Biomedical Data Mining

Extended Abstract

Bird and mammalian lactate dehydrogenase isoenzymes

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Abstract

Lactate dehydrogenase (EC 1.1.1.27, LDH) is an enzyme widely distributed in cells of living systems. It is involved in carbohydrate metabolism catalyzing the interconversion of lactate and pyruvate with nicotinamide adenine dinucleotide as coenzyme both in the cytoplasm as well as in mitochondria. LDH exists in several isoenzymatic forms that differs each other in their kinetic characteristics (Km, kcat), physicochemical properties (different net charge), response to the inhibition by substrate (pyruvate), and immunological response. Their different net charge predetermines their different migration rate in the electric field that is used in separating of these enzymes in research as well as in diagnostic practice. Five somatic LDH isoenzymes are detected in serum and tissues of vertebrates with heart, skeletal muscle and liver being the LDH richest organs. A buffer system of the pH values 8.6 to 8.8 is commonly used for the separation of these isoenzymes enabling to distinguish five LDH molecules in mammals. In the case of bird LDHs, the observation of all five isoforms under this pH condition is very difficult as they produce only one rather diffuse enzymatic zone. Isoelectric focusing technique in the pH range of 3 to 9 was shown to be a convenient method for bird LDH isoenzyme separation producing a good and clear resolution of all five LDH fractions in chicken (adult as well as embryonic), turkey, pheasant, and pigeon. Different pI values of LDHs of bird and mammalian origin with the similar catalytic properties probably reflect the different phylogenesis of bird and mammalian LDH molecules.

Introduction

The use of biomarkers in medicine lies in their ability to detect disease and support diagnostic and therapeutic decisions. They have also a potential value as an important prognostic tool. Clinically useful biomarkers can supplement the clinical diagnosis and help monitoring of the disease, evaluation of treatments, and predicting prognosis and health outcome. Changes in plasma or serum enzymes and isoenzymes are useful indicators of tissue damage in many diseases. Enzyme increases are usually related to their leakage from damaged cells. In humans, the activity and release of a large body of inflammatory mediators and markers of cell damage such as lactate dehydrogenase (LDH, EC 1.1.1.27) have been evaluated as prognostic and monitoring tools of the disease development, activity, and progression. Cytoplasmatic cellular enzymes, like lactate dehydrogenase in the extracellular space, despite no further metabolic function in this space, are still of benefit because they serve as indicators suggestive of disturbances of the cellular integrity induced by pathological condition. Since LDH is an enzyme present in essentially all major organ systems, serum LDH activity is abnormal in a large number of disorders. Many literature sources and reports indicate that the activity of LDH and its isoenzyme patterns show a great variation between animal species and tissue distribution as well. Therefore, it is necessary to understand the composition and distribution of tissue isoenzymes of each animal. The extracellular appearance of LDH is used to detect cell damage or cell death. Increased levels are found in cardiac, hepatic, skeletal muscle and renal diseases, as well as in several haematological and neoplastic disorders. The highest levels of total LDH are seen in pernicious anemia and haemolytic disorders. Liver disorders, such as viral hepatitis and cirrhosis, as well as acute myocardial infarction and pulmonary infarct also show slight elevations of two to three times upper limit of normal. Skeletal muscle disorders and some

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leukaemias contribute to increased LDH levels. Marked elevations can be observed in most patients with acute lymphoblastic leukemia in particular. Because of the many conditions that contribute to increased activity, an elevated total LDH value is a rather nonspecific finding. LDH assays, therefore, assume more clinical significance if separated into isoenzyme fractions.

Conclusion

The fact that the enzyme lactate dehydrogenase is distributed widely in the body required identifying clinical situations in which the determination of lactate dehydrogenase and its isoenzymes in serum are of real value. LDH isoenzyme profiles were the first isoenzyme profiles used in clinical veterinary medicine in an attempt to detect specific organ damage. Even though LDH and its isoenzymes examinations are not used routinely in veterinary laboratory diagnosis, many reports suggested their usefulness in animals. From the clinical perspective, the determination of serum isoenzyme activity is of primary importance, but its determination in biological material from various tissues and organs is also useful. In addition to commonly used blood serum or plasma, LDH activities were also analysed in other body fluids of animals, e.g., synovial fluid, cerebrospinal fluid, milk, and bronchoalveolar lavage fluid. There are many reports suggesting their use within experimental investigations, as well as in diagnosis of organ and metabolic diseases, for example, in cattle.

This work is partly presented at 24th World Chemistry & Systems Biology Conference on October 03-04, 2018 in Los Angeles, USA
October 03-04, 2018 | Los Angeles, USA