BIO TECHNOLOGY boditech

Cardiac

ichroma™ D-Dimer

INTENDED USE

ichroma™ D-Dimer is a fluorescence immunoassay (FIA) for the quantitative determination of D-Dimer in human whole blood/plasma. It is useful as an aid in management and monitoring of post therapeutic evaluation of thromboembolic disease patients.

For *in vitro* diagnostic use only.

INTRODUCTION

D-Dimer, a degradation product of cross-linked fibrin formed during activation of the coagulation system, is commonly used to exclude thromboembolic disease in outpatients suspected of having deep venous thrombosis (DVT) and pulmonary embolism (PE). DVT and PE is relatively common and can cause sudden, fatal embolic events in the pulmonary arteries and other regions.

Measurement of the D-Dimer level in plasma has been used as a screening strategy for subclinical DVT. A systematic review reported that a normal range of a highly sensitive D-dimer level accurately ruled out DVT in patients classified as having a low or moderate clinical probability of DVT. The DVT is a high-risk factor for the stroke because of advanced age, hemiplegia, and coagulation disorders, and DVT can cause paradoxical embolic stroke via a right-to left shunt. Thus, it is important to monitor the level of D-Dimer the incidence and characteristics of DVT in acute stroke patients. The Plasma D-dimer level has proven to be useful for DVT screening in chronic stroke patients undergoing rehabilitation. National and international scientific organizations have suggested the use of these markers when implementing new diagnostic strategies in patients with coronary syndrome. Since D-Dimer is well known to be an important prognostic indicator of heart diseases, its most definitive role is on monitoring post-treatment clinical status and the post therapeutic evaluation of patients.

PRINCIPLE

The test uses a sandwich immunodetection method.

The detector antibodies in buffer bind to antigens in the sample, forming antigen-antibody complexes, and migrate onto nitrocellulose matrix to be captured by the other immobilized antibodies on a test strip.

More antigens in the sample will form more antigen-antibody complexes which lead to stronger fluorescence signal by detector antibodies, which is processed by the instrument for the ichroma™ tests to show D-Dimer concentration in the sample.

COMPONENTS

ichroma™ D-Dimer consists of 'cartridges' and 'detection buffers'.

- The cartridge contains the membrane called a test strip which has anti-D-Dimer at the test line, and streptavidin at the control line. All cartridges are individually sealed in an aluminum foil pouch containing a desiccant, and they are further packaged in a cartridge box.
- The detection buffer contains anti-D-Dimer-fluorescence conjugate, biotin-BSA-fluorescence conjugate, and sodium azide as a preservative in phosphate buffered saline (PBS). It is pre-dispensed in tubes. The detection buffer tubes are packaged in a detection buffer box and further packed in a styrofoam box with ice-pack for the shipment.

WARNINGS AND PRECAUTIONS

- For *in vitro* diagnostic use only.
- Follow the instructions and procedures described in this 'Instructions for use'.
- Use only fresh samples and avoid direct sunlight.
- Lot numbers of all the test components (cartridge, detection buffer and ID chip) must match each other.
- Do not interchange the test components between different lots or use the test components after the expiration date, either of which might yield incorrect test result(s).
- Do not reuse cartridges or detection buffer tubes. A cartridge should be used for testing one sample only. A detection buffer tube should be used for processing of one sample only.
- The cartridge should remain sealed in its original pouch until just before use. Do not use the cartridge, if pouch is damaged or has already been opened.
- Frozen sample should be thawed only once. For shipping, samples must be packed in accordance with local regulations. Sample with severe hemolysis and/or hyperlipidemia must not be used.
- If test components and/or sample are stored in refrigerator, then allow, cartridge, detection buffer and sample to be at room temperature for approximately 30 minutes before use.
- The instrument for ichroma™ tests may generate slight vibration during use.
- Used cartridges, detection buffers and pipette tips should be handled carefully and discarded by an appropriate method in accordance with relevant local regulations.
- The detection buffer contains sodium azide (NaN_3), and it may cause certain health issues like convulsions, low blood pressure, low heart rate, loss of consciousness, lung injury and respiratory failure. Avoid contact with skin, eyes, and clothing. In case of contact, rinse immediately with running water.
- No Biotin interference was observed in **ichroma™ D-Dimer** when biotin concentration in the sample was below 250 ng/mL. If a patient has been taking biotin at dosage of more than 0.03 mg a day, it is recommended to test again 24 hours after discontinuation of biotin intake
- **ichroma™ D-Dimer** will provide accurate and reliable results subject to the below conditions.
  - **ichroma™ D-Dimer** should be used only in conjunction with the instrument for ichroma™ tests.
  - Have to use recommended anticoagulant.

Recommended anticoagulant
Sodium citrate

LIMITATION OF THE TEST SYSTEM

- The test may yield false positive result(s) due to the cross-reactions and/or non-specific adhesion of certain sample components to the capture/detector antibodies.
- The test may yield false negative result(s) due to the non-responsiveness of the antigens to the antibodies which is the most common if the epitope is masked by some unknown components, so therefore not being able to be detected or captured by the antibodies. The instability or degradation of the antigens with time and/or temperature may also cause false negative result as it makes antigens unrecognizable by the antibodies.
- Other factors may interfere with the test and cause erroneous results, such as technical/procedural errors, degradation of the test components/reagents or presence of interfering substances in the test samples.
- Any clinical diagnosis based on the test result must be supported by a comprehensive judgment of the concerned physician in conjunction with clinical symptoms and other relevant test results.

STORAGE AND STABILITY

Storage condition			
Component	Storage temperature	Shelf life	Note
Cartridge	2 - 30°C	20 months	Disposable
Detection buffer	2 - 8°C	20 months	Disposable

- After the cartridge pouch is opened, the test should be performed immediately.

MATERIALS SUPPLIED

REF CFPC-25

Components of **ichroma™ D-Dimer**

- Cartridge box:
  - Cartridge 25
  - ID chip 1
  - Instructions for use 1
- Detection buffer box:
  - Detection buffer tube 25

MATERIALS REQUIRED BUT SUPPLIED ON DEMAND

Following items can be purchased separately with **ichroma™ D-Dimer.** Please contact our sales division for more information.

- Instrument for ichroma™ tests
  - **ichroma™ Reader** REF FR203
  - **ichroma™ II** REF FPRR021
  - **ichroma™ III** REF FPRR037
  - **ichroma™ M3** REF FPRR035
  - **ichroma™-50** REF FPRR022
  - **ichroma™-50 Plus** REF FPRR036
- **Printer** REF FPRR007
- **Boditech D-Dimer Control** REF CFPO-101

SAMPLE COLLECTION AND PROCESSING

The sample type for **ichroma™ D-Dimer** is human whole blood/plasma.

- It is recommended to test the sample within 24 hours after collection when collected sample is stored at room temperature.
- The sample (plasma) should be separated from the clot by centrifugation within 3 hours after the collection of whole blood.
- If testing will be delayed more than 1 day, the sample (plasma) should be frozen at -20 °C.
- The sample (plasma) stored frozen at -20 °C for 3 months showed no performance difference.
- However, the whole blood sample should not be kept in a freezer in any case.
- As a repeated freeze-thaw cycle may affect the test result, do not refreeze previously frozen samples.

TEST SETUP

- Check the contents of **ichroma™ D-Dimer**: Sealed cartridges, detection buffer tubes, an ID chip and an instructions for use.
- Ensure that the lot number of the cartridge matches that of the detection buffer tubes as well as an ID chip.
- If the sealed cartridge and the detection buffer have been stored in a refrigerator, place them on a clean and flat surface at room temperature for at least 30 minutes before testing.
- Turn on the instrument for ichroma™ tests.
- Insert the ID chip into the ID chip port.

※ **Please refer to the instrument for ichroma™ tests operation manual for complete information and operating instructions.**

TEST PROCEDURE

▶ **ichroma™ Reader, ichroma™ II, ichroma™ M3**

Multi test mode

1) Take 10 µL of sample (whole blood/plasma/control) using a pipette and dispense it to the detection buffer tube.
2) Close the lid of the detection buffer tube and mix the sample thoroughly by shaking it about 10~15 times. (The sample mixture must be used immediately. Do not exceed 30 seconds.)
3) Take 75 µL of the sample mixture and dispense it into the sample well of the cartridge.
4) Leave the cartridge at room temperature for 12 minutes.
   ⚠ *Scan the sample-loaded cartridge immediately when the incubation time is over. If not, it will cause inaccurate test result.*
5) To scan the sample-loaded cartridge, insert it into the cartridge holder of the instrument for ichroma™ tests. Ensure proper orientation of the cartridge before pushing it all the way inside the cartridge holder. An arrow is marked on the cartridge especially for this purpose.
6) Press the 'Select' or tap the 'Start' button on the instrument for ichroma™ tests to start the scanning process. (ichroma™ M3 will start the test automatically after inserting.)
7) The instrument for ichroma™ tests will start scanning the sample-loaded cartridge immediately.
8) Read the test result on the display screen of the instrument for ichroma™ tests.

Single test mode

1) The test procedure is same with the 'Multi test mode 1) – 3)'.
2) Insert the sample-loaded cartridge into the cartridge holder of the instrument for ichroma™ tests. Ensure proper orientation of the cartridge before pushing it all the way inside the cartridge holder. An arrow is marked on the cartridge especially for this purpose.
3) Press the 'Select' or tap the 'Start' button on the instrument for ichroma™ tests to start the scanning process.
(ichroma™ M3 will start the test automatically after inserting.)
4) The cartridge goes inside the instrument for ichroma™ tests and will automatically start scanning the sample-loaded cartridge after 12 minutes.
5) Read the test result on the display screen of the instrument for ichroma™ tests.

▶ **ichroma™ III**

1) The test procedure is same with the 'Single test mode'.

▶ **ichroma™-50, ichroma™-50 Plus**

1) Insert the tip array in the tip station.
2) Insert the detection buffer in the reagent station and cover the reagent station to hold the detection buffer tubes in place.
3) Open the lid of the detector diluent and insert the detector diluent in the diluent station.
4) Insert the cartridge magazine with the cartridges into the magazine station.
5) Insert the sample tube into the blood collection tube rack and load the blood collection tube rack into the sampling station (loading part).
6) Tap the button located in the upper side of the No. of test cartridge region to select the ID chip that you want to use.
7) When the selected cartridge slot is activated, set the number of the detector tube by tapping.
8) Set the number of pipette tips by tapping.
9) Tap the 'Start' button on the left upper of the main screen to start test.

INTERPRETATION OF TEST RESULT

- The instrument for ichroma™ tests calculates the test result automatically and displays D-Dimer concentration of the test sample in terms of ng/mL (FEU, Fibrinogen equivalent units).
- Working range: 50-10,000 ng/mL.
- Unit Conversion: DDU x 2 =FEU
  ex) 1 ng/mL (DDU) = 2 ng/mL (FEU)
- Cut-off value: 500 ng/mL

QUALITY CONTROL

- Quality control tests are a part of the good testing practice to confirm the expected results and validity of the assay and should be performed at regular intervals.
- Quality control tests should also be performed whenever there is any question concerning the validity of the test results.
- Control materials are provided on demand with **ichroma™ D-Dimer**. For more information regarding obtaining the control materials, contact Boditech Med Inc.'s Sales Division for assistance.
  (Please refer to the instructions for use of control material.)

PERFORMANCE CHARACTERISTICS

- **Analytical Sensitivity**
  - Limit of blank (LoB) 7.21 ng/mL
  - Limit of detection (LoD) 16.0 ng/mL
  - Limit of quantitation (LOQ) 50.0 ng/mL
- **Analytical Specificity**
  - **Cross-reactivity**
    Biomolecules such as below the ones in the table were added to the test sample(s) at concentrations much higher than their normal physiological levels in the blood. **ichroma™ D-Dimer** test results did not show any significant cross-reactivity with these biomolecules.

Cross reactants	Concentration
Fibrinogen	10 g/L
Troponin Complex	1,000 ng/ml
CK-MB	1,000 ng/ml
NT-proBNP	100 ng/ml
Myoglobin	3,000 ng/ml

  - **Interference**
    Interferents listed in the following table were added to the test sample at the concentration mentioned below. **ichroma™ D-Dimer** test results did not show any significant interference with these materials.

Interferents	Concentration
Bilirubin (unconjugated)	700 µmol/L
Cholesterol	13 mmol/L
Glucose	60 mmol/L
Hemoglobin	10 g/L
Ascorbic acid	300 µmol/L
Triglyceride, total	37 mmol/L
Sodium citrate	2 mg/mL

- **Precision**
  - **Single-site study**
    Repeatability (within-run precision)
    within-laboratory precision (Total precision)
    Lot to lot precision
    3 Lots of **ichroma™ D-Dimer** were tested for 20 days. Each standard material was tested 2 times per day. For each test, each material was duplicated.

D-Dimer [ng/mL]	Repeatability			Within-laboratory precision		
	Mean [ng/mL]	SD	CV (%)	Mean [ng/mL]	SD	CV (%)
400	402.22	22.1	5.5	402.04	23.5	5.9
1600	1602.77	87.8	5.5	1606.88	84.7	5.3
5000	4984.57	285.5	5.7	5008.55	288.3	5.8

D-Dimer [ng/mL]	Lot to Lot precision		
	Mean [ng/mL]	SD	CV (%)
400	400.58	23.9	6.0
1600	1598.45	89.7	5.6
5000	5006.91	284.3	5.7

- **Multi-site study**

  Reproducibility

  1 Lot of ichroma™ D-Dimer was tested for 5 days in 3 different sites (1 person per 1 site, 1 instrument per 1 site). Each standard material was tested 1 time per and 5 replicates per day.

D-Dimer [ng/mL]	Reproducibility		
	Mean [ng/mL]	SD	CV (%)
400	401.47	24.8	6.2
1600	1592.80	106.9	6.7
5000	5039.87	325.5	6.5

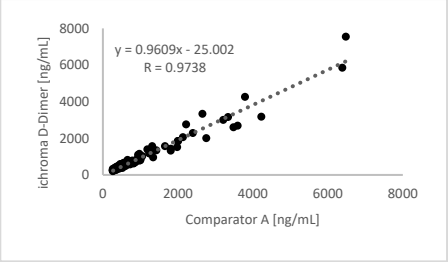
■ **Accuracy**

The accuracy was confirmed by testing with 3 different lots of **ichroma™ D-Dimer**. The tests were repeated 10 times at each concentration of the control standard.

D-Dimer [ng/mL]	Lot 1	Lot 2	Lot 3	AVG	Recovery (%)
5000	5215.04	5271.81	5304.17	5263.67	105.3
3850	4137.89	3935.85	3896.05	3964.73	103.0
1933	1936.33	2049.39	2019.38	2005.26	103.7
1320	1370.27	1403.31	1329.61	1370.08	103.8
860	874.22	908.36	882.11	886.79	103.1
400	409.10	418.20	412.18	414.78	103.7

■ **Comparability**

D-Dimer concentration of 100 clinical samples were quantified independently with **ichroma™ D-Dimer (ichroma™ II)** and **comparator A** as per prescribed test procedures. Test results were compared, and their comparability was investigated with linear regression and correlation coefficient (R). The regression equation and correlation coefficient are as follows.



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Note: Please refer to the table below to identify various symbols

Σ	Sufficient for <n> tests
	Read instruction for use
	Use by Date
LOT	Batch code
REF	Catalog number
	Caution
	Manufacturer
EC REP	Authorized representative of the European Community
IVD	In vitro diagnostic medical device
	Temperature limit
	Do not reuse
CE	This product fulfills the requirements of the Directive 98/79/EC on in vitro diagnostic medical devices

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CE IVD