Fibrinogen

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Fibrinogen

REF		CONTENT		SYSTEM
07153473190	07153473500	210	System-ID 07 2005 9	**cobas t** 511 **cobas t** 711

English

System information

Short name	ACN (application code number)	Information
Fibrinogen	28200	use with Cal Plasma, Con 1, Con P
Fibrinogen_UNI	28201	use with UniCal, UniCon N, UniCon P

Intended use

In vitro assay for the quantitative determination of fibrinogen (Clauss method) in citrated plasma on the indicated **cobas t** analyzers.

The assay is intended as an aid in the detection of hypo- and hyperfibrinogenemia, dysfibrinogenemia and afibrinogenemia.

Summary

Fibrinogen is an important coagulation factor which is synthesized in the liver.[1]
Thrombin converts fibrinogen to fibrin monomers leading to spontaneous fibrin polymerization. The fibrin polymers form a fibrin clot, together with platelets. Fibrin polymers are digested by the fibrinolytic system.
Elevated levels of fibrinogen have been observed during acute-phase reactions[2], pregnancy[3,4] and oral contraception[5,6], menopause[7,8], smoking[9,10], malignancies or chronic inflammatory diseases. Increased fibrinogen concentrations have been associated with thromboembolic states and are considered as risk factors for thrombotic disease.[11,12] Low fibrinogen concentrations can occur during acute or chronic liver disease[13], disseminated intravascular coagulation, thrombolytic therapy, hemodilution and during consumption coagulopathy.[1,14] Chronically low levels may be also related to inherited conditions such as afibrinogenemia[15] or dysfibrinogenemia.[16]
Fibrinogen levels are usually determined for pre-operative screening or in case of unexplained prolonged bleeding.

Test principle

According to the method of Clauss[17], thrombin added in excess to diluted plasma causes the conversion of soluble fibrinogen to insoluble fibrin polymers. The coagulation time is inversely proportional to the fibrinogen concentration of the sample. Due to the presence of a heparin inhibitor in the reagent, also plasma samples of patients under heparin therapy can be assayed reliably.

Reagents - working solutions

cobas t pack

SR[a)] Lyophilized bovine thrombin, approximately 100 NIH[b)] units/mL with stabilizers and buffers.

a) Start reagent

b) National Institute of Health

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.

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

Danger

H334 May cause allergy or asthma symptoms or breathing difficulties if inhaled.

Prevention

P261 Avoid breathing dust.

P284 Wear respiratory protection.

Response

P304 + P340 IF INHALED: Remove person to fresh air and keep comfortable for breathing.

P342 + P311 If experiencing respiratory symptoms: Call a POISON CENTER/doctor.

Disposal

P501 Dispose of contents/container to an approved waste disposal plant.

Product safety labeling follows EU GHS guidance.

Contact phone: all countries: +49-621-7590

Avoid foam formation in all reagents and sample types (specimens, calibrators and controls).

Reagent handling

The reagent in the cassette has been assembled into a ready-for-use unit (**cobas t** pack).

All information required for correct operation is available via the **cobas** link.

Storage and Stability

Store at 2-8 °C.

Store the **cobas t** pack **upright**.

The unopened **cobas t** pack is stable up to the stated expiration date.

Stability of the opened **cobas t** pack:	
on the **cobas t** analyzer	10 days after reconstitution

Do not freeze.

Specimen collection and preparation

Only the specimens listed below were tested and found acceptable:
3.2 % citrated human plasma

Use standard sampling tubes made of plastic or siliconized glass. Strictly observe the ratio of blood (9 parts) to sodium citrate solution 0.11 M (1 part).[18,19]

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 15 minutes at 2500 g or such that the platelet count is < 10000 platelets/µL and assay samples within the given stability period.

Stability:	
at 15-25 °C	4 hours
at -20 °C (± 5 °C)	7 weeks

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Stability:	
at -80 °C (± 5 °C)	11 months

Frozen plasma aliquots should be thawed within 5 minutes at 37 °C in a waterbath, homogenized by carefully mixing without foam formation. It is recommended to assay the samples as soon as possible after thawing. Do not refreeze samples.

Materials provided

See “Reagents – working solutions” section.

Materials required (but not provided)

For ACN 28201

- REF 09618236190, UniCal
- REF 09617990190, UniCon N
- REF 09618163190, UniCon P

For ACN 28200

- REF 07575548190, Cal Plasma
- REF 07530331190, Con 1
- REF 07539665190, Con P

For both ACNs

- REF 07155042190, Owren B
- General laboratory equipment
- Distilled or deionized water
- **cobas t** coagulation analyzer. See User Assistance of the analyzer concerned for additionally required materials.

Assay

For optimum performance of the assays follow the directions given in this document. Refer to the appropriate User Assistance for analyzer-specific assay instructions.

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

Calibration

For calibration, use calibrator kit as listed in the "Materials required (but not provided)" section.

Calibration frequency: full calibration must be performed

- once per lot of Fibrinogen.
- as required following quality control procedures.

Traceability: This method has been standardized against WHO International Standard for Fibrinogen.

Quality control

Controls are required for checking the accuracy and reproducibility of the results.

For quality control, use control kits as listed in the "Materials required (but not provided)" section.

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.

Limitations - interference

The effect of the following endogenous substances and pharmaceutical compounds on assay performance was tested. No impact on results was observed up to the listed concentrations.

Endogenous substances

Compound	Concentration
Conjugated bilirubin	15 mg/dL
Unconjugated bilirubin	15 mg/dL
Hemoglobin	1000 mg/dL
Intralipid	900 mg/dL

Criterion: Recovery within ± 10 % of initial value.

The impact of lipemia, hemoglobin and bilirubin was tested according to Glick.[20]

Drugs: No interference was found at therapeutic concentrations using common drug panels.[21,22]

The presence of direct thrombin inhibitors, such as argatroban, bivalirudin and dabigatran in the sample influence the assay results (decrease in [mg/dL]), which can be of clinical importance.

The fibrinolytic action of Streptokinase (fibrin clot and fibrinogen destruction) prolongs the clotting times and thus alters mg/dL values.

The presence of oritavancin in the sample influences the assay results of Fibrinogen.

Low molecular weight heparin (LMWH): No significant interference was observed in a normal plasma pool spiked with LMWH up to a concentration of 1.5 IU/mL.

Unfractionated Heparin (UFH): No significant interference was observed in a normal plasma pool spiked with UFH up to a concentration of 1.0 IU/mL.

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

Extra wash cycle: The use of special wash steps is mandatory when certain test combinations are run together on **cobas t** analyzers. Refer to the latest version of the carry over evasion list found with the CLEAN and Deproteinizer Method Sheet and the User Assistance for further instructions. Where required, special wash/carry over evasion cycles must be implemented prior to reporting results with this test.

Limits and ranges

Measuring range

60-900 mg/dL

For samples with concentrations from 60 to < 180 mg/dL fibrinogen, the rerun function increases the sample volume by a factor of 4 and the results are automatically calculated applying this factor.

Lower limits of measurement

Limit of Quantitation = 60 mg/dL

The Limit of Quantitation is defined as the lowest amount of analyte in a sample that can be accurately quantitated with a total allowable relative error of ≤ 30 %.

Expected values

193-412 mg/dL

These values correspond to the 2.5th and 97.5th percentiles of results obtained from a total of 200 normal human plasma samples.

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

Repeatability and intermediate precision were determined using human samples and controls in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP05 requirements (2 aliquots per run, 2 runs per day, 21 days). The following results were obtained:

		Repeatability		Intermediate precision	
Sample	Mean (mg/dL)	SD (mg/dL)	CV (%)	SD (mg/dL)	CV (%)
Normal control	273	4.99	1.8	5.90	2.2
Abnormal control	123	1.48	1.2	1.95	1.6
Plasma 1	74.0	0.872	1.2	1.03	1.4

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		Repeatability		Intermediate precision	
Sample	Mean (mg/dL)	SD (mg/dL)	CV (%)	SD (mg/dL)	CV (%)
Plasma 2	128	1.14	0.9	1.61	1.3
Plasma 3	264	3.41	1.3	4.34	1.6
Plasma 4	537	8.47	1.6	13.4	2.5
Plasma 5	778	10.0	1.3	13.3	1.7
Plasma 6	868	9.62	1.1	12.5	1.4

Method comparison

A comparison of the Fibrinogen assay run on the **cobas t** 711 analyzer (y) with an automated coagulation assay (x) gave the following correlation (mg/dL):

Number of samples measured: 135

Deming[23]

y = 1.02x + 12.2 mg/dL

r = 0.994

The fibrinogen concentrations using Fibrinogen reagent were between 67.9 and 897 mg/dL.

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.

For further information, please refer to the appropriate User Assistance for the relevant analyzer and Method Sheets of all necessary components.

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.

Symbols

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

CONTENT	Contents of kit
SYSTEM	Analyzers/Instruments on which reagents can be used
REAGENT	Reagent
CALIBRATOR	Calibrator
→	Volume for reconstitution
GTIN	Global Trade Item Number

CE 0123

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

+800 5505 6606

Roche