BIOSYNEX
Easy Diagnostics for Life

Ref: 1050002

BIOSYNEX® D-dimer

CE

Rapid test for the detection of D-Dimer in human plasma or whole blood

INTENDED USE

The BIOSYNEX® D-dimer test is an immunochromatographic rapid test for the qualitative detection of D-dimer in plasma or whole blood. This test is intended as an aid in the diagnosis of exclusion of a disseminated intravascular coagulation (DIC), a deep venous thrombosis (DVT) and a pulmonary embolism (PE). For professional in vitro diagnostic use only.

SUMMARY

D-dimer testing was originally developed in the diagnosis of a disseminated intravascular coagulation (DIC). In the 1990s, it turned out to be useful in the diagnosis of the thromboembolic process.

D-dimer is a fibrin degradation product, a small protein fragment present in the blood after a blood clot is degraded by fibrinolysis. During coagulation of blood, fibrinogen is metabolized to fibrin by thrombin activation. Fibrin consists of D- and E-units. The cleavage of fibrin leads to so-called D-dimers.

D-dimer concentration may be determined by a blood test to help diagnose thrombosis. Since its introduction in the 1990s, it has become an important test performed in patients suspected of thrombotic disorders. While a negative result practically rules out thrombosis, a positive result can indicate thrombosis but does not rule out other potential aetiologies. Its main use, therefore, is to exclude thromboembolic diseases where the probability is low.

D-dimer testing is of clinical use when there is a suspicion of deep venous thrombosis (DVT) or pulmonary embolism (PE). In patients suspected of disseminated intravascular coagulation (DIC), D-dimer testing may aid in the diagnosis.

PRINCIPLE

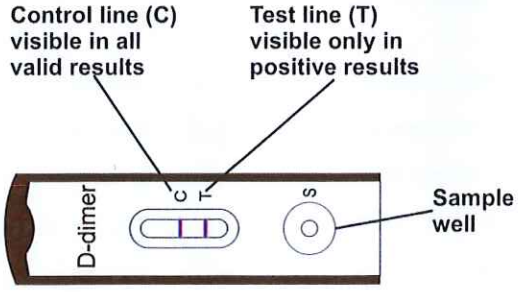
The BIOSYNEX® D-dimer test is intended for use in the detection of D-dimer in plasma or whole blood.

The BIOSYNEX® D-dimer test has been designed to detect D-dimer in plasma or whole blood through visual interpretation of colour development in the test device, which is a sandwich immunoassay. The membrane was pre-coated with an antibody of D-dimer on the test line region (T). During the test the diluted specimen is allowed to react with a colour marked conjugate (anti-D-dimer antibody-gold conjugate) which was submitted on the pad inside the test cassette. The mixture then moves on the membrane chromatographically by capillary action. If D-dimer is present in the specimen, a coloured line with a specific antibody-antigen-conjugate complex will form at the test line region (T) of the membrane.

This complex consists of a colour marked anti-D-dimer antibody, D-dimer from the specimen and the antibody immobilized on the membrane at the test line region (T).

On the other hand, a coloured line will always appear at the control region (C). This control line serves as a procedural indicator for the proper function of the device. It shows that the test procedure has been correct and membrane wicking has occurred.

A distinct colour development in the test line region (T) indicates a positive result and absence of a colour line in the test line region (T) suggests a negative result.



REAGENTS

The test devices include D-dimer antibody coated pointer particles and D-dimer antibodies coated on the membrane.

PRECAUTIONS

- For professional in vitro diagnostic use only
- For single use only
- Do not freeze any components of the test kit
- Do not use components after stated expiration date (see pouch and box label)
- Do not use test if pouch is damaged
- Do not eat, drink or smoke in the area where the specimens or kits are handled
- For professional in vitro diagnostic use only
- For single use only
- Do not freeze any components of the test kit
- Do not use components after stated expiration date (see pouch and box label)
- Do not use test if pouch is damaged
- Do not eat, drink or smoke in the area where the specimens or kits are handled
- Handle all specimens as if they contained infectious agents
- Observe established precautions for microbiological risks throughout all procedures and standard guidelines for appropriate disposal of specimens
- Wear protective clothing such as laboratory coats, disposable gloves and eye protection when specimens are being tested
- Used testing materials should be discarded according to local regulations
- Humidity and high temperature can adversely affect results
- The diluent buffer contains sodium azide (NaN_3) as preservative (0.09%)
- Do not use more than the required amount of liquid
- Bring all reagents to room temperature (15-30°C) before use
- Do not spill the specimens into the result area
- Do not touch the reaction area of the device to avoid contamination
- The test device should remain in the sealed pouch until use
- Interpret results after 10 minutes but not later than 15 minutes
- Store and transport the test device always at 2-30°C
- Avoid cross-contamination of specimens by using a new specimen pipette for each specimen
- The diluent buffer contains sodium azide which may react with lead or copper plumbing to form potentially explosive metal azides. When disposing of these solutions always flush with copious amounts of water to prevent azide build-up
- The potentially infectious materials (e. g. antibodies) or other components of the test (chemicals) do not constitute any danger if test is used according to instructions

STORAGE AND STABILITY

The test kit is to be stored at 2-30°C. The test is stable through the expiry date printed on the sealed pouch. The test must remain in the sealed pouch until use.

MATERIALS

Materials Provided

- Test Devices, single pouched
- Droppers (within pouch)
- Lancets
- Vial with diluent (PBS and 0.09% NaN_3)
- Package insert

Materials Required But Not Provided

- Specimen collection container
- Timer

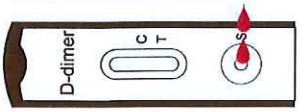
SPECIMEN COLLECTION AND HANDLING

- The BIOSYNEX® D-dimer test (Whole Blood / Plasma) can be performed using whole blood (from vein puncture or finger pad), Citrate, Fluoride or EDTA treated whole blood, or plasma.
- Separate plasma from blood as soon as possible to avoid haemolysis. Preferred anticoagulants are citrate, fluoride, or EDTA. Use only clear, non-haemolysed specimens.
- Testing should be performed immediately after specimen collection. Do not leave the specimens at room temperature for prolonged periods.
- D-dimers are very instable molecules. You can store whole blood and plasma specimens at room temperature only for 8 hours and refrigerated (4°C) only for 1 day.
- Bring specimens to room temperature (15-30°C) prior to testing.
- If specimens are to be shipped, they should be packed in compliance with federal regulations covering the transportation of etiologic agents.

DIRECTIONS FOR USE

Bring tests, diluent buffer, specimens, and/or external controls to room temperature (20-30°C) before testing. Do not open pouches until ready to perform the assay.

1. Remove the test device from its protective pouch (bring the device to room temperature before opening the pouch to avoid condensation of moisture on the membrane), and use it within 1 hour at the latest. For best results, the assay should be performed immediately after opening the sealed pouch. Label the device with patient or control identification.
2. Add **2 drops of whole blood** or **1 drop of plasma** (using the pipette supplied with the test) into the sample well first and then add 1 drop of dilution buffer. **Avoid trapping air**



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bubbles in the specimen well (S) and do not add any liquid to the reaction area.

3. Start the timer as the test starts to run.
   Interpret results after 10 minutes. Do not interpret any results after more than 15 minutes.

INTERPRETATION OF RESULTS

POSITIVE: 2 lines appear. One line appears in the control line area (C) and one line in the test line area (T). A positive result indicates that elevated concentrations of D-dimer have been detected.
NOTE: The intensity of colour in the test area (T) may vary depending on the concentration of D-dimer present in the specimen. Therefore, any shade of colour in the test area (T) should be considered positive.

NEGATIVE: One line appears in the control line area (C). No line appears in the test line area (T). A negative result indicates that no D-dimer is present in the specimen or that the concentration is below the detection level of the test device.

INVALID: Control line fails to appear. Insufficient specimen volume, expired test components or incorrect procedural techniques are the most likely reasons for control line failure. Review the procedure and repeat the test. If the problem persists, discontinue using the test kit immediately and contact your local distributor.

QUALITY CONTROL

Internal Quality Control

An internal procedural control is included in the test. A red line appearing in the control area (C) is an internal positive procedural control. It confirms that sufficient specimen volume was used, and indicates an adequate membrane wicking and a proper procedural technique.

External Quality Control

Good Laboratory Practice recommends performing a positive and negative external control for every kit, and as deemed necessary by internal laboratory procedures. External controls are not supplied with the kit.

EXPECTED VALUES

Increased D-dimer concentrations above the widely accepted cut-off value of 500 ng/ml FEU (fibrinogen equivalent units) are a sign of an active fibrinolysis and have been verified in patients with disseminated intravascular coagulation (DIC), deep venous thrombosis (DVT) and pulmonary embolism.
Increased D-dimer concentrations are observed as well after surgery and injury and during sickle cell anaemia, liver disease, heavy infections, sepsis, inflammation, malign disease or in elderly people. The concentration of D-dimer rises also during a normal pregnancy.

LIMITATIONS

- A negative result may help to exclude to a very high probability disseminated intravascular coagulation (DIC), deep venous thrombosis (DVT) and pulmonary embolism (PE).[1,2]
- As in the case of any diagnostic procedure, the results obtained with this test should be used in conjunction with other information available to the physician, as e.g. the "Wells score" for DVT resp. PE. Especially in the scope of the diagnosis of DIC, the D-dimer result is used to determine the so called "DIC score".[1]
- The sensitivity of immunological rapid tests is lower for patients with moderate or high pre-test probability for thromboembolic infarction (high Wells score) as for patients with low pre-test probability. Hence, for moderate and high pre-test probability an ultrasound examination is recommended irrespective the result of the rapid test.[3]
- False negative readings may occur if the sample is taken either too early after thrombus formation, if testing is delayed for several days or if the sample was taken too late after the occurrence of thromboembolic infarction, as the D-dimer concentration may decrease to normal values as early as 1 week. Additionally, a treatment with anticoagulants prior sample collection may yield a negative result as it prevents thrombus extension.[1,4]
- Increased values of D-dimer after treatment with anticoagulants show further risk of thrombosis.[5]
- A positive result is not an evidence of the existence of the diseases described above. False positive readings can be due to various causes: liver disease, inflammation, malignancy, trauma, pregnancy, recent surgery as well as advanced age.[1,2]
- It is possible that the test does not yield any result if whole blood specimens have a high viscosity or if the whole blood specimens have been stored for more than one day. In this case the test should be repeated with a new test device using fresh specimen from the same patient.

PERFORMANCE CHARACTERISTICS

Analytical Sensitivity

The analytical sensitivity (detection limit) is 500 ng/ml FEU (fibrinogen equivalent units). This is the value indicating a positive result.

Analytical Specificity

The following substances did not interfere with this test: Bilirubin up to 0.2 g/L, lipids (total) up to 15 g/L (with approx. 6 g/L total cholesterol and 4.5 g/L triglycerides), serum protein (total) up to 100 g/L (with approx. 55 g/L albumin and 35 g/L immunoglobulin), haemoglobin up to 1 g/L, rheumatic factor up to 200 IU/ml.

Diagnostic Sensitivity and Specificity

The diagnostic sensitivity and specificity was calculated against Roche Tina-quant® D-dimer Assay yielding following results:

		BIOSYNEX® D-dimer Test		
		positive	negative	Total
Roche Tina-quant® D-dimer Assay	positive	89	1	90
	negative	5	62	67
Total		94	63	157

Diagnostic Sensitivity:	98.9 %
Diagnostic Specificity:	92.5 %
Positive predictive value:	94.7 %
Negative predictive value:	98.4%

Accuracy

The accuracy was compared and checked against Roche Tina-quant® D-dimer Assay. The calculated accuracy is 96.2%.

Precision

Test precision was determined within the same lot (intra-lot-variation) as well as between different lots (inter-lot-variation) with control solutions. Controls with a D-dimer concentration of 0 ng/ml yield negative results. Controls with a D-dimer concentration of 500 ng/ml provide positive results.

LITERATURE

1. Dempfle, Carl-Erik (2005): Bestimmung des D-dimer-Antigens in der klinischen Routine, Deutsches Ärzteblatt Jg. 102, Heft 7, 18. Februar 2005: A428-A432.
2. Fritscher, Claudia (2007): Bedeutung der D-dimer Untersuchung in der Diagnostik der tiefen Beinvenenthrombose, Labor Aktuell Nr.7/2007, 1-8.
3. Brill-Edwards P., Lee A. (1999): D-dimer testing in the diagnosis of acute venous thromboembolism, Thrombosis and Haemostasis; 82(2): 688-94
4. Blackwell Publishing Ltd. (2004): The diagnosis of deep vein thrombosis in symptomatic outpatients and the potential for clinical assessment and D-dimer assays to reduce the need for diagnostic imaging, British Journal of Haematology, 124, 15–25.
5. Thomas, Lothar (2008): Labor und Diagnose (Indikation und Bewertung von Laborfunden für die medizinischen Diagnostik, TH-Books Verlagsgesellschaft mbH, Frankfurt/Main, 7.Auflage, 2008.

SYMBOLS

	Attention, see instructions for use	LOT	Lot number
IVD	For *in vitro* diagnostic use only		Manufacturer
2°C 30°C	Store between 2-30°C		Do not reuse
Σ	Tests per kit	REF	Catalog number
	Expiry	DIL	Extraction Buffer

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