3-17P (S.A. 15 mc/μm)(II) respectively, were run, both with adrenal tumor slices, according to Weliky and Engel (1962). A control expe-

riment with C^{14}-D and H^3-D sulfate was run at the same time (III). Recoveries were checked by using C^{14}-compounds when possible, and the trace contents in D or D sulfate of the starting material thoroughly analyzed by taking them through the procedure used for the incubates.

The results indicate the sulfation of D and 17P, some split of D sulfate, and a much better yield of D sulfate from 17P than from 17P sulfate. The increase of H^3/S^{35} ratio in D sulfate after H^3-17P S^{35}-sulfate incubation indicates, either a split of H^3-17P S^{35}-sulfate to H^3-17P followed by formation of H^3-D and then sulfation, and/or a split of formed H^3-D S^{35}-sulfate to H^3-D followed by resulfation. In any case, most of the D sulfate formed from 17P sulfate comes through the sulfate pathway. These in vitro experiments analyzing immediate precursors of D sulfate, show that adrenal "desmolase" can act on a steroid sulfate, as suggested by Lieberman's work. However, the better yield of D sulfate formation from 17P than from its sulfate implicates further studies in order to define the actual physiological pathways.

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