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Fatty Acid Composition of Phospholipids in Epithelium and Stroma of Human Benign Prostatic Hyperplasia

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BACKGROUND. Although it is well known that prostatic 5α-reductase is active only in its membrane-bound form, rather limited information is available concerning the composition of cellular lipids in human BPH. Therefore, in the present study, the phospholipid fatty acid composition and content in epithelium and stroma of human BPH have been investigated for the first time.

METHODS. Phospholipids separated on TLC plates were methylated and fatty acid methyl esters were analyzed by capillary gas chromatography.

RESULTS. The fatty acid composition of total phospholipids was significantly different between epithelium and stroma. In particular, the percentage of oleic acid was significantly higher in epithelium as compared with stroma, whereas that of arachidonic acid was significantly lower in epithelium than in stroma. In addition, significant differences between epithelium and stroma were found in regard to the fatty acid composition of the main phospholipid subclasses. Another remarkable finding were the age-dependent changes of the fatty acid composition in human BPH.

CONCLUSIONS. This study shows that the fatty acid composition of phospholipids is significantly different between epithelium and stroma of human BPH. Furthermore, age-dependent alterations of the fatty acid composition were found. Further studies are needed to determine whether the endogenous hormonal milieu in the prostate modulates the fatty acid composition of the prostatic cells, as well as what impact such modulation could have on the properties of membrane proteins, i.e., enzymes like the 5α-reductase and receptors, which are thought to be affected by alterations in membrane fluidity or composition, or both. *Prostate 36:235–243, 1998.*

KEY WORDS: **fatty acid composition; phospholipids; human BPH; 5α-reductase**

INTRODUCTION

The activity and properties of a variety of membrane-bound enzymes have been demonstrated to be affected by changes of the membrane lipid composition [1,2]. At the cellular level of the human prostate, such a membrane-bound enzyme is the testosterone 5α-reductase [3,4]. It catalyzes the conversion of testosterone to 5α-dihydrotestosterone (DHT). DHT rather than testosterone is known to promote the normal prostatic growth. It most likely also gives rise to the development of the human benign prostatic hyperplasia (BPH) with age. Thus, as a result of its DHT-forming capacity, the testosterone 5α-reductase plays a central role regarding the normal and abnormal growth of the human prostate as well. This fact is underlined by finasteride, a 5α-reductase inhibitor, which in many patients induces a shrinkage of the enlarged prostate [5].

Earlier own studies have shown significant differences in the 5α-reductase activity between epithelium and stroma of the human prostate [3,6–8]. The highest

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DHT-forming capacity was found in epithelium of the normal prostate. With age, 5α-reductase activity in epithelium decreased gradually to a level that was found in stroma over the entire age range. The regulatory forces for those differences in 5α-reductase activity between epithelium and stroma of the human prostate are more or less unknown. In principle, they could operate both at the gene level, which is known to express at least two types of 5α-reductase, and at the posttranslational level.

To address the posttranslational level, of interest is the composition of the lipid environment, in which the 5α-reductase has to be embedded in order to gain its active state [4]. As a result, we recently analyzed the lipids in the BPH [9]. The phospholipids were found to be the major portion, followed by cholesterol and glyceride glycerols. Moreover, related to wet weight and to protein, the lipid concentration was two- to threefold higher in BPH epithelium than in stroma.

The present study deals with the content of fatty acids in various phospholipids extracted from the epithelium and stroma of human BPH. For the first time, our studies indicate significant differences in fatty acid composition of phospholipids between epithelium and stroma. Furthermore, age-dependent alterations of the fatty acid composition were found.

MATERIALS AND METHODS

Chemicals

Silica gel 60 H was obtained from Merck AG (Darmstadt, Germany), fatty acid methyl ester and phospholipid standards were purchased from Sigma Chemical Co. (St. Louis, MO). All other chemicals were obtained from Merck AG (Darmstadt, Germany), Serva (Heidelberg, Germany), and Boehringer (Mannheim, Germany).

Tissue Specimens

BPH tissue (n = 17) was obtained from patients undergoing suprapubic prostatectomy. In each instance, written consent for the use of tissue in this study was given. The age of the patients ranged from 57 to 83 years (mean 69 years). After surgical extirpation, the tissue was immediately chilled in ice-cold 150 mmol/L NaCl. All tissue specimens were divided into small pieces and stored in plastic tubes at −196°C. Representative sections from all tissue specimens were fixed in phosphate-buffered formalin, embedded in paraffin, and stained with hematoxylin and eosin (H&E). The histology of all examined prostates was that of glandular–stromal hyperplasia.

Tissue Preparation

The prostatic epithelium and stroma were separated according to Cowan et al. [10], with minor modifications as follows [11]. Aliquots of minced tissue were thawed in an ice bath and homogenized after addition of 4 vol (w/v) of 10 mM Tris buffer (2 mM EDTA, 5 mM NaN_3, 10 mM $MgCl_2 \cdot 6\ H_2O$, pH 7.5, at 4°C) with a Bühler homogenizer HO 4 (Bühler Laborgerätebau, Tübingen, Germany) in three periods of 30 sec at 8,000 rpm with cooling intervals of 30 sec. The homogenate was filtered through nylon gauze (pore size 150 μm) under slight suction. The filtrate was centrifugated at 1,800*g* for 10 min, the pellet resuspended in 4 vol of Tris buffer (w/v), and defined as epithelium. The tissue retained after filtration was homogenized in four volumes of Tris buffer (w/v) with an Ultra Turrax (Jahnke and Kunkel, Staufen, Germany) in three periods of 30 sec, with 30-sec cooling intervals. The homogenate was passed through nylon gauze under strong suction. The retained tissue was resuspended in four volumes of Tris buffer (w/v), and defined as stroma. Using this separation procedure, the relative purity of the epithelial as well as the stromal fraction was more than 83%; estimated by measuring acid phosphatase as a marker for epithelial cells and hydroxyproline as a marker for stromal elements in both tissue fractions [6,11–13].

Lipid Extraction and Fatty Acid Analysis

The pellets were subjected to lipid extraction according to the method of Folch et al. [14] using chloroform-methanol, 2:1 (v/v). The fatty acid concentration of total phospholipids were determined by adding before lipid extraction diheptadecanoyl-sn-glycero-3-phosphocholine of known weight as internal standard to all samples. The lipid extracts were dried under nitrogen and lipid residues were redissolved in chloroform:methanol, 2:1 (v/v) for further analysis. Phospholipids and neutral lipids of the total lipid extract were separated from each other on thin-layer chromatography (TLC) plates coated with silica gel 60 H. Plates were developed using a solvent system composed of petrolether:ethylether:acetic acid, 78:20:2 (v/v). The major classes of phospholipids were separated from each other on TLC plates coated with silica gel 60 H using a two-dimensional TLC system. The solvent system used in the first dimension was chloroform:methanol:water:acetic acid, 50:30:4:3 (v/v), and chloroform:methanol:25% ammonia, 65:25:6 (v/v) in the second dimension.

Phospholipids separated on TLC plates were methylated for 3 hr in a heating block at 80°C with 3 ml

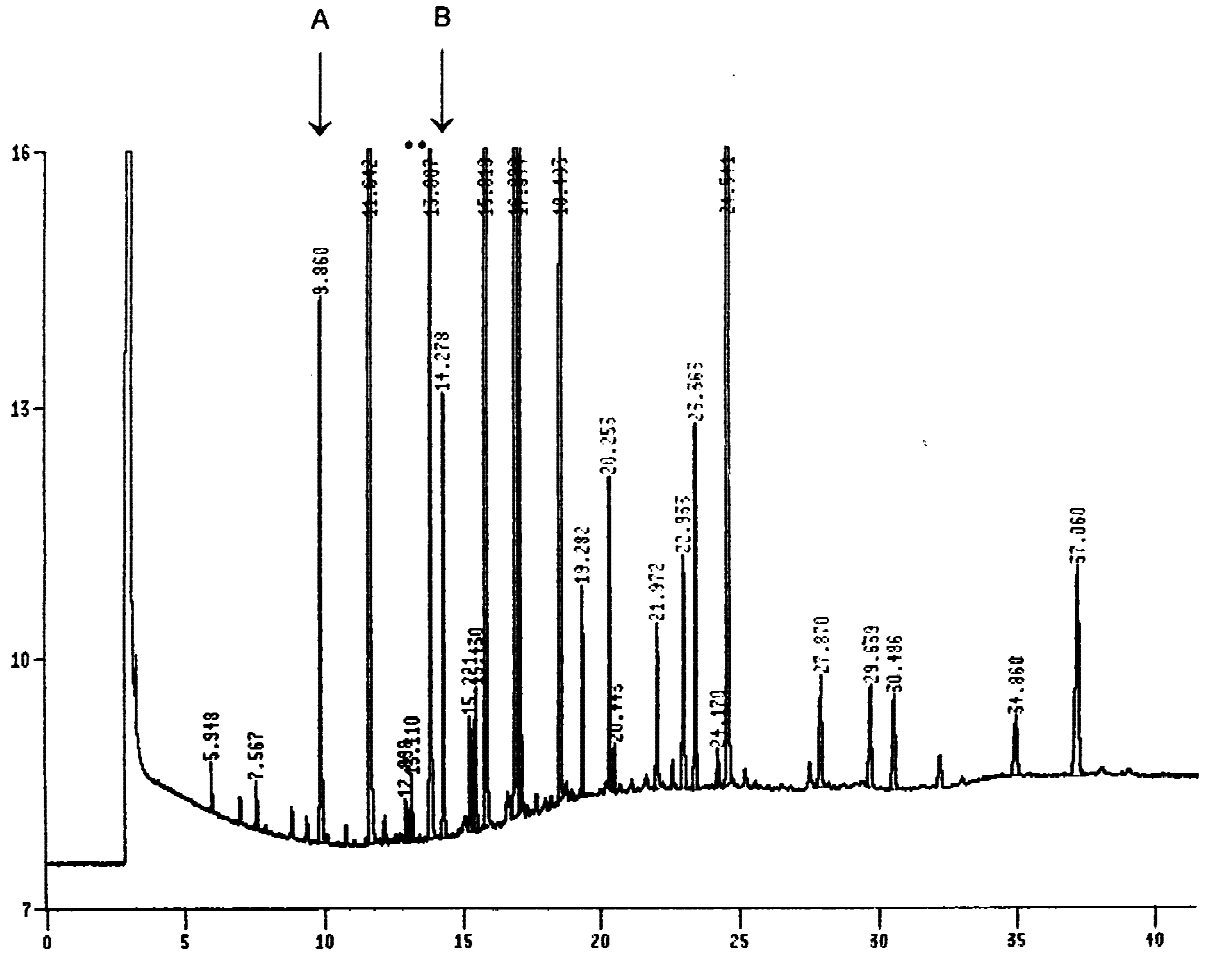

Fig. 1. Analysis of total phospholipid fatty acids in human BPH by gas chromatography. *Arrows*, the two unidentified peaks A (retention time: 9.860 min) and B (retention time: 14.278 min). ••, internal standard heptadecanoic acid C 17:0 (retention time: 13.807 min).

methanolic hydrochloric acid. Fatty acid methyl esters were extracted into n-hexane, taken to dryness under a stream of nitrogen, dissolved in 100 μl n-hexane, and then analyzed by capillary gas chromatography (GC) using a Hewlett Packard 5890 gas chromatograph. Samples were injected onto a 50-m wall coated open tubular (WCOT) fused silica, CP Sil 88, capillary column with 0.22-mm internal diameter. Helium was used as carrier gas and pre-column split ratio was 50:1. Rise in column temperature was programmed at 150°C for 10 min, then 5°C/min to 195°C. Total run time for each sample was programmed to 40 min. Injector temperature was fixed at 270°C and detector temperature was fixed at 300°C. Fatty acid methyl ester concentrations were determined using a flame ionization detector. Fatty acid methyl ester peaks were identified on the basis of retention times, using known standards under the same conditions. The fatty acids of total phospholipids were quantified by the comparison of the area (percentage) of each peak on the chromatogram with that of internal standard heptadecanoic acid C17:0 (Fig. 1) (retention time: 13.807 min) of known weight.

Other Methods

Acid phosphatase activity (EC 3.1.3.2) was measured by the method of Walter and Schütt [15]. The statistical significance of the means was determined by Student's *t*-test. The significance of age-related changes was determined by the Spearman rank correlation coefficient (R). $P < 0.05$ was considered significant.

RESULTS

Fatty Acid Composition of Total Phospholipids in Epithelium and Stroma of Human BPH

Analysis of the phospholipid fatty acids in epithelium and stroma by GC (Fig. 1) showed that the main fatty acids were palmitic (C16:0), stearic (C18:0), oleic

TABLE I. Fatty Acid Composition (mean ± SEM; n = 15) of Total Phospholipids in Epithelium and Stroma of Human BPH

	(wt%)		(nmol/g wet wt)	
Fatty acid	Eptihelium	Stroma	Epithelium	Stroma
C 14:0	0.3 ± 0.04	0.4 ± 0.03**	93 ± 21	47 ± 5*
A	2.7 ± 0.11	2.4 ± 0.12	212 ± 23[a]	57 ± 5**[a]
C 16:0	20.2 ± 0.24	19.4 ± 0.32	5,974 ± 506	1,894 ± 103**
C 16:1	0.5 ± 0.04	0.8 ± 0.06**	143 ± 15	81 ± 10**
B	2.0 ± 0.10	4.0 ± 0.10**	144 ± 11[a]	102 ± 7**[a]
C 18:0	14.0 ± 0.35	16.8 ± 0.29**	3,671 ± 274	1,481 ± 84**
C 18:1 (n-9)	21.8 ± 0.64	12.3 ± 0.18**	6,045 ± 609	1,102 ± 75**
C 18:1 (n-7)	3.0 ± 0.09	2.1 ± 0.07**	826 ± 92	184 ± 16**
C 18:2	8.6 ± 0.25	7.5 ± 0.20**	2,290 ± 171	682 ± 54**
C 18:3	1.6 ± 0.07	0.5 ± 0.04**	441 ± 50	43 ± 4**
C 20:0	1.0 ± 0.04	0.7 ± 0.03**	246 ± 23	54 ± 3**
C 20:2	0.9 ± 0.10	0.5 ± 0.04**	244 ± 27	39 ± 6**
C 20:3	2.4 ± 0.12	2.3 ± 0.10	586 ± 66	192 ± 17**
C 20:4	9.5 ± 0.43	15.9 ± 0.26**	2,271 ± 146	1,316 ± 82**
C 22:0	1.7 ± 0.07	1.3 ± 0.06**	361 ± 30	93 ± 6**
C 22:4	0.7 ± 0.07	1.8 ± 0.07**	143 ± 13	132 ± 8**
C 22:5	0.6 ± 0.09	1.4 ± 0.05**	122 ± 20	111 ± 9**
C 22:6	3.2 ± 0.14	3.6 ± 0.22	757 ± 79	281 ± 33**
C 24:0	0.8 ± 0.10	1.1 ± 0.10	172 ± 23	71 ± 8**
C 24:1	0.7 ± 0.09	1.7 ± 0.13**	138 ± 19	113 ± 10

[a]Concentration (μg/g wet weight ± SEM).
*$P < 0.05$; **$P < 0.005$, epithelium versus stroma.

(C18:1 [n–9]), linoleic (C18:2), and arachidonic (C20:4) acid.

As shown in Table I, between epithelium and stroma of human BPH there were significant differences in the fatty acid composition of the total phospholipids. In particular, the percentage (weight % ± SEM) of oleic acid was significantly ($P < 0.001$) higher in epithelium (21.8 ± 0.64) as compared with stroma (12.3 ± 0.18), whereas that of arachidonic acid was significantly ($P < 0.001$) lower in epithelium (9.5 ± 0.43) than in stroma (15.9 ± 0.26). Related to wet weight (nmol/g wet wt ± SEM), almost always significantly ($P < 0.05$) higher fatty acid concentrations were found in epithelium as compared with stroma. Moreover, the ratio of saturated to unsaturated fatty acids (mean ± SEM) was significantly ($P < 0.001$) lower in epithelium (0.71 ± 0.01) than in stroma (0.79 ± 0.02).

Both in epithelium and in stroma, the GLC analysis of phospholipid fatty acids showed two unidentified peaks (Fig. 1A, B and Table I). The percentage (weight % ± SEM) of peak B was significantly ($P < 0.001$) lower in epithelium (2.0 ± 0.10) than in stroma (4.0 ± 0.10). In order to characterize these peaks, GLC was performed before and after hydrogenation (data not shown). Peaks A and B both disappeared after hydrogenation, indicating that these molecular species are, by nature, unsaturated.

Relationship Between the Fatty Acid Composition of Total Phospholipids and the Donor's Age

The fatty acid composition of total phospholipids in epithelium and stroma was examined for age-dependent alterations. Plotting the percentage (weight % of total fatty acids) of each fatty acid versus the donor's age, in epithelium a significant age-dependent decrease of oleic acid was found ($P < 0.01$), whereas in stroma the amount of oleic acid remained rather constant over the whole age range (Fig. 2A). Moreover, as opposed to stroma, the concentration (μmol/g wet wt) of total fatty acids in epithelium decreased significantly ($P < 0.05$) with age (Fig. 2B).

Fatty Acid Composition of the Main Phospholipid Subclasses in Epithelium and Stroma of Human BPH

In epithelium and stroma, the percentage fatty acid composition of phosphatidylcholine (PC), phosphatidylethanolamine (PE), phosphatidylserine (PS), phosphatidylinositol (PI), and sphingomyelin (SM) was analyzed (Table II). The main fatty acids of PC were palmitic and oleic acid. Palmitic acid also was the main component of SM, whereas the content of this fatty acid was relatively low in PE and PS. PS and PI

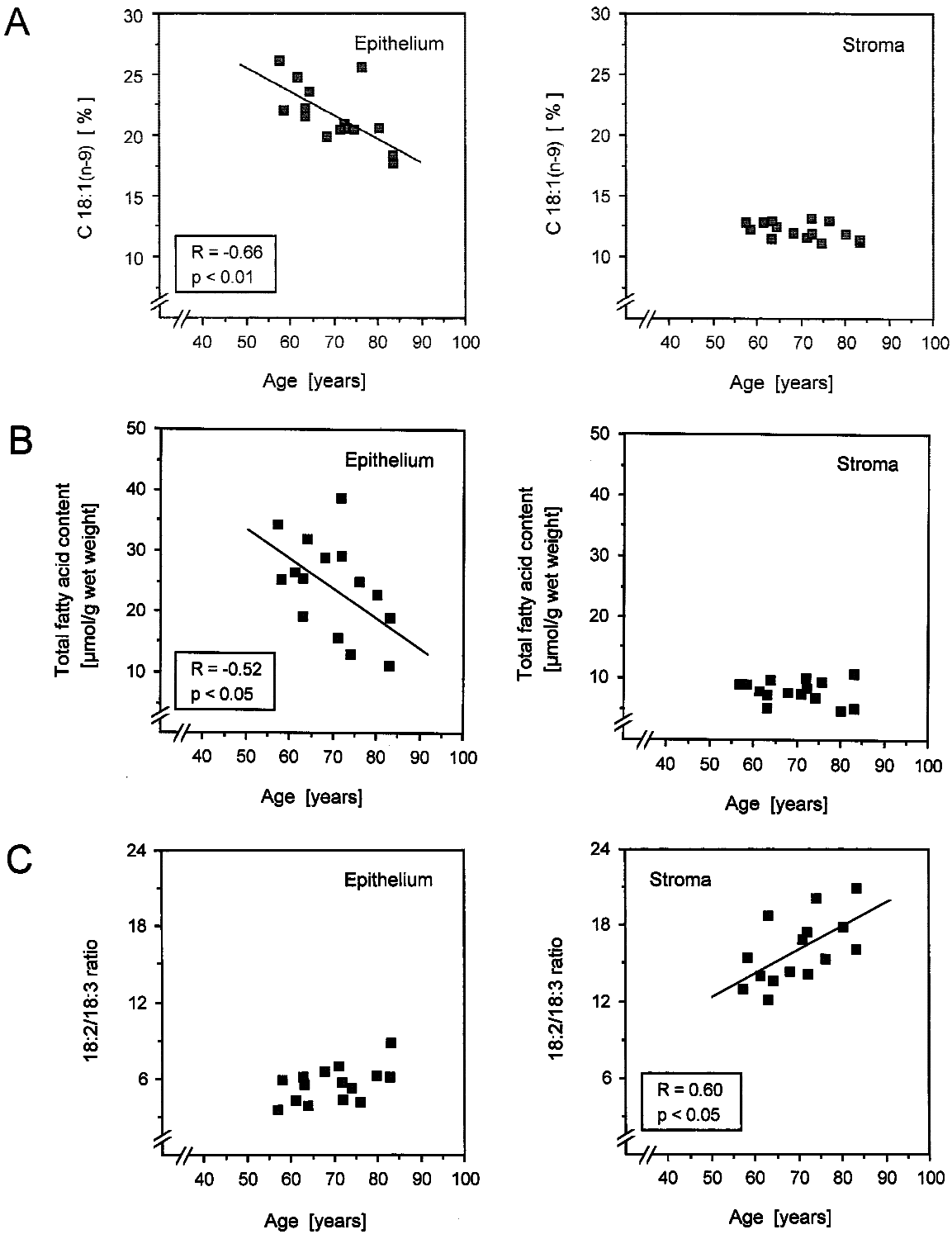

Fig. 2. Age-dependent alterations of oleic acid (expressed as weight % of total fatty acids) **(A),** fatty acid content of total phospholipids **(B),** and 18:2/18:3 ratio **(C)** in epithelium and stroma (n = 5). The significance of the age-related changes was determined by the Spearman rank correlation coefficient (R).

contained mainly stearic acid, as well as substantial amounts (>10%) of oleic acid. SM fatty acids showed a high percentage of 20-, 22-, and 24-carbon chain length. In contrast to the other phospholipid fractions, arachidonic acid represents less than 1% of the fatty acids in SM.

As already mentioned, fatty acid analysis of total phospholipids showed two unidentified peaks (A and

TABLE II. Fatty Acid Composition (Mean ± SEM) of Various Phospholipid Subclasses in Epithelium and Stroma of Human BPH[†]

	Phosphatidylcholine		Phosphatidylethanolamine		Phosphatidylserine		Phosphatidylinositol		Sphingomyelin	
Fatty acid	Epithelium (n = 8)	Stroma (n = 9)	Epithelium (n = 8)	Stroma (n = 8)	Epithelium (n = 6)	Stroma (n = 9)	Epithelium (n = 6)	Stroma (n = 9)	Epithelium (n = 8)	Stroma (n = 9)
C 14:0	—	0.3 ± 0.09*	0.2 ± 0.12	0.1 ± 0.14	—	—	—	—	1.2 ± 0.83	0.3 ± 0.17
A	0.2 ± 0.12	0.2 ± 0.09	5.8 ± 0.42	4.8 ± 0.71	—	—	—	0.8 ± 0.55	1.1 ± 1.11	0.1 ± 0.06
C 16:0	30.4 ± 0.62	31.1 ± 1.66	11.3 ± 1.51	8.9 ± 0.99	5.0 ± 1.21	8.1 ± 1.07	20.0 ± 3.04	13.3 ± 1.87	36.0 ± 3.78	42.2 ± 1.70
C 16:1	0.1 ± 0.06	0.3 ± 0.12	—	—	—	—	—	—	0.1 ± 0.06	—
B	0.1 ± 0.05	0.2 ± 0.08	4.4 ± 0.48	8.8 ± 1.86*	—	2.0 ± 1.06	0.4 ± 0.39	0.5 ± 0.45	1.2 ± 1.17	—
C 18:0	12.2 ± 0.63	17.1 ± 1.08**	16.2 ± 1.34	19.4 ± 2.28	44.3 ± 1.33	45.9 ± 2.67	34.7 ± 3.11	51.0 ± 3.61**	8.8 ± 0.51	14.9 ± 1.73*
C 18:1 (n-9)	28.4 ± 1.32	15.6 ± 0.52**	24.4 ± 1.24	11.2 ± 1.11**	23.1 ± 0.93	22.3 ± 2.21	12.7 ± 0.92	11.6 ± 1.31	13.8 ± 2.93	3.7 ± 1.68*
C 18.1 (n-7)	3.4 ± 0.10	2.8 ± 0.15**	2.8 ± 0.21	1.4 ± 0.17**	2.0 ± 0.27	1.5 ± 0.83	3.4 ± 0.78	0.4 ± 0.37**	2.4 ± 0.98	0.9 ± 0.44
C 18:2	10.5 ± 0.95	11.5 ± 0.72	5.0 ± 0.37	2.5 ± 0.37**	3.4 ± 0.28	1.4 ± 0.69*	3.5 ± 0.79	1.9 ± 0.65	3.9 ± 0.92	2.8 ± 1.34
C 18:3	1.5 ± 0.02	0.4 ± 0.06**	2.5 ± 0.13	0.7 ± 0.13**	3.2 ± 0.26	0.5 ± 0.17**	0.6 ± 0.38	—	0.2 ± 0.09	—
C 20:0	0.1 ± 0.05	0.1 ± 0.05	0.2 ± 0.09	0.2 ± 0.07	2.1 ± 0.27	0.7 ± 0.22**	0.8 ± 0.49	2.5 ± 1.66	6.6 ± 1.50	4.4 ± 0.99
C 20:2	1.4 ± 0.12	0.6 ± 0.08**	0.8 ± 0.19	0.2 ± 0.07*	0.9 ± 0.33	0.1 ± 0.08*	1.5 ± 0.48	—**	0.2 ± 0.12	—*
C 20:3	2.3 ± 0.18	2.7 ± 0.19	2.0 ± 0.32	1.4 ± 0.25	3.7 ± 0.43	1.7 ± 0.47*	2.6 ± 1.00	0.3 ± 0.32*	0.1 ± 0.08	0.2 ± 0.17
C 20.4	5.5 ± 0.56	11.2 ± 1.12**	11.5 ± 2.03	16.7 ± 3.06	5.7 ± 0.90	11.0 ± 2.71	8.0 ± 3.11	12.8 ± 3.34	0.1 ± 0.05	0.6 ± 0.48
C 22:0	0.2 ± 0.12	0.4 ± 0.14	0.7 ± 0.23	0.1 ± 0.08*	1.0 ± 0.29	0.5 ± 0.20	0.7 ± 0.49	1.1 ± 0.73	7.0 ± 2.01	9.4 ± 1.43
C 22:4	—	0.4 ± 0.14*	0.5 ± 0.20	1.6 ± 0.53	—	0.3 ± 0.19	0.3 ± 0.25	—	—	—
C 22:5	—	0.3 ± 0.12*	0.3 ± 0.19	1.6 ± 0.51*	—	0.3 ± 0.19	1.0 ± 0.71	—	—	—
C 22:6	0.6 ± 0.19	0.9 ± 0.22	7.5 ± 2.32	4.4 ± 1.10	2.5 ± 0.85	0.3 ± 0.34*	0.6 ± 0.64	—	—	—
C 24:0	—	0.8 ± 0.29*	—	—	—	—	0.5 ± 0.54	—	5.5 ± 1.42	8.7 ± 1.26
C 24:1	—	—	—	0.7 ± 0.47	—	—	—	—	8.7 ± 5.04	10.6 ± 1.63

[†]Results are expressed as percentage of total fatty acids.
*$P < 0.05$; **$P < 0.005$, epithelium versus stroma. (—) = not detected or present at less than 0.1%.

TABLE III. Fatty Acid Substrate/Product Ratios (Mean ± SEM; n = 15) in Epithelium and Stroma of Human BPH

Ratio	Epithelium	Stroma
18:0/18:1 (n-9)	0.65 ± 0.03	1.37 ± 0.04*
18:2/18:3	5.63 ± 0.36	15.64 ± 0.79*
18:2/20:4	0.92 ± 0.03	0.47 ± 0.02*
18:3/20:4	0.18 ± 0.01	0.03 ± 0.00*

*$P < 0.001$ epithelium versus stroma.

B in Tables I and II). Both peaks were present at the highest level in the chromatogram of PE (Table II). Concerning peak B, its percentage (weight % ± SEM) was significantly ($P < 0.05$) lower in epithelium (4.4 ± 0.48) than in stroma (8.8 ± 1.86). In PC, PS, PI, and SM, respectively, peaks A and B were found, if at all, in rather small amounts.

Turning to differences in the fatty acid composition between epithelium and stroma, significant differences were found in PC and PE, especially with regard to oleic and arachidonic acid. Moreover, in epithelium always a higher percentage of oleic acid was found as compared with stroma, whereas the opposite was true regarding the arachidonic acid (Table II).

Estimated Desaturase and Elongase Activity by Fatty Acid Substrate/Product Ratios

The following fatty acid substrate/product ratios were used as indexes of desaturase and elongase activity: 18:0/18:1 (n-9) (Δ9-desaturase activity), 18:2/18:3 (Δ6-desaturase activity), 18:2/20:4 and 18:3/20:4 (Δ5 Δ6-desaturases and elongase activity). Both for epithelium and stroma of human BPH, the mean values of these ratios are summarized in Table III. As compared with stroma, in epithelium a significantly ($P < 0.001$) lower 18:0/18:1 (n–9) and 18:2/18:3 ratio were found. By contrast, the 18:2/20:4 and 18:3/20:4 ratio were significantly ($P < 0.001$) higher in epithelium as compared with stroma. Finally, as opposed to epithelium in stroma, the 18:2/18:3 ratio increased significantly ($P < 0.05$) with the donor's age (Fig. 2C).

DISCUSSION

The aim of the present study was to describe in detail the fatty acid composition of phospholipids extracted from epithelium and stroma of human BPH. As yet, such a comprehensive study has not been undertaken. In fact, already a few previous studies have dealt with the composition of phospholipids and fatty acids in homogenate of human and rat prostatic tissue [16–19]. However, in those studies the prostatic tissue has not been separated in epithelium and stroma.

Epithelium and stroma are the two histoanatomical compartments of the prostate, which are of special interest because of their mutual growth-regulating interaction. It is widely assumed that such stroma–epithelium interaction, on which DHT might have an impact, is not only relevant regarding the normal but also regarding the abnormal growth of the prostate, leading in almost all men with increasing age to a more or less symptomatic BPH.

The precise cellular events responsible for the normal and abnormal growth in epithelium and stroma are not fully understood. Within this context, little attention has been paid to the lipid environment in epithelium and stroma, although generally a close relationship is well known between phospholipids and biomembrane processes such as fluidity and cellular function [1,2,20]. Moreover, in light of the assumed impact of DHT on prostate growth, it is worthwhile to mention that for its activity the DHT-forming 5α-reductase requires a close association with lipids [4]. Therefore, our detailed analysis of the lipid composition in epithelium and stroma may serve as a database, on which androgen-dependent processes in the prostate could hopefully be better understood.

As far as the total phospholipids are concerned, both in epithelium and stroma of human BPH we found that palmitic and stearic acid were the main saturated fatty acids, while oleic, linoleic and arachidonic acid were the main unsaturated one. This finding is in accordance with the fatty acid pattern found in most animal cell membranes [21] as well as in the whole tissue homogenates from human prostate carcinoma and BPH [16–18]. However, a more accurate comparison between epithelium and stroma revealed significant differences regarding the fatty acid composition in the total phospholipid fraction. In epithelium, the amount of oleic acid was significantly higher than in stroma, whereas the opposite held true for the arachidonic acid. Moreover, the ratio of saturated to unsaturated fatty acids was significantly higher in stroma as compared with epithelium. Both, an increase in chain length and in the ratio of saturated to unsaturated fatty acids are known to lead to a decrease in the fluidity of cell membranes [1,2,20]. Thus, compared with epithelium, our data provide some indications of a decreased membrane fluidity in stroma.

In addition, significant differences between epithelium and stroma were found as far as the fatty acid composition of the main phospholipid subclasses is concerned. However, the biological significance of those differences remains to be determined. This holds also true regarding the two unidentified peaks. In their study on the phospholipid fatty acid composition

in rat ventral prostate, Pulido et al. [19] described the presence of three unidentified peaks. Two of these peaks, again detectable at highest levels in phosphatidylethanolamine, showed a retention time comparable to that of the unidentified peaks A and B in our analysis.

Another remarkable finding are the age-dependent changes of the fatty acid composition in human BPH, the biological significance of which however are at present unknown. So far, the effects of age on fatty acid composition has been investigated in various animal tissues [22–26]. Within this context, a significant age-dependent increase in some long-chain polyunsaturated fatty acids as well as an age-dependent decrease of palmitoleic acid, oleic acid, and linoleic acid was found in phospholipids from liver membrane of rats [22]. Moreover, in adipose tissue of male and female Fischer rats, oleic acid increased slightly in both sexes from the age of three to five weeks. Thereafter, up to the 13th week, oleic acid showed a further increase in female rats, whereas in male rats it dropped [23].

Finally, it is interesting to note that in stroma a significant age-dependent increase of the 18:2/18:3 ratio was found. Within this context, it is known that the formation of saturated and unsaturated fatty acids is regulated by the fatty acid elongation and desaturation pathways. The differences in the fatty acid substrate/product ratios, as well as the age-dependent alteration of such a ratio (vide supra) may indicate that these pathways probably differ between epithelium and stroma of human BPH. It is unclear whether a fatty acid desaturase activity exists in human prostatic tissue. It is known that desaturase activity is influenced by diet, hormones, and age [27–33], so it is thinkable that such a direct link between hormones, aging, fatty acid composition, and desaturase activity actually exists in the human prostate. It is also interesting to note that, in epithelium and stroma, the content of DHT and estrogens is strikingly different in regard to age-dependent alterations [34]. Further studies are needed to determine whether the endogenous hormonal milieu in the prostate modulates the fatty acid composition and desaturase activity of the prostatic cells and what impact such modulation could have on the properties of membrane proteins, i.e., enzymes and receptors, which are supposed to be affected by alterations in membrane fluidity and/or composition. Within this context, Dave et al. were able to demonstrate, in the rat, an inverse relationship in prostatic prolactin binding capacity and membrane lipid microviscosity [35]. Moreover, in vitro fluidization of prostatic membrane exhibited an age-dependent modification of prolactin binding. Thus, changes in membrane fluidity with aging are of prime importance in modulating the accessibility of prolactin receptors in the prostate gland. Furthermore, the significant differences in the lipid composition between epithelium and stroma, as well as the age-dependent alterations reported in this study support our hypothesis that lipids could be somehow involved in the modulation of the 5α-reductase activity. Such support is also given by our very recent studies indicating that 5α-reductase activity can be modulated in vitro by the addition of phospholipases and phospholipids [36,37].

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