LACTATE/LAC

Lactate is measured amperometrically. The enzyme lactate oxidase, immobilized in the lactate biosensor, selectively converts lactate to pyruvate and hydrogen peroxide (H_2O_2). The liberated hydrogen peroxide is oxidized at a platinum electrode to produce a current which is proportional to the sample lactate concentration.

$$\text{L-Lactate} + O_2 \xrightarrow{\text{Lactate Oxidase}} \text{Pyruvate} + H_2O_2$$

$$H_2O_2 \xrightarrow{\text{Platinum electrode}} 2H^+ + O_2 + 2e^-$$

See below for information on factors affecting results. Certain substances, such as drugs, may affect analyte levels *in vivo.*[1]

If results appear inconsistent with the clinical assessment, the patient sample should be retested using another cartridge.

Intended Use

The test for lactate, as part of the i-STAT System, is intended for use in the *in vitro* quantification of lactate in arterial, venous, or capillary whole blood.

The i-STAT lactate test is useful for (1) the diagnosis and treatment of lactic acidosis in conjunction with measurements of blood acid/base status, (2) monitoring tissue hypoxia and strenuous physical exertion, and (3) diagnosis of hyperlactatemia.

Contents

Each i-STAT cartridge contains one reference electrode (when potentiometric sensors are included in the cartridge configuration), sensors for the measurement of specific analytes, and a buffered aqueous calibrant solution that contains known concentrations of analytes and preservatives. For cartridges that contain a sensor for the measurement of lactate, a list of reactive ingredients is indicated below:

Reactive Ingredient	Biological Source	Minimum Quantity
Lactate	N/A	1.8 mmol/L
Lactate Oxidase	*Aerococcus viridans*	0.001 IU

Metrological Traceability

The i-STAT System test for lactate measures L-lactate amount-of-substance concentration in the plasma fraction of arterial, venous, or capillary whole blood (dimension mmol L^{-1}) for *in vitro* diagnostic use. Presently, no international conventional reference measurement procedure or international conventional calibrator for lactate is available. Lactate values assigned to i-STAT's controls and calibration verification materials are traceable to i-STAT's working calibrator prepared from sodium L-lactate (Sigma-Aldrich

Fluka, >99 % purity). i-STAT System controls and calibration verification materials are validated for use only with the i-STAT System and assigned values may not be commutable with other methods. Further information regarding metrological traceability is available from Abbott Point of Care Inc..

Expected Values

Test/Abbreviation	Units*	Reportable Range	Reference[2] Range (arterial)	Reference[2] Range (venous)
Lactate/Lac	mmol/L	0.30 – 20.00	0.36 – 1.25	0.90 – 1.70
	mg/dL	2.7 – 180.2	3.2 – 11.3	8.1 – 15.3

To convert a lactate result from mmol/L to mg/dL, multiply the mmol/L value by 9.01.

The i-STAT reference ranges for whole blood listed above are similar to reference ranges derived from serum or plasma measurements with standard laboratory methods.

The reference range shown above is intended to be used as a guide for the interpretation of results. Since reference ranges may vary with demographic factors such as age, gender and heritage, it is recommended that reference ranges be determined for the population being tested.

* The i-STAT System can be configured with the preferred units.

Clinical Significance

Elevated levels of lactate are mainly found in conditions of hypoxia such as shock, hypovolumia, and left ventricular failure; in conditions associated with diseases such as diabetes mellitus, neoplasia, and liver disease; and in conditions associated with drugs or toxins such as ethanol, methanol, or salicylates.[2]

Hyperlactatemia is an indicator commonly used to detect tissue hypoperfusion, particularly in the case of sepsis,[3-5] but also in trauma[6-8] and surgical[9-11] settings.

Performance Characteristics

The typical performance data summarized below was collected in health care facilities by health care professionals trained in the use of the i-STAT System and comparative methods.

Precision data were collected using CLSI guideline EP5-A[12]. Duplicates of each level of control were tested on three lots of cartridges over 20 days for a total of 120 replicates.

Method comparison data were collected using CLSI guideline EP9-A[13]. Venous blood samples, collected in sodium heparin Vacutainer® tubes, and arterial blood samples, collected in blood gas syringes, were analyzed in duplicate on the i-STAT System. In the plasma study, a portion of each specimen was centrifuged, and the separated plasma was analyzed on the comparative method.

Deming regression analysis[14] was performed on the first replicate of each sample. In the method comparison table, n is the number of specimens in the data set, Sxx and Syy refer to the estimates of imprecision based on the duplicates of the comparative and the i-STAT methods respectively, Sy.x is the standard error of the estimate, and r is the correlation coefficient.*

*The usual warning relating to the use of regression analysis is summarized here as a reminder: For any analyte, “if the data is collected over a narrow range, the estimate of the regression parameters are relatively imprecise and may be biased. Therefore, predictions made from these estimates may be invalid”.[12] The correlation coefficient, r, can be used as a guide to assess the adequacy of the comparative method range in overcoming this problem. As a guide, the range of data can be considered adequate if r>0.975.

Precision Data (mmol/L)	Aqueous Control	n	Mean	SD	%CV
	Level 1	120	6.35	0.08	1.21
	Level 3	120	0.81	0.03	3.27

Method Comparison (mmol/L)	Radiometer ABL 725 **(whole blood vs. whole blood)**	Hitachi 917 **(i-STAT whole blood vs. Hitachi plasma)**
n	47	47
Sxx	0.123	0.084
Syy	0.136	0.079
Slope	1.02	1.06
Int't	0.12	-0.32
Sy.x	0.18	0.17
Xmin	0.80	1.77
Xmax	14.20	14.24
r	0.998	0.997

Factors Affecting Results*

Special collection procedures are necessary to prevent changes in lactate both during and after the blood is drawn. For steady state lactate concentrations, patients should be at rest for 2 hours and fasting. Venous samples should be obtained without the use of a tourniquet or immediately after the tourniquet is applied. Both venous and arterial samples may be collected into heparinized syringes.

Samples for lactate should be analyzed immediately on drawing as lactate increases by as much as 70% within 30 minutes at 25 ºC as a result of glycolysis.[2]

Interference studies were based on CLSI guideline EP7-A2.[15] Test concentrations used were as per the CLSI guideline unless otherwise indicated.

When added to a plasma pool the following substances (at the concentrations indicated) were found to interfere with the i-STAT lactate assay:

Substance	Test Concentration (mmol/L)	Interference
Bromide	37.5	Use another method. See Note below
Glycolic Acid	10.0 [16]	Increased i-STAT lactate results. Use another method.
Hydroxyurea	0.92	Increased i-STAT lactate results. Use another method.

The following substances are known not to significantly interfere with the i-STAT lactate assay at the stated test concentrations:

Substance	Test Concentration (mmol/L)
Acetaldehyde	0.045 [16]
Acetaminophen	1.32
Acetylcysteine	10.2
Ascorbate	0.34
Bromide *(therapeutic)*	2.5 [17,18,19]
Dopamine	0.006
Formaldehyde	0.133 [16]
β-Hydroxybuterate	6.0 [20]
Pyruvate	0.31
Salicylate	4.34
Uric Acid	1.4

Notes:

1) Hydroxyurea is a DNA synthesis inhibitor used in the treatment of various forms of cancer, sickle cell anemia, and HIV infection. This drug is used to treat malignancies including melanoma, metastatic ovarian cancer, and chronic myelogenous leukemia. It is also used in the treatment of polycythemia vera, thrombocythemia, and psoriasis. At typical doses ranging from 500 mg to 2 g/day, concentrations of hydroxyurea in patients' blood may be sustained at approximately 100 to 500 µmol/L. Higher concentrations may be observed soon after dosing or at higher therapeutic doses.

2) Glycolic acid is a product of ethylene glycol metabolism. Unexpected increased lactate concentrations caused by glycolic acid may be a clue to the possibility of ethylene glycol ingestion as the cause of an otherwise unknown high anion gap metabolic acidosis.[21,22] In a study of 35 patients who had ingested ethylene glycol, initial glycolic acid concentrations of 0 to 38 mmol/L corresponded to ethylene glycol levels of 0.97 - 130.6 mmol/L.[22]

3) Bromide has been tested at two levels; the CLSI recommended level and a therapeutic plasma concentration level of 2.5 mmol/L. The latter is the peak plasma concentration associated with halothane anesthesia, in which bromide is released. APOC has not identified a therapeutic condition that would lead to levels consistent with the CLSI recommended level. Bromide at a concentration of 37.5 mmol/L decreased i-STAT lactate results, while a therapeutic range of bromide (2.5 mmol/L) did not significantly interfere with i-STAT lactate results.

* It is possible that other interfering substances may be encountered. The degree of interference at concentrations other than those listed might not be predictable.

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