Bioavailability of potassium from potatoes and potassium gluconate: A randomized dose response trial

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Running head: Potassium bioavailability

Abbreviations: Aix, augmentation index; BMI, body mass index; DBP, diastolic blood pressure; SBP, systolic blood pressure; K, potassium

Abstract

Background: Bioavailability of potassium should be considered in setting requirements, but bioavailability from individual foods has not been determined. Potatoes provide 19-20% of potassium in the American diet.

Objective: The aim of this study was to compare bioavailability and dose response of potassium from non-fried white potatoes with skin (targeted at 20, 40, and 60 mEq K) and French fries (40 mEq) with potassium gluconate at the same doses when added to a basal diet containing ~ 60 mEq potassium .

Design: Thirty five healthy, normotensive men and women with a mean age of 29.7+11.2 years and BMI of 24.3+4.4 kg/m2 (mean + SD) were enrolled in this single-blind, cross-over, randomized controlled trial. Participants were partially randomized to order of testing for 9, 5-day interventions of additional potassium: 0 mEq (control repeated at phase 1 and phase 5), 20 mEq, 40 mEq, 60 mEq potassium per day consumed as a potassium gluconate supplement or as unfried potato or 40 mEq from French fries completed at phase 9. Bioavailability of potassium was determined from AUC of serial blood draws and cumulative urinary excretion during a 24 hour period and kinetic analysis. The effect of potassium source and dose on change in blood pressure and augmentation index (AIx) was determined.

Results: Serum potassium AUC increased with dose (p<0.0001) and did not differ due to source (p=0.53). Cumulative 24 hour urinary potassium also increased with dose (p<0.0001) and was greater with potato than supplement (p<0.0001). Kinetic analysis showed absorption efficiency was high across all interventions (>94+12%). There were no significant differences in change in blood pressure or AIx with treatment source or dose.

Conclusions: Bioavailability of potassium is as high from potatoes as from supplements. Future studies that include fecal potassium measurements will be necessary to determine whether retention varies due to source and in hypertensive individuals for effect of dietary potassium on blood pressure.

Key Words: potassium, bioavailability, blood pressure, normotensive, adults, controlled diet

Introduction

Potassium is a shortfall nutrient according to the 2015 Dietary Guidelines for Americans (1). Only 3% of Americans meet the recommended Adequate Intake of 4700 mg/d for potassium (2). The average potassium (K) intake of Americans is just about half of the recommended intake and among consumers, potatoes provided about 19-20% of potassium in the diet (3). In setting requirements for most minerals, bioavailability is usually considered. However, little is known about the bioavailability of potassium and what is known is from potassium salt supplementation (5-7) rather than food.

A few studies have examined potassium kinetics and developed models to describe potassium metabolism. Ginsburg and Wilde (1) measured tissue distribution of a 42K following IV injection in rats for 7 hr. Organs differed with respect to how rapidly they took up tracer; they were divided into fast (kidney), intermediate (liver), slow (muscle), very slow (brain, RBC), and other (bone). However, the predicted mass of potassium in each compartment did not match the measured amount of potassium. The authors concluded that each organ contained > 2 exchange pools, and that the six pools existed across organs rather than one pool per organ. Leggett and Williams (2) proposed an anatomically-based model for humans that can be used for predicting flows and tissue distribution. The control of potassium movement between extracellular and intracellular fluid, and regulation of potassium excretion has been modeled by scaling up a model based on detailed studies in canines to humans (10). Physiological models contain a large number of parameters and are useful for predictions.

Recommended dietary potassium intakes were determined primarily to optimize protection against hypertension and secondarily to protect against stroke and coronary heart disease (3).

Hypertension affects approximately 27% of the global population and is a major risk factor for stroke, congestive heart failure, myocardial infarction, and peripheral vascular disease (11). Nutritional interventions that lower blood pressure are important strategies to prevent these chronic diseases given that poor diet was a major factor associated with death in the US in 2000 (12). Diets high in potassium relative to sodium have been associated with reduced blood pressure (13-15). Therefore, the aims of this study were to compare bioavailability, kinetics, and dose response of potassium from white potatoes and potassium gluconate and to study the effect of each source and dose on blood pressure. For kinetic analysis, we used the simplest model to fit data as we were interested in estimating two parameters, absorption and excretion.

Methods

*Participants*

Healthy, normotensive men and women aged 20-60 y and with a BMI between 15-35 m/kg2 were enrolled in this study and followed between 2013 and 2014. Exclusionary criteria included hypertension or hypotension or diseases such as kidney malabsorption disorders which are known to affect potassium absorption, taking medication known to affect electrolyte metabolism or contain high levels of potassium or sodium, smoking, taking illegal drugs, pregnancy and nut allergy.

Participants were recruited from the West Lafayette and Lafayette area by online and poster advertisements. At a screening visit, participants signed a consent form and were screened for eligibility including a brief medical history, blood pressure, height and weight measurements and blood draw to measure a routine blood chemistry panel, lipid panel and complete blood count. Participants completed a 4-day food record at baseline and between phases 8 and 9 to assess habitual dietary intake and a baseline 24 hour urine sample was provided.

This study was conducted according to the guidelines laid down in the Declaration of Helsinki and the Institutional Review Board of Purdue University approved all procedures involving human subjects. Written informed consent was obtained from all subjects. The present study was registered at Clinicaltrials.gov ID: NCT01881295.

*Study Design*

The study consisted of nine 5-day intervention periods separated by a minimum of a 7 day washout period. In a 9 phase cross-over design participants received a control diet containing 60 mEq K from normal foods excluding potatoes plus additional K (0-60 mEq) from potatoes or potassium gluconate supplements in a partially randomized order. Control phases (+0 mEq K) were assigned as phases 1 and 5. The diet containing French fries (+40 mEq K) was assigned as phase 9 and was optional. The remaining dietary interventions (+20 mEq, +40 mEq, +60 mEq potassium as potassium gluconate pills or unfried potatoes) were assigned to phases 2,3,4,6,7, and 8 in randomized sequence according to a computer generated randomized allocation assigned by the statistician. In order to blind the doses of supplements potassium gluconate and placebo pills were combined to provide the same number of pills for each assigned dose. Potato supplementation could not be blinded. For three days subjects arrived daily at the Purdue Clinical and Translational Sciences Institute clinical Research Center to receive their assigned meals which were consumed in a free living setting. On day 4 subjects consumed their meals in the clinic as part of a 24 hour clinical bioavailability study. On the fifth day subjects continued the controlled diet in a free living setting after fasting blood and blood pressure measurements were assessed. On the morning of day 6 the subjects returned for blood pressure and Pulse Wave Analysis .

*Controlled Diets*

Potato or potassium supplements were added in quantities described above to a controlled diet containing approximately 60 mEq/d potassium from foods excluding potatoes. All foods and drinks were controlled during each intervention period and mineral-free water was provided ad libitum. Participants were assigned to one of four energy levels (6700, 8400, 10000, 11700 KJ) based on energy requirements estimated by Harris-Benedict equations (16) to maintain body weight. Three meals and 2 snacks were provided on days 1, 2, 3 and 5 as pack-out meals. Subjects were required to return any uneaten food when they returned to the clinic the following day. Potassium gluconate and placebo pills for each day were split by dose to be consumed at breakfast, lunch and dinner. On day 4, 2 identical test meals, each containing half of the total assigned potassium were provided at 0 hours (~ 7 am) and 5 hours (~ 12 N). A third meal was provided at 11.5 hours (~ 6:30 pm) and 1 snack was consumed after 12 hours (7 pm). Potassium gluconate or placebo pills were given mid-meal at 0 and 5 hours. During the 24 hour clinical bioavailability study, sodium was kept constant between 1925-2400 mg/d for all interventions.

*Potassium Gluconate and Potatoes*

Potassium (2.3 mEq/pill) as potassium gluconate and placebo pills were provided by Delavau, Philadelphia, USA. Potatoes, french fries and prepared potato products were provided by McCain Foods Limited. Three different fresh potato batches were used in the study: 1 batch from Washington and 2 batches from Idaho containing 0.1, 0.07, and 0.06 mEq, respectively. Potato servings were adjusted accordingly for the correct potassium dose.

*Compliance*

All food and drinks which were not consumed were returned, weighed and recorded for compliance. All potassium gluconate supplements that were not consumed were returned and counted.

*Anthropometric Measurements*

Height and weight were measured at baseline and weight was measured on the 4th day of each intervention phase.

*Potassium Bioavailability and Kinetics (Primary Outcome Measure)*

On day 4, participants collected urine for 24 hours starting from the second collection on day 4 until the first collection on day 5. Samples from the 24 hour period were pooled at baseline, 2, 4, 6, 8, 10, 12 and 24 hours and frozen at -20 °C for later analysis.

On day 4, blood was drawn at baseline and following breakfast containing half of one of the intervention doses of potassium either as potassium gluconate or potato, blood was drawn at 0.5, 1, 2, 3, 3.5, 4, 4.5, 5, 8, 9, 12 and 24 hours post breakfast meal and frozen at -80 °C for later analysis. Serum potassium was measured by atomic absorption spectrophotometry (AAS, 5100 PC, Perkin Elmer, Waltham MA). Urinary potassium was measured by Inductively Coupled Plasma Optical Emission Spectroscopy (ICP-OES, Optima 4300, Perkin Elmer, Waltham MA)

*Model Development*

Control period:

Data consisted of plasma potassium concentration and urine potassium excretion over a 24 h period. The data from subjects with at least 8 treatment periods (n=19) were analyzed by compartmental modeling using WinSAAM (17). A 2-compartment model was used initially based on a model prosed by ~~in~~ Jasani and Edmonds (18). Total body potassium, determined by whole body counting of the long-lived radioisotope, 40K, has been reported to range from 66 to 173 g (18). We assumed that whole body potassium content of our subjects was 100 g. To satisfy this assumption, it was necessary to add a third compartment to the model.

Two models were set up with identical parameter values. The first ‘tracer’ model was used to calculate steady state masses. The masses were used as the initial condition of the second tracee model. The tracee model also had a ‘dosing’ compartment which contained the potassium in each meal. Parameter values (represented by the arrows between compartments) were made adjustable and fitted by a least squares fitting routine in WinSAAM to minimize residuals, between observed data and model calculated values, to optimize the fit of the model to the whole body potassium, plasma and urine potassium during the control period. It was necessary to allow the parameter for urinary excretion to change during the 12-24 hr period, as urinary excretion of potassium decreased overnight. A fit was considered acceptable when there were no consistent deviations between the urine data, and the calculated values, the pattern of the plasma data were fitted by the model, and parameter fractional standard deviations were less than 0.75.

Absorption, as a fraction of ingested potassium absorbed, was calculated as the ratio of the pathway from compartment 8 into compartment 1, over the sum of the pathways out of compartment 8 (i.e., pathways labeled 1/(1+2)). Urinary excretion, represented by pathway 3, was expressed as fraction of compartment 1 going to urine (i.e., pathway 3/(3+4)) and return of potassium from compartment 2 was expressed as a fraction of the turnover of compartment 2 (i.e., pathway 5/(5+6)).

Intervention:

Another tracee model, with the same initial conditions as during the control period, was set up to represent the intervention period. The treatment model had an additional dosing compartment for the treatments. The model was fitted to data for each subject. Parameter values were compared to those of the control period preceding the treatment. It was found that data during the treatment periods could be fitted by allowing 3 parameters to vary from the control period; release from the second compartment back to the first compartment, and urinary excretion during the day and overnight periods. In some subjects, the intervention data could be fitted by allowing absorption to vary, rather than movement from compartment 2 to compartment 1, but all subjects could be fitted with this pathway varying, and these results are presented.

*Blood Pressure and Arterial Stiffness*

Fasting arterial blood pressure (secondary outcome measure) was measured on days 1, 2, 3, 5 and 6 using an upper arm blood pressure monitor (Omron BP791IT). On day 4, blood pressure was measured at 0, 6 and 11 hours.

Participants were seated for 10 minutes before blood pressure was measured in a seated position, 3 times, with 1 minute between measurements. On the morning of days 1 and 6, central augmentation index (AIx) was calculated by pulse wave analysis (PWA). Peripheral pressure waveforms were measured from the radial artery at the wrist by tonometry using a SphygmoCor device (Atcor Medical, Sydney, Australia). The radial waveform was converted to calculated central aortic pressure using Atcor software, version 9. AIx was expressed as aortic Pressure divided by pulse pressure, expressed as a percentage. Larger AIx values suggest greater arterial stiffness.

*Side Effects*

Participants were asked daily to report any side effects or discomfort and completed an adverse effects questionnaire at the end of day 4 recording abdominal pain, bloating, flatulence, diarrhea and stomach noises on a scale of 0-5, where 0 was none and 5 was a lot.

*Statistical Analysis*

Area under the curve (AUC) was calculated using the trapezoidal rule. In a plot of serum potassium data versus time, lines were drawn from each observation to the x axis and the observations were connected by line segments. The areas of the resulting trapezoids were summed to obtain the AUC. A mixed linear model that included terms for subject, intervention period, and sex was used to analyze serum potassium 24-hour AUC and 24-hour urinary potassium. There were nine intervention periods: two controls (0 mEq), potassium source (supplement or potato) crossed with dose (~20, 40, 60 mEq), and French fries (~40 mEq). Contrasts were constructed to estimate the linear effects of dose (~20, 40, 60 mEq), the main effect of source of potassium, the interaction of dose and source, and the difference between French fries and the other ~40 mEq interventions. Covariates included age, BMI, height, and weight. A similar model was used to analyze the change in blood pressure from day 1 to day 6, averaged over the last two of the three replicates, with the control period change as a covariate.

For kinetic analysis, parameters between control periods, each intervention compared to control periods, and between potato and K salt interventions for each dose were compared using Paired t-tests. Differences were significant for P<0.05.

Since little is known about the bioavailability of potassium, variance from previous calcium studies were used for power calculations which indicates a sample size of 26 was required to reach 80% power to see significant differences between interventions.

All statistical analyses were performed using SAS Version 9.3.

**Results**

*Recruitment*

Fifty nine participants were screened to take part in the study, 54 participants met the inclusionary criteria and were recruited to the study. Forty five participants began the study, 42 participants completed the first intervention phase and 35 participants took part in at least 2 intervention phases and were included in the final analysis. (See **Figure 1**). Baseline characteristics of men and women and the entire group are given in **Table 1**. Distribution by sex was nearly equal and subjects met inclusion criteria for healthy normotensive.

*Analysis of Intervention*

By analysis, potassium intervention for potatoes was 18.5, 37, and 55.5 mEq/d. The potassium gluconate provided supplement 0, 20, 40, or 60 mEq potassium/d.

*Habitual Dietary Potassium*

Two 4-day food diaries were analyzed for habitual dietary potassium intake. Average potassium intake was 2344+753 mg/d (mean+SD). No difference was found between dietary potassium intake for men compared with women ( 2550+857 and 2175+635 mg/d, p=0.16).

*Compliance (%)*

Returned potassium gluconate supplement and placebo pills were counted. Food not consumed was returned and weighed. Overall compliance for test days was 99-100% for all interventions. Urinary potassium increased linearly with dose as an objective indicator of compliance.

***Potassium Bioavailability***

For 24-hour serum potassium AUC, there were no effects of sex (p=0.053) or interaction of dose by potassium source (p=0.25). No difference between supplement and potato was found (14.8 mEq potassium/d, 95% CI -31 to 61, p=0.53). The difference between French fries and the average of 40 mEq supplement and potato was not statistically significant (29.9 mEq potassium/d, 95% CI -52 to 111, p=0.47). Results were summarized using the linear effect of dose (p<0.0001, slope=2.15 (se=0.44)), see **Figure 2**. For 24-hour urinary potassium, no effects of sex (p=0.54) or interaction of dose by potassium source (p=0.35) were found. Potassium source was statistically significant with potato having higher values than supplement (p<0.0001, estimate of difference=522 (se=0.60)). The difference between French fries and 40 mEq supplement was not statistically significant (p=0.42), but the difference between French fries and 40 mEq potato was statistically significant (p=0.003). Results were summarized using the parallel linear effect of dose for each source (p<0.0001, slope=16.7(se=1.3)), see **Figure 3**. No statistically significant effects for blood pressure or AIx (pulse wave) were found. The covariates had essentially no affect on the results.

*Kinetic Analysis*

The kinetic model developed is shown in **Figure 4**. Kinetic analysis showed that potassium absorption was high (>94±12%) and did not differ between control and any of the intervention periods (**Table 2**). Thus, total absorbed potassium increased with dose. Fractional urinary excretion during the day (i.e., 0 to 12 hr) was higher for all treatments compared to controls (Table 2). The increases were higher for potato than for K salt at 40 and 60 mEq doses. Excretion overnight (i.e., 12-24 hr) was less than half the daytime value (Table 2 and **Figure 5**); only 60 mEq supplement from potato was higher than control.

For the control period, 2% of potassium in compartment 1 went to urine, and this increased to 5% for the 60 mEq supplement period (Table 2). The value was significantly higher in the 60 mEq potato period (5.8%). The return of potassium from compartment 2 to compartment 1 increased from 41% in the control to 45% in the 60 mEq potato period, but did not differ between interventions (Table 2).

The 40 mEq French fry intervention did not differ from the 40 mEq supplement intervention, but excretion from 40 mEq French fry was less than 40 mEq from potato (0.22±0.05/h and 0.24±0.05/h, respectively). This translated into a smaller fraction of compartment 1 being excreted with the 40 mEq French fry intervention (4.3±0.9%) than with the 40 mEq potato intervention (4.7±0.9%), (data not shown).

The calculated mass of compartments 1, 2, and 3 were 0.97±0.1, 2.9±1.1, and 92±8 g respectively. The volume of distribution of compartment 1 was estimated by making it adjustable for the control period for the first subject. When it was adjustable it increased parameter uncertainty and did not improve the fit of the other subjects and so it was fixed at 7.5 L for all subjects. Other fixed parameters were transfer into compartment 2 from compartment 1 at 4.9/hr, into compartment 3 from compartment 2 at 2.61/h and from compartment 3 into compartment 2 at 0.073/h.

*Blood Pressure and Arterial Stiffness*

There were no significant differences in blood pressure change between day 1 and day 6 with potassium dose (SBP p=0.34, DBP p=0.69), potassium source (SBP p=0.39, DBP p=0.49) or sex (SBP p=0.86, DBP p=0.51). There were no significant differences in blood pressure change between day 1 and day 6 with French fry intervention compared to the equivalent average potassium gluconate and potato dose (SBP p=0.46, DBP p=0.49).

Similarly, change in AIx between day 1 and day 6 did not differ significantly between potassium dose (p=0.93), potassium source (p=0.82) or sex (p=0.99).

*Side Effects/Symptoms*

Subjects were asked to evaluate gastrointestinal symptoms including abdominal pain, bloating, flatulence, diarrhea and stomach noises after consuming the various interventions for 4 days. Symptoms were rated on a scale of 0 (none) to 5 (extreme symptom). The average of all subjects and interventions was < 1 for all symptoms (range 0.2-0.8) indicating very mild, if any gastrointestinal discomfort with either the pill or potato inventions.

**Discussion**

Although apparent potassium absorption has been estimated from total diets (19,20), little is known about the bioavailability of potassium from individual sources. Previously only urinary potassium was used to assess potassium bioavailability from potassium salt supplementation (5-7). In this study, we have shown that urinary potassium excretion increases with potassium dose and was higher with potato and French fries than with potassium gluconate. For the first time serum potassium is reported in response to intake. Serum potassium increased with dose and did not differ due to source.

Kinetic analysis showed that potassium absorption efficiency was high (>94+12%) and similar to previously reported balance studies in 4 subjects (>90%) and similar to apparent potassium absorption from a total diet of 84% (19). The kinetic analyses show that absorption efficiency does not decrease with dose so that the total amount absorbed is approximately equivalent to the ingested dose. Higher excretion of potassium occurs during the day, rather than overnight. During a 24 h period, urinary potassium excretion varies with activity and fluctuations in potassium intake with meals (21). In mice, activity alters gene expression of potassium channels in the collecting duct in the kidney (22). With respect to meals, enteric solute sensors are considered to respond to dietary potassium (and other ions) by signaling the kidney to rapidly alter ion excretion or resorption. The circadian pattern of potassium excretion, where excretion is higher during the day and lower at night, is due to higher concentration of potassium in the collecting ducts rather than changes in flow (23). It has been hypothesized that dysregulation of these circadian rhythms may contribute to changes in blood pressure and development of hypertension (22).

The estimated average habitual dietary potassium intake of participants in our study of 2340 mg/d was comparable to the estimated average potassium intake of Americans from the 2003-2006 representative sample of 2591 mg/d (2).

We found no differences in blood pressure due to potassium dose or source. This is at odds with a cross over study by Vinson et al. where purple potato consumption decreased blood pressure in overweight, hypertensive individuals over 4 weeks (24). The differences between these results and ours may be explained by the duration of the studies, the type of potatoes and the higher blood pressure of the overweight individuals in the Vinson et al. study compared with the healthy participants in our study. Ours was a short study in a healthy population and it is possible than in a longer study in a larger population of hypertensive participants would have given the power to see decreases in blood pressure from both potassium salt and potatoes. Effect of sodium reduction interventions on reducing blood pressure is established by one week according to a recent meta-analysis (25). Assuming blood pressure response to increasing dietary potassium is equally rapid, baseline blood pressure may be the larger predictor of response.

Strengths of this study are its novel aim to assess bioavailability of potassium from a food, especially one that is a dominant vegetable source of dietary potassium. The controlled diet, prolonged clinical visits, and cross-over design are other strengths. Limitations include the small sample size using a convenience sample which limits generalizability. The small sample size in a normotensive population and short duration of the intervention likely precluded our ability to determine the relationship of potassium intake to blood pressure. We were unable to determine potassium retention in the absence of a balance study or sweat collection; losses can be high under conditions of high temperature (28), though not in moderate climates (29).

**Conclusions**

This is a unique study, which compares the bioavailability of potassium from food with that from a salt. The results suggest that bioavailability of potassium is higher from potatoes than from supplements which is a positive message for potassium nutrition from food. A longer balance study in a hypertensive population is needed to determine net potassium balance and if the greater potassium bioavailability from potatoes compared with that from potassium salt leads to improved cardiovascular risk profiles.

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**Author Responsibilities were:**

CMW, BRM, GPM: study concept and design; CJM-C, BRM, PJL: acquisition of data; CJM-C, BRM, LDM, GPM, CMW: analysis and interpretation of data; MW: kinetic analysis and interpretation; LDM and GPM: statistical analysis; CJM-C, BRM, LDM, GPM, MW, and CMW: drafting of manuscript; CMW: obtainment of funding.

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**References**

1. Scientific Report of the 2015 Dietary Guidelines Advisory Committee http://www.health.gov/dietaryguidelines/2015-scientific-report/ Accessed July 23, 2015.

2. Fulgoni VL,3rd, Keast DR, Bailey RL, Dwyer J. Foods, fortificants, and supplements: Where do Americans get their nutrients? J Nutr 2011;141(10):1847-1854.

3. Food and Nutrition Board, Institute of Medicine, Dietary Reference Intakes for Water, Potassium, Sodium, Chloride, and Sulfate. 2005. National Academies Press, Washington DC,

4. Storey ML, Anderson PA. Contributions of white vegetables to nutrient intake: NHANES 2009-2010. Adv Nutr 2013;4(3):335S-44S.

5. Bechgaard H, Shephard NW. Bioavailability of potassium from controlled-release tablets with and without water loading. Eur J Clin Pharmacol 1981;21(2):143-147.

6. Betlach CJ, Arnold JD, Frost RW, Leese PT, Gonzalez MA. Bioavailability and pharmacokinetics of a new sustained-release potassium chloride tablet. Pharm Res 1987;4(5):409-411.

7. Melikian AP, Cheng LK, Wright GJ, Cohen A, Bruce RE. Bioavailability of potassium from three dosage forms: suspension, capsule, and solution. J Clin Pharmacol 1988;28(11):1046-1050.

8. Ginsburg JM, Wilde WS. Distribution kinetics of intravenous radiopotassium. The American journal of physiology 1954;179(1):63-75.

9. Leggett RW, Williams LR. A model for the kinetics of potassium in healthy humans. Phys Med Biol 1986;31(1):23-42.

10. Young DB. Control of Potassium. U.S.A.: Morgan & Claypool Life Sciences, 2013.

11. WHO. Global atlas on cardiovascular disease prevention and control. Geneva: World Health Organization (WHO); 2011.

12. Mokdad AH, Marks JS, Stroup PF, Gerberding JL. Actual causes of death in the United States, 2000. JAMA 2004;291:1238-1246.

13. Zhang Z, Cogswell MD, Gillespie C, Fan J, Loustalot F, Dai S, Carriquiry AL, Kuklina EV, Hong Y, Merritt R, Yang Q. Association between usual sodium and potassium intake and blood pressure and hypertension among U.S. adults: NHANES 2005-2010. PLoS One, 2013. 8(10): p. e75289.

14. Ang Q, Liu T, Kuklina EV, Flanders WD, Hong Y, Gillespie C, Chang MH, Gwinn M, Dowling N, Khoury MJ, Hu FB. Sodium and potassium intake and mortality among US adults: prospective data from the Third National Health and Nutrition Examination Survey. Arch Intern Med, 2011. 171(13): p. 1183-91.

15. Binea A, Jaeger J, Hu Y, Singh A, Simmerman D. Daily potassium intake and sodium-to-potassium ratio in the reduction of blood pressure: a meta-analysis of randomized controlled trials. J Hypertens 205;33:1509-1520.

16. Harris JA, Benedict FG. A Biometric Study of Human Basal Metabolism. Proc Natl Acad Sci U S A 1918;4(12):370-373.

17. Greif P, Wastney M, Linares O, Boston R. Balancing needs, efficiency, and functionality in the provision of modeling software: a perspective of the NIH WinSAAM project. Adv Exp Med Biol 1998;445:3-20.

18. Jasani BM, Edmonds CJ. Kinetics of potassium distribution in man using isotope dilution and whole-body counting. Metab Clin Exper 1971;20(12):1099-106.

19. Holbrook JT, Patterson KY, Bonder JE, Douglas LW, Veillon C, Kelsay JL, Mertz W, Smith JC Jr. Sodium and potassium intake and balance in adults consuming self-selected diets. Am J Clin Nutr 1984, 40(4):786-793.

20. Kodama N, Morikuni E, Matsuzaki N, Yoshioka YH, Takeyama H, Yamada H, Kitajima H, Nishimuta M. Sodium and potassium balances in Japanese young aduls. J Nutr Sci Vitaminol (Tokyo) 2005; 51(3):161-168.

21. Agarwal R, Afzalpurkar R, Fordtran JS. Pathophysiology of potassium absorption and secretion by the human intestine. Gastroenterology 1994;107(2):548-71.

22. Palmer BF. Regulation of Potassium Homeostasis. Clin J Am Soc Nephrol 2015;10(6):1050-60. doi: 10.2215/CJN.08580813.

23. Steele A, deVeber H, Quaggin SE, Scheich A, Ethier J, Halperin ML. What is responsible for the diurnal variation in potassium excretion? Am J Physiol 1994;267(2 Pt 2):R554-60.

24. Vinson JA, Demkosky CA, Navarre DA, Smyda MA. High-antioxidant potatoes: acute in vivo antioxidant source and hypotensive agent in humans after supplementation to hypertensive subjects. J Agric Food Chem 2012;60(27):6749-6754.

25. Graudal N, Hubeck-Graudal T, Jurgens G, McCarron DA. The significance of duration and amount of sodium reduction intervention in normotensive and hypertensive individuals: A meta-analysis. Adv Nutr 2015;6:169-177.

26. Alburto NJ, Hanson S, Gutierrez H, Hooper L, Elliott P, Cappuccio FP. Effect of increased potassium intake on cardiovascular risk factors and disease: systematic review and meta-analyses. BMJ 2013;346:f1378.

27. Cappuccio FP, MacGregor GA. Does potassium supplementation lower blood pressure? A meta-analysis of published trials. J Hypertens 1991;9:465-473.

28. Sriboonlue P, Prasongwatana V, Suwantrai S, Bovornpadungkitti S, Tungsanga K, Tosukhowong P. Potassium needed for maintaining its balance in healthy male subjects residing in an area of low potassium intake and with a high environmental temperature. J Med Assoc Thai 1999; 82(7):690-700.

29 Palacios C, Wigertz K, Weaver CM. Comparison of 24-hour whole body versus patch tests for estimating body surface electrolyte losses. Intl J Sport Nutr Exerc Metab 2003; 13(4):479-488.

*Table 1. Baseline Characteristics1*

|  |  |  |  |
| --- | --- | --- | --- |
|  | **All\***  **Mean (SD)** | **Men**  **Mean (SD)** | **Women**  **Mean (SD)** |
| **n** | 35 | 16 | 19 |
| **Age (y)** | 29.7 (11.2) | 29.2 (8.6) | 30.2 (13.2) |
| **Height (cm)** | 170.0 (9.7) | 177.4 (7.4) | 163.9 (6.6) |
| **Weight (kg)** | 70.5 (15.0) | 76.4 (13.2) | 65.5 (15.0) |
| **BMI (kg/m2)** | 24.3 (4.4) | 24.4 (4.8) | 24.2 (4.2) |
| **Systolic Blood Pressure (SBP) (mmHg)** | 107.8 (8.5) | 112.0 (7.4) | 104.2 (7.9) |
| **Diastolic Blood Pressure (DBP) (mmHg)** | 70.9 (7.2) | 70.2 (6.1) | 71.5 (8.2) |

1 Includes only those participants that completed at least 2 phases.

*Table 2: Model (Figure 4) parameter values with interventions (Mean, SD, n=19).*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Intervention | | | | | | |
|  |  |  | Supplement | | | Potato | | |
| Parameter | Unit | Control | 20 mEq | 40 mEq | 60 mEq | 20 mEq | 40 mEq | 60 mEq |
| Absorption | (Fraction) | 0.94 | 0.95 | 0.93 | 0.94 | 0.94 | 0.95 | 0.95 |
| (SD) |  | 0.12 | 0.10 | 0.13 | 0.14 | 0.13 | 0.11 | 0.11 |
| Urine excretion-daytime | (Fraction/h) | 0.098 | 0.1711 | 0.2091 | 0.2591 | 0.1951 | 0.2441,2 | 0.3001,3 |
| (SD) |  | 0.014 | 0.057 | 0.045 | 0.038 | 0.051 | 0.051 | 0.046 |
| Urine excretion-overnight | (Fraction/h) | 0.043 | 0.046 | 0.053 | 0.051 | 0.043 | 0.045 | 0.0521 |
| (SD) |  | 0.027 | 0.022 | 0.029 | 0.025 | 0.021 | 0.026 | 0.025 |
| Compartment 1 going to urine | (Fraction) | 0.020 | 0.0341 | 0.0411 | 0.0501 | 0.0381 | 0.0471,2 | 0.0581,3 |
| (SD) |  | 0.003 | 0.011 | 0.008 | 0.007 | 0.010 | 0.009 | 0.008 |
| Pathway from compartment 2 to compartment 1 | (Fraction/h) | 1.808 | 2.0451 | 1.7691 | 1.7881 | 1.8161 | 2.021 | 2.1661 |
| (SD) |  | 0.616 | 0.819 | 0.449 | 0.470 | 0.394 | 0.901 | 0.858 |
| Compartment 2 to compartment 1 | (Fraction) | 0.409 | 0.4371 | 0.4061 | 0.4081 | 0.4141 | 0.4311 | 0.4501 |
| (SD) |  | 0.084 | 0.103 | 0.059 | 0.058 | 0.041 | 0.115 | 0.103 |

1Significantly different, P(< 0.05), Paired t-test from control,

2Potato at 40 mEq was different from supplement at 40 mEq

3potato at 60 mEq was different from supplement at 60 mEq.

Figure Legends

Figure 1. Flow Diagram of Potassium Bioavailability Study. The study design included a partial randomization scheme. All subjects were assigned to Control 1 as the first phase and Control 2 as the fifth phase. The French Fry intervention was an option as the last phase of the study. All other potato and K salt interventions were assigned in a random sequence.

Figure 2. Mean Serum Potassium( ± 95% CI) measured by Area Under the Curve determined by serial blood draws at 0.5, 1, 2, 3, 3.5, 4, 4.5, 5, 8, 9, 12 and 24 hours post breakfast meal containing either 0, 18.5, 37, or 55.5 mEq potassium from potatoes or potassium gluconate or 37 mEq from French fries. There were no differences due to source of potassium (p=0.53) and no interaction of dose by potassium source (p=0.25). A general linear mixed model with contrasts was used to analyze the 241 observations. N per group = 25-35 except for French fries where n = 17

Figure 3. Cumulative urinary potassium as a result of increasing doses from potatoes or potassium gluconate (p <0.0001, slope = 16.7 ±1.31). Excretion from potato interventions is ~ 522 mg greater than from supplements (p<0.0001). Urinary excretion from French fry intervention is 422 mg less than potato (p=0.0028) but not different from the supplement at the same dose (p=0.42). Gender of participant had no effect on any urinary comparisons (p=0.54). A general linear mixed model with contrasts was used to analyze the 241 observations. N per group = 25-35 except for French fries where n = 17

Figure 4. Model of K kinetics. Numbers in circles are compartment numbers; numbers next to the arrow are pathway numbers, for reference. The boxes on compartments 60 (and 61) indicate that the value of the compartment was set to the amount of K in each meal (or treatment).The triangles on compartment 1 and 6 indicate compartments that were sampled, plasma and urine respectively.

Figure 5. Fit of model in Figure 4 to plasma K, and urine K, over time in one representative subject; (lines are model calculated values, symbols are observed data; triangles and solid lines are control and dotted lines and squares are treatment); after 60 mEq of K as gluconate (A, B), and as potato (C,D). The increase in plasma K at 0, 6 and 12 h are due to intake of meals; treatment was also taken at 0 and 6 h. Urine excretion occurred at a faster rate during the day (0-12 h) than overnight (12-24 h).

Excluded (n=14)

* Not meeting inclusion criteria ( n=5)
* Declined to participate ( n=9)

Assessed for Eligibility (n=59)

**Enrollment**

All participants who completed at least 2 phases of the study were included in the analysis (n=35)

**Control 2** n=27)

**Control 1** (n=42)

**Allocation**

(n= completed intervention phase)

Randomized to all interventions (n=45)

**Analysis**

**Lost to follow-up at various phases of the study (n=28)**

Withdrew from study for lack of interest before study started (n=3)

Discontinued intervention for lack of time and scheduling conflicts (n=21)

Discontinued intervention because of dislike of diet (n= 3)

Discontinued intervention because of inability to complete serial blood draws (n=1)

**Follow-Up**

**French Fries 40 mEq** (n=17)

**Salt 20 mEq** (n=27)

**Potato 60 mEq** (n=27)

**Potato 40 mEq** (n=28)

**Salt 60 mEq** (n=25)

**Salt 40 mEq** (n=29)

**Potato 20 mEq** (n=28)



Control Phase 1 and Phase 5 \*

Supplement ○

Potato □

French Fries Δ

Mean AUC serum potassium (mmol/L)

4300

3800

3300

2800

2300

0 20 40 60

Potassium dose (mEq/d)



5000

4000

3000

2000

1000

Cumulative urinary K (mg/d)

0 20 40 60

Potassium dose (mEq/d)

Control Phase 1 and Phase 5 \*

Supplement ○

Potato □

French Fries Δ

Potato Dose – solid line

Supplement Dose – dashed line

1

2

3

6

8

Model of K Kinetics

Urine

Feces

‘Meals’

‘Treatments’

60

61

1

2

3

4

5

6



A

B

C

D