Potassium Bicarbonate

Potassium bicarbonate (also known as potassium hydrogen carbonate or potassium acid carbonate), is a colorless, odorless, slightly basic, salty substance. Potassium bicarbonate is “generally recognized as safe”.

Potassium bicarbonate is soluble in water, and is often found added to bottled water to affect taste; however, it is not soluble in alcohol. Decomposition of the substance occurs between 100°C and 120°C into \( \text{K}_2\text{CO}_3 \) (potassium carbonate), \( \text{H}_2\text{O} \) (water), and \( \text{CO}_2 \) (carbon dioxide). In concentrations greater than 0.5%, \( \text{KHCO}_3 \) can have toxic effects on plants (potassium bicarbonate has widespread use in crops, especially for neutralizing acidic soil, and is also under consideration as an organic fungicide, although there is no evidence of human carcinogenicity, no adverse effects of overexposure, and an undetermined LD\(_{50}\).

Physically, potassium bicarbonate occurs as a crystal or a soft white granular powder. It has a CAS No [298-14-6]. It is manufactured by reacting potassium carbonate with carbon dioxide and water:

\[
\text{K}_2\text{CO}_3 + \text{CO}_2 + \text{H}_2\text{O} \rightarrow 2 \text{KHCO}_3
\]

Potassium bicarbonate is very rarely found in its natural form, the mineral called kalicinite.

Uses

The compound is used as a source of carbon dioxide for leavening in baking, extinguishing fire in dry chemical fire extinguishers, acting as a reagent, and a strong buffering agent in medications. Potassium bicarbonate is used as a fire suppression agent (“BC dry chemical”) in some dry chemical fire extinguishers, as the principal component of the Purple-K dry chemical. It is the only dry chemical fire suppression agent recognized by the National Fire Protection
Association for firefighting at airport crash rescue sites. It is about twice as effective in fire suppression as sodium bicarbonate.

It is used as a base in foods to regulate pH. It is a common ingredient in club soda, where it is used to soften the effect of effervescence.

Potassium bicarbonate is an effective fungicide against powdery mildew.

**What is potassium bicarbonate?**

Potassium is a mineral that is found naturally in foods and is necessary for many normal functions of your body, especially the beating of your heart.

Potassium bicarbonate is used to prevent or to treat a potassium deficiency (hypokalemia).

Potassium bicarbonate may also be used for other purposes not listed in this medication guide.

**Important information about potassium bicarbonate?**

Avoid taking potassium supplements or using other products that contain potassium without first asking your doctor. Salt substitutes or low-salt dietary products often contain potassium. If you take certain products together you may accidentally get too much potassium. Read the label of any other medicine you are using to see if it contains potassium.

There are many other medicines that can interact with potassium bicarbonate. Tell your doctor about all the prescription and over-the-counter medications you use. This includes vitamins, minerals, herbal products, and drugs prescribed by other doctors. Do not start using a new medication without telling your doctor. Keep a list with you of all the medicines you use and show this list to any doctor or other healthcare provider who treats you.
Before taking this medication, tell your doctor if you are allergic to any drugs, or if you have:

- kidney disease;
- Addison’s disease;
- stomach ulcer or an intestinal blockage;
- chronic diarrhea (colitis).

If you have any of these conditions, you may not be able to use potassium bicarbonate, or you may need a dose adjustment or special tests during treatment.

Pregnancy category C. This medication may be harmful to an unborn baby. Tell your doctor if you are pregnant or plan to become pregnant during treatment. It is not known whether potassium bicarbonate passes into breast milk or if it could harm a nursing baby. Do not use this medication without telling your doctor if you are breast-feeding a baby.

**How to take potassium bicarbonate?**

Use this medication exactly as directed on the label, or as prescribed by your doctor. Do not use it in larger amounts or for longer than recommended.

Take each dose with a full glass of water. Take potassium bicarbonate with food or milk to lessen stomach upset.

Drop the effervescent tablets into a glass of water (at least 4 ounces, or one-half cup). Allow the tablets to dissolve completely and then drink this mixture right away. Do not save it for later use.

Do not stop taking this medication without first talking to your doctor. If you stop taking potassium bicarbonate suddenly, your condition may become worse. Store potassium bicarbonate at room temperature away from moisture and heat.
Take the missed dose as soon as you remember. If you are more than 2 hours late in taking your medicine, skip the missed dose and wait until your next regularly scheduled dose. Do not take extra medicine to make up the missed dose.

Seek emergency medical attention if you think you have used too much of this medicine.

Overdose symptoms may include numbness or tingling in your hands or feet, uneven heart rate, paralysis, feeling like you might pass out, chest pain or heavy feeling, pain spreading to the arm or shoulder, nausea, sweating, general ill feeling, or seizure (convulsions).

**Potassium bicarbonate side effects**

Get emergency medical help if you have any of these signs of an allergic reaction: hives; difficulty breathing; swelling of your face, lips, tongue, or throat. Stop using potassium bicarbonate and call your doctor at once if you have any of these serious side effects:

- confusion;
- uneven heartbeat;
- unusual tiredness, weakness, heavy feeling in your legs;
- severe stomach pain cramping; or
- black, bloody, or tarry stools.

Less serious side effects may include:

- nausea, vomiting, diarrhea, or upset stomach;
- a rash;
- slight tingling in the hands or feet; or
- anxiety.

This is not a complete list of side effects and others may occur. Tell your doctor about any unusual or bothersome side effect.

**What other drugs will affect potassium bicarbonate?**
The following drugs can interact with potassium bicarbonate. Tell your doctor if you are using any of these:

- digoxin (Lanoxin);
- an ACE inhibitor such as benazepril (Lotensin), captopril (Capoten), fosinopril (Monopril), enalapril (Vasotec), lisinopril (Prinivil, Zestril), moexipril (Univasc), perindopril (Aceon), quinapril (Accupril), ramipril (Altace), or trandolapril (Mavik);
- a beta-blocker such as atenolol (Tenormin), labetalol (Normodyne, Trandate), metoprolol (Lopressor, Toprol), propranolol (Inderal, InnoPran), sotalol (Betapace), timolol (Blocadren);
- a diuretic (water pill) such as amiloride (Midamor, Moduretic), chlorothiazide (Dioril, others), hydrochlorothiazide (Hydrodiuril, HCTZ, others), indapamide (Lozol), metolazone (Zaroxolyn), spironolactone (Aldactone, Aldactazide), or triamterene (Dyrenium, Dyazide, Maxzide);
- aspirin or other NSAIDs (non-steroidal anti-inflammatory drugs) such as ibuprofen (Motrin, Advil), naproxen (Aleve, Naprosyn), diclofenac (Voltaren), etodolac (Lodine), indomethacin (Indocin), ketoprofen (Orudis), and others; or
- a steroid such as prednisone (Deltasone, Orasone), hydrocortisone (Cortef, Hydrocortone), dexamethasone (Decadron, Hexadrol), and others.

This list is not complete and there may be other drugs that can interact with potassium bicarbonate or affect your condition. Tell your doctor about all your prescription and over-the-counter medications, vitamins, minerals, herbal products, and drugs prescribed by other doctors. Do not start a new medication without telling your doctor.

To be sure this medication is helping your condition, your blood may need to be tested often. Your heart rate may also be checked using an electrocardiograph or ECG (sometimes called an EKG) to measure electrical activity of the heart. This test will help your doctor.
determine how long to treat you with potassium. Do not miss any scheduled appointments.

Serious side effects of potassium include uneven heartbeat, muscle weakness or limp feeling, severe stomach pain, and numbness or tingling in your hands, feet, or mouth.

What is potassium bicarbonate and potassium citrate?

Potassium is a mineral that is found in many foods and is needed for several functions of your body, especially the beating of your heart.

Potassium bicarbonate and potassium citrate is used to prevent or to treat low blood levels of potassium (hypokalemia). Potassium levels can be low as a result of a disease or from taking certain medicines, or after a prolonged illness with diarrhea or vomiting.

Potassium bicarbonate and potassium citrate may also be used for other purposes other than those listed in this medication guide.

Potassium-rich foods

Potassium-rich foods include: squash, baked potatoes (skin on), spinach, lentils, broccoli, Brussels sprouts, zucchini, kidney or navy beans, raisins, watermelon, orange juice, bananas, cantaloupe, and low-fat milk or yogurt. Consume only the daily amounts recommended by your doctor or nutrition counselor.

What other drugs will affect potassium bicarbonate and potassium citrate?

The following drugs can interact with potassium bicarbonate and potassium citrate. Tell your doctor if you are using any of these:

- eplerenone (Inspra);
- digoxin (digitalis, Lanoxin);
- quinidine (Quinaglute, Quinidex, Quin-Release);
• a bronchodilator such as ipratropium (Atrovent) or tiotropium (Spiriva);
• an ACE inhibitor such as benazepril (Lotensin), captopril (Capoten), fosinopril (Monopril), enalapril (Vasotec), lisinopril (Prinivil, Zestril), moexipril (Univasc), perindopril (Aceon), quinapril (Accupril), ramipril (Altace), or trandolapril (Mavik); or
• any type of diuretic (water pill) such as bumetanide (Bumex), chlorothiazide (Diaril), chlorthalidone (Hygroton, Thalitone), ethacrynic acid (Edecrin), furosemide (Lasix), hydrochlorothiazide (HCTZ, HydroDiaril, Hyzaar, Lopressor, Vasoretic, Zestoretic), indapamide (Lozol), metolazone (Mykrox, Zarxolyn), or torsemide (Demadex).

This list is not complete and there may be other drugs that can interact with potassium bicarbonate and potassium citrate. Tell your doctor about all your prescription and over-the-counter medications, vitamins, minerals, herbal products, and drugs prescribed by other doctors. Do not start a new medication without telling your doctor.

Potassium bicarbonate (KBC) potently reduces urine calcium excretion in adult humans, including patients with hypertension or calcium urolithiasis, and postmenopausal women. In the latter, who have substantial risk of calcium deficiency, it remains unknown whether the observed short-term urine calcium-lowering effect of KBC persists over years.

We studied 170 postmenopausal women randomized to KBC 30, 60, or 90 mmol/d (KBC treatment), or placebo, for up to 36 months. Each received a multivitamin with 400 IU vitamin D, and calcium carbonate as needed to produce a total dietary calcium intake of at least 30 mmol daily.

Daily urine calcium excretion (UCaV) did not differ among groups at baseline (all-groups mean ± SD, 155 ± 83 mg/d). From 1–36 months of KBC treatment, adjusting UCaV for creatinine (Cr) excretion, each
dose of KBC reduced UCaV \((P < 0.01)\) with a dose-dependent trend \((P = 0.05)\). The reduced UCaV/Cr persisted throughout the KBC treatment period (up to 36 months) in all KBC, and the greatest reductions occurred in the subjects with greatest baseline UCaV/Cr \((\Delta \text{UCaV/Cr} \text{ vs. baseline UCaV/Cr}; P < 0.001)\).

Twenty-eight percent of the subjects had high baseline calciuria \((\text{UCaV/Cr} > 200 \text{ mg Ca/1000 mg Cr})\). With baseline UCaV/Cr of 250 mg/1000 mg Cr, KBC 60 mmol decreased UCaV/Cr by 55.8 mg/1000 mg Cr, a potential daily calcium retention that over a 36-month period would accumulate up to 55,845 mg of calcium, nearly 5% of bone calcium content.

KBC treatment induced a dose-dependent decrease in UCaV/Cr that persisted up to 36 months, with the greatest decreases occurring in those women with the greatest baseline UCaV, nearly a third of whom had high baseline calciuria. Thus, one can pre-select postmenopausal women most likely to have the urine calcium-lowering effect of KBC and predict their potential bone calcium increase.

AGE-RELATED BONE MASS decline entails loss of bone calcium. Bone might lose calcium in part because its alkaline calcium salts titrate non-carbonic acids endogenously produced in response to habitual ingestion of the net acid-producing diets typical of Western countries. The acid-liberated bone calcium disappears in urine, proportionate to the magnitude of the diet net acid load. Although the kidney daily excretes the bulk of the diet net acid load, the body retains a small fraction sufficient to induce a persisting low-grade metabolic acidosis, which ensures continued titration of the alkaline salts of bone, with attendant loss of calcium and phosphorus in urine. The diet-induced low-grade metabolic acidosis that persists further contributes to the external losses of calcium by direct impairment of renal calcium re-absorptive efficiency, a characteristic of metabolic acidosis.
Eating a diet that produces little or no net acid, or neutralizing the diet’s acid with an exogenously administered basic salt such as potassium bicarbonate (KBC), decreases the demand for bone base, and hence presumably decreases the amount of bone breakdown and amount of bone calcium released. This in turn leads to a decrease in urine calcium excretion.

Previously, we demonstrated, in 18 postmenopausal women fed a nutritionally standard, high-protein diet for 2 months supplemented with KBC (60–120 mmol/d for 18 d), that plasma bicarbonate increased significantly \((P = 0.03)\) and that net acid production, as estimated by renal net acid excretion, decreased \((P < 0.001)\), greater in the women taking the 120-mmol dose of \(\text{KHCO}_3\) than in the women taking the 60-mmol dose. Calcium balance improved, slightly more so in the group given the higher dose of \(\text{KHCO}_3\), and in all subjects the improvement in calcium balance was mirrored by an improvement in phosphate balance. Other investigators have also shown a short-term effect of KBC or citrate to lower urine calcium excretion.

The question remains whether the urine calcium-lowering effect of KBC persists over years, as would be necessary to substantially improve or prevent bone lost from its titration by endogenous produced non-carbonic acids. However, such a persisting effect remains undemonstrated.

Studies demonstrates that in normal postmenopausal women eating a typical diet, supplementing dietary potassium with potassium bicarbonate induces a reduction in urinary excretion of calcium that persists over a period of up to 36 months. More importantly, the women at the greatest risk for body calcium loss (i.e. hypercalciuric subjects at baseline) had the greatest decline in urinary excretion of calcium and would potentially derive the greatest benefit from treatment with potassium bicarbonate.

Assuming a urine calcium excretion at baseline of 250 mg/1000 mg Cr \((71 \text{ mmol}/100 \text{ mmol Cr})\), a woman receiving 60 mmol/d of
KHCO$_3$ would have a decrease in urinary excretion of calcium of approximately 55 mg/1000 mg Cr per day (15.5 mmol/100 mmol Cr per day). Because absolute Cr excretion averaged 931 mg/d in this group, a reduction of 55 mg Ca/1000 mg Cr per day converts to an absolute reduction of 51 mg Ca per day. Retained over 36 months, without change in intestinal calcium absorption, this amount of calcium would accumulate to more than 55,845 mg (1396 mmol) of calcium, a potential saving of bone calcium content of nearly 5%, assuming a total bone calcium content of approximately 1200 g. Previous studies with KHCO$_3$ administration confirm no change in intestinal calcium absorption.

Yet, no one has studied the effect of long-term (months or years) of KHCO$_3$ administration on intestinal calcium absorption. Because body calcium content increases because of renal calcium retention, intestinal calcium absorption might decrease, perhaps secondary to reduced PTH-driven calcitriol production. Yet, even if intestinal calcium absorption decreases over time (months or years), unless it does so commensurately with the reduction in urine calcium excretion, calcium balance will remain on the positive side.

Many factors can affect urine calcium excretion, including dietary calcium and sodium intake, vitamin D intake, PTH levels, thyroid function, and renal function. Sodium intake, as judged by urine sodium excretion, remained unchanged within and between groups during the 36 months of the study. A non-significant decline in renal function occurred in all groups over time, with the slope of the change in renal function nearly identical in all groups.

More than one quarter of the women in this study had high baseline calciuria. High urine calcium excretion is often seen in women with osteoporosis and can be an important predictor for both low bone mass and kidney stones. Supplementation of the diet with a potassium alkalinizing salt has been shown to decrease the incidence of kidney stones in subjects with a propensity to form kidney stones and to prevent bone loss in patients with calcium urolithiasis and
reduce bone resorption in postmenopausal women. This study suggests that one can pre-select the postmenopausal women most likely to benefit from long term KHCO$_3$ and potentially decrease the incidence of osteoporosis.

Abbreviations: Cr, Creatinine; KBC, potassium bicarbonate; UCaV, urine calcium excretion.

**Potassium Bicarbonate Reduces Urinary Nitrogen Excretion in Postmenopausal Women**

Although plasma acidity does not perceptibly increase from day to day, a gradual increase does occur over time as renal acid-base regulatory function declines with increasing age. Therefore, although it appears that bone completely neutralizes the small fraction of retained acid daily, an even smaller fraction escapes bone neutralization and a slight retention of acid accumulates in body fluids to account for the increasing acidity with advancing age.

Previously we demonstrated that low grade chronic metabolic acidosis exists normally in humans eating ordinary diets that yield normal net rates of endogenous acid production (EAP), and that the degree of acidosis increases with age. We hypothesize that such diet-dependent and age-amplifying low grade metabolic acidosis contributes to the decline in skeletal muscle mass that occurs normally with aging. This hypothesis is based on the reported finding that chronic metabolic acidosis induces muscle protein breakdown, and that correction of acidosis reverses the effect. Accordingly, in 14 healthy postmenopausal women residing in a General Clinical Research Center and eating a constant diet yielding a normal EAP rate, we tested whether correcting their “physiological” acidosis with orally administered potassium bicarbonate (KHCO$_3$; 60-120 mmol/day for 18 days) reduces their urinary nitrogen loss. KHCO$_3$ reduced EAP to nearly zero, significantly reduced the blood hydrogen ion concentration ($P < 0.001$), and increased the plasma bicarbonate concentration ($P < 0.001$), indicating that pre-KHCO$_3$
diet-dependent EAP was significantly perturbing systemic acid-base equilibrium, causing a low grade metabolic acidosis. Urinary ammonia nitrogen, urea nitrogen, and total nitrogen levels significantly decreased. The cumulative reduction in nitrogen excretion was $14.1 \pm 12.3$ g ($P < 0.001$). Renal creatinine clearance and urine volume remained unchanged.

We conclude that in postmenopausal women, neutralization of diet-induced EAP with KHCO$_3$ corrects their preexisting diet-dependent low grade metabolic acidosis and significantly reduces their urinary nitrogen wasting. The magnitude of the KHCO$_3$-induced nitrogen-sparing effect is potentially sufficient to both prevent continuing age-related loss of muscle mass and restore previously accrued deficits. (J Clinical Endocrinol Metab 82: 254-259, 1997)

In disorders that cause chronic metabolic acidosis, protein degradation in skeletal muscle is accelerated (1-3), increasing the production of nitrogen (N) end products that are eliminated in the urine, thereby inducing negative N balance. This disturbance of N metabolism apparently results directly from the acidosis, not from its cause or from other sequelae of the underlying acidosis-producing disorder, because it occurs with widely differing acidosis-producing conditions, and it is reversible by administration of alkali, which corrects the acidosis but not its cause. Acidosis-induced proteolysis appears to be an acid-base homeostatic mechanism. By releasing increased amounts of amino acids, in particular glutamine, which is used by the kidney for synthesis of ammonia, the kidney can increase the excretion of acid (as ammonium) in the urine, thereby mitigating the severity of the acidosis.

One cause of chronic metabolic acidosis is eating a diet whose metabolism yields non-carbonic acids (e.g. sulfuric acid) in excess of base (e.g. bicarbonate). Such diets induce a chronic low grade metabolic acidosis even in healthy subjects; the severity of the acidosis correlates with the net rate of endogenous acid production (acid minus base). Net acid-producing diets are typical of those
ingested by the inhabitants of industrialized countries, where consumption of foods rich in acid precursors (animal foods) is disproportionate to that of foods rich in base precursors (vegetable foods). Habitual ingestion of such diets has been linked to clinical disorders, in particular nephrolithiasis and osteoporosis, in which diet-induced acid production has been identified as contributing to their pathogenesis.

Because of the attendant low grade chronic acidosis, habitual ingestion of typical net acid-producing diets might chronically sustain a slightly increased state of protein breakdown and consequent N wasting. Conceivably, low grade N wasting is a tonic “normal” state in adult humans, accounting for the normal progressive decrease in muscle mass as adults get older. Indeed, diet-dependent acidosis induced muscle wasting might be amplified by age because diet-dependent metabolic acidosis tends to increase in severity with age, which, in turn, appears to result from the normal age-related decline in the function of the kidney.

Discussion

The findings of the present study indicate that in healthy postmenopausal women:

1) Reducing the diet net acid load from normal to nearly zero with exogenous base (\(\text{KHCO}_3\)) significantly reduces blood acidity and increases the plasma bicarbonate concentration, indicating that the unsupplemented normal diet net acid load was significantly perturbing systemic acid-base equilibrium, causing a low grade metabolic acidosis.

2) Correction of the diet-dependent metabolic acidosis causes a significant reduction in urinary N excretion, comprising nearly equal reductions in urinary ammonia and urea excretion

3) N-sparing effect is reversed by withholding the exogenous base.
Because blood acidity decreased significantly and plasma bicarbonate increased significantly when the diet-dependent net acid load was eliminated, the preexisting net acid load must have been significantly perturbing systemic acid-base equilibrium, in effect causing a low grade metabolic acidosis. Because meat based diets typically yield positive nonzero rates of net endogenous acid production, and because the functional integrity of the kidneys progressively declines during adulthood, chronic low grade age-related metabolic acidosis is the norm in adult humans.

When the net acid load increases from zero to values typical of net acid-producing diets, the kidney increases net acid excretion to a new steady state approaching the new net acid load, thus stabilizing blood acid-base equilibrium, but not before a new steady state has developed with significantly greater blood acidity and lower plasma bicarbonate concentrations, the levels of which are determined in part by the magnitude of the acid load and the prevailing functional integrity of the kidney.

Failure to recognize the respective roles of the diet net acid load and the age-related impaired renal acid-base regulatory integrity has prevented recognition of the low grade acidotic state that exists in otherwise healthy adults, whose acidotic plasma acid-base composition traditionally has been viewed as normal. Rather, the truly non-acidotic state is defined as the plasma acid-base composition when the diet net acid load is zero and renal function is unimpaired, as in young adulthood.

It is understandably difficult to think “metabolic acidosis” when the values for plasma acid-base composition are in the range traditionally considered normal. As the term metabolic acidosis implies pathophysiological sequelae, if such sequelae were not present with normal diet net acid loads one might remain skeptical despite the arguments presented above, but, in fact, such acidosis-induced pathophysiological conditions as negative calcium and phosphorus balance and accelerated bone resorption appear to be a consequence
of the normal diet acid load and are significantly improved by normalizing blood acid-base composition by neutralizing the diet net acid load with small amounts of exogenous base.

As noted, the degree of metabolic acidosis manifested by the plasma acid-base composition underestimates the severity of the pathophysiological injury caused by the acid-base disturbance. With diet-dependent chronic metabolic acidosis, renal and extra-renal homeostatic adaptations occur that serve to minimize disturbances in $[H^+]_b$ and $[\text{HCO}_3^-]_p$, but these adaptations themselves are detrimental. Those include decreased renal citrate production and excretion, hypercalciuria, dissolution of bone, protein catabolism and muscle wasting, and progression of renal disease.

Thus, homeostatic mitigation of the disturbance of extracellular acid-base equilibrium requires the body to accept certain deleterious trade-offs. Although the degree of diet-dependent metabolic acidosis is mild as judged by the degree of perturbation of blood acid-base equilibrium, it cannot be considered mild as judged by its negative biological effect.

Chronic metabolic acidosis is a recognized cause of renal N wasting. N loss occurs both in conditions in which net endogenous acid production is abnormally high, such as chronic ketoacidosis induced by dietary carbohydrate deficiency, and in conditions in which the endogenous acid load is not increased but the acid excretory and/or bicarbonate re-absorptive capacity of the kidney is impaired, such as the acidosis caused by advanced renal insufficiency. In both conditions, the N wasting and attendant negative N balance are reversed on correction of acidosis by the administration of exogenous alkali. Consistent with that effect of alkali, in children with chronic renal acidosis, correction of acidosis with alkali therapy reverses growth retardation and permits the attainment and maintenance of normal stature.
Metabolic acidosis induces N wasting in part by directly increasing the rate of protein degradation in skeletal muscle without commensurately increasing the rate of protein synthesis. That proteolytic effect has been attributed to two acidosis-induced disturbances in skeletal muscle cells: stimulation of an ATP- and ubiquitin-dependent proteolytic pathway and enhancement of the oxidation of proteolytically released branched chain amino acids (valine, leucine, and isoleucine), preventing their reuptake for protein synthesis. Non-branched chain amino acids, especially glutamine, released into the circulation in increased supply, are made available to the kidney for the generation and excretion of ammonium, thereby eliminating muscle N and precluding its reuse for protein synthesis.

Additional mechanisms operate during chronic metabolic acidosis to facilitate renal excretion of ammonium and promote N wasting. Chronic metabolic acidosis causes an adaptive increase in renal glutamine extraction and ammonia production. Glutamine becomes the major source of the increased ammonium excreted in the urine. Acidosis also stimulates hepatic production of glutamine, which serves to sustain the acidosis-augmented rates of renal glutamine extraction and utilization.

Consistent with the above considerations, in our subjects, correction of diet-dependent acidosis was accompanied by a reduction in urinary ammonium excretion, which returned to control when the acidosis was allowed to recur by discontinuing the KHCO₃ supplement. However, in addition to the reduction in NH₄⁺ N excretion during KHCO₃ administration, a sustained reduction in UUN excretion also occurred, suggesting that the higher pretreatment excretion rates of urea were contributing to the acidosis-induced N wasting. The reductions in urea and ammonia excretion contributed about equally to the N-sparing effect.

Because no detectable reduction occurred in creatinine clearance with KHCO₃ administration, the observed reduction in urea excretion was not attributable to a reduced filtered load of urea caused by a reduced
glomerular filtration rate. Similarly, because urine flow was not reduced, reduced urea excretion was not attributable to increased passive urea absorption secondary to increased renal water reabsorption. Otherwise, assuming a urea distribution space equal to total body water, the resultant near doubling of the serum urea N concentration would have been easily detected. Alternatively, if the reduction in urea excretion was due to reduced endogenous net urea production, the requisite reduction in serum urea N (<0.4 mg / dL) would have been too small to observe. Accordingly, the reduction in urea excretion during KHCO$_3$ administration is consistent with a reduced net rate of urea production, but inconsistent with either reduced a glomerular filtration rate or increased renal urea reabsorption.

We believe that the most straightforward interpretation of the findings in this study is this. KHCO$_3$ administration reduced the net endogenous acid production and corrected the preexisting low grade metabolic acidosis, raising urine pH and reducing the total rate of renal ammonia production. As a consequence, both the excretion of ammonia in the urine and the delivery of ammonia to the systemic circulation via the renal vein decreased. The reduction in urinary ammonia contributed directly to the improvement in N balance. The reduction in ammonia delivery to the systemic circulation via the renal vein in addition contributed indirectly to improvement in N balance by limiting substrate (viz, ammonia) availability for hepatic urea production, thereby reducing external loss of N as urinary urea. In addition, by correcting the preexisting low grade metabolic acidosis, KHCO$_3$ decreased the pretreatment rate of muscle proteolysis, thereby limiting the availability of amino acids for both urea and ammonia production, further contributing to the improvement in N balance.

Reduction of urea excretion during alkali administration has been observed in other acidotic states. Papadoyannakis et al. reported significant reductions in urinary urea and total urinary N excretion in response to sodium bicarbonate administration in patients with renal
acidosis. In fasting subjects with ketoacidosis, administration of bicarbonate salts reduced urea N excretion significantly in some studies, but not in others. Hannaford et al. reported a significant reduction in urinary urea excretion in response to the administration of combined sodium bicarbonate and potassium chloride in fasting obese subjects with ketoacidosis. Gougeon-Reyburn et al. using a very low calorie diet (<500 Cal) made up almost exclusively of protein, found no significant change in urea excretion in response to either sodium or KHCO$_3$. The reason for the difference in response of urea excretion between the studies of Hannaford and Gougeon-Reyburn is not clear.

Whether the renal N-sparing effect of KHCO$_3$ administration translates to improved whole body N balance is not specifically answered in this study because we did not also measure fecal N excretion. Fecal N excretion is a small fraction (<12%) of the total N excretion, however, and does not change with alkali administration. Papadoyannakis et al. found no change in daily measured stool N losses during sodium bicarbonate treatment of patients with renal acidosis, although urinary N excretion decreased significantly. Further studies are necessary to determine the effects of KHCO$_3$ administration on N balance and Lean Bone Mass.

Potassium bicarbonate, but not sodium bicarbonate, reduces urinary calcium excretion and improves calcium balance in healthy men. Previous studies demonstrated that the administration of NaHCO$_3$ or sodium citrate had either only a small effect to reduce urinary Ca excretion or no effect, but that potassium citrate significantly reduced urinary Ca excretion.

In order to further evaluate and compare the effects of NaHCO$_3$ and of KHCO$_3$, we performed ten metabolic balances in healthy men during 18 control days, 12 days of NaHCO$_3$, 60 mmol/day and 12 days of KHCO$_3$, 60 mmol/day. Six subjects were fed a low Ca diet (5.2 ±0.7 SD mmol/day) and three of these were also given calcitriol (0.5 µg 6-hourly). Four subjects ate a normal Ca diet (19.5 ±1.3...
mmol/day). For all 10 subjects, KHCO₃ administration reduced urinary Ca excretion from control by -0.9 ± 0.7 mmol/day, P < 0.001. Net intestinal Ca absorption did not change detectably so that Ca balances became less negative by a +0.9 ± 0.9 mmol/day; P = 0.01. KHCO₃ administration was also accompanied by more positive PO₄ and Mg balances. NaHCO₃ administration had no significant effect on urinary Ca excretion or Ca balance. NaHCO₃ and KHCO₃ administration were accompanied by equivalently more positive Na or K balances, respectively and equivalently more negative acid balances (HCO₃ retention). Neither NaHCO₃ or KHCO₃ altered fasting serum HCO₃ concentrations, blood pH, serum 1,25-(OH)₂-D or PTH concentrations.

We conclude that KHCO₃ promotes more positive Ca balances by either enhancing renal Ca retention or skeletal Ca retention or both.