ANNALES
UNIVERSITATIS MARIAE CURIE-SKŁODOWSKA
LUBLIN-POLONIA
VOL. LX, N1, 20 SECTIO D 2005

Department of Biochemistry and Molecular Biology, Medical University of Lublin

BOLESŁAW FLORIAŃCZYK

Enzymes in the urine

The emergence of enzymes in the urine comes as a result of the functioning of the same mechanisms that are observed in general proteinuria. However, there is a certain peculiarity to the process. Compared with the overall values of protein the enzymatic protein concentration is minimal and can only be expressed by its catalytic activity. Morover, the urine is not a natural environment for the enzymes, the fact that may modify their physical-chemical and catalytic properties.

THE ORIGINATING SOURCES OF THE URINE ENZYMES

The enzymes present in the urine can be of renal or extrarenal origin. Therefore, we can distinguish two main sources of enzymes: a) renal (renal tubules, renal pelves, the epithelial cells of the urinary tract) and b) extrarenal (plasma, leukocytes, erythrocytes). An increase in the activity of the urine enzymes of extrarenal origin is a manifestation of an impaired functioning of the renal glomerule while an increase in the activity of the renal enzymes suggests damage to renal tubules (2,5,7).

ENZYMES OF EXTRARENAL ORIGIN

The main source of the extrarenal enzymes is the plasma. The enzymes present in the normal urine typically have the molecular weight of less than 70. 000. Those are for example: miramidase (m. w. of 15,000); ribonuclease (m. w. of 13,000); carboxypeptidase (m. w. of 31,000); uropepsinogen (m. w. of 42,000); amylase (m. w. of 45,000); lipase (m. w. of 48,000); urokinase (m. w. of 55,000).

However, also in normal conditions the activity of enzymes possessing a molecular weight of more than 70,000 can be observed, e. g. LDH* (m. w. of 120,000); AP (m. w. of 300,000). Still, in the overall enzymatic activity of the urine the role of those enzymes is negligible.

If we assume a similar mechanism for the filtration of the high-molecular enzymes as we do for the non-enzymatic proteins, i. e. the capability of the molecule's shrinking via dissociation, the potential role of the molecular charge and changes in the spatial structure of the enzymatic protein as well as partial proteolysis in the renal tubule, then their passage from the plasma to the urine seems possible. We may thus consider it to be a regular phenomenon that certain high-molecular enzymes are present in the urine of healthy people.

---

* List of abbreviations: AAP – alanyloaminopeptydase (E.C. 3.4.1.2), AlAT – alanine aminotrasferase (E.C. 1.1.1.27, AP – alcaline phosphatase (E.C. 3.1.3.2), AW – carbonic anhydrase (E.C. 4.2.1.1), AspAT – aspartic aminotransferase (E.C. 2.6.1.1), gamma-GTP – gammaglutamyltranspeptidase, GLDH – glutamate dehydrogenase (E.C. 1.4.1.4), LAP – leucyloaminopeptydase (E.C. 3.4.1.1), LDH – lactic dehydrogenase (E.C. 1.1.1.27), MDH – malic dehydrogenase (E.C. 1.1.1.37),

The presence of high-molecular enzymatic proteins is also connected with the question of selectivity of the basement membrane of the renal glomerule and the clearance of the enzymatic proteins. The results of clearance studies indicate that the "glomerular sieve" works either as a selective or non-selective filter. The higher the selectivity of proteinuria the higher the albumin clearance compared with that of the proteins bearing a higher molecular weight. A reverse situation is observed in the states of lost selectivity i. e. when albumin clearance is raised by the clearance of the proteines bearing a higher molecular weight (6). The clearance of the proteins is inversely proportional to their molecular weight. Individual enzymatic proteins observed in the urine show a higher clearance co-efficient at a lower molecular weight. In pathological conditions, with a significant proteinuria, there is a possibility of the migration of most plasmatic enzymes (3,6,8,9).

MORPHOTIC ELEMENTS AS AN ORIGINATING SOURCE OF URINE ENZYMES

Erythrocytes and leukocytes can pass over the renal filter, autolyse in low-osmotic primary urine, in proximal tubules or in more remote segments of the urinary tract causing an increase of the enzyme activity in the urine. A similar effect is observed in the case of the passage of the morphotic elements of the blood from the blood vessels of the bladder and the lower urinary tract (6). Periductal macrophages may also give rise to the enzyme presence in the urine, particularly to that of muramidase, since macrophages contain large amounts of that enzyme (4).

RENAL TISSUE AS A SOURCE OF ENZYMES IN THE PLASMA AND IN THE URINE

In physiological conditions the activity of the enzymes in the plasma (in body fluids) is correlated with the organ's mass. Thus the skeletal muscles and the liver are the two main sources of the enzymes in the plasma. Considering the kidneys and their relatively small mass as well as the passage of the enzymes not only to the bloodstream but also to the urine we may venture a statement that the process of flushing the enzymes from the kidney into the blood is less spectacular than their passing from the other organs having the same mass as the kidney. Apart from this, we have to take into consideration the arrangement of the enzymes in the respective parts of the nephron as well as the relative mass of those individual structures.

Table 1. Examples of the enzyme presence in particular segments of the nephron

Nephrone structures	The enzyme name
Proximal tubule	Gamma-GTP LDH GLDH AspAT AW LAP AP
Henle's loop	MDH AlAT
Distal tubule	LDH GLDH AspAT AW

The proximal tubules are known to have the largest amount of enzymes whereas a significantly smaller number of those is present in the Henle's loop and the distal tubule. The renal glomerule itself is characterized by the smallest amount of enzymes (2).

Considering the fact that the activity of the enzymes is confined to the sinuous tubules, which constitute about 85% of the renal cortex, we can draw a conclusion that the enzymes of the renal origin which diffuse into the blood and urine will mainly come from the cortex, at least in the physiological conditions. In pathological situations the release of the enzymes into the plasma from the affected organ may be more vigorous owing not only to the death of a cell but also due to an increase in the permeability of the cytomembrane (1,7).

NEPHROPATHY

In pathological states of the kidneys we witness considerable changes in the activity of the enzymes in the urine. The most characteristic are changes in the activity of the enzymes specific to the renal tissue and those that are observed in more significant amounts there. These include gamma-glutamylo-tranpeptidase, arylsulphatase, trechalase, beta glucoronidase, leucyloaminopeptydase, urokinase and renin (5). As with the renal threshold for low-molecular substances (e. g. glucose or amino acids) there may be a renal threshold for enzymatic proteins. We should also consider the crossing of the renal threshold by the enzymatic proteins in the absence of the metabolic block.

In nephropathies there is an increased passage of the enzymes originating from glomerular filtration as well as of those removed from the brush border of the renal tubules. Increased permeability of the protein in the glomerules (pathological states affecting renal glomerules) encourages a hialine accumulation of proteins in the proximal tubular cells. Changes in the proximal tubular cells are also caused by increased endocytosis of the plasmatic proteins. Increased removal of the tubular enzymes is a result of protein nephrosis similar to osmotic nephrosis. The increased removal of AAP and lysozyme on the administration of gentamycin has also been observed. It can be explained by increased pinocytosis in the presence of gentamycin in the proximal tubular cells, which involves the increased removal of the enzymes. Also, the increased activity in the urine of the enzymes in hyperthyroidism can be explained by an increased pinocytosis of the proteins in the proximal tubule, the overloading of the tubular cells and, in consequence, the flushing of retrostructures with large amounts of lysosomal enzymes into the lumen of the tubule (5).

If there is a hyperenzymuria with an intact glomerular membrane, the enzymatic activity is exclusively a renal response to some extrarenal pathological conditions. Such a conclusion is justified by the following data: a) In liver pathologies AAP appears sooner in the urine than in the plasma; b) Enzymes typical for renal tissue appear in the urine; c) Enzymes with a higher molecular weight than expected judging from the size of the molecular sieve in the glomerules appear in the urine; d) There is a lack of correlation between the enzyme activity in the plasma and that in the urine (2,5).

REFERENCES

1. Eijan A.M. et al.: Cathepsin B levels in urine from bladder cancer patients. Oncol. Rep., 7, 1395, 2000.
2. Floriańczyk B.: Aktywność niektórych enzymów w moczu ludzi chorych na białaczki. Praca doktorska, Lublin 1981.
3. Floriańczyk B.: Współczynniki oczyszczania dla niektórych enzymów u ludzi chorych na białaczki. Diagn. Lab., 19, 235, 1983.
4. Lutz W., Krajewska B.: Biomarkers in diagnosis of kidney diseases caused by chemical toxins. Med. Pr., 48, 205, 1997.
5. Maruhn D. et al.: Normal limits of urinary exretion of eleven enzymes. Clin. Chem., 22, 1567, 1976.
6. Mattenheimer H.: Enzymes in the urine. Medical Clinics of North America., 55, 1495, 1971.
7. Sakai T.: Biomarkers of lead exposure. Ind. Health, 38, 127, 2000.

8. Pirtskalaishvili G. et al.: Use of urine-based markers for detection and monitoring of bladder cancer. Tech. Urol., 5, 179, 1999.
9. Preston R.A., Epstein M.: Renal parenchymal disease and hypertension. Semin. Nephrol., 15, 138, 1995.

SUMMARY

The emergence of enzymes in the urine comes as a result of the functioning of the same mechanisms that are observed in general proteinuria. The enzymes present in the urine can be of renal or extrarenal origin. Therefore, we can distinguish two main sources of enzymes: renal (renal tubules, renal pelves, the epithelial cells of the urinary tract) and extrarenal (plasma, leukocytes, erythrocytes). An increase in the activity of the urine enzymes of extrarenal origin is a manifestation of an impaired functioning of the renal glomerule while an increase in the activity of the renal enzymes suggests damage to renal tubules.

Enzymy w moczu

Pojawienie się enzymów w moczu jest wynikiem funkcji tych samych mechanizmów, jakie działają w odniesieniu do ogólnej proteinurii. Wyróżniamy dwa główne źródła enzymów: nerkowe (kanaliki nerkowe, miedniczki nerkowe, komórki nabłonka dróg moczowych) oraz pozanerkowe (osocze, leukocyty, erytrocyty). Wzrost aktywności enzymów w moczu pochodzenia pozanerkowego świadczy o zaburzonej funkcji kłębka nerkowego, natomiast wzrost aktywności enzymów nerkowych świadczy o uszkodzeniu kanalików nerkowych.