FRA

cobas®

Fructosamine

Order information

REF	CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
04537939 190	Fructosamine 150 tests	System-ID 07 3756 9	Roche/Hitachi **cobas c** 311, **cobas c** 501/502
11098993 122	Precimat Fructosamine (3 x 1 mL)	Code 581	
11098985 122	Precinorm Fructosamine (3 x 1 mL)	Code 321	
11174118 122	Precipath Fructosamine (3 x 1 mL)	Code 322	

English

System information

For **cobas c** 311/501 analyzers:

FRA: ACN 667

For **cobas c** 502 analyzer:

FRA: ACN 8667

Intended use

In vitro test for the quantitative determination of glycated proteins (fructosamine) in human serum and plasma on Roche/Hitachi **cobas c** systems.

Summary[1,2,3,4]

Fructosamine represents non-enzymatic glycation attached to blood and tissue proteins. The formation of fructosamine is a two-step reaction, which is dependent on the glucose concentration. As a first step a Schiff Base is formed by the reversible coupling of glucose to protein which, in a second step, is transformed by non-reversible Amadori rearrangement to the corresponding ketoamine. This ketoamine is designated as fructosamine. The formation of fructosamine increases with the level of blood glucose. Metabolization occurs within 1 to 3 weeks, corresponding to the turnover of most serum proteins. The concentration of fructosamine thus reflects the average of the continuously varying blood glucose concentrations during this period, serving as a blood glucose memory.

Fructosamine is therefore a rapid indicator of glycemia in the diagnosis and management of diabetes mellitus.

Test principle

Colorimetric test by reaction with nitroblue tetrazolium.[5,6,7]

The colorimetric test for fructosamine (glycated protein) is based on the ability of ketoamines to reduce nitroblue tetrazolium in alkaline medium. The rate of formation of formazan is directly proportional to the fructosamine concentration and is measured photometrically.

Reagents - working solutions

R1 Nitroblue tetrazolium: 1.2 mmol/L; uricase (microbial): ≥ 12 µkat/L; pH 7.5; non-reactive buffer; stabilizer; surfactants

R2 Carbonate buffer: 1.5 mol/L; pH 10.4

R1 is in position B and R2 is in position C.

Precautions and warnings

For in vitro diagnostic use.
Exercise the normal precautions required for handling all laboratory reagents.
Disposal of all waste material should be in accordance with local guidelines.
Safety data sheet available for professional user on request.

For USA: For prescription use only.

This kit contains components classified as follows in accordance with the Regulation (EC) No. 1272/2008:

Danger

H315 Causes skin irritation.

H318 Causes serious eye damage.

H412 Harmful to aquatic life with long lasting effects.

Prevention:

P273 Avoid release to the environment.

P280 Wear eye protection/ face protection.

Response:

P305 + P351 + P338 + P310 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a POISON CENTER or doctor/ physician.

P362 + P364 Take off contaminated clothing and wash it before reuse.

Product safety labeling primarily follows EU GHS guidance.

Contact phone: all countries: +49-621-7590, USA: 1-800-428-2336

Reagent handling

Ready for use

Storage and stability

FRA

Shelf life at 2-8 °C:	See expiration date on **cobas c** pack label.
On-board in use and refrigerated on the analyzer:	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 (free from hemolysis): Collect serum using standard sampling tubes.
Plasma (free from hemolysis): Li-heparin and K_2-EDTA 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.

Stability:	3 days at 15-25 °C[8]
	2 weeks at 2-8 °C[8]
	2 months at (-15)-(-25) °C[9]

Materials provided

See “Reagents – working solutions” section for reagents.

Materials required (but not provided)

- See “Order information” section
- General laboratory equipment

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.

The performance of applications not validated by Roche is not warranted and must be defined by the user.

Application for serum and plasma

cobas c 311 **test definition**

FRA

Fructosamine

Assay type	Rate A	
Reaction time / Assay points	10 / 52-57	
Wavelength (sub/main)	700/546 nm	
Reaction direction	Increase	
Unit	µmol/L	
Reagent pipetting		Diluent (H_2O)
R1	60 µL	28 µL
R2	12 µL	20 µL

Sample volumes	*Sample*	*Sample dilution*	
		Sample	Diluent (H_2O)
Normal	6 µL	–	–
Decreased	3 µL	–	–
Increased	6 µL	–	–

cobas c 501 **test definition**

Assay type	Rate A	
Reaction time / Assay points	10 / 63-70	
Wavelength (sub/main)	700/546 nm	
Reaction direction	Increase	
Unit	µmol/L	
Reagent pipetting		Diluent (H_2O)
R1	60 µL	28 µL
R2	12 µL	20 µL

Sample volumes	*Sample*	*Sample dilution*	
		Sample	Diluent (H_2O)
Normal	6 µL	–	–
Decreased	3 µL	–	–
Increased	6 µL	–	–

cobas c 502 **test definition**

Assay type	Rate A	
Reaction time / Assay points	10 / 63-70	
Wavelength (sub/main)	700/546 nm	
Reaction direction	Increase	
Unit	µmol/L	
Reagent pipetting		Diluent (H_2O)
R1	60 µL	28 µL
R2	12 µL	20 µL

Sample volumes	*Sample*	*Sample dilution*	
		Sample	Diluent (H_2O)
Normal	6 µL	–	–
Decreased	3 µL	–	–
Increased	12 µL	–	–

Calibration

Calibrators	S1: H_2O S2: Precimat Fructosamine
Calibration mode	Linear
Calibration frequency	2-point calibration • after reagent lot change • as required following quality control procedures

Traceability: This method has been standardized against fructose polylysine standard.

Quality 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

Roche/Hitachi **cobas c** systems automatically calculate the analyte concentration of each sample.

Limitations – interference

Criterion: Recovery within ± 10 % of initial value at a fructosamine concentration of 285 µmol/L.

Icterus:[10] No significant interference up to an I index of 5 for conjugated and unconjugated bilirubin (approximate conjugated and unconjugated bilirubin concentration: 85 µmol/L (5 mg/dL)).

Hemolysis:[10] No significant interference up to an H index of 100 (approximate hemoglobin concentration: 62 µmol/L (100 mg/dL)).

Lipemia:[10] No significant interference up to an L index of 1800. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Drugs: No interference was found at therapeutic concentrations using common drug panels.[11,12]

Exception: Levodopa causes artificially high fructosamine results. Oxytetracycline causes artificially high fructosamine results.

Other: Ascorbic acid levels of up to 170 µmol/L (30 mg/L) do not significantly interfere with the test.

In hydremic states (pregnancy for instance) it may be favorable to relate fructosamine to protein using the following formula:

$$\text{Fructosamine}_{corr} = \frac{\text{measured fructosamine} \times 72}{\text{measured total protein (in g/L)}}$$

Dysproteinemic states may affect fructosamine values.[4]

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[13]

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

ACTION REQUIRED

Special Wash Programming: The use of special wash steps is mandatory when certain test combinations are run together on Roche/Hitachi **cobas c** systems. The latest version of the carry-over evasion list can be found with the NaOHD-SMS-SmpCln1+2-SCCS Method Sheets. For further instructions refer to the operator's manual. **cobas c** 502 analyzer: All special wash programming necessary for avoiding carry-over is available via the **cobas** link, manual input is not required.

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

Limits and ranges

Measuring range

14-1000 µmol/L

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:2 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 2.

Lower limits of measurement

Lower detection limit of the test

14 µmol/L

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 the lowest standard (standard 1 + 3 SD, repeatability, n = 21).

Expected values[6,14]

Fructosamine concentrations were determined in 555 apparently healthy subjects between the ages of 20 and 60. A reference range of 205 to 285 µmol/L was determined in this study for adults without diabetes. In a poorly controlled diabetic population, mean fructosamine values were reported to be 396 µmol/L (range 228-563 µmol/L). A fructosamine concentration above the established expected value is an indicator for hyperglycemia during the preceeding 1-3 weeks or longer.

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 (n = 21) and intermediate precision (3 aliquots per run, 1 run per day, 21 days). The following results were obtained:

Repeatability	*Mean*	*SD*	*CV*
	µmol/L	*µmol/L*	*%*
Precinorm Fructosamine	262	4	1.6
Precipath Fructosamine	498	4	0.7
Human serum 1	262	2	0.9
Human serum 2	208	2	1.0
Intermediate precision	*Mean*	*SD*	*CV*
	µmol/L	*µmol/L*	*%*
Precinorm Fructosamine	262	4	1.5
Precipath Fructosamine	489	6	1.2
Human serum 3	266	4	1.5
Human serum 4	210	4	1.8

Method comparison

Fructosamine values for human serum and plasma samples obtained on a Roche/Hitachi **cobas c** 501 analyzer (y) were compared with those determined on Roche/Hitachi 917/MODULAR P analyzers (x), using the corresponding Roche/Hitachi reagent.

Sample size (n) = 231

Passing/Bablok[15]	Linear regression
y = 0.968x + 15.0 µmol/L	y = 0.967x + 15.5 µmol/L
τ = 0.946	r = 0.998

The sample concentrations were between 166 and 836 µmol/L.

References

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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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