Metabolism of orally administered *rac*-1-*O*-[1'-^{14}C]dodecylglycerol and nutritional effects of dietary *rac*-1-*O*-dodecylglycerol in mice

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Abstract The metabolism of orally administered *rac*-1-*O*-[1'-^{14}C]dodecylglycerol was investigated in mice. The substrate was rapidly absorbed in the intestine and then incorporated into ether glycerolipids of various organs,and tissues in high proportions. In intestine and liver, however, large amounts of *rac*-1-*O*-[1'-^{14}C]dodecylglycerol were catabolized by oxidative cleavage of the ether bond followed by degradation of the radioactive cleavage product, i.e., lauric acid, to water-soluble metabolites that were excreted in the urine at a fast rate. The feeding of a *rac*-1-*O*-dodecylglycerol-containing diet (1 g *rac*-1-*O*-dodecylglycerol/kg body weight × day) given over a period of 4 weeks did not significantly alter body weights or organ weights of mice. Analysis of total lipids revealed that high proportions of the substrate were incorporated into ether lipids of all organs and tissues during the feeding period, generally accompanied by a remarkable increase in saturated acyl moieties and a concomitant decrease of linoleoyl moieties of total lipids. Yet, 4 weeks after removal of the *rac*-1-*O*-dodecylglycerol-containing diet, the lipids of murine organs and tissues showed a close resemblance to those of the control group. — **Weber, N.** Metabolism of orally administered *rac*-1-*O*-[1'-^{14}C]dodecylglycerol and nutritional effects of dietary *rac*-1-*O*-dodecylglycerol in mice. *J. Lipid Res.* 1985. **26:** 1412-1420.

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Ether glycerolipids having a 1-*O*-dodecylglycerol backbone are minor but ubiquitous substituents of mammalian cells (1-3). Recently, it was found that *rac*-1-*O*-dodecylglycerol has excellent bacteriostatic effects (4, 5). Moreover, 1-*O*-dodecylglycerol is a mild nonionic surfactant (6) qualitatively similar to monoglyceride surfactants that are frequently used as food emulsifiers (7-9). Little is known, however, regarding the use of *rac*-1-*O*-dodecylglycerol as a food additive (10, 11). In the current study, the metabolism and nutritional effects of this substance in mice were, therefore, investigated.

MATERIALS AND METHODS

Chemicals

[1-^{14}C]Lauric acid (1.34 GBq/mmol) was purchased from Amersham Buchler (Braunschweig, West Germany). Methyl [1-^{14}C]laurate was derived from the fatty acid by the reaction with diazomethane. [1-^{14}C]Dodecanol (37 MBq/mmol) was prepared from methyl [1-^{14}C]laurate by reduction with lithium aluminium hydride (12) and purified by TLC on silica gel H (E. Merck, Darmstadt, West Germany) with hexane-diethyl ether (80:20, vol/vol). *rac*-1-*O*-[1'-^{14}C]Dodecylglycerol (37 MBq/mmol) was prepared from [1-^{14}C]dodecanol and *rac*-isopropylideneglycerol (EGA-Chemie, Steinheim, West Germany) by the method of Baumann and Mangold (13). The radiochemical purity of the labeled dodecylglycerol was better than 98%. *rac*-1-*O*-Dodecylglycerol was synthesized by the same procedure starting from dodecan-1-ol (E. Merck).

Acetylations were carried out in acetic anhydride-pyridine 1:1 (vol/vol) at room temperature. Methyl esters derived from acyl lipids were prepared by transmethylation (14).

Animals

Female NMRI mice (Winkelmann Versuchstierzucht, Borchen, West Germany), weighing 20-25 g, were used. The animals were maintained at 22°C and 60% humidity and given feed and water ad libitum throughout the experiment.

Abbreviations: TLC, thin-layer chromatography; GLC, gas-liquid chromatography.

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Administration of *rac*-1-*O*-[1'-^{14}C]dodecylglycerol

Labeled dodecylglycerol (37 MBq/mmol) (148 kBq/animal) was administered by stomach tube in 0.05 ml of a 5% aqueous dispersion of phosphatidylcholines ('Essentiale-Nattermann,' A. Nattermann, Cologne, West Germany) to three animals fasted for 12 hr. Distilled water, 2 ml/animal, was injected intraperitoneally 1 hr after administration of the radioactive substrate in order to get larger volumes of urine.

Feeding experiment

The mice were weighed and divided into two groups of eight animals each. Group 1 was given 'Altromin' standard (Altromin International, Lage, West Germany) and group 2 received the same diet containing 4 g of *rac*-1-*O*-dodecylglycerol/kg for 4 weeks. Every week the total food consumption and the weight gain of each group were determined. Feces of both groups were collected over a period of 24 hr every week. Three additional animals that had received the diet with *rac*-1-*O*-dodecylglycerol for 4 weeks were given the 'Altromin' standard diet for a further period of 4 weeks.

Extraction procedures

The animals of the metabolic study were killed by cervical dislocation 2 hr after administration of the radioactive substrate. Urine, about 2 ml/animal, was collected immediately. The animals were exsanguinated by section of the aorta. Organs and tissues (stomach, intestine, liver, kidneys, heart, lungs, spleen, brain, femoral muscle tissue, and adipose tissue from the perirenal region) from three animals were quickly removed from the carcasses and weighed. Each type of tissue was pooled and homogenized in 4 ml of chloroform–methanol 1:2 (vol/vol) per 1 g of tissue using an Ultra Turrax blender (IKA-Werke, Staufen, West Germany). After centrifugation, pellets were reextracted twice with chloroform–methanol 2:1 (vol/vol). Radioactivity was determined by liquid scintillation counting in aliquots of total extracts of each tissue as well as in aliquots of pellets. Total extracts were diluted with chloroform and water and the phases were separated by centrifugation (15). Radioactivity in both chloroform and water phases was determined by liquid scintillation counting.

At the end of the feeding period, the animals of the nutritional experiment were killed and organs and tissues were rapidly dissected as described above. Subsequently, the total lipids were extracted according to an established procedure (15).

Determination of radioactivity

Solutions were mixed with 'Aquasol-2' (NEN-Chemicals, Dreieich, West Germany) and radioactivity was determined by liquid scintillation counting in a Tri-Carb C 2425 Instrument (Packard Instruments Company, Downers Grove, IL). The distribution of radioactive fractions on thin-layer chromatograms was determined with a Berthold Automatic TLC-Linear Analyzer LB 282 in combination with a data acquisition system LB 500 (BF-Vertriebsgesellschaft, Wildbad, West Germany). Radio gas–liquid chromatography was carried out in a Perkin-Elmer F 22 Instrument (Perkin-Elmer Bodenseewerk, Überlingen, West Germany) equipped with a thermal conductivity detector, in combination with a Packard Gas Proportional Counter Model 894 (Packard Instruments Company). Peak areas were measured with a Spectra Physics Minigrator System (Spectra Physics, Darmstadt, West Germany). Methyl esters of radioactive fatty acids were analyzed on a glass column, 1.8 m × 4 mm, packed with 10% Silar 5 CP on Gas Chrom Q, 100–120 mesh (Applied Science Laboratories, State College, PA) with helium (40 ml/min) as carrier gas; the temperature was programmed from 180 to 230°C, 2°C/min. Separations of labeled alkyldiacetylglycerols were carried out on a glass column, 1.8 m × 3 mm, packed with 10% OV-101 (Applied Science Laboratories) using a temperature program from 220–260°C (4°C/min) and then kept at 260°C for 15 min (16).

Gas–liquid chromatography

GLC was carried out in a Perkin-Elmer F 22 Instrument equipped with flame ionization detectors. Analyses of fatty acid methyl esters and alkyldiacetylglycerols were carried out as described above. Alkyl acetates were separated on Silar 5 CP using a temperature program from 160–235°C (4°C/min) and then kept at 235°C for 20 min. Peak areas were determined using a Spectra Physics Autolab IV B system (Spectra Physics).

Analysis of radioactively labeled lipids

The total lipids of each tissue were fractionated on layers of silica gel H using chloroform–methanol–water 65:25:4 (vol/vol) (17) and the distribution of radioactivity in the various fractions was determined with the thin-layer chromatogram scanner. The fractions of choline glycerophospholipids, ethanolamine glycerophospholipids, and less polar lipids were eluted from the adsorbent with chloroform–methanol–water 1:2:0.8 (vol/vol) (15). Choline glycerophospholipids and ethanolamine glycerophospholipids were purified by rechromatography using the same solvent system as described above.

Choline glycerophospholipids were identified by co-chromatography of aliquots with a standard and by staining with Dragendorff reagent (17) and Dittmer-Lester reagent (18); ethanolamine glycerophospholipids were identified by co-chromatography of aliquots with a standard and by staining with ninhydrin reagent (19) as well as Dittmer-Lester reagent (18).

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The less polar lipids were further fractionated on layers of silica gel H using hexane–diethyl ether–acetic acid 80:20:1 (vol/vol) (20) twice, and the distribution of radioactivity in the various lipid classes was determined as described above. The fractions containing alkylglycerols, diacylglycerols plus alkylacylglycerols, triacylglycerols, and alkyldiacylglycerols were identified by co-chromatography with standards. The lipid fractions were each isolated and eluted from the adsorbent with water-saturated diethyl ether.

The fractions of choline glycerophospholipids, ethanolamine glycerophospholipids, diacylglycerols plus alkylacylglycerols, and alkyldiacylglycerols from each tissue were subjected to hydrogenolysis with $LiAlH_4$ (12). The resulting mixtures of long-chain alcohols and alkylglycerols were separated on layers of silica gel H with hexane–diethyl ether 2:8 (vol/vol) and identified by co-chromatography with standards; the distribution of radioactivity was determined by scanning. Long-chain alcohols and alkylglycerols were isolated and acetylated. The resulting alkylacetates and alkyldiacetylglycerols were purified by TLC on layers of silica gel H with hexane–diethyl ether 3:2 (vol/vol). Labeled triacylglycerols isolated from intestine and liver were each transmethylated (14); the resulting fatty acid methyl esters were purified by TLC on layers of silica gel H with hexane–diethyl ether 8:2 (vol/vol) and identified by co-chromatography with standards. Labeled alkylacetates, alkyldiacetylglycerols, and methyl esters of fatty acids were analyzed by radio-GLC as described above.

In order to determine radioactive 1-alkenyl moieties, the fraction of alkylglycerols derived from ethanolamine glycerophospholipids by hydrogenolysis with $LiAlH_4$ was treated with concentrated HCl in diethyl ether (21). The reaction mixture, i.e., long-chain aldehydes plus 1-*O*-alkylglycerols, was subjected to $LiAlH_4$ reduction and the resulting long-chain alcohols and 1-*O*-alkylglycerols were fractionated by TLC as described above; the distribution of radioactivity was determined by scanning.

Analysis of lipids of the feeding experiment

The total lipids extracted from organs and tissues of mice from groups 1 and 2 of the feeding experiment were isolated as described above. Aliquots of total lipids of the various organs and tissues were subjected to hydrogenolysis with $LiAlH_4$ and the resulting long-chain alcohols were acetylated. Alkylacetates were purified by TLC and analyzed by GLC as described above. 1-*O*-Alkylglycerols plus 1-*O*-(1'-alkenyl)glycerols, derived from total lipids, were treated with conc. HCl in ether and the reaction products were further derivatized and purified as described above. The resulting alkylacetates derived from 1-alkenyl moieties and the alkyldiacetylglycerols were analyzed by GLC as described above.

Statistical analysis

Statistical evaluation of differences between groups of body weights and organ weights was performed using the Student's *t*-test for unpaired values.

RESULTS AND DISCUSSION

Metabolism of *rac*-1-*O*-[1'-^{14}C]dodecylglycerol

Recently, it was demonstrated that *rac*-1-*O*-dodecylglycerol is a highly potent antibacterial agent (4, 5) having mild surfactant activity (6, 7). In order to study the metabolism of this substance that may be useful as an antibacterial food additive, radioactively labeled *rac*-1-*O*-dodecylglycerol was orally administered to mice.

Radioactivity was measured in extracts of various tissues including blood as well as in urine of mice 2 hr after oral administration of radioactive *rac*-1-*O*-dodecylglycerol and the distribution of radioactivity was determined in chloroform and water phases (**Table 1**). This procedure allows an assessment of the proportions of labeled lipophilic and hydrophilic metabolites from the distribution of radioactivity in extracts from tissues between the organic solvent and water. Stomach, intestine, heart, and liver contained the highest levels of radioactivity. Large proportions of radioactivity that were not extractable with organic solvents were found in urine. Moreover, high levels of radioactivity were detected in aqueous phases of extracts from intestine, liver, kidneys, and blood. These data indicate a high rate of

TABLE 1. Radioactivity in extracts from various tissues and in urine of mice 2 hr after oral administration of *rac*-1-*O*-[1'-^{14}C]dodecylglycerol and distribution of radioactivity in chloroform and water phases

Tissue		Distribution of Radioactivity[a] % in CHCl3	Distribution of Radioactivity[a] % in H2O
	dpm/100 mg		
Stomach	172,000	82	18
Intestine	36,500	52	48
Liver	12,400	52	48
Kidneys	10,200	36	64
Heart	16,800	90	10
Lungs	7,300	75	25
Spleen	6,500	78	22
Muscle	2,700	67	33
Adipose tissue	5,700	82	18
Brain	2,800	66	34
Blood (dpm/100 μl)	1,800	36	64
Urine (dpm/100 μl)	85,200	Tr[b]	>99

[a] From three animals.
[b] Tr, trace (<1%).

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degradation to radioactive water-soluble metabolites of *rac*-1-*O*-[1'-^{14}C]dodecylglycerol in these organs. The results given in Table 1 are in good agreement with our findings on the extensive degradation to water-soluble products of lauroyl moieties derived from dodecyl β-glycosides by oxidizing enzyme systems of cells (22). Similarly, larger proportions of water-soluble catabolic products were observed to be formed in the intestine of rats fed 1,2-di-*O*-octylglycerol rather than in those fed 1,2-di-*O*-alkylglycerols having long-chain alkyl groups (23). Relatively low proportions of radioactive water-soluble metabolites were found in extracts of heart.

Table 2 records the distribution of radioactivity in fractions of glycerolipids of various murine organs and tissues 2 hr after oral administration of labeled *rac*-1-*O*-dodecylglycerol. It is evident from the data listed in Table 2 that high proportions of radioactivity were incorporated predominantly into diradylglycerophosphocholines and alkyldiacylglycerols. Appreciable labeling of ethanolamine glycerophospholipids and diradylglycerols was also observed in most organs and tissues. Large amounts of radioactively labeled substrate were found in stomach indicating that only small amounts of the substrate were metabolized in this organ. Similar results were observed previously with alkyl β-glycosides as substrates (22). Substantial proportions of radioactive dodecylglycerol were also detected in the lipids of brain. Remarkably high levels of labeled triacylglycerols were detected exclusively in intestine and liver. The relatively high amounts of these labeled acyl glycerolipids suggest that the ether bond of the substrate was oxidatively cleaved predominantly in intestine and liver.

Table 3 shows the distribution of radioactivity in alkyl and acyl moieties of glycerolipids from murine organs and tissues 2 hr after oral administration of *rac*-1-*O*-[1'-^{14}C]dodecylglycerol. The data summarized in Tables 2 and 3 indicate that high proportions of ether lipids, predominantly alkylacylglycerophosphocholines containing radioactive alkyl moieties, were formed in all tissues. Labeled alkyl moieties exclusively consisted of [^{14}C]dodecyl groups as shown by radio-GLC analysis. These findings agree with observations on the formation of complex ether lipids in rat intestinal mucosa starting from 1-*O*-alkylglycerols as precursors (24). Remarkably large proportions of radioactive acyl moieties derived from dodecyl moieties by oxidative cleavage of the ether bond occurred in all labeled lipids isolated from liver as compared to other tissues. In all organs and tissues, diradylglycerophosphoethanolamines generally contained higher levels of radioactive acyl moieties than the corresponding choline glycerophospholipids; remarkably large proportions of labeled acyl moieties (>70%) were found in ethanolamine glycerophospholipids of liver. These findings again support the view that the substrate was oxidized in liver at a fast rate.

These results, taken together with the data from Tables 1 and 2, indicate that *rac*-1-*O*-dodecylglycerol was oxidized preferentially in intestine and liver rather than in other organs and tissues. Our data agree with earlier findings that intestine and liver of various mammals have the highest enzymatic activites for oxidative cleavage of ether bonds as compared to other tissues (25, 26). In addition, the tetrahydropteridine-dependent alkyl monooxygenase of rat liver cells has been found to attack both enantiomers of *rac*-1-*O*-dodecylglycerol with the same specificity (27). Moreover, it is well known that unesterified alkylglycerols are the best accepted substrates for this enzyme in the degradation of ether lipids (26). These data agree with

TABLE 2. Distribution of radioactivity in glycerolipid classes of various murine tissues 2 hr after oral administration of *rac*-1-*O*-[1'-^{14}C]dodecylglycerol

	Distribution of Radioactivity[a] in						
Tissue	Diradylglycerophosphocholines	Diradylglycerophosphoethanolamines	Other Polar Lipids	Dodecylglycerol	Diradylglycerols	Triacylglycerols	Alkyldiacylglycerols
	%						
Stomach	6	Tr[b]	Tr	82	5	Tr	6
Intestine	35	15	Tr	18	11	4	17
Liver	37	13	2	6	7	13	22
Kidneys	60	6	6	6	3	Tr	19
Heart	60	9	Tr	4	8	Tr	19
Lungs	62	7	Tr	4	11	Tr	16
Spleen	57	7	Tr	3	9	Tr	24
Muscle	59	9	4	4	7	Tr	17
Adipose tissue	40	11	4	7	8	Tr	30
Brain	21	11	3	39	16	Tr	10
Blood	39	3	5	7	8	Tr	38

[a] From three animals.
[b] Tr, trace (<1%).

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TABLE 3. Distribution of radioactivity in alkyl and acyl moieties of glycerolipids from murine organs and tissues 2 hr after oral administration of *rac*-1-*O*-[1'-^{14}C]dodecylglycerol

	Distribution of Radioactivity[a] in Radyl Moieties of Various Glycerolipids							
	Diradylglycero-phosphocholines		Diradylglycerophos-phoethanolamines		Diradylglycerols		Alkyldiacyl-glycerols	
Tissue	Alkyl[b]	Acyl	Alkyl[c]	Acyl	Alkyl[b]	Acyl	Alkyl[b]	Acyl
				%				
Stomach	96	4	84	16	97	3	94	6
Intestine	90	10	86	14	88	12	92	8
Liver	45	55	28	72	65	35	85	15
Kidneys	90	10	73	27	82	18	93	7
Heart	98	2	93	7	97	3	99	Tr[d]
Lungs	92	8	78	22	91	9	98	2
Spleen	96	4	91	9	98	2	97	3
Muscle	97	3	91	9	94	6	95	5
Adipose tissue	97	3	92	8	93	7	99	Tr
Brain	66	34	83	17	95	5	97	3
Blood	86	14	81	19	72	28	98	2

[a] From three animals.
[b] Consisting exclusively of radioactive 1-*O*-dodecyl moieties.
[c] [^{14}C]Dodecyl moieties containing traces of 1-alkenyl groups.
[d] Tr, trace (<1%).

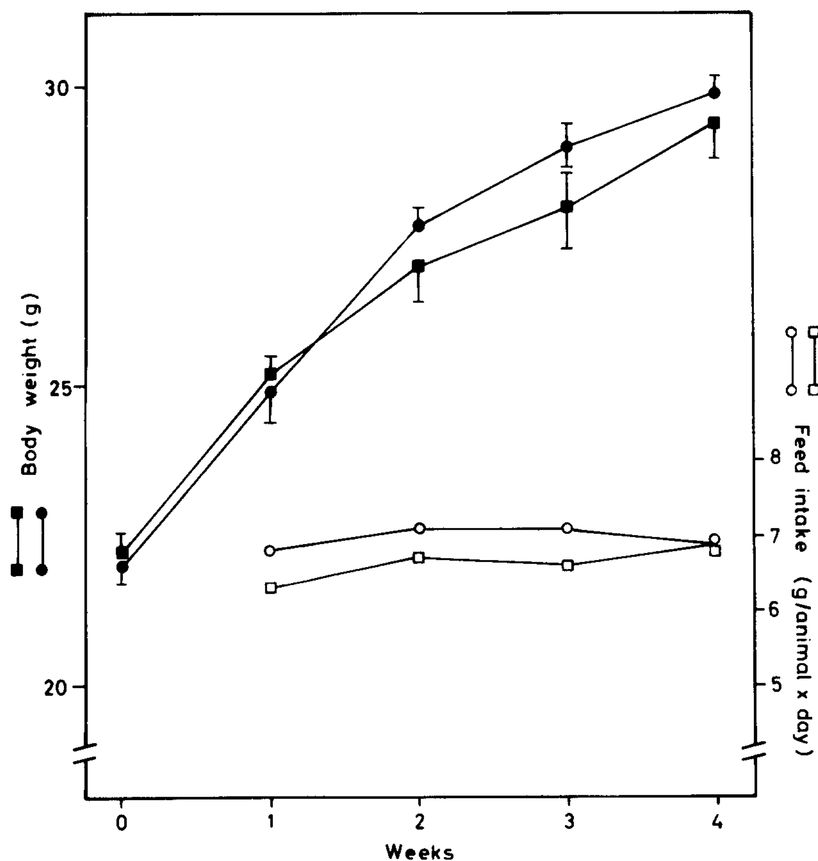

Fig. 1. Effects of standard diet and *rac*-1-*O*-dodecylglycerol-containing diet administered for 4 weeks on body weight and food intake of mice. Values of body weight are mean ± SEM, n = 8; there are not statistically different values, $P > 0.2$; values of food intake are mean. Standard diet (●—●, ○—○); *rac*-1-*O*-dodecylglycerol-containing diet (■—■, □—□).

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findings of the present study that the radioactivity in the fraction of dodecylglycerol decreased from more than 80% in the stomach to less than 20% in intestine and 6% in liver.

The products of oxidation were, however, somewhat different in intestine and liver. High proportions of radioactive water-soluble metabolites were found in both organs (Table 1), but the glycerolipids of liver had additionally incorporated large amounts of labeled acyl moieties (Table 3). The findings reported here suggest that in intestine the substrate was predominantly catabolized to water-soluble compounds, such as carboxylic acids or amino acids. Radioactive acyl moieties that had been detected in glycerolipids, e.g., triacylglycerols, of intestine might be formed by oxidative cleavage of the ether bond of the substrate followed by chain elongation of the resulting lauric acid and/or by de novo synthesis from [^{14}C]acetate. This is evident from the analysis of methyl esters derived from triacylglycerols of intestine which were found to contain labeled lauroyl (74%), myristoyl (19%), and palmitoyl (7%) moieties. In liver, apart from substantial proportions of labeled water-soluble metabolites, large amounts of radioactive acyl moieties were detected in various glycerolipids, e.g., the label of triacylglycerols was found to be located exclusively in lauroyl moieties. All these observations indicate that the substrate was oxidized at a faster rate in liver than in intestine. Moreover, these results are consistent with our findings on the metabolism of ether lipids in rats after intravenous injection of *cis*-9-octadecenol (28) as well as with findings by others that medium-chain fatty acids are oxidized faster than long-chain fatty acids (29, 30).

Nutritional effects of dodecylglycerol

rac-1-*O*-Dodecylglycerol was found to have a minimum inhibitory concentration of 4 mg/l with gram-positive bacteria as test organisms (4, 5). We have given a 1,000-fold excess, i.e., 4 g of *rac*-1-*O*-dodecylglycerol/kg standard diet, to mice in order to study its suitability as a food additive.

Standard diet as well as dodecylglycerol-containing diet were administered to mice for 4 weeks and the effects on body weight and food intake were measured (**Fig. 1**). The average food consumption of dodecylglycerol-containing diet was 6-7 g per mouse and day, i.e., about 1 g of *rac*-1-*O*-dodecylglycerol/kg body weight and day; the food intake of both groups of animals was quite similar. The results given in Fig. 1 also show that the body weight of mice that

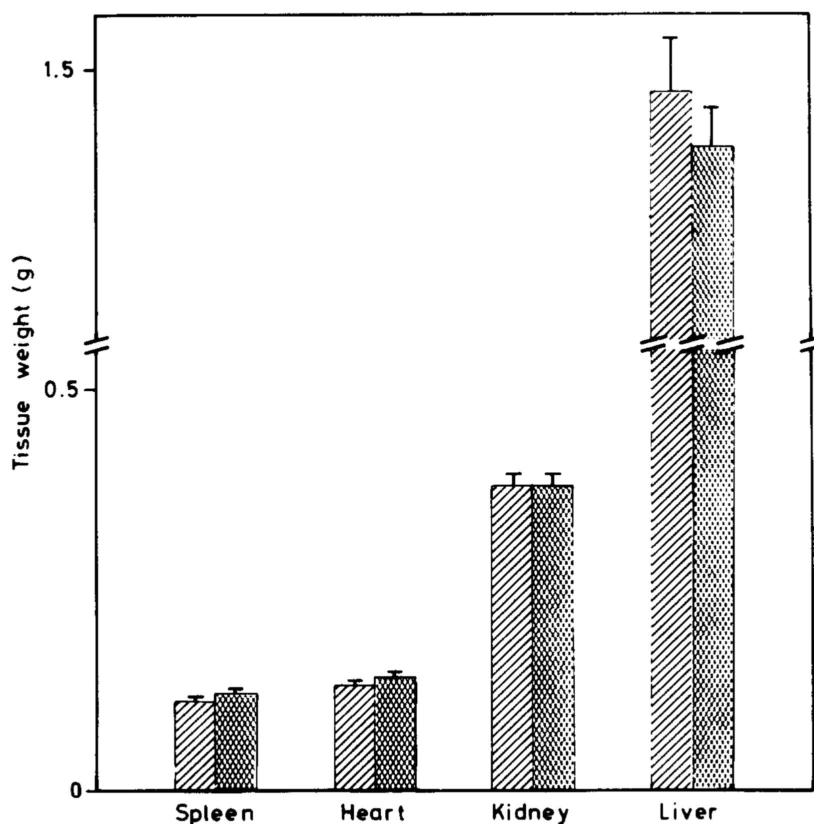

Fig. 2. Effects of standard diet and *rac*-1-*O*-dodecylglycerol-containing diet administered for 4 weeks on weights of various organs of mice. Values are mean ± SEM, n = 8; there are no statistically different values, $P > 0.2$. Standard diet, right column; *rac*-1-*O*-dodecylglycerol-containing diet, left column.

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had received the dodecylglycerol-containing diet was not statistically different ($P > 0.2$) from the body weight of the control group. A somewhat reduced food intake by the animals of the dodecylglycerol group at the beginning of the feeding period might be due to a slightly bitter taste of the substrate (as checked by the author) that was added to standard diet in relatively high concentration.

Fig. 2 shows the effects of standard diet and *rac*-1-*O*-dodecylglycerol-containing diet administered for 4 weeks on weights of spleen, heart, kidneys, and liver of mice. Obviously, the weights of the various organs of both groups of animals were not statistically different ($P > 0.2$).

The composition of alkyl moieties of ether lipids was studied in total lipids of murine organs and tissues as well as in feces. The 1-*O*-alkyl moieties of ether glycerolipids of all tissues of mice that had received standard diet consisted mainly of hexadecyl, octadecyl, and *cis*-9-octadecenyl groups, i.e., the common pattern of alkyl moieties in ether glycerolipids of mammalian cells (1). In addition to these alkyl moieties, high proportions of 1-*O*-dodecyl groups derived from both alkylacylglycerolipids and unmetabolized substrate were detected in total lipids of various tissues of mice that had received the *rac*-1-*O*-dodecylglycerol-containing diet (data not shown). Similar results were observed by other authors who had fed various 1-*O*-alkylglycerols containing long-chain alkyl moieties to rats (24, 31, 32). Only traces of ether glycerolipids containing 1-*O*-dodecyl moieties, however, were found in total lipids of most organs and tissues from animals that had received the *rac*-1-*O*-dodecylglycerol-containing diet over a period of 4 weeks and then the standard diet for an equal length of time. Small proportions of ether lipids containing 1-*O*-dodecyl moieties were detected only in adipose tissue and muscle. These results again support the view that ether lipids having a 1-*O*-dodecylglycerol backbone were catabolized in mammalian cells at a fast rate. Only trace amounts of 1-*O*-dodecylglycerol derived from both ether glycerolipids and unmetabolized substrate were detected in the total lipids of feces (10 μg of 1-*O*-dodecylglycerol/g of feces).

Analyses of alkylacetates derived from 1-alkenyl moieties of plasmalogens of total lipids revealed that the pattern of chain-lengths and degree of unsaturation of these substituents remained almost unchanged in plasmalogens of both experimental groups (data not shown). In contrast, the composition of acyl moieties was altered to

TABLE 4. Composition of acyl moieties in total lipids of various organs and tissues of mice that had received standard diet or *rac*-1-*O*-dodecylglycerol-containing diet over a period of 4 weeks

Tissue[b]	Type of diet	Composition of Acyl Moieties[a]						
		<16	16:0	16:1	18:0	18:1	18:2	>18[c]
					%			
Stomach	Standard	1	21	3	12	32	23	8
	Dodecylglycerol	1	25	4	13	30	19	8
Intestine	Standard	2	23	1	25	16	28	5
	Dodecylglycerol	1	30	1	30	20	14	4
Liver	Standard	1	28	2	17	20	25	7
	Dodecylglycerol	1	34	2	24	20	16	3
Kidneys	Standard	2	30	3	17	33	12	2
	Dodecylglycerol	1	31	3	21	25	15	4
Heart	Standard	1	27	2	33	17	16	4
	Dodecylglycerol	1	24	1	27	16	27	4
Lungs	Standard	2	39	6	13	26	11	3
	Dodecylglycerol	2	46	5	15	23	7	2
Spleen	Standard	2	32	3	17	28	13	5
	Dodecylglycerol	2	35	4	18	27	10	4
Brain	Standard	Tr[d]	30	1	28	33	2	6
	Dodecylglycerol	Tr	30	1	28	32	1	8
Adipose tissue	Standard	2	23	5	4	33	30	3
	Dodecylglycerol	2	24	5	4	36	26	3
Muscle	Standard	2	22	6	5	34	27	4
	Dodecylglycerol	3	24	6	6	35	22	4
Blood	Standard	2	33	2	16	20	21	6
	Dodecylglycerol	2	37	3	18	17	17	6

[a] Number of carbon atoms:number of double bonds.
[b] From eight animals.
[c] Including 18:3 and odd-numbered acyl moieties.
[d] Tr, trace (<1%).

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an appreciable extent in total lipids of various organs and tissues of mice that had received the *rac*-1-*O*-dodecylglycerol-containing diet for 4 weeks as compared to the control group (**Table 4**). A remarkable decrease of linoleoyl moieties was observed in total lipids of most tissues, especially intestine and liver, accompanied by an increase in saturated acyl moieties (16:0 plus 18:0). Only trace amounts of lauroyl moieties were detected in total lipids of the various tissues of both groups of animals.

It is conceivable that the modification of alkylacylglycerophosphocholines in cell membranes by dodecyl moieties may lead to a limitation of membrane functions. As a consequence, the regulation of the biophysical properties of membranous ether glycerophospholipids may be the reason for the shift of acyl groups that was detected predominantly in intestine and liver. These observations are in good agreement with findings on glycerophospholipids in animals (33) and plant cells (34) as well as with earlier studies on yeast cells (35) and artificial phospholipid membranes (36), indicating that permeability is markedly increased by substituting long-chain saturated radyl groups in phospholipids by short-chain or unsaturated radyl moieties. Further studies regarding these observations are in progress.

In summary, our data clearly show that *rac*-1-*O*-[1'-^{14}C]dodecylglycerol is converted to common intermediates of ether lipid metabolism in mammals (26, 28, 37, 38). Two major routes for the metabolism are observed: *a*) the substrate enters the pathway of ether glycerolipid biosynthesis as a direct precursor (24), and *b*) *rac*-1-*O*-dodecylglycerol as well as ether lipids derived therefrom are oxidized by the action of an alkyl monooxygenase (26). Lauric acid thus formed is not esterified into acyl glycerolipids to an appreciable amount, but further oxidized to acetate and other water-soluble compounds at a fast rate. Only trace amounts of the substrate are excreted in feces. Obviously, feeding of a *rac*-1-*O*-dodecylglycerol-containing diet does not significantly alter body weight and organ weights of mice.

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