The Presence of Isoprenoid Compounds in Human Organs *

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All tissues and cells so far investigated in various experimental systems contain isoprenoid substances, mainly dolichol.[1] Subcellular fractionation has demonstrated that dolichol is a constituent of all membranes indicating its role in the structure itself. While the function of dolichol is not yet clearly established, dolichyl-P has a well known role in the glycoprotein synthesis. Some preliminary data indicated that human tissues could contain much higher amounts of isoprenoid substances than organs of various experimental animals. Organs of chicken, pig, rat, rabbit and bovine origin have a dolichol content in the range of 10–150 μg/g wet weight. In this study we had the aim to analyze the polyisoprene pattern of human tissues in order to obtain some possible information about the functional implication of these substances.

Organ material was removed from diceased patients around the age of 70, within 2 d after death. Histological investigation was performed to exclude tissues with major pathological changes. Tissue homogenates were extracted and purified by chromatography as described earlier.[2] Alkaline hydrolysis was applied for removal of phospholipids. Dolichol and dolichyl-P were quantitated by high performance liquid chromatography (HPLC).

Since autopsy material was used in the investigations one can always question the results in view of the possible action of degradative enzymes. We have compared autopsy samples from various organs with biopsy and surgical materials and have analyzed both the dolichol and the dolichyl-P content. The results demonstrated that no degradation of polyprenols occurred in the autopsy material; therefore, the results we obtained could be considered as reliable. The dolichol content of human organs is shown in Table 1. The endocrine organs such as adrenal, pituitary gland, testis, thyroid gland and also pancreas have a dolichol content between 1.5 and 7.0 mg/g. The lipid content in other organs is lower but still

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Table 1. Dolichol content in human organs. Human autopsy material was extracted with lipid solvents and purified by DEAE-Sephadex chromatography. After alkaline hydrolysis and extraction, dolichol was quantitated by HPLC.[2] The values represent the mean of 6–11 measurements.

Tissue	Dolichol μg/g wet weight
Adrenal gland	1598
Brain	279
Heart	185
Kidney	192
Liver	452
Lung	247
Pancreas	1440
Pituitary gland	7168
Small intestine	153
Spleen	114
Testis	1542
Thyroid gland	1960

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Table 2. Dolichyl-P content in human organs. The lipid was dephosphorylated prior to HPLC measurements. The acid hydrolysis was conducted in the presence of HCl (0.3 M), first at 20 °C for 40 min, and then by an incubation at 65 °C for 45 min. The total dolichol represents the sum of the free alcohol (Table 1) and the amount of dolichyl-P. The values represent the mean of 5–7 measurements.

	Dolichyl-P, μg per g wet weight		
	without acid hydrolysis	with acid hydrolysis	% of total dolichol
Adrenal gland		51.1	3.1
Heart	6.5	13.1	6.6
Kidney		12.7	6.2
Liver	6.1	18.8	4.0
Lung	9.7	13.3	5.1
Pancreas	9.4	30.9	2.1
Pituitary gland		283.1	3.8
Spleen	1.8	3.3	2.8
Testis	68.3	72.7	4.5
Thyroid gland	9.4	13.8	0.7

Table 3. Composition of dolichol and dolichyl-P in human tissues. The individual dolichols and dolichyl-P were separated and quantitated by HPLC using C18 reversed phase column. The values represent the mean of 5 experiments.

	Composition (% of total)				
Tissue	D17	D18	D19	D20	D21
Dolichol					
Aorta	2	32	55	10	1
Liver	4	12	49	27	8
Stomach	1	22	53	23	1
Dolichyl-P					
Aorta	3	20	47	23	7
Liver	1	28	42	26	3
Stomach	2	30	48	18	2

considerable. The high content in the pituitary gland is quite surprising. We have analyzed the phospholipid and neutral lipid composition of this organ and found that even the total phospholipids (6 mg/g) are below the dolichol value. Subcellular fractionations suggested that dolichol is present in all membranes but considerable enrichment could be observed in the lysosomes. To find out more about the structural and functional role of this lipid the pituitary gland seems to be a good starting point.

The amount of dolichyl-P in various tissues is of great importance since the polyprene is an essential intermediate in the establishment of the *N*-glycosidically linked oligosaccharide chains. A great deal of experimental evidence is also available, demonstrating that the phosphorylated intermediate is the rate limiting factor in several glycosyl transferase reactions.[3] The amount of dolichyl-P in the different organs is variable but never more than a few per cent (Table 2). In most cases, acid hydrolysis prior to HPLC determination increases the dolichyl-P amount considerably. This means that a large part of the intermediate is glycosylated during *in vivo* conditions. It is not clear, however, if the whole

dolichyl-P pool participitates in the transfer of all monosaccharides or if there is some specialization.

The dolichol fraction in various human tissues – composed of a family of polyprenes, among them the dolichol with 19 isoprene residues – is dominating (Table 3). The amount of D 18 and D 20 is smaller, while D 17 and D 21 are minor components. This general pattern, however, displays a certain variation concerning the per cent distribution. The distribution of individual polyprenes follows a similar pattern, in the case of dolichyl-P, and here again an internal variation is observed. The variation in the dolichyl-P pattern is not the same as it is with the free alcohol; this emphasizes that the synthesis of free alcohol and its phosphorylated form are regulated by different mechanisms.

The results described above demonstrate that the high content of dolichol is a universal property of human organs and tissues. Obviously, the age may be an important factor since in some tissues there is a tendency toward increase with age.[4] Dietary conditions do not appear to influence the dolichol content. The fact that the free alcohol and its phosphorylated derivative are not broken down in the autopsy material provides a possibility to investigate the amount, structure and distribution of polyprenol in human organs and tissues. There are indications that pathological conditions change the amount and composition of dolichol, this may explain some functional anomalies.[5] The distribution and composition of dolichyl-P shows no relation to that of dolichol, raising the question whether or not an interrelationship between these compounds is present. It is probable that dolichol and dolichyl-P are regulated by separate biosynthetic mechanisms.

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