

Detection of Folate RBC in Erythrocytes with Roche e801

Test Name: In vitro test for the quantitative determination of folate in erythrocytes (red blood cells, RBCs) on Roche/Hitachi Cobas e systems.

Method Name: Whole blood is treated with ascorbic acid until the erythrocytes are lysed and analysis is performed using the hemolysate. In the Elecsys FOL assay, a folate specific antibody labeled with a ruthenium complex is used to determine the folate concentration.

Results: Technical Range: 0.2-6 g/dL
Reportable Range: 0.31-5.61 g/dL

Reference Ranges: ≥ 366 ng/mL

Clinical Significance: Folate belongs to the family of B-group vitamins composed of an aromatic pteridine ring linked through a methylene group to p-aminobenzoic acid and a glutamate residue. Folate (folic acid) is vital for normal cellular functions and plays an essential role in nucleic acid synthesis, methionine regeneration, shuttling and redox reactions of one-carbon units required for normal metabolism and regulation.

The folate metabolism can be exemplified as a cycle, where folate facilitates the transfer of one-carbon units from one molecule to another required in various biochemical reactions: for example, tetrahydrofolate (THF) accepts a single carbon unit from serine, which is reduced in a number of steps to 5-methyltetrahydrofolate (5-MTHF). 5-MTHF gives its methyl group to homocysteine, which is - with involvement of methionine synthase and vitamin B12 - enzymatically converted to methionine. The resulting THF starts again the cycle of methyl group synthesis. From methionine, the methyl groups are transferred to S-adenosylmethionine (SAM). SAM serves as a methyl group donor in several methylation reactions, like DNA, RNA and protein methylation.

The methionine cycle is highly sensitive to folate deficiency: with a low folate status, the ability of the cell to re-methylate homocysteine is impaired and this results in increased homocysteine concentrations in plasma.

Folate also plays an essential role in the synthesis of purine and pyrimidine precursors of nucleic acids. Altered distribution of methyl groups and impaired DNA synthesis play an essential role in the development of cancers. Abnormal folate status has also been linked with cardiovascular diseases, neural tube defects, cleft lip and palate, late pregnancy complications, neurodegenerative and psychiatric disorders. Folate belongs to the group of essential vitamins, i.e. it cannot be synthesized by the human organism and therefore must be absorbed from diet. Primary sources of folates are green and leafy vegetables, sprouts, fruits, brewer's yeast and liver.

Folate deficiency can be caused by decreased nutritional intake, poor absorption of ingested folate in the intestine or increased demand of folate, for example during physical activity or pregnancy. Deficiency of folate can also be a result of liver diseases or impaired folate metabolism due to genetic defects or drug interactions.

A clinical manifestation of both folate and vitamin B12 deficiency is the so called megaloblastic (macrocytic) anemia: due to the affected DNA synthesis and cell maturation, especially involving the cells of erythropoiesis, the total count of erythrocytes is significantly reduced. The hemoglobin synthesis capacity however is normal, which leads to abnormally large erythrocyte precursors (“macrocytes” or “megaloblasts”), which have an elevated hemoglobin content (“hyperchromic anemia”). Serum folate concentrations may be affected by recent folate intakes, whereas red blood cell (RBC) folate is a measure of the folate intake across the 90-120 days lifespan of erythrocytes. Thus, folate concentrations in RBC give a more accurate picture of a patient’s underlying folate status than serum folate concentrations and are considered by experts as the better measure for folate status.

Because vitamin B12 and folate are closely interrelated in the cellular one-carbon unit metabolism, and hematologic and clinical consequences of the two vitamin deficiency states might be similar, it is advisable to determine both parameters simultaneously in patients with the relevant symptoms of vitamin deficiency.

Submission Criteria:

For specimen collection and preparation only use suitable tubes or collection containers.

Only the specimens listed below were tested and found acceptable.

Hemolysate prepared from whole blood treated with anticoagulants Na-heparin or K3-EDTA.

The sample types listed were tested with a selection of sample collection tubes that were commercially available at the time of testing, therefore 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.

Storage and Stability: **Whole blood:**
28 days at -20°C

Rejection Criteria:

Rejection criteria include but are not limited to:

1. Specimens containing fibrin or clots.
2. Excessive platelet clumping
3. Leaking specimens
4. Substandard mixing or collection
5. Expired or improperly stored collection tubes.
6. Improperly filled tubes based on collection tube manufacturer’s guidelines.
7. Contaminated specimens (IV fluid, foreign particles, etc.)

8. Specimens not analyzed within the appropriate time frame.
9. Samples not shipped at appropriate temperature.
10. Samples without 2 proper identifiers or samples having identifiers that do not match the electronic or paper lab requisition.

Authorization: Diagnostic testing can only be performed with approval from an authorized provider/agency.

Turn Around Time: 1 day.

Instructions for Whole Blood Specimen Submission

General Information

The detection of folate in erythrocytes is performed using a Roche cobas i58 analyzer.

Specimens must be collected and stored at -20°C if to be analyzed within 28 days. Please be aware that storing specimens at $\leq -70^{\circ}\text{C}$ ($\leq -94^{\circ}\text{F}$) is not permissible.

Specimens MUST be received at Reditus Laboratories within 28 days of collection.

Collection Instructions for EDTA Whole Blood Specimen

1. Do not use expired collection tubes. Store collection tubes as per manufacturers recommendations. Use standard venipuncture practices for collecting samples. Filled 12 x 75 mm EDTA tubes are preferred. EDTA microtubes and raised bottom tubes are also acceptable.
2. Ensure that the patient's name, date-of-birth, and time/date of collection are recorded on the specimen tube along with the name or initials of the individual collecting the sample.
3. Complete all the demographic information on a sample requisition form through the approved electronic submission process
4. Refrigerate the specimen between 2-8°C (36-46°F) and ship or courier the specimen(s) within 48 hours.
5. The specimen(s) *must* be received at the laboratory **no later than** 48 hours *from the time of collection*.
 - a. **Avoid shipping specimens over weekends or holidays** as they may not be received at the laboratory and cold-packs will not maintain the required 2-8°C (36-46°F) specimen temperature.
 - b. Ensure that specimens shipped by commercial carrier are shipped with **overnight delivery**. If shipping on a Friday for Saturday delivery, ***you must include Saturday Delivery*** during shipment, or the specimens will not be received until the following non-holiday business day. Failure to receive specimens within 24 hours of shipment will result in specimens being rejected from testing.
6. For any questions pertaining to sample collection, storage, or shipping, please contact the Reditus Laboratories using the below contact information.

Instructions for Specimen Transport

1. **Messenger/Courier by ground transport.** Place specimen(s) into a biohazard labeled bag and seal securely. Place the test requisition(s) on the outside of the biohazard labeled bag. Place the sealed biohazard bag and test requisition(s) inside the shipping container. Place cold packs, which have been frozen for at least 24 hours, in the leak-proof outer container. The shipping container must be rigid, such as a Styrofoam cooler, and labeled with the UN 3373 Biological Substance Category B marking. Close securely.
2. **Commercial carrier by ground/air transport.** Place the specimen(s) inside a biohazard labeled bag and seal securely. Place the test requisition(s) on the outside of the biohazard labeled bag. Place the sealed bag and completed test requisitions(s) inside the outer shipping container. Place cold packs, which have been frozen for at least 24 hours, in the leak-proof outer container. Label the outer shipping container with Reditus Laboratories address listed below. Complete the return address section to include the name of the person shipping the package, business name and address, and a business phone number. The shipping container must include the UN3373 Biological Substance Category B marking.
3. *Ship specimens by overnight delivery* to the attention of Clinical Chemistry at Reditus Laboratories. This can be accomplished by use of local courier, shipping corporations or U.S. Postal Service.
 - a. **If specimens are shipped on a Friday for Saturday delivery, you must include/indicate Saturday delivery** during shipment, or the specimens will not be received until the following non-holiday business day. Failure to receive specimens within 24 hours of shipment will result in specimens being rejected from testing.

4. The specimen(s) must be received at the laboratory **no later than** 48 hours *from the time of collection* and 24 hours from the time of shipment. Do not ship specimens over weekends or holidays as they will not be received, and cold-packs will not maintain the required 2-8°C (36-46°F) specimen temperature.

NOTE: Testing may be delayed, or specimens may be considered UNSATISFACTORY if the above instructions are not followed or the requisition form is not filled out completely. If there are any questions about specimen collection, handling, or shipping please contact the Reditus Laboratories to speak with laboratory personnel.

Ship specimens by a local courier or overnight by commercial carrier to the designated laboratories indicated below.

Send to: Reditus Laboratories
200 Enterprise Drive
Pekin, IL 61554

Phone: (469) 498-0222

Website: <https://www.redituslabs.com/>