CERU

Ceruloplasmin

cobas®

Specific proteins

Order information

REF	CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
20764663 322	Ceruloplasmin (100 tests)	System-ID 07 6466 3	COBAS INTEGRA 400 plus COBAS INTEGRA 800
03555941 190	Calibrator f.a.s. PAC (3 × 1 mL)	System-ID 07 6810 3	
04567021 190	Prealbumin/Ceruloplasmin Control Set[a)] for Precinorm PC (3 x 1 mL) for Precipath PC (3 x 1 mL)	 System-ID 07 6853 7 System-ID 07 6854 5	
20756350 322	NaCl Diluent 9 % (6 × 22 mL)	System-ID 07 5635 0	
05117003 190	PreciControl ClinChem Multi 1 (20 × 5 mL)	System-ID 07 7469 3	
05947626 190	PreciControl ClinChem Multi 1 (4 × 5 mL)	System-ID 07 7469 3	
05947626 160	PreciControl ClinChem Multi 1 (4 × 5 mL, for USA)	System-ID 07 7469 3	
05117216 190	PreciControl ClinChem Multi 2 (20 × 5 mL)	System-ID 07 7470 7	
05947774 190	PreciControl ClinChem Multi 2 (4 × 5 mL)	System-ID 07 7470 7	
05947774 160	PreciControl ClinChem Multi 2 (4 × 5 mL, for USA)	System-ID 07 7470 7	

a) Not for use in the US; US customers should use a suitable commercially available control.

English

System information

Test CERU3, test ID 0-666

Intended use

In vitro test for the quantitative immunological determination of ceruloplasmin in human serum and plasma on COBAS INTEGRA systems.

Summary[1,2,3,4,5]

Ceruloplasmin is a protein with a molecular weight of 150 kDa. Each molecule can reversibly bind eight atoms of copper. Ceruloplasmin carries at least 95 % of all copper in plasma. The protein is synthesized by the liver and shows an acute phase response. Decreased levels are found in primary biliary cirrhosis, primary biliary atresia, and in some cases of severe hepatitis. The decreased levels are due to the limitations of total liver metabolism rather than to a defect in specific ceruloplasmin synthesis. In some congenital disorders, such as Wilson's disease, ceruloplasmin is also found to be decreased.

As ceruloplasmin is increasingly expressed during the acute-phase response it is generally detected in elevated levels during all inflammatory diseases. In addition, raised levels are seen in reticuloendothelial neoplasia, biliary obstruction, estrogen therapy, and pregnancy.

Various methods have been described for the measurement of ceruloplasmin. The most commonly used are turbidimetry, nephelometry, and radial immunodiffusion.

Test principle[2]

Immunoturbidimetric assay.

Human ceruloplasmin forms a precipitate with a specific antiserum which is determined turbidimetrically at 340 nm.

Reagents - working solutions

R1 Accelerator
Polyethylene glycol (PEG) 50 g/L, in phosphate buffer; preservative

SR Anti-ceruloplasmin T antiserum (rabbit) specific for human ceruloplasmin > 0.42 g/L in phosphate buffer; preservative

R1 is in position B and SR is in position C.

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

Storage and stability

Shelf life at 2-8 °C	See expiration date on **cobas c** pack label
COBAS INTEGRA 400 plus system	
On-board in use at 10-15 °C	8 weeks
COBAS INTEGRA 800 system	
On-board in use at 8 °C	8 weeks

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
Plasma: Li-heparin plasma.

The sample types listed were tested with a selection of sample collection tubes 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 materials which could affect the test results in some cases. When processing samples in primary tubes (sample collection systems), follow the instructions of the tube manufacturer.

Centrifuge samples containing precipitates before performing the assay.

Samples and controls are automatically prediluted 1:21 (1 + 20) with NaCl solution by the instrument.

Stability:[6]	3 days at 2-8 °C
	4 weeks at (–15)-(–25) °C

Materials provided

See "Reagents – working solutions" section for reagents.

Materials required (but not provided)

NaCl Diluent 9 %, Cat. No. 20756350322, system-ID 07 5635 0 for automatic sample dilution and standard serial dilutions. NaCl Diluent 9 % is placed in its predefined rack position and is stable for 4 weeks on-board COBAS INTEGRA 400 plus/800 analyzers.

Assay

For optimum performance of the assay follow the directions given in this document for the analyzer concerned. Refer to the appropriate operator's manual for analyzer-specific assay instructions.

Application for serum and plasma

COBAS INTEGRA 400 plus test definition

Measuring mode	Absorbance
Abs. calculation mode	Endpoint
Reaction mode	D-R1-S-SR
Reaction direction	Increase
Wavelength A	340 nm

Calc. first/last	33/55
Typical prozone effect	> 12.8 g/L (> 1280 mg/dL or > 95.5 µmol/L)
Antigen excess check	No
Predilution factor	21
Unit	g/L

Pipetting parameters

		Diluent (H_2O)
R1	100 µL	
Sample	20 µL	5 µL
SR	20 µL	5 µL
Total volume	150 µL	

COBAS INTEGRA 800 test definition

Measuring mode	Absorbance
Abs. calculation mode	Endpoint
Reaction mode	D-R1-S-SR
Reaction direction	Increase
Wavelength A	340 nm
Calc. first/last	44/82
Typical prozone effect	> 13.2 g/L (> 1320 mg/dL or > 98.5 µmol/L)
Antigen excess check	No
Predilution factor	21
Unit	g/L

Pipetting parameters

		Diluent (H_2O)
R1	100 µL	
Sample	20 µL	5 µL
SR	20 µL	5 µL
Total volume	150 µL	

Calibration

Calibrator	C.f.a.s. PAC
Calibration dilution ratio	1:6.3, 1:8.5, 1:11, 1:21, 1:40, 1:105, performed automatically by the instrument
Calibration mode	Logit/log 5
Calibration replicate	Duplicate recommended
Calibration interval	Each lot and as required following quality control procedures

Enter the assigned lot-specific ceruloplasmin value of the undiluted calibrator indicated in the package insert for C.f.a.s. PAC.

Traceability: This method has been standardized against the IFCC/BCR/CAP reference preparation CRM 470 (RPPHS 91/0619) for 14 serum proteins.[7]

Quality control

Reference range	Precinorm PC* or PreciControl ClinChem Multi 1
Pathological range	Precipath PC* or PreciControl ClinChem Multi 2
Control interval	24 hours recommended
Control sequence	User defined
Control after calibration	Recommended

*Not for use in the US; US customers should use a suitable commercially available control.

For quality control, use control materials as listed in the "Order information" section. 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

COBAS INTEGRA analyzers automatically calculate the analyte concentration of each sample. For more details, please refer to Data Analysis in the Online Help (COBAS INTEGRA 400 plus/800 analyzers).

Conversion factors:[8]	g/L × 7.46 = µmol/L
	g/L × 100 = mg/dL
	mg/dL × 0.0746 = µmol/L

Limitations - interference

Criterion: Recovery within ± 10 % of initial value.

Icterus:[9] No significant interference up to an I index of 60 for conjugated and unconjugated bilirubin (approximate conjugated and unconjugated bilirubin concentration: 1026 µmol/L or 60 mg/dL).

Hemolysis:[9] No significant interference up to an H index of 1000 (approximate hemoglobin concentration: 621 µmol/L or 1000 mg/dL).

Lipemia (Intralipid):[9] No significant interference up to an L index of 50. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

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

Rheumatoid factors: No significant interference up to a rheumatoid factors level of 400 IU/mL.

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[10]

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

b) 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.

ACTION REQUIRED

Special Wash Programming: The use of special wash steps is mandatory when certain test combinations are run together on COBAS INTEGRA analyzers. Refer to the CLEAN Method Sheet for further instructions and for the latest version of the Extra wash cycle list.

Where required, special wash/carry-over evasion programming must be implemented prior to reporting results with this test.

Limits and ranges

Measuring range

0.08-1.4 g/L (0.597-10.4 µmol/L or 8.00-140 mg/dL) (typical measuring range)

The upper and lower limits of the measuring range depend on the actual calibrator value.

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:3 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 3.

Determine samples having lower concentrations via the rerun function. For samples with lower concentrations, the rerun function reduces the sample predilution factor to 10.5. The results are automatically multiplied by the reduced predilution factor.

Lower limits of measurement

Lower detection limit of the test:
0.03 g/L (0.224 µmol/L or 3.00 mg/dL)

The lower detection limit represents the lowest measurable analyte level that can be distinguished from zero. It is calculated as the value lying 3 standard deviations above that of a zero sample (zero sample + 3 SD, repeatability, n = 30).

Expected values[11]

Male: 0.15-0.30 g/L (15.0-30.0 mg/dL or 1.12-2.24 µmol/L)

Female: 0.16-0.45 g/L (16.0-45.0 mg/dL or 1.19-3.36 µmol/L)

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 COBAS INTEGRA 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:

	Level 1	Level 2
Mean	0.20 g/L (1.52 µmol/L or 20.4 mg/dL)	0.35 g/L (2.59 µmol/L or 34.7 mg/dL)
CV repeatability	3.6 %	2.4 %
CV intermediate precision	3.9 %	2.7 %

Method comparison

Ceruloplasmin values for human serum samples obtained on a COBAS INTEGRA 400 analyzer (x) with the COBAS INTEGRA Ceruloplasmin reagent were compared to those determined with the same reagent on a COBAS INTEGRA 800 analyzer (y) and with Tina-quant Ceruloplasmin reagent on a Roche/Hitachi 917 instrument (y).

COBAS INTEGRA 800 analyzer

Sample size (n) = 73

Passing/Bablok[12]	Linear regression
y = 1.05x - 0.005 g/L	y = 1.04x - 0.001 g/L
τ = 0.9330	r = 0.9965
SD (md 95) = 0.015	Sy.x = 0.007

The sample concentrations were between 0.08 and 0.68 g/L (0.597 and 5.07 µmol/L or 8.00 and 68.0 mg/dL).

Roche/Hitachi 917 analyzer

Sample size (n) = 82

Passing/Bablok[12]	Linear regression
y = 1.05x + 0.002 g/L	y = 1.03x + 0.005 g/L
τ = 0.8886	r = 0.9917
SD (md 95) = 0.023	Sy.x = 0.010

The sample concentrations were between 0.08 and 0.68 g/L (0.597 and 5.07 µmol/L or 8.00 and 68.0 mg/dL).

References

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2 Halls DJ, Fell GS, Dunbar PM. Determination of copper in urine by graphite furnace atomic absorption spectrometry. Clin Chim Acta 1981;114:21-27.

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6 Tietz NW, ed. Clinical Guide to Laboratory Tests, 3rd ed. Philadelphia, PA: WB Saunders Company 1995;122-123.

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8 Young DS, Huth EJ. SI Units For Clinical Measurement. American College of Physicians, 1998.

9 Glick MR, Ryder KW, Jackson SA. Graphical Comparisons of Interferences in Clinical Chemistry Instrumentation. Clin Chem 1986;32:470-475.

10 Bakker AJ, Mücke M. Gammopathy interference in clinical chemistry assays: mechanisms, detection and prevention. Clin Chem Lab Med 2007;45(9):1240-1243.

11 Data on file at Roche Diagnostics.

12 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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Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com

Distribution in USA by:
Roche Diagnostics, Indianapolis, IN
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