

# Diuretic Drug Information

## Classification

Diuretics elevate the rate of bodily urine excretion (diuresis). All diuretics increase the excretion of water from the body, although each class of diuretics does so in a distinct way employing different mechanisms of action. In medicine, diuretics are used to treat heart failure, liver cirrhosis, hypertension and certain kidney diseases. Side effects include dehydration, hypotension, disturbed electrolyte balance, muscle cramps and weakness.

Diuretics are prescription drugs with relatively low potential for abuse among the general population. They are not classified as Controlled Substances in the United States. There are several categories of diuretics:

- High ceiling loop diuretics such as furosemide, bumethanide and ethacrynic acid may cause substantial diuresis. They inhibit the body's ability to reabsorb sodium in the kidney which leads to retention of water in the urine as water normally follows sodium back into the extracellular fluid.
- Thiazides such as hydrochlorothiazide, cause moderate diuresis. They act as carbonic anhydrase inhibitors with the major site of action in the renal distal tube. They enhance excretion of sodium, potassium, calcium and chlorine ions.
- Potassium sparing diuretics such as amiloride, triamterene and spironolactone do not promote the secretion of potassium into the urine; thus potassium is spared and not lost as much as in other diuretics.
- Osmotic diuretics like mannitol, glucose and other sugars are filtered in the kidneys, but cannot be reabsorbed leading to elevated water elimination with urine.
- Low ceiling diuretics—the term is used to indicate a pharmacological profile with rapidly flattening dose effect curve (in contrast to "high ceiling", where the relationship is close to linear). The thiazides usually fall into this category.

## Metabolism

Most diuretics are excreted in urine with minimal metabolites. A few exceptions include spironolactone metabolizing into canrenone and canrenoic acid; and triamterene, which in the body undergoes conversion to hydroxytriamterene sulfate.

## Abuse

Diuretics are sometimes abused by people with eating disorders for weight loss. Use of diuretics in sports is prohibited. Increased urine flow would reduce concentrations of banned performance enhancing substances in urine such as anabolic steroids, thus complicating their detection in doping control (masking). In sports where weight categories are involved diuretics are abused as weight reducing agents. Diuretic abuse in sports is unethical and dangerous for athlete health (dehydration). Diuretic testing is a part of routine doping control in sports.

## **Methods of Analysis**

Methylation and gas chromatography/mass spectrometry (GC/MS) have been traditionally used for diuretic screening and confirmation in athletic doping control. In recent years, liquid chromatography/tandem mass spectrometry (LC/MS/MS) has been successfully applied for direct analysis of unextracted urine.