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QUARTERLY

Proteoglycans of human umbilical cord arteries✪

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Proteoglycans (PGs) were dissociatively extracted from human umbilical cord arteries (UCAs) with 4 M guanidine hydrochloride containing Triton X-100 and protease inhibitors, purified by Q-Sepharose anion exchange chromatography and lyophilized. They were analysed by gel filtration, SDS/PAGE and agarose gel electrophoresis before and after treatment with chondroitinase ABC. It was found that the PG preparation was especially enriched in chondroitin/dermatan sulphate PGs. The predominant PG fraction included small PGs that emerged from Sepharose CL-2B with K_{av} = 0.74. Their molecular mass, estimated by SDS/PAGE, was 160–200 kDa and 90–150 kDa, i.e. it was typical for biglycan and decorin, respectively. Treatment with chondroitinase ABC yielded the core proteins of 45 and 47 kDa, characteristic for both small PGs. Remarkable amounts of the 45 kDa protein were detected in non-treated PG samples, suggesting the presence of free core proteins of biglycan and decorin. Large PGs were present in lower amounts. In intact form they were eluted from Sepharose CL-2B with K_{av} = 0.17 and 0.43. Digestion with chondroitinase ABC yielded the core proteins with a molecular mass within the range of 180–360 kDa but predominant were the bands of 200, 250 and 360 kDa. The large PGs probably represent various forms of versican or perlecan bearing chondroitin sulphate chains.

Extracellular matrix is a mixture of macromolecules forming a network that contributes essentially to the normal function of the arterial wall [1]. Proteoglycans are important constituents of the matrix, although they are also present in basement or plasma membranes,

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Abbreviations: 6-AHA, 6-aminohexanoic acid; CS, chondroitin sulphate; CSPG, chondroitin sulphate proteoglycan; CS/DSPG, chondroitin/dermatan sulphate proteoglycan; DS, dermatan sulphate; GAG, glycosaminoglycan; HS, heparan sulphate; HSPG, heparan sulphate proteoglycan; NEM, *N*-methylmaleimide; PG, proteoglycan; PMSF, phenylmethylsulphonyl fluoride; UCA, umbilical cord artery.

and in secretory granules of the cells [1, 2]. These compounds are built of backbone protein cores covalently attached to sulphated glycosaminoglycans (GAGs). Many different, genetically distinct core proteins combine with various GAG chains to form macromolecules expressing specific features [2, 3].

Arterial proteoglycans perform numerous functions. Because of their hydrophilicity they create water-filled compartments that maintain viscoelastic and turgor pressures within the vascular wall [1]. Proteoglycans participate also in the regulation of vascular permeability, lipid metabolism, hemostasis and thrombosis [1, 4]. In addition, they interact with vascular extracellular matrix molecules and cells, as well as with growth factors and cytokines to regulate vascular cell adhesion, migration and proliferation [1].

The most abundant arterial proteoglycans (PGs) include versican, decorin, biglycan and perlecan [1]. Versican is a large PG (over 1000 kDa) containing multiple chondroitin sulphate (CS) chains. Another large proteoglycan is perlecan, localized mainly in basement membranes [1]. It has a very large core protein (400–470 kDa) and 3–10 heparan sulphate (HS) and/or CS chains [3]. Decorin and biglycan are small leucine-rich PGs (core protein of about 45 kDa) with one or two CS/DS (dermatan sulphate) chains, respectively [3, 5, 6]. Vascular smooth muscle cells are the main producers of arterial PGs, although other cell types, especially endothelial cells, are also involved in the synthesis of those macromolecules [1, 4].

The umbilical cord forms the connection between the placenta and the foetus. It contains one vein and two arteries surrounded by Wharton's jelly and covered by simple amniotic epithelium [7]. Umbilical cord arteries (UCAs) receive blood from the foetus. It was found from previous studies that umbilical cord arteries have the same GAG species [8, 9] as the adult arteries [8, 10]. The UCAs, however, are especially rich in hyaluronic acid (non-sulphated GAG, not covalently bound to PG protein cores) [8, 9] and contain a lesser amount of HS [8]. Those results suggested that UCA proteoglycans had some peculiarities not shared by PGs of other arteries.

Most studies on arterial PGs were performed on adult vessels, especially on aortal tissues. Proteoglycans of the UCA have not been characterized to date. For those reasons we decided to explore PG composition of that tissue. Here we show that the proteoglycan preparation obtained by dissociative extraction of UCA contains at least three individual populations. Their core proteins are substituted mainly by CS/DS chains and show some characteristics of decorin, biglycan and versican. The existence of other PG species, especially of perlecan, should not be excluded.

MATERIALS AND METHODS

Tissue material. Studies were performed on 10 UCAs taken from 10 newborns delivered by healthy mothers aged 23–36. The babies were born between the 38th and 41st week of gestation. Sections (20 cm long) of the umbilical cords were excised beginning from their placental end. UCAs were carefully dissected from the umbilical cord immediately after delivery and stored at –20°C.

Extraction and isolation of UCA proteoglycans. The general schema of PG extraction proposed by Hascall *et al.* [2] was applied with some modifications. Briefly, the samples of UCAs were thawed, washed with cold (4°C) physiological saline to remove blood residues, blotted with filter paper and finely cut into small pieces. They were suspended in cold (4°C) extracting buffer which included 4 M guanidine-HCl and 2% (v/v) Triton X-100 in 0.1 M sodium acetate (pH 5.8), and five protease inhibitors: 0.1 M 6-AHA, 0.01 M EDTA-Na_2, 0.01 M NEM, 0.005 M benzamidine-HCl and 0.001 M PMSF. The samples were homogenized with a knife homogenizer (four times, at 20 000 r.p.m. at 4°C for 15 s) and extracted with 10 vol. (v/w) of ex-

tracting buffer at 4°C for 24 h with constant stirring. The mixture was centrifuged at 6 000 × ***g*** at 4°C for 30 min. The supernatant was collected (1st extract) and the pellet was submitted to second extraction and centrifugation in the same conditions as above, except that five volumes (v/w) of extracting buffer were used.

The final pellet that remained after the second extraction was suspended in five volumes of a solution containing 0.05% (w/v) papain, 0.005 M cysteine-HCl and 0.01 M EDTA-Na_2 in 0.1 M phosphate buffer, pH 6.5. The hydrolysis was carried out at 60°C for 18 h with occasional shaking. The reaction was stopped by heating at 100°C for 5 min. The samples were cooled to room temperature and centrifuged at 6 000 × ***g*** for 30 min. The supernatant was collected and tested for the concentration of sulphated GAGs (see below) to estimate the amount of PGs insoluble under conditions of the extraction.

The 1st and 2nd extracts were combined (separately for individual tissue samples) and dialysed (4°C) against the buffer containing 7 M urea, 0.5% (w/v) Triton X-100, 0.1 M NaCl and a mixture of protease inhibitors (0.01 M 6-AHA, 0.01 M EDTA-Na_2, 0.005 M benzamidine-HCl, 0.001 M NEM, 0.001 M PMSF) in 0.05 M Tris/HCl, pH 6.5. The dialysed samples were applied to a Q-Sepharose Fast Flow anion-exchange column (10 cm × 1.5 cm) containing 5 ml of the resin equilibrated with the same urea-containing buffer. The column was washed with 5 × 5 ml of the equilibrating buffer, followed by 10 × 5 ml of the buffer containing 0.5% (w/v) Chaps instead of barely dialyzable Triton X-100. Proteoglycans were eluted with the Chaps-containing buffer in which NaCl concentration was elevated from 0.1 M to 2 M. The purified PGs were dialysed against double distilled water at 4°C with constant stirring, frozen (–20°C) and lyophilized.

Gel filtration. Lyophilized PGs, containing 250 μg of chondroitin 4-sulphate equivalents (derived in equal amounts from individual preparations), were dissolved in 0.5 ml of the eluting buffer composed of: 7 M urea, 0.5% (v/v) Triton X-100, 0.3 M NaCl, a mixture of protease inhibitors (0.01 M 6-AHA, 0.01 M EDTA-Na_2, 0.005 M benzamidine-HCl, 0.001 M NEM, 0.001 M PMSF) in 0.05 M Tris/HCl, pH 6.5. The samples were applied onto a Sepharose CL-2B column (50 cm × 1 cm), and eluted at a flow rate of 0.15 ml/min, at room temperature. Fractions of 1 ml were collected. The PG content in individual fractions was estimated by measuring the concentration of sulphated GAGs (see below). The column was calibrated with Blue Dextran for the void volume (V_o) and phenol red for the total volume (V_t).

Chondroitinase ABC digestion. Lyophilized PGs were treated with chondroitinase ABC (Sigma) to obtain free protein cores of CS/DSPGs. The reaction mixture included PGs (approx. 60 μg of chondroitin 4-sulphate equivalents) and chondroitinase ABC (0.06 U) in 0.1 ml of 0.05 M Tris/HCl buffer (pH 8.0), containing 0.06 M sodium acetate, bovine serum albumin (BSA) (0.14 mg/ml) and a mixture of protease inhibitors (0.01 M 6-AHA, 0.01 M EDTA-Na_2, 0.01 M benzamidine-HCl, 0.005 M NEM, 0.001 M PMSF). The reaction was carried out at 37°C for 4 h with occasional shaking. Control incubation (without the enzyme) was performed in the same conditions. The reactions were stopped by adding 0.1 ml of SDS/PAGE sample buffer (0.125 M Tris/HCl, pH 6.8, 4% (w/v) SDS, 40% (w/v) glycerol, 10% (v/v) 2-mercaptoethanol, 0.01% (w/v) Bromophenol Blue) or sample buffer for agarose electrophoresis (0.1 M Tris, 0.768 M glycine, pH 8.6, 1% (w/v) SDS, 0.01% (w/v) Bromophenol Blue) and heated at 100°C for 5 min. The effects of digestion were evaluated by electrophoretic methods (see below).

Electrophoretic techniques. SDS/PAGE of PG samples (prepared as above) was performed on 1 mm-thick isocratic gels (7.5% separating with 6% stacking gels, and 5% separating with 3.5% stacking gels) under reducing conditions, according to the procedure of Laemmli [11]. Protein molecular mass mark-

ers from Sigma (Sigmamarkers, Wide range) were used. Electrophoresis was run at a constant current of 20 mA.

The gels were stained with silver [12] without or with pre-staining with Alcian Blue/Coomassie Brilliant Blue R-250. Pre-staining was performed as described by Vilim & Krajickova [13], except that ten times higher concentration of Coomassie Brilliant Blue R-250 (0.0025%) was applied to better visualize PG protein cores released after chondroitinase ABC treatment.

For agarose electrophoresis PG samples (0.2 ml) in the sample buffer for agarose electrophoresis (see above) were mixed with 0.1 ml of the sample gel containing 1% (w/v) agarose, 15% (v/v) glycerol, 0.2% (w/v) SDS, 0.05 M Tris, 0.384 M glycine, pH 8.6, heated at 100°C for 10 min, and immediately layered under the electrophoresis buffer into the preformed well. PGs or their digests were separated on 2 mm-thick, slab agarose gels (1.2%, w/v) in 0.1 M Tris/acetate buffer, pH 6.8, in a vertical manner [14]. Electrophoresis was run at 50 V for 90 min. PGs were stained overnight with Toluidine Blue [15].

Sulphated GAGs were assayed in duplicate samples by the dimethylmethylene blue binding method [16] using chondroitin 4-sulphate (Sigma) as a standard.

Protein was determined by the modified method of Bradford [17] that enables linearization of the calibration curve over a wide range of protein concentrations.

RESULTS

Extractability of proteoglycans from umbilical cord arteries

We found that 1 g of UCAs contains 4.00 ± 1.44 mg of sulphated GAGs (reflecting the presence of PGs). About 80% of sulphated GAGs (3.13 ± 1.13 mg/g of wet tissue) were solubilized by two extractions with buffered 4 M guanidine-HCl/2% Triton X-100 solution. The course of extraction and purification of UCA proteoglycans is summarized in Table 1. The yield was approximately 1.65 mg of sulphated GAGs/g of wet UCA.

Heterogeneity of UCA proteoglycans

The elution profile of the PG preparation on Sepharose CL-2B column (Fig. 1) shows that the PGs were poorly separated, although three individual peaks can be distinguished. The most prominent one corresponds to PGs eluted with K_{av} = 0.74, which suggests the prevalence of small PGs in the UCA. Two minor peaks are less retarded (K_{av} = 0.17 and K_{av} = 0.43) as in the case of large PGs.

Table 1. Extraction and purification of proteoglycans from human umbilical cord artery.

Values are given as means ±S.D. for 10 preparations.

Purification step	Sulphated GAG [mg/g of wet tissue]	Sulphated GAG/protein ratio
Starting material	4.00 ± 1.44	–
4 M guanidine-HCl/ 2% Triton X-100 extraction (combined extracts)	3.13 ± 1.13	0.055 ± 0.012
Q-Sepharose anion-exchange chromatography	1.65 ± 0.58	0.890 ± 0.180

Electrophoretic characterization of UCA proteoglycans

To estimate the molecular mass of UCA proteoglycans and of their core proteins, they were subjected to SDS/PAGE, both as intact

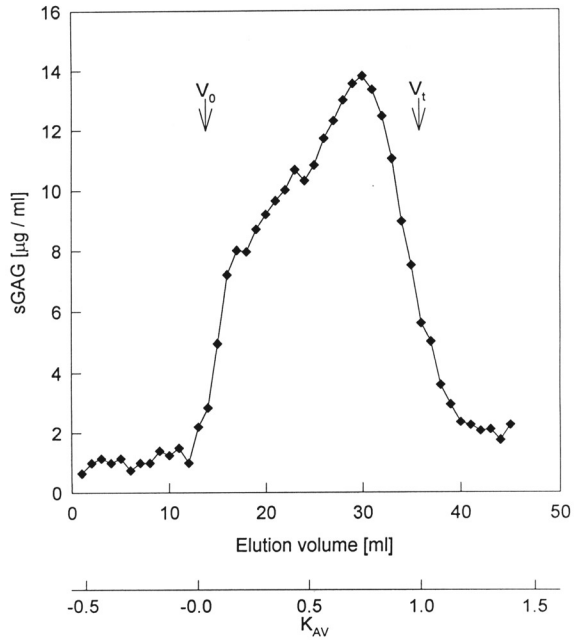

Figure 1. Gel filtration of proteoglycans isolated from umbilical cord arteries on Sepharose CL-2B.

Fractions of 1 ml were collected and assayed for sulphated GAG (sGAG) concentration.

PGs and after treatment with chondroitinase ABC (Figs. 2, 3 and 4). Electrophoretic separation on 7.5% gel, sequentially stained with Alcian Blue/Coomassie Blue and silver, revealed two broad bands, with a molecular mass of 160–200 kDa and 90–150 kDa, respectively (Fig. 2, lane 1). The broad, faint band, visible on the top of stacking gel, probably corresponds to large PGs. The sharp band visible at 45 kDa became much more intensive after the action of chondroitinase ABC (Fig. 2, lane 2) and therefore may be considered a core protein of CS/DSPGs. Treatment with the enzyme resulted also in appearance of a new band of about 47 kDa and a strongly stained band of about 70 kDa (Fig. 2, lane 2) which is also visible in the case of chondroitinase ABC alone (lane 3), and corresponds probably to BSA present in the enzyme preparation as a stabilizer. The other bands (Fig. 2, lane 1) probably reflect the presence of contaminating proteins as they did not disappear after chondroitinase ABC treatment (lane 2). The action of this enzyme resulted in almost complete disappearance of all PG-containing bands (Fig. 2, lane 2).

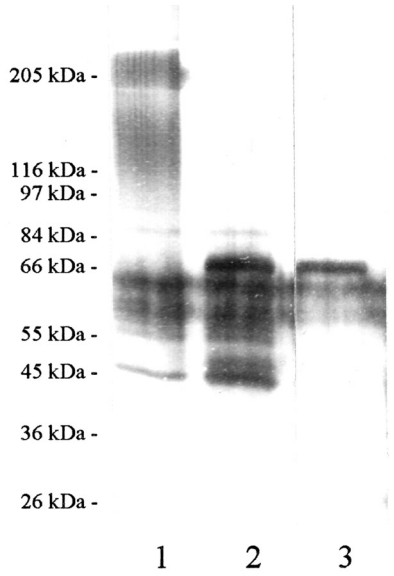

Figure 2. SDS/PAGE of UCA proteoglycans and their core proteins after treatment with chondroitinase ABC.

Electrophoresis was performed on 7.5% gel stained with Alcian Blue/Coomassie Brilliant Blue R-250 followed by silver staining. Lane 1, intact UCA proteoglycans; lane 2, UCA proteoglycans treated with chondroitinase ABC; lane 3, chondroitinase ABC.

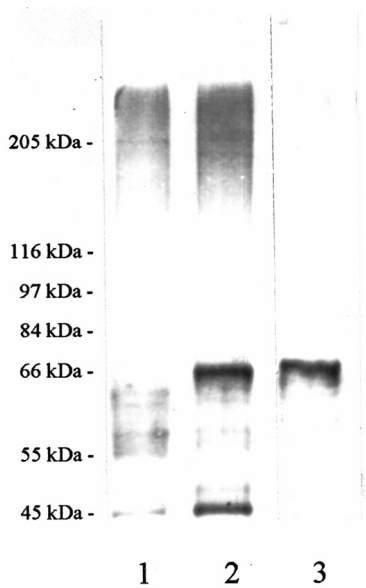

Figure 3. SDS/PAGE of UCA proteoglycans and their core proteins after treatment with chondroitinase ABC.

Electrophoresis was performed on 7.5% gel stained with silver. Lane 1, intact UCA proteoglycans; lane 2, UCA proteoglycans treated with chondroitinase ABC; lane 3, chondroitinase ABC.

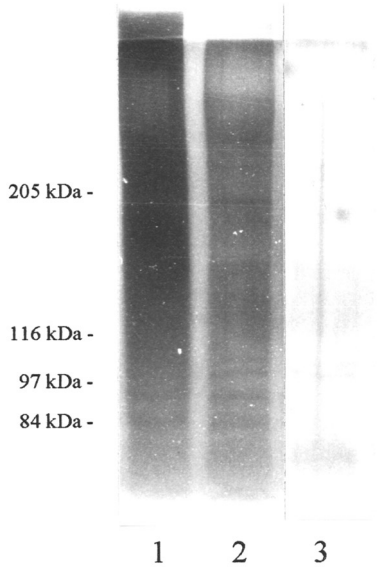

Figure 4. SDS/PAGE of UCA proteoglycans and their core proteins after treatment with chondroitinase ABC.

Electrophoresis was performed on 5% gel stained with Alcian Blue/Coomassie Brilliant Blue R-250 followed by silver staining. Lane 1, intact UCA proteoglycans; lane 2, UCA proteoglycans treated with chondroitinase ABC; lane 3, chondroitinase ABC.

Omission of pre-staining prevented the detection of intact PG bands (Fig. 3, lane 1) as GAG chains are poorly stained with silver without pre-staining with Alcian Blue. However, the core protein bands are clearly visible. Three bands are worthy of notice: a doublet of 45 kDa- and 47 kDa-bands described above (see Fig. 2) and the band of about 200 kDa. The intensity of the latter strongly increased after chondroitinase ABC treatment (Fig. 3, lane 2), suggesting that it was a free PG protein core. New bands of about 180, 250 and 260 kDa also appeared after the action of the enzyme.

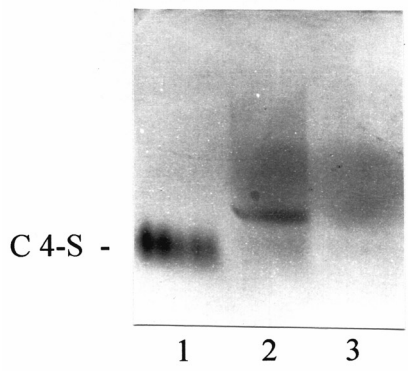

Figure 5. Agarose gel electrophoresis of UCA proteoglycans and their chondroitinase ABC digests.

The samples were analysed on 2 mm-thick slab gels of 1.2% agarose (8 cm × 8 cm) and stained with Toluidine Blue. Lane 1, chondroitin 4-sulphate (C 4-S, standard); lane 2, UCA proteoglycan mixture; lane 3, UCA proteoglycan mixture after digestion with chondroitinase ABC.

To better visualize PG core proteins of higher molecular mass, electrophoresis was performed on 5% gel (Fig. 4). Lane 1 shows that a part of the high molecular PG fraction did enter the separating gel. Chondroitinase ABC digestion yielded new bands with a molecular mass of 180–360 kDa. The most prominent were the bands of 200 kDa, 250 kDa and 360 kDa (lane 2). The bands poorly contrasted with the background, pointing to the presence of proteoglycan(s) other than CS/DSPG.

Electrophoretic mobility of UCA proteoglycans and their chondroitinase ABC digests on 1.2% agarose gel is presented in Fig. 5. As can be seen, non-digested PGs separated into four bands (lane 2). The mobility of the fastest one was only slightly lower than that of standard chondroitin 4-sulphate (lane 1). The predominant, sharp band migrated close behind the fastest one (lane 2). Two broad slower migrating bands probably represent large PGs. Chondroitinase ABC treatment resulted in disappearance of most of Toluidine Blue stainable material (lane 3).

DISCUSSION

Proteoglycan content of the umbilical cord artery is very similar to that obtained for adult arteries. It was reported that 1 g of wet human aorta contained approximately 1.3 mg of uronic acids [10], which constitute on an average one third of the sulphated GAG mass. The two-step extraction procedure we applied was more efficient than one-step procedures [10, 18], even if they were performed at higher temperature [18] or for a longer time [10] as

they resulted in extraction of 35–67% of total tissue PG. The higher efficiency (about 80%) we have obtained was probably caused not only by the additional step of extraction but also by the presence of Triton X-100, which was able to solubilize membrane-bound PGs. However, it has been suggested that such a procedure should generally solubilize 80–100% of the proteoglycans [2]. Therefore our results point that the UCA shares with other arteries some resistance to dissociative solvents. Such a resistance might be caused by strong binding or mechanical entrapment of PGs in the network of other components of the extracellular matrix, especially elastin [18].

The elution profile of UCA proteoglycans on Sepharose CL-2B column points to relative prevalence of small PGs in the examined material. The main peak (K_{av} = 0.74) is similar as in the case of arterial smooth muscle cells [4, 19] and aorta [10], where it is often most prominent and featured by K_{av} values of 0.58 to 0.86 [4, 10, 19]. Such a peak in those tissues mainly reflects the presence of CS/DSPGs [4, 10] with core protein of 45 kDa [4], which is characteristic of decorin and biglycan [5, 6]. Two minor peaks of large PGs of the UCA (K_{av} = 0.17 and 0.43) may be compared to similar but single peaks (K_{av} values of 0.20–0.39) that have been reported for arterial smooth muscle cells [4, 19] and aorta [10, 20]. In the case of those tissues the peaks contain large CSPGs [4, 10, 19, 20] able to aggregate with hyaluronic acid [4, 10] as in the case of versican [1, 3]. Indeed, the PG of arterial smooth muscle cells, eluted with K_{av} = 0.2, was proved to be versican [19]. Therefore, the peak with K_{av} = 0.17 we have obtained may also contain that proteoglycan. Also the second peak (K_{av} = 0.43) might contain versican-like PGs as it was suggested in the case of arterial PG with K_{av} = 0.39 [20]. However, the presence of perlecan can not be excluded because its molecular mass is intermediate between those of versican and small PGs [1, 3].

SDS/PAGE confirmed the prevalence of small PGs among other UCA proteoglycans. The main bands of intact PGs have a molecular mass of 160–200 kDa and 90–150 kDa, typical for biglycan and decorin, respectively [21, 22]. The most intensive core protein bands released after chondroitinase ABC treatment also point to the predomination of the proteoglycans mentioned above. The mobility of the 45 kDa-band is characteristic of the core protein of biglycan [6], and the doublet band of 45 kDa and 47 kDa is typical for two variants of the decorin core protein, having two or three N-linked oligosaccharides [5]. Significant amounts of decorin and/or biglycan seem to be present as free core proteins (see Fig. 2, 3, lane 1). This phenomenon might be caused by a high biosynthetic potential of PG-producing cells as it was observed in the case of *in vitro* studies on overexpression of the two PGs, high amounts of which were produced in the form free of sulphated GAG chains [23, 24]. The high molecular bands (Fig. 3 and 4, lane 2), most probably correspond to versican-like core proteins. Versican is the main large CSPG of the arterial wall [1]. Core proteins of versican produced by aortal smooth muscle cells [19], appear at about 450, 360, and 330 kDa when resolved by SDS/PAGE. On the other hand, smaller core proteins were also described, both for bovine aorta (170 kDa) [20] and for human cartilage (170 kDa and 200 kDa) [25]. This striking variability in size could be caused by species or tissue dependent differences, distinct glycosylation patterns, and by the action of proteases within the tissue or during the purification procedure. The multiple forms of core protein could have also resulted from alternative splicing. Indeed, at least three of the four known splice variants of versican were detected in human aorta [26] and mouse endothelial cells [27].

Core proteins of perlecan might also form some of the high molecular bands of UCA PGs. Perlecan is one of the major arterial PGs

[1]. Although it is generally considered to be HSPG [1, 3], it can also carry CS chains [3, 28, 29]. The core proteins of perlecan isolated from some tissues have a molecular mass of about 220 kDa [28, 29], 260 kDa [28], 330 kDa and 400 kDa [29]. Therefore it cannot be excluded that some of high molecular bands of chondroitinase ABC-treated UCA proteoglycans, especially those of 200 kDa and 250 kDa, might be related to perlecan. This suggestion is partly supported by the presence of the 200 kDa-band in non-treated PG preparation (Fig. 3, lane 1) since perlecan may be secreted as a free core protein [28].

Agarose electrophoregram of UCA proteoglycans also suggests the predomination of small PGs. They seem to be focused in two faster migrating bands. The fastest of them, because of its mobility relative to chondroitin 4-sulphate, may correspond to decorin [15]. The mobility of the second, predominant band strongly resembles that of biglycan [15]. The more retarded two bands seem to represent large PGs, such as versican or perlecan.

It can be concluded from both polyacrylamide and agarose electrophoregrams presented above that the UCA is very rich in CS/DSPGs. Other PG populations, such as HSPGs, seem to be very rare in the UCA. Studies on GAG level revealed a much lower amount of HS in the UCA wall than in adult vessels [8]. High content of CS/DSPGs may contribute significantly to the functional behaviour of the UCA. The degradation of CS/DS chains of the arterial PGs was reported to increase the stiffness of vascular wall and alter the myogenic properties of the artery [30]. A high amount of CS/DSPGs may therefore ensure significant elasticity and adaptability that enable the UCA to adjust to the variable shape of the umbilical cord. They may also confer on the UCA a high resistance to rapid alterations of transmural pressures during intrauterine life or delivery. In such a way CS/DSPGs may prevent disturbances in blood transport to the placenta. On the other hand, low HSPG content is thought to increase vascular wall permeability [4] and therefore it might facilitate the exchange of water and various solutes between the UCA blood and the surrounding Wharton's jelly and amniotic fluid.

It is evident from the results presented above that small PGs, most probably decorin and biglycan, predominate among the UCA proteoglycans. Decorin binds to collagen and regulates the diameter and organization of the collagen fibrils [1, 3, 5] that are important constituents of the UCA wall [8, 31]. In addition, decorin is able to bind cytokines, such as transforming growth factor-β [3, 5]. Biglycan also shows transforming growth factor-β-binding activity [3, 6] and is probably involved in the control of endothelial cell migration [6].

Large proteoglycans seem to be present in the UCA in lower amounts. Most of them probably constitute versican-like PGs. Versican is known to destabilize cell adhesion and facilitate cell growth and proliferation [32]. Perlecan, which may also be present in the form of CSPG in our preparations, appears to promote the adhesion of cells, such as endothelial [3, 33] and vascular smooth muscle cells [33].

There is some evidence that proteoglycans with GAG chains other than CS or DS do exist in the UCA. They might include a HS-containing form of perlecan, syndecans, glypicans or keratan sulphate proteoglycan, lumican, which were identified in the vascular wall [1]. However, because of their rarity in our preparations, they were not characterized in this study. The identity of such PGs remains to be established.

It is well known that the state of the vascular system of mother and placenta plays an important role in the intrauterine development of the foetus [34]. Pregnancy-associated pathological conditions are known to cause rearrangement of the extracellular matrix of the UCA and Wharton's jelly. This is especially evident in the case of preeclampsia (EPH-gestosis), which is accompanied by an increase in collagen content [7, 31], decrease in

the amount of elastin [35], and premature replacement of hyaluronic acid by sulphated GAGs [9]. Such changes are considered to affect the mechanical properties of these vessels and disturb fetal blood circulation. The role of UCA proteoglycans in the pathomechanism of preeclampsia was not studied yet. In this paper we present proteoglycan composition of the umbilical cord artery for the first time. Although our work was performed on healthy subjects, it may be expected to facilitate future research explaining several aspects not only of preeclampsia, but also of other prenatal pathological conditions.

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