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Department of Biochemistry and Molecular Biology, Department of Oncology
Medical University of Lublin

BOLESŁAW FLORIAŃCZYK, AGNIESZKA BASIŃSKA,
LUDMIŁA GRZYBOWSKA-SZATKOWSKA,
MARIA MAZURKIEWICZ, MARTA STRYJECKA-ZIMMER

Beta-glucuronidase activity in patients with breast cancer and head and neck cancer

β-glucuronidase (β-GR) has a systemic name of glucuronohydrolase of β-D-glucuronides (EC 3.2.1.31.). The enzyme catalyses the hydrolysis of β -D-glucuronides – the compounds arising as a result of the combination of β -D-glucuronic acid and a number of both exo-and endogenous compounds containing hydroxylic, carboxylic, amine, imine or thiolic groups (1, 9). These compounds comprise, among others: tyroxine, corticosteroids, estrogens, testosterone, aldosterone, catecholamines, bilirubin and many drugs and poisons. The origination of glucuronides constitutes one of the detoxicating mechanisms, because physiological compounds or those introduced from the outside lose their biological activity or toxic characteristics after combining with the glucuronic acid. Those compounds are better dissolved in water as glucuronides, which favours their ridding from the organism. The enzyme affects exclusively β-glycoside bonds of glucuronides. It does not decompose either α-glucuronides or β-glucupyranosides, but it hydrolyses β-galacturonides (8).

Changes in the activity can be observed in different physiological and pathological conditions (11,12). This is why a lot of research has been conducted on the enzyme. The studies on the changes of β-glucuronidase activity influenced by different factors in physiological as well as pathological conditions have been done using experimental animals as well as humans (8)

The aim of this work was to determine the activity of beta-glucuronidase in the blood serum of patients with breast cancer and head and neck cancer.

MATERIAL AND METHODS

The experimental material were the blood serum samples of patients with breast cancer (n = 24, *ca ductale invasivum*, stage $T_1.T_2,N_0,M_1$) and head and neck cancer (n = 25, stage III^0 and IV^0, histopathology: squamous cell carcinoma). The patients had not been exposed to any prior chemo--or radiotherapy. Blood serum obtained from healthy people served as a control (n = 20). The activity of β-glucuronidase was determined using F i s h m a n et al. method (14). It consists in the colorimetric measurement of the quantity of phenolphtalein freed from the substrate. The results were analyzed statistically by means of the Cohran-Cox test accepting the differences as intrinsic at the intrisicity level of $p<0.05$. The results were presented in the table.

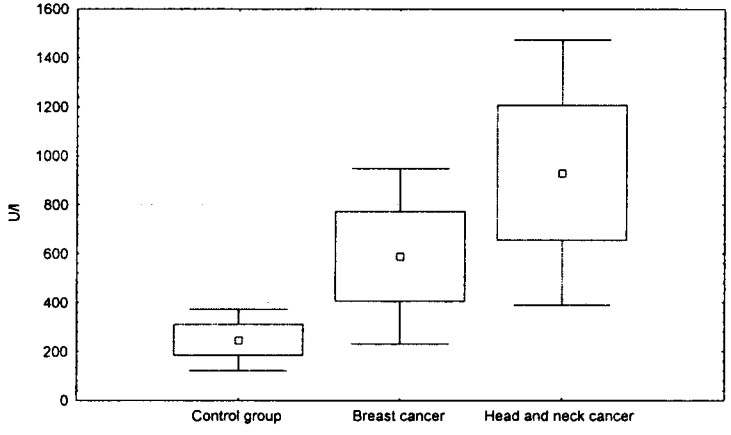
RESULTS

The results of the experiment are presented in Table 1 and Figure 1. As follows from the numeric data presented in the table, median β-GR activity in the blood serum of control group.

246.67 U/l. The mean β-GR activity in the blood serum of breast cancer and head and neck cancer were 597.12 and 940.51 U/l respectively.

Table 1. The activity of beta-glucuronidase in the blood serum of patients with breast cancer and head and neck cancer

Investigated group	Mean value	Standard deviation	Significance level
Control group	246.67	64.07	
Breast cancer	597.12	198.44	$p < 0.05$
Head and neck cancer	940.51	306.42	$p < 0.05$



Ryc.1. Beta-glucuronidase activity in the breast cancer and head and neck cancer

DISCUSSION

In our studies we found an increased beta-glucuronidase activity in the blood serum of patients with breast cancer and larynx cancer. The mean activity of beta-glucuronidase in the blood serum of patients with breast cancer is 2 times higher and in the blood serum of patients with head and neck cancer is over 3.5 times higher in comparison with the mean level of this activity in the control group.

Research into β-glucuronidase activity in human malignancies is numerous (3, 4, 5, 6, 7, 10, 13, 15). In 1947 Anlyan (cit. from S z c z e k l i k) showed that β-glucuronidase activity is higher compared with respective healthy tissue both in primary malignancies and in lymph node or other distant metastases. In further experiments Fishman and Anlyan (cit. from S z c z e k l i k) stated a high activity of β-glucuronidase in stomach, breast, colon, uterus, penile, lung, skin and brain cancer. It follows from clinical studies that increased enzyme activity in the plasma can accompany neoplasms of different location. This cannot be considered a permanent phenomenon. Irrespective of the starting point level, β-glucuronidase activity changes in liver metastases. When the lesion is small, the activity increases, whereas if the neoplastic process covers a larger area, the activity drops.

Golbarg (cit. from S z c z e k l i k) showed β-glucuronidasuria to be within the normal amounts in stomach, breast and cervical cancer. Increased values appear in patients with pancreatic cancer. Costa and Piper (cit. from S z c z e k l i k) examined β-glucuronidase activity in stomach cancer. They observed an increase in the activity of the enzyme in gastric juice. β-glucuronidase appears in gastric juice side by side with other non-proteolytic enzymes. The substrates are glu-

curonides of extra-hepatic origin. The enzyme appears in gastric juice as a result of the passage from a high-concentration environment to the extracellular fluid. Kim et al. (cit. from Konarska) detected the enzyme increase approaching 1,000 Fishman units among 93% of 32 stomach cancer patients. According to them that increase was evidently due to a higher content of the enzyme in neoplastic cells, which, while breaking down, supplied the juice with it, an increased permeability of neoplastic cells and the presence of enzyme activators or absence of inhibitors in neoplastic patients.

As regards malignancies of the central nervous system an increase in β-glucuronidase activity in cerebro-spinal fluid was observed (8). Anlyan and Starr (cit. from Szczeklik) found this regularity in 60% of glioblastoma multiforme patients. β-glucuronidase is one of the biochemical markers used in the diagnostics of the urinary bladder cancer. The first to point this out were Boyland et al. (cit. from Rokicki). The above observation was confirmed by subsequent researchers, who agreed that the phenomenon appeared in 72–75% of those affected. Simultaneoulsly, Costa (cit. from Rokicki) showed an increase in the activity of β-glucuronidase in cancer and papilloma tissues as compared with the healthy tissue of the urinary bladder. β-glucuronidase activity varies in many disease processes including neoplasms. It is therefore significant for medical diagnosis.

In anti-neoplastic treatment it has long been considered noteworthy to include glucuronides as therapeutics. Such drugs could be administered for neoplasms with a high activity of β-glucuronidase. It is imaginable for a non-toxic drug to change into a toxic compound in a neoplastic cell showing a high activity of the enzyme (2).

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SUMMARY

β-glucuronidase (EC 3.2.1.31.) is a lysosomal enzyme catylysing the decomposition of β-D-glucuronides – compounds arising as a result of the combination of β-D-glucuronic acid and a number of compounds both exo- and endogenous, containing hydroxylic, carboxylic, amine, imine or thiol groups. These compounds comprise, among others: tyroxine, corticosteroids, estrogens, testosterone, aldosterone, catecholamines, bilirubin and many drugs and poisons. The activity of β-glucuronidase increases in many pathological conditions. In our studies we found an increased beta-glucuronidase activity in the blood serum of patients with breast cancer and larynx cancer. The mean activity beta-glucuronidase in the blood serum of patients with breast cancer is 2 times higher and in the blood serum of patients with head and neck cancer is over 3.5 times higher in comparison with the mean level of this activity in the control group.

Aktywność β-glukuronidazy u pacjentów z rakiem sutka i rakiem głowy i szyi

β-glukuronidaza (E.C. 3.2.1.31.) jest enzymem lizosomalnym katalizującym rozkład β-D-glukuronidów – związków powstałych w wyniku połączenia kwasu β-D-glukuronowego z szeregiem związków, zarówno egzo- jak i endogennych, zawierających grupy hydroksylowe, karboksylowe, aminowe, iminowe lub tiolowe. Aktywność β-glukuronidazy zmienia się w wielu stanach patologicznych. W naszych badaniach stwierdziliśmy podwyższoną aktywność beta-glukuronidazy w surowicy krwi u pacjentów z rakiem sutka oraz z rakiem gardła. U pacjentów z rakiem sutka aktywność tego enzymu była ponad 2-krotnie wyższa, a u pacjentów z rakiem głowy i szyi – 3,5-krotnie wyższa w porównaniu z aktywnością enzymu w grupie kontrolnej.