Vitamin C and urine test strips
Handling the impact on erythrocytes and glucose results
Urine test strips
A reliable tool in diagnostic

A well proven diagnostic tool
The utilization of urine test strips, within both hospitals and outpatient services alike, is routinely practiced. Urine test strips provide not only a sophisticated means of ensuring rapid diagnostic success, but are also quite cost effective. Some authors consider the microscopic examination of urine samples to be unnecessary if the macroscopic urinary inspection and urine strip testing are normal.1-4 Although such recommendations have to be evaluated in context, taking into account all aspects of the individual patient’s medical history, urine test strips have rightly earned a high degree of trust throughout the modern medical community.

From ancient times until today
It is quite common for medical staffs to use urine specimens to diagnose selective conditions, but from ancient times until the Victorian era, urine analysis was the primary diagnostic tool. It could be said that laboratory medicine started 6000 years ago with the analysis of human urine, termed uroscopy until the 17th century. Today we refer to this practice as urinalysis.5 Considered as the pathfinder of modern test strip urinalysis is the Viennese chemist Fritz Feigl. Feigl in the 1920s published his results referred to as the “spot reaction” method, a more rapid testing method for certain urine compounds by filter paper impregnation with particular reagents.

Diagnostic reliability of urine test strips
Today urine test strips are a widely used simple procedure for rapid and reliable detection, as well as, semi-quantitative determination of particular parameters. However, the presence of certain agents, or even the improper handling of the urine specimen itself, could interfere with the test’s ability to deliver reliable results. Apart from contamination (e.g. germicides) or the prolonged exposure to light and room-temperature, physicians should be cognizant of the potential existence of metabolites occurring from drugs or nutrients in the patient’s urine. Of particular importance is the presence of high amounts of Vitamin C, which can cause false-negative results for the parameters erythrocytes (hemoglobin) and glucose, two very important indicators for a couple of severe diseases.

Impacts on diagnostic reliability
- **Handling**: Prolonged exposure to light and room-temperature alter the concentration of certain metabolites.
- **Nutrition**: Enhanced concentrations of nutrition metabolites (e.g. Vitamin C) may alter test pad functionality.
- **Contamination**: e.g. with hospital germicides may alter pH level of the specimen.
- **Patient’s medication**: Metabolites from drugs in the patient’s urine may interfere with the detectability of some parameters.

From the many parameters that could interfere with the reliability of urine test strips, Vitamin C is of vital importance.

Diagnostic reliability of urine test strips can be influenced by improper handling, contamination of the urine sample, metabolites from drugs or nutrition.
Sources of Vitamin C in modern nutrition

Vitamin C is widely distributed in fruits and vegetables, as well as, artificially added in commercially available food and beverages.

**Nutrition and Vitamin C**

Vitamin C, probably the most famous amongst the vitamins, is also referred to as ascorbic acid or ascorbate. It belongs to the water-soluble class of vitamins. Vitamin C is widely distributed in fruits and vegetables thus making it relatively easy to acquire the recommended daily dosage essential for meeting the requirements of a balanced diet. In addition, the enhanced use of Vitamin C as an additive in many foods and beverages, as well as, the presence of Vitamin C in several health supplements creates the potential for the general population to be exposed to excessively large amounts of ascorbic acid on a daily basis. The food industry routinely uses Vitamin C as a natural antioxidant, to preserve color, to enhance aroma, and as a nutritional additive. The meat processors use Vitamin C to facilitate the reduction of both the amount of added nitrite, as well as, residual nitrite content in their products. The addition of Vitamin C to fresh flour is commonly used to reduce the 4-8 weeks of maturation time flour would normally have to undergo after milling, thus improving its baking qualities.

**Catabolism of Vitamin C**

Vitamin C can be absorbed by active transport in the intestine. Up to 100 mg/day the absorption level is at 80-98%. Higher levels reduce the efficiency of absorption. The average body tissue of an adult stores only 1.2-2.0 g presumably maintained by taking 60-75 mg per day. The total body pool of ascorbic acid is saturated by taking approximately 140 mg per day. The average half life of Vitamin C amounts to 10-20 days, being inversely proportional to the dosage. Urinary excretion starts with plasma ascorbate concentrations of about 1.2-1.8 mg/dL. They are considered to be the renal threshold. Threshold urinary excretion of ascorbic acid was reported at already 60 mg doses per day. Ingestion of higher doses of Vitamin C results in increased and unchanged excretion without re-absorption by the kidneys.

**Sources of Vitamin C in modern nutrition**

1. **Vitamin C availability in general**
   - The accessibility of Vitamin C within the commercially available food supply more than covers the individual daily requirement

2. **Vitamin C as a product feature**
   - Due to its widely accepted associated health benefits, the food and beverage industry routinely adds ascorbic acid to its list of ingredients as a promotional benefit

3. **Vitamin C as a health supplement**
   - The increased level of public interest for personal health care has led to an increase in self-prescribed overmedication with readily available over-the-counter drugs (e.g. Vitamin C, as well as, many other popular vitamins in western countries)

4. **Vitamin C as a preservative**
   - Ascorbic acid is routinely used in the food industry as an inexpensive preservative, a discoloration inhibitor and an antioxidant

---

**Vitamin C**

**Healthy, powerful and interfering**

---

**Urinary excretion of Vitamin C**

<table>
<thead>
<tr>
<th>Higher doses of Vitamin C result in unchanged excretion</th>
<th>Total body pool of Vitamin C is saturated at 140 mg per day</th>
<th>Average adult stores only 1.2-2.0 g in body tissue</th>
</tr>
</thead>
</table>

**The impact on urinalysis**

As a result of increased consumption, high Vitamin C concentrations of >400 mg/L are increasingly found in urine samples. The presence of such high concentrations has been known to cause significant problems with urine strip testing.

Vitamin C reduces the oxidized indicator substances which can lead to false-negative results when analyzing glucose and erythrocytes (hemoglobin). Such serious progressive illnesses as diabetes mellitus, glomerulonephritis, and bladder tumors could go underdiagnosed.

**Prevention of false-negative results**

The understanding of these false-negative results has contributed to the development of suitable approaches to minimize the interference of ascorbic acid, thus preventing false-negative results from occurring in the future when using urine test strips. One obvious approach has been to test urine specimens at least 10 hours after the last intake of Vitamin C. Another approach may be as simple as the use of urine test strips that include an additional pad for the detection of Vitamin C thus verifying a urine sample is free of this substance. However, if Vitamin C is detected, time-consuming patient revisits and retests might be inevitable. These revisits are both costly for the patient and physician, and might lead to delayed treatment.

Certainly, a more differentiated approach would be to use urinalysis test strips that are resistant to ascorbic acid, like the Combur-Test® strip.

---

**Prevent against false-negative results and potential under diagnoses**

<table>
<thead>
<tr>
<th>Option 1</th>
<th>Use Vitamin C resistant tests like Roche’s Combur-Test® strip*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Option 2</td>
<td>Use strip with additional pad that indicates the presence of Vitamin C. Use option 3, if positive and repeat test</td>
</tr>
<tr>
<td>Option 3</td>
<td>Avoid Vitamin C as much as possible. Instruct your patient to avoid additional Vitamin C consumption for at least 10 h prior to revisiting your practice</td>
</tr>
</tbody>
</table>

---

**Average adult stores only 1.2-2.0 g in body tissue**

---

**Urinary excretion of Vitamin C**

<table>
<thead>
<tr>
<th>&gt; 60 mg per day</th>
<th>140 mg per day</th>
<th>60-75 mg per day</th>
</tr>
</thead>
</table>

---

**Vitamin C as a preservative**

Vitamin C is detected, time-consuming patient revisits and retests might be inevitable. These revisits are both costly for the patient and physician, and might lead to delayed treatment.

**Option 3**

Certainly, a more differentiated approach would be to use urinalysis test strips that are resistant to ascorbic acid, like the Combur-Test® strip.*
Combur-Test® strips* Resistant to Vitamin C

**The Combur-Test® strip* promise**
Patients revisits and – even more important – patients retests could be avoided just by eliminating interference from Vitamin C. Even at high levels up to 790 mg/L, Vitamin C in the specimen, Combur-Test® strips* provide reliable results for the disease-critical parameters of glucose and erythrocytes (hemoglobin).

**Iodate impregnation makes the difference**
In order to diminish the interference, ascorbic acid can be oxidized to dehydroascorbate acid, by incorporating an oxidant into the test strips. It was shown that mercuric acetate is able to eliminate the negative impact of ascorbic acid.13 Also impregnation with iodate removes interference of ascorbic acid effectively.30 The latter is used in Combur-Test® strips*. An iodate-impregnated reagent paper is added in the erythrocytes (hemoglobin) and glucose test pads in order to guarantee reliable results.

**Most resistant compared to competitors**
Recent tests have discovered that some urine test strips available on the market are reporting a potentially dangerous false-negative result for glucose and erythrocytes (hemoglobin) even in the presence of small amounts of Vitamin C.

In a study performed by Nagel et al., five very common 10-parameter urine test strips from different manufacturers were compared. Combur-Test® strips* showed the best error tolerance against Vitamin C even in the lowest, but clinically relevant concentrations of glucose and erythrocytes (hemoglobin).34

**Summary**

Problems exist with test strip urinalysis in the presence of Vitamin C that may influence the test’s ability to provide clinically secure results.

**Vitamin C is common and widely used**
A higher intake of ascorbic acid in the general population is triggered by lifestyle and health awareness, and by the food and beverage industry where it is used as a preservative, an antioxidant and a health supplement.

**Iodate impregnation of the test area is an optimal solution**
An iodate impregnated component significantly reduces the effect of ascorbic acid interference. Tests have discovered that some urine test strips available on the market are reporting a potentially dangerous false-negative result for glucose and erythrocytes (hemoglobin) even in the presence of small amounts of Vitamin C. These false-negative results could have serious consequences for doctor and patient alike.

In order to diminish the interference, ascorbic acid can be oxidized to dehydroascorbate acid, by incorporating an oxidant into the test strips. It was shown that mercuric acetate is able to eliminate the negative impact of ascorbic acid.21 Also impregnation with iodate removes interference of ascorbic acid effectively.22 The latter is used in Combur-Test® strips*. An iodate-impregnated reagent paper is added in the erythrocytes (hemoglobin) and glucose test pads in order to guarantee reliable results.

**Most resistant compared to competitors**
Recent tests have discovered that some urine test strips available on the market are reporting a potentially dangerous false-negative result for glucose and erythrocytes (hemoglobin) even in the presence of small amounts of Vitamin C.

In a study performed by Nagel et al., five very common 10-parameter urine test strips from different manufacturers were compared. Combur-Test® strips* showed the best error tolerance against Vitamin C even in the lowest, but clinically relevant concentrations of glucose and erythrocytes (hemoglobin).23

**In summary**

Problems exist with test strip urinalysis in the presence of Vitamin C that may influence the test’s ability to provide clinically secure results.

**Vitamin C interferes with the reliability of urine test strips**

High ascorbic acid concentrations of >400 mg/L are increasingly being found in the urine samples tested by laboratories.25 The presence of such high concentrations is known to cause significant problems with urine strip testing because ascorbic acid can, and often will, lead to false-negative results. In particular, there are specific inconsistencies when analyzing glucose and erythrocytes (hemoglobin).

**Combur-Test® strip* provides best results even at high concentrations of ascorbic acid**

Combur-Test® strip* detects even low concentrations of glucose and erythrocytes (hemoglobin) in the presence of Vitamin C giving you accurate results you can rely on.

**Combur-Test® strips* showed the best error tolerance against Vitamin C in the specimen, even at lowest concentrations of glucose and erythrocytes.**34

The presence of high amounts of Vitamin C in the patient’s urine is very common. Combur-Test® strips* could help to prevent patient revisits caused by unreliable test results.
References


* Combur-Test® is marketed under Chemstrip® Test in the USA and Canada
** Combur-10 Test® UX has been used for the comparison

COBAS, LIFE NEEDS ANSWERS, CHEMSTRIP, COMBUR-TEST and COMBUR 10 TEST are trademarks of Roche.

©2010 Roche

Roche Diagnostics Ltd.
CH-6343 Rotkreuz
Switzerland
www.roche.com