ISE-I

ISE Indirect

cobas®

ISE Applications

English

Intended use

The ISE module of the COBAS INTEGRA systems is intended for use in the quantitative determination of sodium, potassium, and chloride in diluted serum and plasma using ion-selective electrodes.

Summary[1]

Electrolytes are involved in most major metabolic functions in the body. Sodium, potassium, and chloride are amongst the most important physiological ions and the most often assayed electrolytes. They are supplied primarily through the diet, absorbed in the gastrointestinal tract, and excreted by the kidneys.

Sodium is the major extracellular cation and functions to maintain fluid distribution and osmotic pressure. Some causes of decreased levels of sodium include prolonged vomiting or diarrhea, diminished reabsorption in the kidney and excessive fluid retention. Common causes of increased sodium include excessive fluid loss, high salt intake, and increased kidney reabsorption.

Potassium is the major intracellular cation and is critical to neural and muscle cell activity. Some causes of decreased potassium levels include reduced intake of dietary potassium or excessive loss of potassium from the body by prolonged vomiting, diarrhea, or increased kidney excretion. Increased potassium levels may be caused by dehydration or shock, severe burns, diabetic ketoacidosis, and retention of potassium by the kidney.

Chloride is the major extracellular anion and serves to regulate the balance of extracellular fluid distribution. Similar to the other ions, common causes of decreased chloride include reduced dietary intake, prolonged vomiting, reduced renal reabsorption as well as some forms of acidosis and alkalosis. Increased chloride values are found in dehydration, kidney failure, some forms of acidosis, high dietary or parenteral chloride intake, and salicylate poisoning.

Test principle

Ion-selective electrodes, using automatically diluted specimens (ISE Indirect).

Precautions and warnings

Pay attention to all precautions and warnings listed in Section 1 / Introduction of this Method Manual.

For USA: For prescription use only.

Reagent handling

Ready for use.

Specimen collection and preparation

For specimen collection and preparation only use suitable tubes or collection containers.

Only the specimens listed below were tested and found acceptable. Serum or plasma, free from hemolysis.

The only acceptable anticoagulants are lithium or ammonium heparin.

For sodium and chloride determinations serum is the specimen of choice. For potassium determinations, the use of plasma is preferable since the rupture of platelets during the coagulation process leads to a higher serum potassium concentration compared to plasma.

For plasma specimens, use only lithium or ammonium heparin.

If heparinized plasma is used, ensure that the collection tubes are filled with the correct volume of blood. Underfilling of heparin tubes can result in a high concentration of heparin in the sample which has been shown to result in a small but significant underestimation of sodium when measured by ion-selective electrode methods.[2]

High Li-heparin concentrations can cause interference and downward drift on sodium measurements.

It is not recommended to use primary tubes with a Li-heparin concentration higher than in standard commercially available tubes for adults. The standard Li-heparin tubes tested have a Li-heparin concentration of 17 IU/mL (14.3 USP/mL) and show no interference on sodium measurements. A downward drift can be expected if the Li-heparin concentration is twice this amount or higher.

The sample types listed were tested with a collection of sample collection tubes containing Li-heparin that were commercially available at the time of testing, i.e. not all available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing Li-heparin concentrations which could affect the test results in some cases.

It is important to follow tube supplier's recommendations concerning the filling volume and tube handling after blood collection, ensuring that there is no further impact on sodium measurements.

The operational life of the chloride electrode may be reduced when using plasma samples. In addition, patient results may also be elevated. Therefore always carefully evaluate chloride results derived from plasma samples.

Samples should be separated from the clot or cells promptly after collection. Grossly lipemic specimens should be cleared by ultracentrifugation or ultrafiltration.

The specimens are automatically diluted 1:6 (1+5) by the instrument.

Note

Serum separator tubes containing acrylic, ester, styrene, urethane or olefin based gels may be used for sample collection as long as they are used in accordance with the manufacturer's recommended procedures. It is especially important that storage temperature, adequate mixing and clotting times at sufficient g-forces for sufficient time periods are respected. Ensure also correct filling levels and ensure a minimum of 1 cm sample above gel layer. If these precautions are not taken, it is possible to accidentally coat the sample probe with gel (interfering with proper sample level detection), or even to aspirate gel into the ISE system (resulting in a clogged system). Inadequate mixing of plasma tubes can cause interference with micro fibrin clots.

It is strongly recommended to avoid silicone-type gels, due to risk of silicon oil contaminations. Today's global tube suppliers do not employ silicone based gels at all, but it may be that silicone gels are in use by small local suppliers. In addition, tubes that exhibit a layer of clear liquid, which rises to the top of the serum after centrifugation, should not be used for direct sample aspiration, in order to prevent coating the sample probes and interfering with ISE system.

It is possible to clog the sample probes or the ISE tubing with gel or clots if these precautions are not taken.

The stabilities of the electrolytes in the specimen (separated serum or plasma) kept in tightly closed tubes are given in the table below:[3]

	15-25 °C	2-8 °C	(-15)-(-25) °C
Sodium	14 days	14 days	stable
Potassium	14 days	14 days	stable
Chloride	7 days	7 days	stable

Application for serum and plasma
COBAS INTEGRA 400 plus/800 test definition

Measuring mode		ISE
Test range	*Sodium*	20-250 mmol/L
	Potassium	0.2-30 mmol/L
	Chloride	20-250 mmol/L
Unit		mmol/L

Pipetting parameters

Sample	20 µL
Diluent (H_2O)	100 µL

Calibration

Calibrators	ISE Solutions 1, 2
	ISE Calibrator Indirect/Urine
Calibration replicate	Single
Calibration interval	Five hours (main calibration)
	Every sample (one-point calibration)

Once opened, ISE Solution 1 and 2 are stable on-board up to 2 weeks.

Once opened, ISE Calibrator Indirect/Urine is stable on-board up to 8 weeks.

Note

Any ISE mode change (between direct, indirect, and urine) is initiated using ISE Solution 1 as a dummy sample in an appropriate dilution.

ISE Solution 3 is used during maintenance procedures (COBAS INTEGRA 800 analyzers only).

Quality control

Reference range	Precinorm U, Precinorm U plus, or PreciControl ClinChem Multi 1*
Pathological range	Precipath U, Precipath U plus, or PreciControl ClinChem Multi 2*
Control interval	5 hours recommended
Control sequence	User defined
Control after calibration	Recommended

*not for use in the US

For quality control, use control materials as listed above. In addition, other suitable control material can be used.

The control intervals and limits should be adapted to each laboratory's individual requirements. Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

Follow the applicable government regulations and local guidelines for quality control.

Calculation

Refer to the Section "Principle of Measurement" in the general description "Ion-Selective Electrode Module".

Limitations - interference

Criterion: Recovery within ± 10 % of initial value.

Serum, plasma

Hemolysis: Avoid hemolyzed specimens.

Sodium and chloride: No significant interference up to a hemoglobin level of 10 g/L.

Potassium: No significant interference up to a hemoglobin level of 0.06 mmol/L (1 g/L).

Potassium concentration in erythrocytes is 25 times higher than in normal plasma. The level of interference may be variable depending on the exact content of erythrocytes.

Icterus: No significant interference

Lipemia: No significant interference

Drugs: Therapeutic drug interference was tested according to the recommendations of the VDGH[a)]. No interferences were found.

Exceptions:
Chloride
Acetylsalicylic acid causes artificially high chloride concentrations.
In addition to the tested drug panel, salicylic acid was measured. Including the highest concentration (3 mmol/L), no significant interference was detected. Falsely high chloride values have been reported from patients receiving perchlorate medication. This is due to an interference of perchlorate ions with chloride ISE determinations.

For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

a) Verband der Diagnostica und Diagnostica Geräte Hersteller. Refer to section 1 / Introduction of this Method Manual for a list of drugs tested and their concentrations.

Expected values[4]

ISE indirect and flame emission photometry

Serum (adults)	Sodium	136-145 mmol/L
	Potassium	3.5-5.1 mmol/L
	Chloride	98-107 mmol/L
Plasma (adults)	Sodium	136-145 mmol/L
	Potassium	3.4-4.5 mmol/L
	Chloride	98-107 mmol/L

Plasma potassium levels are reported to be lower than serum levels.[1]

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

Specific performance data

Representative performance data on the analyzers are given below. Results obtained in individual laboratories may differ.

Precision

Precision was determined using human samples and controls in an internal protocol with repeatability and intermediate precision (2 aliquots per run, 2 runs per day, 20 days). The following results were obtained:

Sodium	Level 1	Level 2
Mean	112 mmol/L	138 mmol/L
CV repeatability	0.3 %	0.2 %
CV intermediate precision	1.0 %	0.6 %

Potassium	Level 1	Level 2
Mean	4.25 mmol/L	6.92 mmol/L
CV repeatability	0.4 %	0.3 %
CV intermediate precision	0.8 %	0.8 %

Chloride	Level 1	Level 2
Mean	101 mmol/L	86.7 mmol/L
CV repeatability	0.7 %	0.8 %
CV intermediate precision	1.2 %	1.5 %

Method comparison

Sodium and potassium values for human serum samples obtained on the COBAS INTEGRA 700 ISE module (y) were compared to those determined on a COBAS MIRA analyzer (x) and an alternative manufacturer's system (x).

Chloride values for human serum samples obtained on the COBAS INTEGRA 700 ISE module (y) were compared to those determined on a COBAS INTEGRA 700 analyzer (previous chloride electrode) (x).

Samples were measured in duplicate. Sample size (n) represents all replicates.

Sodium

		COBAS MIRA analyzer
Method		ISE direct
Sample size	(n)	208
Corr. coeff.	(r)	0.985
	(r_s)	0.976
Lin. regression		y = 1.021x - 8.7 mmol/L
Passing/Bablok[5]		y = 1.022x - 9.0 mmol/L

The sample concentrations were between 116 and 174 mmol/L.

		Alternative system
Method		ISE indirect
Sample size	(n)	208
Corr. coeff.	(r)	0.994
	(r_s)	0.980
Lin. regression		y = 0.964x + 1.2 mmol/L
Passing/Bablok[5]		y = 0.948x + 3.5 mmol/L

The sample concentrations were between 116 and 176 mmol/L.

Potassium

		COBAS MIRA analyzer
Method		ISE direct
Sample size	(n)	208
Corr. coeff.	(r)	0.996
	(r_s)	0.996
Lin. regression		y = 0.968x - 0.07 mmol/L
Passing/Bablok[5]		y = 0.958x - 0.03 mmol/L

The sample concentrations were between 3.96 and 7.60 mmol/L.

		Alternative system
Method		ISE indirect
Sample size	(n)	208
Corr. coeff.	(r)	0.999
	(r_s)	0.998
Lin. regression		y = 0.999x - 0.09 mmol/L
Passing/Bablok[5]		y = 0.996x - 0.08 mmol/L

The sample concentrations were between 3.96 and 7.45 mmol/L.

Chloride

		COBAS INTEGRA 700 analyzer
Method		ISE indirect
Sample size	(n)	100
Corr. coeff.	(r)	0.988
	(r_s)	0.967
Lin. regression		y = 0.988x - 0.05 mmol/L
Passing/Bablok[5]		y = 1.000x - 1.01 mmol/L

The sample concentrations were between 85 and 117 mmol/L.

References

1 Tietz NW, Pruden EL, Siggaard-Andersen O. Electrolytes. In: Burtis CA, Ashwood ER, eds. Tietz Textbook of Clinical Chemistry. 2nd ed. Philadelphia: WB Saunders Co 1994;1354-1374.

2 Mann SW, Green A. Interference from heparin in commercial heparinised tubes in the measurement of plasma sodium by ion selective electrode: a note of caution. Ann Clin Biochem 1986;23:355-356.

3 Young DS. Storage of specimen. In: Effects of Preanalytical Variables on Clinical Laboratory Tests. 1st ed. Washington: AACC Press 1993;4:269-278.

4 Tietz NW, ed. Clinical Guide to Laboratory Tests, 3rd ed. Philadelphia: WB Saunders, 1995;124-127(chloride), 840-841 (lithium), 502-507 (potassium), 562-565 (sodium).

5 Bablok W, Passing H, Bender R, et al. A general regression procedure for method transformation. Application of linear regression procedures for method comparison studies in clinical chemistry, Part III. J Clin Chem Clin Biochem 1988 Nov;26(11):783-790.

A point (period/stop) is always used in this Method Sheet as the decimal separator to mark the border between the integral and the fractional parts of a decimal numeral. Separators for thousands are not used.

Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard.

CONTENT	Contents of kit
→	Volume after reconstitution or mixing
GTIN	Global Trade Item Number

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