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

Materials required (but not provided):

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 for health care professionals. Exercise the normal precautions required for handling all laboratory reagents.

Infectious or microbial waste:
Warning: handle waste as potentially biohazardous material. Dispose of waste according to accepted laboratory instructions and procedures.

Environmental hazards:
Apply all relevant local disposal regulations to determine the safe disposal.

Safety data sheet available for professional user on request.

For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

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.

Prevention:

P264 Wash skin thoroughly after handling.

P280 Wear protective gloves/ eye protection/ face protection.

Response:

P302 + P352 IF ON SKIN: Wash with plenty of water.

P332 + P313 If skin irritation occurs: Get medical advice/attention.

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

P305 + P351 + P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.

P310 Immediately call a POISON CENTER /doctor.

Product safety labeling 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: Collect serum using standard sampling tubes.
Plasma: 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.

See the limitations and interferences section for details about possible sample interferences.

Sample stability claims were established by experimental data by the manufacturer or based on reference literature and only for the temperatures/time frames as stated in the method sheet. It is the responsibility of the individual laboratory to use all available references and/or its own studies to determine specific stability criteria for its laboratory.

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**

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

Calibration interval may be extended based on acceptable verification of calibration by the laboratory.

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 or 5 mg/dL).

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

As tested according CLSI recommendation Methyldopa causes artificially high fructosamine results.[13]

Ascorbic acid: No significant interference from ascorbic acid up to a concentration of 170 µmol/L (30 mg/L).

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.[14]

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 required in certain cases.

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[6,15]

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

The data obtained on **cobas c** 501 analyzer(s) are representative for **cobas c** 311 analyzer(s).

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[16]	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.

The data obtained on **cobas c** 501 analyzer(s) are representative for **cobas c** 311 analyzer(s).

References

1 Johnson RN, Metcalf PA, Baker JR. Fructosamine: a new approach to the estimation of serum glycosylprotein. An index of diabetic control. Clin Chim Acta 1983;127:87-95.

2 Armbruster DA. Fructosamine: structure, analysis, and clinical usefulness. Clin Chem 1987;33(12):2153-2163.

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12 Sonntag O, Scholer A. Drug interference in clinical chemistry: recommendation of drugs and their concentrations to be used in drug interference studies. Ann Clin Biochem 2001;38:376-385.

13 CLSI. Interference testing in Clinical Chemistry; Approved Guideline-Second Edition. CLSI document EP7-A2, Wayne, Pennsylvania, 2005.

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

15 Melzi d'Eril GV, Bosini T, Solerte SB, et al. Performance and clinical significance of the new fructosamine assay in diabetic patients. Wien Klin Wochenschr Suppl 1990;180:60-63.

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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.

Any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established.

FRA

Fructosamine

cobas®

Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard (for USA: see dialog.roche.com for definition of symbols used):

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

FOR US CUSTOMERS ONLY: LIMITED WARRANTY

Roche Diagnostics warrants that this product will meet the specifications stated in the labeling when used in accordance with such labeling and will be free from defects in material and workmanship until the expiration date printed on the label. THIS LIMITED WARRANTY IS IN LIEU OF ANY OTHER WARRANTY, EXPRESS OR IMPLIED, INCLUDING ANY IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR PARTICULAR PURPOSE. IN NO EVENT SHALL ROCHE DIAGNOSTICS BE LIABLE FOR INCIDENTAL, INDIRECT, SPECIAL OR CONSEQUENTIAL DAMAGES.

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Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com
+800 5505 6606

Roche

Distribution in USA by:
Roche Diagnostics, Indianapolis, IN
US Customer Technical Support 1-800-428-2336