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Urine test strip analysis, concentration range and its interpretations of the parameters

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Abstract

Urinalysis is a simple urine analysis performed in many healthcare settings and at home that reveals important diagnostic information. Diabetes mellitus, kidney failure, renal, liver diseases, hydration, urinary tract infection, and metabolic abnormalities are among the diseases studied. Urinalysis is simple to perform using a urine test strip, but the results must be correctly interpreted. Urinalysis is a noninvasive, widely available, and reasonably priced method. A urine test strip is a paper or plastic dipstick with a chemically impregnated pad that is one of the simplest, cheapest, and most effective in vitro diagnostic devices for screening urine. The reference ranges, detection limits, and chemical analysis of common urine constituents such as occult blood, glucose, protein, ketones, leukocytes, nitrite, urobilinogen, bilirubin, pH, specific gravity, ascorbic acid, microalbumin, and creatinine are discussed in this article.

Keywords: Urine; Urinalysis; Biomarkers; Urine test strip; Colorimetric test

1. Introduction

Urinalysis is the examination of urine for certain groups of physical, chemical, and microscopic parameters in the urine, such as byproducts of normal and abnormal metabolism, cells, cellular fragments, and bacteria. It is one of the most readily available and cost-effective sets of screening tests for the diagnosis of some common diseases. It is used to assess the appearance, concentration, and content of urine and is used to detect and/or manage a wide range of medical disorders, such as urinary tract infections, kidney disease, liver problems and diabetes [1]. Urinalysis helps many disorders to be detected in their early stages by identifying substances that are not normally present in the urine or by measuring abnormal levels of certain parameters.

Urine, a waste product of the body, can give us immense information about health conditions or disorders of certain organs [2, 3]. Urine is a biological fluid interminably produced and excreted from the body and provides important information on the states of disease or body dysfunction before another fluid composition is altered to a significant extent. Therefore, the examination of urine is an aid in the diagnosis and monitoring of the course of treatment of certain diseases. Normal urine color is typically transparent and yellow or amber on visual inspection, and any other color is considered abnormal (Fig. 3.) [7]. A midstream urine sample collected for urinalysis in the first morning can be an accurate detection of some parameters and reduces the risk of the sample being contaminated.

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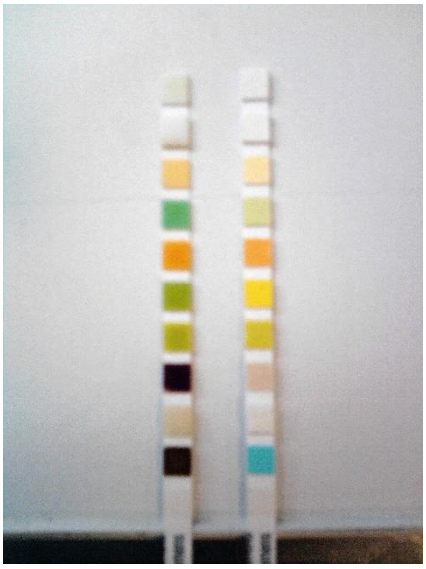

Figure 1 Colour changes of urine strip

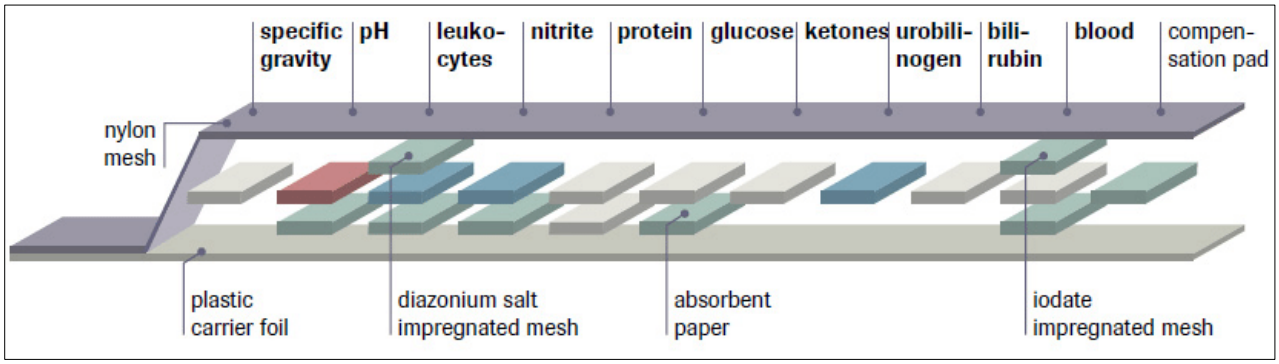

Figure 2 Representative parameters of urine test strips cross-section created by conventional manufacturing (Source: Roche Diagnostics USA)

2. Material and methods

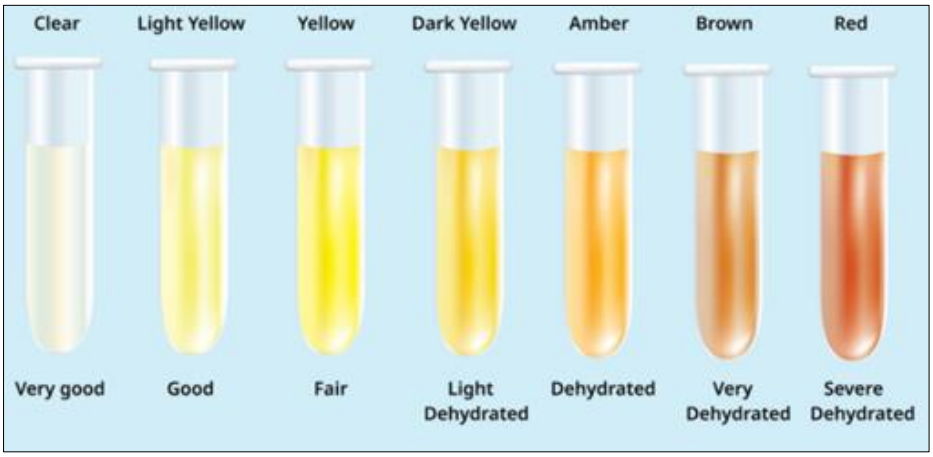

Figure 3 Common colors of urine

The urine reagent test strip is a paper with various pads impregnated with chemicals that react with the compounds present in urine producing a characteristic color change in a certain concentration. The reading of the results can often be done by comparing the color chart with the labels attached to the bottle after dipping for appropriate seconds [9].

The test may provide information on the status of carbohydrate metabolism, the acid-base balance of the body, kidney, and liver function, and urinary tract infection [8]. The manufacturers recommend the test strips to be stored in the original airtight container to maintain reagent reactivity and to obtain accurate results, urine collection, storage, and handling must be sterile and follow standard procedures [9].

Table 1 The color/Odour of urine is variable in the following disease conditions

Color	**Possible causes/ disorder**	**Odour diseases**	**Diseases**
Color less	Fatty disease, diabetes mellitus, Polyuria	Fruity odour	ketosis
Yellowish brown	Bile pigment, Fever	Cabbage type odour	methionine Malabsorption
Reddish brown	Hemoglobin in urine, hemorrhage, menstrual contamination	Maple sugar odour	maple sugar urine disease (MSUD)
Milky	Presence of Fat	Mousy	phenylketonuria
Dark Yellow	Fever	Rancid odour	tyrosine
Dark green	typhoid and cholera	Foul	Urinary Tract Infection, Vaginitis
Black	Due to Melanin (Melanoma) or Homogentisic acid in Alkaptonuria		

The most common dipstick examination of urine involves screening for abnormal levels of urinary occult blood, bilirubin, urobilinogen, ketones, protein, nitrite, glucose, pH, specific gravity, leukocytes, ascorbic acid, microalbumin, creatinine, calcium and so on. Recent chemical technological signs of progress have provided for the development of reagent test strips (dipsticks) that allow for the rapid, simultaneous determination of these substances. Abnormal urine chemistry results not only aid in the assessment of renal disorders but can also disclose many systemic disorders. Several manufacturers have developed reagent test strips that will provide results in 1-2 min. Instructions for each brand of reagent strips must be reviewed and adhered to carefully to avoid reporting misinterpreted results.

A dipstick, commonly called a urine reagent strip, is usually a thin plastic stick with several separate test pads that have chemicals impregnated affixed. The reagent strips are commonly used for qualitative and semiquantitative determination of one or more analytes in a urine sample i.e., qualitative strips only show positive or negative, whereas, semi-quantitative strips provide an estimation of a quantitative result; trace, 1+, 2+, 3+ and 4+ in addition to providing a positive or negative reaction via a change in color of the pad for substances are present or if certain levels are above or below normal. The analysis is fast and convenient; however, false-positive and false-negative results can occur depending on different conditions.

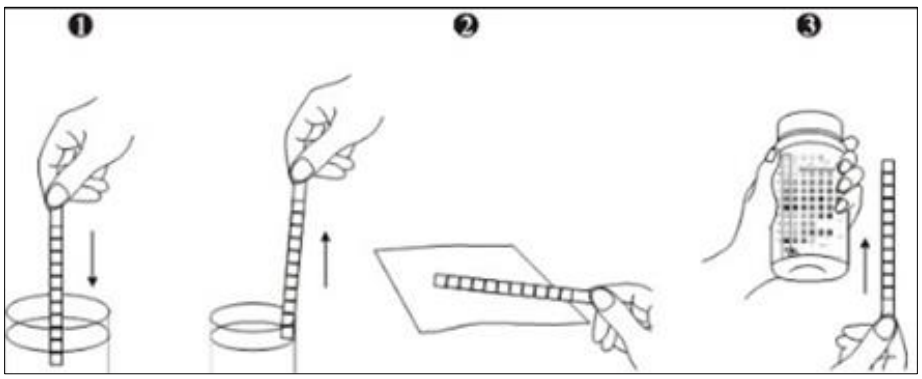

Figure 4 Urine test strip visual test procedure

3. Results

Urine test strips are commonly used to perform chemical examinations of urine in most clinical laboratories. When the test strip is immersed completely into a well-mixed urine sample and let the strip stands for the time necessary for the chemical reactions to occur, i.e., one minute for all except leukocytes which is two minutes, the color change on the pads starts to appear and are compared with the color charts of each test provided by the manufacturer. Nowadays, automated urine chemistry analyzers are developed by manufacturers to read the results, which reduces the limitations of visual reading such as timing errors and variations in color interpretation. The degree of color change on a test pad can give an estimate of the amount of substance present. The manufacturers recommend urinalysis is often done in conjunction with or may be followed by a microscopic examination for any abnormal results.

Table 1 Expected concentration levels in urinalysis strips

Test	**SI Unit**	**Reportable Range**						
		Neg.	**Trace**	**+ 1**	**+ 2**	**+ 3**	**+4**	
BLO	RBC/µL	Neg.	10	25	80	200	250	
BIL	mg/dL	Neg.	-	1	2	4	6	
URO	mg/dL	0.1	1	2	4	8	12	
KET	mg/dL	Neg.	5	15	40	80	160	
PRO	mg/dL	Neg.	15	30	100	300	1000	2000
NIT	mg/dL	Neg.	0.05	10				
GLU	mg/dL	Neg.	100	250	500	1000	2000	
pH	-	5	6	6.5	7	7.5	8	9
SG	-	1.000	1.005	1.010	1.015	1.020	1.025	1.030
LEU	WBC/µL	Neg.	15	70	125	250	500	
ASA	mg/dL	Neg.	10	20	40	50		
MA	mg/L	10	30	80	150			
CRE	mg/dL	10	50	100	200	300		
Calcium	mg/dL	1	5	10	20	40	50	

Depending on the manufacturer, the number of analytical pads and measurement ranges on the test strip may differ. Most of the test strips have one negative for analytes that do not exist in normal urine and a field for analytes present in urine in a small amount, whereas there is a various levels in ascending concentration of analyte for positive results in the reading.

Table 2 Common reported ranges in the test strip

Test Item	**Negative/Normal**	**Positive/Abnormal**
Blood	Negative/0	1+ ~ 3+ (10 ~ 250 RBC/µL)
Bilirubin	Negative/0	+ ~ +++ (0.5 ~ 3 mg/dL)
Urobilinogen	0.1 ~ 1 mg/dL	2.0 ~ ≥ 8.0 mg/dL
Ketones	Negative/0	+/- ~ +++(5 ~ 100 mg/dL)
Protein	Negative/0	+/- ~ +++ (30 ~ 1000 mg/dL)
Nitrite	Negative/0	Positive
Glucose	Negative/0	+/- ~ +++ (100 ~ 2000 mg/dL)

pH	5.0 ~6.0	6.5 ~ 9.0
Specific Gravity	1.005~1.020	1.010 ~ 1.030
Leukocytes	Negative/0	+ ~ +++ (15 ~ 500 WBC/ μL)
Ascorbic Acid	Negative/0	N/A
Microalbumin	< 10mg/L	20 ~ 200 mg/L
Creatinine	< 10 mg/dL	100 ~ 300 mg/dL
Calcium	10 mg/dL/Normal	<10 and >10 mg/dL

4. Discussion

The most frequently performed chemical tests using reagent test strips are described below

4.1. Occult blood (hemoglobin)

Hemoglobin is not normally present in urine. It may appear

If there is intravascular hemolysis, allowing hemoglobin to be filtered into the urine, or if red cells break apart within the urinary tract, these allow hemoglobin to be liberated. If there is intravascular hemolysis so that hemoglobin is filtered into the urine, or if red cells break apart within the urinary tract, liberating hemoglobin. This test is used to detect hemoglobin in the urine (hemoglobinuria). Hemoglobin is an oxygen-transporting protein found inside red blood cells (RBCs). Its presence in the urine indicates occult blood in the urine (known as hematuria).

A small number of RBCs are normally present in urine and usually result in a "negative" chemical test. An increased amount of hemoglobin and/or an increased number of RBCs are detected as a "positive" chemical test result. The results of this test are typically interpreted along with those from the microscopic examination of urine to determine whether RBCs are present in the urine. A positive result on this test with no RBCs present may indicate the presence of hemoglobin in the urine (which can occur when RBCs have broken apart) or myoglobin from muscle injury. Blood in the urine is not a normal finding, but it is not uncommon and not necessarily a cause for alarm. Your healthcare practitioners will investigate further to try to determine the source and underlying cause of the blood and may request repeat testing to determine whether the blood is persistent.

4.2. Glucose

Glucose is normally present in human urine in small amounts. Glucose is usually not detectable because ketones, ascorbic acid, or other substances found in urine may cause false negative results by reagent strips even when urinary glucose approaches abnormal values near 100 mg/dl. Depending on the manufacturer, from 4-5 categories (Neg./Normal, Trace, 1+, 2+, 3+, 4+ were used to report urinary strip glucose results in a concentration range of 50-2000 mg/dL the most common among them is reported from 100-2000 mg/dL. In the most common test strips, the glucose concentration of 100 mg/dL (5.5 mmol/L) was defined as a trace or normal result. The positive results or presence of glucose in the urine sample are called glucosuria. It results from either an excessively high glucose level in the blood, such as may be seen with people who have uncontrolled diabetes mellitus or a reduction in the "renal threshold;" when blood glucose levels reach a certain concentration, the kidneys begin to eliminate glucose from the urine to decrease blood concentrations. Sometimes the threshold concentration is reduced and glucose enters the urine sooner, at a lower blood glucose concentration.

Large amounts of urinary glucose suggest diabetes mellitus, or, rarely, renal glycosuria. Some other conditions that can cause glucosuria include hormonal disorders, liver disease, medications, and pregnancy. When glucosuria occurs, other tests such as fasting blood glucose are usually performed to further identify the specific cause.

4.3. Protein

Protein enters the urine either because of altered glomerular permeability or because of tubular damage. The common test strips report 15-2000mg/dL concentrations of urinary protein as 5-6 categories (Neg. trace, 1+, 2+, 3+, and 4+). The most common test strip protein concentration ranges from 15-1000 mg/dL. The protein test pad provides a rough estimate of the amount of albumin in the urine. All medical laboratories assigned the first measurement field to the negative category of urinary proteins. Protein enters the urine either because of altered glomerular permeability or

because of tubular damage. Glomerular proteinuria always includes a large component of albumin. Albumin makes up about 60% of the total protein in the blood. Normally, there will be no protein or a small amount of protein in the urine. When urine protein is elevated, a person has a condition called proteinuria.

Proteinuria may occasionally be seen in healthy individuals. Healthy people can have temporary or persistent proteinuria due to stress, exercise, fever, aspirin therapy, or exposure to a cold, for example. Repeat testing may be done once these conditions have resolved to determine whether the proteinuria is persistent.

If trace amounts of protein are detected, and depending on the person's signs, symptoms, and medical history, a repeat urinalysis and dipstick protein may be performed at a later time to see if there is still protein in the urine or if it has dropped back to undetectable levels.

If a large amount of protein is detected on a urinalysis and/or if the protein persists in repeated tests, a 24-hour urine protein test may be used as a follow-up test. Since the dipstick primarily measures albumin, the 24-hour urine protein test also may be ordered if a healthcare practitioner suspects that proteins other than albumin are being released into the urine.

4.4. Ketones

Ketone bodies appear in the urine as a consequence of accelerated fat metabolism. β-Hydroxybutyric acid is quantitatively the greatest, followed by acetoacetic acid and acetone. Ketones are not normally found in the urine. The test strip reported ketone concentration in 5-6 categories in ranges from 5 – 160 mg/dL (Neg., Trace, 1+, 2+, 3+, 4+). In all available test strips, the first measurement was defined as a negative result. Ketones are intermediate products of fat metabolism and are produced when glucose is not available to the body's cells as an energy source. They can form when a person does not eat enough carbohydrates (for example, in cases of fasting, starvation, or high-protein diets) or when a person's body cannot use carbohydrates properly. When carbohydrates are not available, the body metabolizes fat instead to get the energy it needs to keep functioning. Strenuous exercise, exposure to cold, frequent, prolonged vomiting, and several digestive system diseases can also increase fat metabolism, resulting in ketonuria.

In a person who has diabetes, ketones in urine may also be an early indication of insufficient insulin. With insufficient insulin, a diabetic cannot process glucose and instead metabolizes fat. This can cause ketones to build up in the blood, resulting first in ketosis and then progressing to ketoacidosis, a form of metabolic acidosis. Excess ketones and glucose are dumped into the urine by the kidneys to flush them from the body. This condition, called diabetic ketoacidosis (DKA), is most frequently seen with uncontrolled type 1 diabetes and can be a medical emergency. (See the article on Ketones and Diabetes.)

4.5. Leukocyte

Leukocyte counts were reported as 5-6 categories from 15-500Leu/μL (neg., trace, 1+, 2+, 3+, 4+) depending on the manufacturer. Leukocytes or also known as white blood cells are a central part of the immune system. Leukocyte esterase test in urine is a screening test used to determine the presence of white blood cells [8]. Esterase level is directly proportional to the number of leukocytes present in a urine sample. Only a very few levels of leukocytes, if any, are normally found in urine. High levels or positive results of leukocytes in urine may indicate an infection in the urinary track or kidney or underlying inflammatory medical problems. Urinary tract infection (UTI) is the most common cause of leukocytes in the urine [10-12]. In case of high leukocytes resulting in urine, screening should be supported with a microscopic examination.

The detection of leukocytes in the urine suggests a possible Urinary Tract Infection (UTI) somewhere in the urinary tract system including the bladder, urethra, and kidneys. The lower urinary tract and especially the bladder and urethra are common sites for infection. A UTI usually happens when bacteria enter the urinary tract through the urethra. They then multiply in the bladder. The test for Leukocyte Esterase is purely indicative and should not be solely relied on for diagnosis. The positive results for the nitrite test are also an indication of bacterial infection.

The color development read at 120 seconds is proportional to leukocytes in urine. The results can be negative and positive and are mostly reported semiquantitatively as trace, 1+, 2+, and 3+. The dipsticks are sensitive to 10-15 leukocytes per microliter of urine.

4.6. Nitrite

The Nitrite test is a screening test for possible infections caused by nitrate-reducing bacteria. Most of the bacteria that cause UTIs can reduce nitrate to nitrite. Since not all bacteria are capable of converting nitrate to nitrite, someone can still have a UTI despite a negative nitrite test. The results of this test will be considered along with the leukocyte esterase and microscopic examination. The nitrite test is a rapid, indirect method for detecting bacteriuria. The reaction principle is based on the bacterial reduction of dietary nitrate, which is normally present in urine, to nitrite, which is not normally present. Different from other dipstick parameters, the color intensity is not proportional to the number of bacteria, but the results are reported as positive or negative. A positive test result for nitrite and leukocytes can commonly indicate a UTI [10-11]. Any color development in the reaction area is considered positive. Colored substances in urine and prolonged storage of urine at room temperature may result in a false positive result.

4.7. Urobilinogen

Urobilinogen appears in urine when there are abnormalities in bilirubin metabolism or liver function. The concentration of urobilinogen reported in various test strips ranges from 0.1-12 mg/dL (normal, trace, 1+, 2+, 3+, 4+). The lowest urobilinogen concentration detected by the common urine test strip is 0.1mg/dL. This test screens for urobilinogen in the urine. The results are considered along with those for urine bilirubin.

Urobilinogen is normally present in urine in low concentrations. It is formed in the intestine from bilirubin, and a portion of it is absorbed back into the blood. Positive test results may indicate liver diseases such as viral hepatitis, cirrhosis, liver damage due to drugs or toxic substances, or conditions associated with increased RBC destruction (hemolytic anemia). When urine urobilinogen is low or absent in a person with urine bilirubin and/or signs of liver dysfunction, it can indicate the presence of hepatic or biliary obstruction.

4.8. Bilirubin

Bilirubin appears in urine when there are abnormalities in bilirubin metabolism or liver function. Most manufacturers used 4 categories to report urinary bilirubin concentration in the range of 0.5 - 4mg/dL (Neg., 1+, 2+, 3+). This test screens for bilirubin in the urine. Bilirubin is not present in the urine of normal, healthy individuals. It is a waste product that is produced by the liver from the hemoglobin of RBCs that are broken down and removed from circulation. It becomes a component of bile, a fluid that is released into the intestines to aid in food digestion.

In certain liver diseases, such as biliary obstruction or hepatitis, excess bilirubin can build up in the blood and is eliminated in urine. The presence of bilirubin in urine is an early indicator of liver disease and can occur before clinical symptoms such as jaundice develop.

The results of this test will be considered along with the result of urobilinogen (below). If positive, the healthcare practitioner will likely follow up with other laboratory tests, such as a liver panel, to help establish a diagnosis.

4.9. pH

Urinary pH is an expression of proton (hydrogen ion) concentration in urine. Mostly, urine has pH of about 6, which is slightly acidic, however, depending on the acid-base status, the urinary pH ranges from low 4.5 (acidic) to 7 neutral (neither acidic nor alkaline) or as high as 9 (alkaline). The acid-base balance of the body is mainly maintained by the kidneys. The pH of urine in the body can be affected by any condition that produces acids or bases in the body, such as acidosis or alkalosis, or the ingestion of acidic or basic foods or certain treatments.

Thus, the acidic urinary pH indicates that there are few hydrogen ion acceptors in urine and the nonionic diffusion of NH_3 into the tubular lumen is relatively hampered. Whereas, the alkaline pH of the urine shows that there are phosphates and other solutes that efficiently accept hydrogen ions, and diffusion of NH_3 into the tubular lumen is enabled.

The formation of crystals in basic urine and precipitate out to form crystals in acidic urine depending on the dissolved substances in urine is being produced in the kidneys, a kidney stone or "calculus" can develop. By modifying urine pH through diet or medications, the formation of these crystals can be reduced or eliminated.

The urine is acidic in reaction to following disease conditions such as diabetes mellitus, ketoacidosis, prolonged starvation, febrile illness in children, or strenuous exercise, while the urine can be alkaline in reaction to following diseased condition such as severe vomiting, diarrhea, hyperventilation, or prolonged use of diuretic drugs.

4.10. Specific gravity

The specific gravity of urine depends on a person's state of hydration. Normally, urine-specific gravity is measured by the weight of the number of solutes dissolved in urine. Normal urine always contains solutes dissolved in it; therefore, the specific gravity is higher than 1.000 (specific gravity of pure water). The normal specific gravity of an adult should be in between 1.016 and 1.022 as it simply indicates a person's state of hydration. Under normal conditions, all urine has some substances in it, a urine specific gravity of 1.000 (pure water SG) is not possible. The urine test strip-specific gravity test is based on the apparent pKa change concerning ionic concentration. The color development is proportional to the ionic concentration. Normal urine has a specific gravity within the range of 1.001 to 1.035 to measure with a dipstick at 0.005 levels indicating low ionic and increased ionic concentration in urine. Elevated specific gravity is associated with diabetes mellitus with increased urinary glucose.

Knowing the urine concentration helps healthcare practitioners understand whether a urine specimen they are evaluating is the best one to detect a particular substance. For example, if they are looking for very small amounts of protein, a concentrated morning urine specimen would be the best sample. When the protein is present in large amounts, all common methods are affected. There is no convenient correction factor for reagent strips. Specific gravity is increased in Excessive sweating, acute nephritis albuminuria, and all cases of oliguria. Specific gravity is decreased in diabetes insipidus, chronic nephritis, and all cases of Polyuria.

Table 3 The common concentration of interference observed and its effect on various tests is summarized below:[10]

Analyte	Interfering Analyses and Concentration	Impact on test result
Blood	Nitrofurantion ≥200 mg/L	+1
	Ascorbic acid ≥30 mg/dL	-1
	Leukocytes ≥500 WBC/μL	+1
	Albumin ≥1000 mg/dL	-1
	Formaldehyde ≥150 mg/dL	+1
	Bilirubin ≥4 mg/dL	+1
	Urobilinogen ≥20mg/dL	-1
	NaCl (Specific gravity) ≥1.040	-1
	Nitrofurantoin ≥30 mg/dL	+1
	Riboflavin ≥50 mg/dL	+1
Bilirubin	Selenium ≥2000 mg/L	+1
	p-amino salicylic acid ≥12500 mg/L	+1
	Urobilinogen ≥120 mg/L	+1
	Penicillin ≥7000 mg/L	+1
	Ascorbic acid ≥40 mg/dL	+1
Urobilinogen	p-amino salicylic acid ≥12500 mg/L	+1
	Azogantrinsin (Sulfamethoxazol) ≥1000 mg/L	+1
	Bilirubin ≥4 mg/dL	+1
	Formaldehyde ≥150 mg/dL	-1
	Nitrofurantion ≥40 mg/dL	+1
	Phenazopyridine ≥37 mg/dL	+1
	Riboflavin ≥25 mg/dL	+1
	Selenium ≥220 mg/dL	+1
Ketone	Formalin ≥1500 mg/L	+1

	Captopril ≥50 mg/L	+1
	NaCl (Specific gravity) ≤1.000	+1
	Bilirubin ≥4 mg/dL	+1
Protein	Sodium acetate ≥2800 mg/dL	+1
	High pH >9	+1
	Acetaminophen ≥500 mg/L	+1
	Bilirubin ≥6 mg/dL	+1
	Hemoglobin ≥5 mg/dL	+1
	Riboflavin≥25 mg/dL	-1
	Urobilinogen≥20 mg/dL	-1
	Acetaminophen50 mg/dL	+1
	Nitrofurantion ≥20 mg/dL	+1
Nitrite	Ascorbic acid ≥40 mg/dL	-1
	Bilirubin≥4 mg/dL	+1
	Nitrofurantoin≥20 mg/dL	+1
	Phenazopyridine≥37 mg/dL	+1
	Riboflavin≥50 mg/dL	+1
	Selenium≥300 mg/dL	+1
	Urobilinogen≥15 mg/dL	+1
Glucose	Chlorine Bleach ≥100 mg/L	+1
	Mecetronium Etilsulfate ≥40 mg/L	+1
	Ascorbic acid ≥40 mg/dL	-1
	Ketones ≥40 mg/dL	-1
	NaCl (Specific gravity) ≤1.000	+1
	Bilirubin ≥6 mg/dL	+1
	Formaldehyde ≥150 mg/dL	+1
pH	-	-
Specific gravity	pH≥ 9	+1
Leukocytes	Glucose ≥2000 mg/dL	-1
	Albumin ≥1000 mg/dL	-1
	Formaldehyde ≥1000 mg/L	+1
	Captopril ≥100 mg/L	-1
	Tetracycline ≥400 mg/L	+1
	Bilirubin ≥4 mg/dL	+1
	Formaldehyde ≥150 mg/dL	+1
	Urobilinogen ≥15 mg/dL	+1
Microalbumin	Bilirubin ≥4 mg/dL	+1
	Hemoglobin ≥5 mg/dL	+1

	Urobilinogen ≥15 mg/dL	+1
	pH ≥9	+1
	Acetaaminophen 50 mg/dL	+1
	Potassium Chloride ≥1500 mg/dL	-1
Creatinine	Chlirine Bleach ≥1%	+1
	Hemoglobin ≥5 mg/dL	+1
	Nitrofurantion ≥30 mg/dL	+1
	Riboflavin ≥37 mg/dL	+1
	Urobilinogen ≥20 mg/dL	-1

5. Additional parameters available on dipsticks

Some brands of reagent strips are offering additional test parameters including calcium, creatinine, and microalbumin. In addition, some brands of reagent strips include a test pad for ascorbic acid. Excess ascorbic acid can interfere with the chemical reactions of bilirubin, blood, and glucose and may result in false low or negative results in these parameters. Detecting the presence of ascorbic acid may help correlate negative results with other findings.

5.1. Ascorbic Acid (Vitamin C)

Occasionally, people taking vitamin C or multivitamins may have large amounts of ascorbic acid in their urine. When this is suspected to be the case, a laboratorian may test the sample for ascorbic acid (vitamin C) because it has been known to interfere with the accuracy of some of the results of the chemical test strip, causing them to be falsely low or falsely negative. Examples of tests that may be affected include urine dipstick tests for glucose, blood bilirubin, nitrite, and leukocyte esterase.

5.2. Microalbumin

Normal urine contains very little protein: usually less than 10 mg/dL or 100 mg per 24 hours is excreted.[5] Persistent microalbuminuria indicates a high probability of damage to the kidney glomerular filtration capacity.[10] Albuminuria is the term used when albumin levels reach >200 mg/L in the urine.6 Microalbuminuria is the term used when albumin levels in the urine are 20-200 mg/L.[10] Even though only a small amount of albumin is present in the urine in microalbuminuria, this can be an indicator that the patient has the beginnings of kidney damage.[11] Patients with microalbuminuria have an elevated risk of developing progressive renal disease as well as an increased risk of cardiovascular disease.[13] Action taken by a healthcare practitioner (HCP) at this stage can halt or reverse the damage to the kidneys.[16] The Micral-Test strip is an easy-to-use test designed to deliver quick and accurate results, specific for human albumin and sensitive across the diagnostic range. Suitable for all patient groups, the Micral-Test strip is a cost-efficient way to gain actionable health information. [14-16]

The test is also used to screen samples for microalbuminuria, which may help determine which patients are at risk of developing early kidney damage. The development of glomerular damage, in the absence of nephropathy, may be predicted by microalbuminuria. Patients with the highest risk are those with diabetes and hypertension, followed by patients who have immune disorders or have been exposed to nephrotoxins. Microalbuminuria may also be an early indication of developing preeclampsia during pregnancy.

5.3. Creatinine

Creatinine is a waste product of creatine, an amino acid contained in muscle tissue and found in urine. A person may attempt to foil a test by drinking excessive amounts of water or diuretics such as herbal teas to “a flush” the system. Creatinine and specific gravity are two ways to check for dilution and flushing. Low creatinine and specific gravity levels may indicate dilute urine. The absence of creatinine (<5 mg/dl) is indicative of a specimen not consistent with human urine. Creatinine levels vary based on age, gender, and health history. Higher levels in the urine may reveal impaired kidney function or kidney disease. Some compounds, physical properties (e.g., high pH, high SG) and high concentrations of yellow pigment may lead to higher CR readings. It helps in the diagnosis and treatment of renal diseases and can be used to monitor renal dialysis, in addition to as a calculation basis for measuring of other urine analytes. Daily Creatinine excretion related to muscle mass is usually constant.

5.4. Calcium

High levels of calcium in the urine can show hyperparathyroidism, milk-alkali syndrome, idiopathic hypercalciuria, sarcoidosis, renal tubular acidosis, vitamin D intoxication, use of loop diuretics, or kidney failure. Abnormally low calcium in the urine may signal malabsorption disorders, vitamin D deficiency, hypoparathyroidism, or use of thiazide diuretics. A large concentration of magnesium ions in urine will elevate the calcium result.

5.5. Potential interferes on the test results

False-negative results may occur with high specific gravity and in urines containing glucose and protein. [2,9,11] Significantly high levels of protein or glucose can contribute to increased specific gravity. In such an environment, white blood cells will crenate and be unable to release esterase. Various drugs and chemicals interfere with this test. Check the packaging insert of the reagent strip manufacturer for specifics concerning interfering substances. Some drugs and chemicals that may cause false-negative results include ascorbic acid, oxalic acid, cephalexin, cephalothin, gentamicin, and tetracycline.

Table 4 Summary of urine test strip analysis

Parameter	Expected Results	Interpretation of Results	Causes of False Positives (or Increase)	Causes of False Negatives (or Decrease)
Blood	Negative	Positive: hematuria: trauma, infection, inflammation, infarction, calculi, neoplasia, coagulopathy hemoglobinuria: myoglobinuria	bleach contamination; high levels of bromide or iodide; bitch in heat	poorly mixed urine
Bilirubin	Negative	Positive: can be normal in dogs; ALWAYS abnormal in cats; indicates liver disease, bile duct obstruction, starvation; hemolysis; pyrexia	high doses of chlorpromazine; etodolac metabolites	ascorbic acid; nitrites
Glucose	Negative to Trace	Positive: Chronic or transient hyperglycemia; post administration of certain drugs; rarely-Fanconi-like syndrome	hydrogen peroxide; bleach	ascorbic acid; ketones; increased specific gravity; cold urine; expired reagent strips
Ketones	Negative	Positive: starvation; insulinoma; diabetes mellitus; persistent hypoglycemia; high-fat low carbohydrate diets; glycogen storage disease	pigmented urine	old urine sample
Protein	Negative to Trace	hemorrhage; urinary infection; intravascular hemolysis; renal disease	alkaline urine; disinfectant residue	dilute or acidic urine
Specific Gravity	1.005 to 1.030		moderate to high levels of protein	alkaline urine
pH	5.0 to 8.0	Acidic: meat diet; acidosis; low chloride; acidifying agents Alkaline: vegetable-based diet; bacterial infection; alkalosis; urine exposed to air for extended times; administration of alkalinizing agents; postprandial tide	glucose in urine	

Urobilinogen	0.1 to 1.0 mg/dL	Positive: hemolytic crisis; intestinal or hepatic dysfunction	elevated reagent strip temperature	old urine sample, formalin residue in the collection container
Leukocytes	Negative	pyuria	common in cats, and if fecal contamination	often occurs; tetracycline; high glucose; high specific gravity; voided sample in animal with pyometra or prostatitis
Nitrite	Negative	bacterial infection		common in kids

6. Conclusion

In conclusion, we summarize that the analyte concentration reporting ranges are different for different manufacturers. However, they all agree on lower or negative concentration, whereas the variations in the positive results did not significantly affect the diagnosis since most parameters should not exist in normal urine. The dipstick portion of urinalysis is an important diagnostic and monitoring laboratory test system. To ensure accurate results, certain sample collection, handling, and testing techniques must be strictly followed. The causes of false positive and negative test results also should be considered when evaluating urine dipstick results. Because the dipstick test is easy to perform and economical, all practices should be able to perform this test in-house rather than submitting samples to an outside laboratory. In-house, laboratory analysis also provides more accurate results and prevents age-induced artifacts that may lead to false positive and false negative test results.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data Availability

The data used to support the findings of this study are included in the article.

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