SANTA BARBARA NUTRIENTS®

KetoCitra®

Medical Food
Ready-to-Mix Powder

KetoCitra® produces a specially formulated solution containing an ionic mixture of D,L-beta-hydroxybutyrate, citrate, and inorganic electrolytes (potassium, calcium, magnesium).

Flavor: Lemonade (naturally flavored)
Size: 13.76 oz (390 g) for 60 servings or one month supply*
Serving Size: One rounded scoop (6.5 g). Recommended two servings (two rounded scoops) per day for a total of 13 g/day.

KetoCitra® is a medical food for the daily dietary management of individuals with mild to moderate stages (CKD stages 1-3) of autosomal-dominant polycystic kidney disease (ADPKD) and is intended to be used under medical supervision. Please carefully read the directions for use, warnings and contraindications prior to using this product. KetoCitra® is not intended for individuals with advanced ADPKD (CKD stages 4-5), hyperkalemia (high potassium levels), or those with severely impaired renal function or impaired electrolyte homeostasis. ***Prior to using* KetoCitra® *for the first time your physician should check your blood electrolyte status.***

Made in the USA of imported and domestic ingredients under strict cGMP standards.

Manufactured for Santa Barbara Nutrients, Inc.
Santa Barbara, CA 93106, USA · 805-272-0029
Visit **SantaBarbaraNutrients.com** for more information

Covered under U.S. Pat. No. 11,013,705 & U.S., Mexican Pat. No. 395975, and foreign patents pending

Scan the **QR code** to the left to obtain the latest package insert or to reorder KetoCitra®.

NOTICE: THIS PRODUCT IS INTENDED TO BE USED UNDER THE SUPERVISION OF A PHYSICIAN

Product Features

Per day, two servings (two rounded scoops; total 13g/day) of KetoCitra® provide

- **5.3 g of Beta-Hydroxybutyrate (BHB)**
- **3.5 g Citrate**
- **600 mg Potassium**
- **300 mg Calcium**
- **250 mg Magnesium**
- **51 mEq Alkaline Base Load**

Kidney Friendly
Gluten Free
Natural Flavor
Naturally Derived Sweetener
Sodium Free
Dairy Free
Keto Friendly
Sugar Free
Soy Free
Vegan

Description: KetoCitra® is a specially formulated medical food containing a mixture of *D,L*-beta-hydroxybutyrate (BHB), citrate and mineral salts (potassium, calcium, magnesium), for the dietary management of individuals with mild to moderate ADPKD (CKD stages 1-3). ADPKD is a genetically inherited disease that is characterized by metabolic defects, renal cyst growth, progressive chronic kidney disease and other serious complications. Metabolic abnormalities in renal cells in ADPKD lead to preference of glucose as energy source to sustain disease progression over the ketone body BHB (1–15). Additional metabolic abnormalities in ADPKD lead to metabolic acidosis accompanied by acidification of the urine, and low urinary citrate levels (hypocitraturia). Furthermore, individuals with ADPKD frequently have high levels of uric acid (hyperuricemia) and even clinical gout. Altogether, these conditions may increase the risk for kidney stones (nephrolithiasis) and associated renal injury which may further accelerate disease progression (16–27). KetoCitra® provides specifically modified nutritional support to address the unique nutrient needs of individuals with ADPKD by increasing circulating levels of the ketone body BHB, and normalizing urine pH and urinary citrate.

Due to these disease-specific metabolic abnormalities, conventional, carbohydrate-predominant diets consumed by most individuals in industrialized societies may worsen the progression of ADPKD. High carbohydrate intake leads to high blood glucose and insulin levels, overweight, obesity, metabolic syndrome, and diabetes which have been associated with more rapid progression of ADPKD (7, 15, 28, 29). Such diets lead to persistently high levels of blood glucose and low levels of blood BHB. Dietary intake of oxalate, inorganic phosphate and purines - in combination with low urine pH and hypocitraturia found in ADPKD – increase the risk of kidney stones (nephrolithiasis) due to renal tubular calcium or uric acid crystal precipitation that may cause renal injury and exacerbate ADPKD progression (16, 25).

Individuals with ADPKD may benefit from nutritional management with the goal to address these metabolic abnormalities by raising circulating levels of the natural ketone body BHB to healthy levels, and by supporting a normal, neutral urine pH and normal urine citrate levels. KetoCitra® is intended to facilitate the nutritional management of individuals with ADPKD by providing a preferred cellular energy substrate, the ketone BHB, instead of problematic glucose, and by providing citrate and an alkali base load. KetoCitra® is formulated to be kidney-safe by avoiding sodium and by providing BHB as a blend of mineral salts that avoids excessive intake of any one mineral. These minerals are carefully chosen to provide additional nutritional support. Calcium and magnesium – especially when taken with meals – bind food-derived oxalate and inorganic phosphates and lower their gastrointestinal absorption, thereby further lowering the risk, through dietary intervention, of renal precipitation of calcium oxalate and calcium phosphate microcrystals that may accelerate ADPKD disease progression (30–32).

These distinctive nutritional requirements cannot feasibly be met by altering the normal diet because ADPKD is a chronic, slowly progressive disease that requires management for years or decades. Attempting to modify the diet alone to address the distinctive nutritional requirements of ADPKD is not feasible. Also, circulating BHB levels can be raised by extended fasting or by using a strict ketogenic diet. However, such extensive dietary changes are very difficult to adhere to for most individuals, especially in the long term, and may also increase the risk of malnutrition, kidney stone formation, and other adverse effects (33–38). Increased citrate intake can be achieved by consuming lemon juice or lemonade (39, 40). However, the required large amounts make this unfeasible in the long term, and consumption of large quantities of lemon juice/lemonade may lead to excessive sugar intake and increased risk of tooth erosion (39, 41–43).

KetoCitra® can be taken by itself without any other changes to the normal diet. However, it is recommended to use KetoCitra® as part of an overall nutritional management program in conjunction with sensible dietary changes under medical supervision.

KetoCitra® has been developed, labeled, and should be used in accordance with the legal definition of "Medical Food", as defined in section 5(b) of the Orphan Drug Act (21 U.S.C. 360ee (b) (3)) and incorporated into Food and Drug Administration (FDA) regulations: "a food which is formulated to be consumed or administered enterally under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation." The FDA does not evaluate the safety or health benefits of medical foods prior to marketing, and there is no FDA premarket review or clearance of medical foods.

Medical foods, like KetoCitra®, are specially formulated foods intended for the dietary management of individuals with certain medical conditions with distinctive nutritional requirements, which cannot be managed by altering a normal diet. Medical foods must be used under the supervision of a physician.

Ingredients: All ingredients in KetoCitra® are Generally Recognized as Safe (GRAS) under their conditions of use. Please refer to the Nutrition Information Table below for additional information and the full list of ingredients.

Macronutrient Profile: KetoCitra® does not contain fat or protein. An insignificant amount of carbohydrate is contributed by the natural flow agent (soluble corn fiber) and by the natural flavoring (lemon extract and lemon juice concentrate combined with gum acacia). 15 kcal (Calories) of energy per recommended serving (6.5 g) are provided in the form of citrate from citric acid and beta-hydroxybutyrate (BHB), a naturally occurring ketone body used as an energy substrate by nearly all tissues in the body including muscle, brain and heart.

D,L-Beta-Hydroxybutyrate (BHB): KetoCitra® contains mineral salt forms of the ketone body BHB as a racemic mixture. KetoCitra® provides a blend of mineral salts (potassium, calcium, and magnesium) in order to deliver the maximum amount of BHB while minimizing the total content of any one mineral.

Citrate: KetoCitra® provides citrate in the form of citric acid. Upon dissolving KetoCitra® in water, the citric acid is partially neutralized by the other ingredients of KetoCitra® to provide a balanced overall level of acidity.

Minerals: KetoCitra® contains a blend of important electrolytes (potassium, calcium, and magnesium). KetoCitra® is formulated without sodium because dietary sodium intake is associated with accelerated disease progression in ADPKD and other forms of chronic kidney disease (44, 45). Each recommended serving of KetoCitra® is formulated to provide 51 mEq of alkaline base in the form of mineral salts of organic acids.

Flavoring and Sweetener: No artificial flavors or sweeteners are used in KetoCitra®. To avoid introducing sugar which would raise blood glucose and insulin and antagonize ketosis, KetoCitra® uses a naturally derived sweetener from the leaves of the plant species Stevia rebaudiana. KetoCitra® is pleasantly flavored using a blend of dehydrated natural lemon extract and lemon juice concentrate absorbed on gum acacia, a type of natural fiber commonly derived from a species of acacia tree.

Soluble Corn Fiber: To preserve the powder consistency and prevent clumping, KetoCitra® contains soluble corn fiber, a non-digestible carbohydrate that meets the FDA definition of dietary fiber. This dietary fiber is not digested in the same manner as cornstarch. Instead, it is fermented by microflora in the colon. (46, 47). The soluble corn fiber used in KetoCitra® is non-GMO.

No unnecessary ingredients included: Many ingredients that are commonly found in processed foods or dietary supplements may be renal stressors and potentially harmful to individuals with ADPKD. KetoCitra® is specially formulated with kidney-safety in mind and avoids any unnecessary fillers, bulking agents or other artificial or potentially harmful ingredients.

- No artificial flavors.
- No colorings.
- No whiteners.
- No phosphates.
- No preservatives.

Nutrition Information and Complete Ingredient Listing

Nutrition Information

60 Servings per Container	Recommended Serving size: One rounded scoop (6.5g)		
	Per serving size (1 rounded scoop, 6.5g)	Per daily servings (2 rounded scoops, 13g)	Per 100g Powder
Calories (kcal)	**15**	**30**	**231**
Total Fat	**0g**	**0g**	**0g**
Total Carbohydrates	**<1g**	**<1.5g**	**<10g**
Dietary Fiber	**0.5g**	**1g**	**8g**
Sugars	**<0.1g**	**<0.1g**	**<0.5g**
Protein	**0g**	**0g**	**0g**
Beta-Hydroxybutryrate	**2.65g**	**5.3g**	**41g**
Citrate	**1.75g**	**3.5g**	**27g**
Potassium	**300mg**	**600mg**	**4.6g**
Calcium	**150mg**	**300mg**	**2.3g**
Magnesium	**125mg**	**250mg**	**1.9g**
Sodium	**0mg**	**0mg**	**0mg**
Base Equivalents	**25.5 mEq**	**51 mEq**	**392 mEq**

Ingredients: Citric Acid, Magnesium Beta-Hydroxybutyrate, Potassium Beta-Hydroxybutyrate, Calcium Beta-Hydroxybutyrate, Soluble Corn Fiber, Natural Lemon Flavor (Arabic Gum, Lemon Extract, Lemon Juice Concentrate), Purified Stevia Leaf Extract (Reb A 98%)

Directions: The recommended adult serving amount is one rounded scoop, taken two times per day, for a total of two rounded scoops (13 g/day). Twice per day, shake or stir vigorously one rounded scoop (approx. 6.5 g) of KetoCitra® with 8-16 oz of water and drink slowly (during one hour or more), preferably with a meal. Once reconstituted, any unused mixture should be refrigerated and consumed within 24 hours.

Your physician may recommend a different serving size or frequency based on clinical assessment, including your blood electrolyte levels. This may affect the number of servings per container. First time users begin with half serving (half of one rounded scoop, approx. 3.3 g) twice per day for one week to assess tolerance and gradually increase to recommended serving size. In case of gastrointestinal discomfort or any other signs of intolerance, reduce serving size or discontinue use of product, and consult your physician.

Contents sold by weight, not volume. Some settling may occur during shipping and handling. Serving size is measured by weight with a scoop included for your convenience. The amount of product contained in one rounded scoop may be above or below 6.5 grams due to variations in handling and product density.

Serving Size Determination: KetoCitra® is to be used under medical supervision. Prior to using KetoCitra® for the first time, your healthcare practitioner should review your metabolic blood panel, renal function, and body's ability to handle the electrolytes contained in KetoCitra® (potassium, calcium, magnesium). The healthcare practitioner will need to consider patient body weight, medical conditions, medications, dietary intake, and renal function when determining the serving size and frequency.

The serving size may be increased or decreased depending on your level of renal function and other medical considerations. Increasing the serving size will provide a higher intake of BHB and citrate but will also lead to a higher intake of electrolytes. It is recommended that your healthcare practitioner regularly monitors your blood levels of potassium, calcium and magnesium, and may adjust the serving size of KetoCitra® accordingly.

Urine pH: KetoCitra® is intended to help normalize the urine pH (acidity). Metabolic changes in individuals with ADPKD frequently lead to abnormally acidic urine with a low pH value that may increase the risk of renal crystal precipitation which may detrimentally affect ADPKD progression. Normal, well-balanced urine pH is in the neutral range of pH 6.0-7.0. Your healthcare practitioner should monitor your urine pH and may adjust the serving size of KetoCitra® accordingly. You may wish to utilize the pH measuring strips included with KetoCitra® to regularly monitor your urine pH and communicate the values to your healthcare practitioner.

KetoCitra® should not be used together with other urine alkalizing agents such as sodium bicarbonate unless recommended by your physician.

Warnings and Contraindications:

- KetoCitra® contains significant amounts of the electrolytes potassium, calcium, and magnesium and is not suitable for individuals with advanced stage chronic kidney disease or other causes of severely impaired renal function or impaired electrolyte homeostasis.
- The potassium contained in KetoCitra® may increase blood potassium levels in individuals with hyperkalemia. KetoCitra® is contraindicated in patients with hyperkalemia (or who have conditions predisposing them to hyperkalemia), as a further rise in serum potassium concentration may become dangerous. Such conditions include chronic renal failure, uncontrolled diabetes mellitus, acute dehydration, extensive tissue breakdown, or the administration of a potassium-sparing diuretic.

Before using* KetoCitra®, *a qualified healthcare practitioner should review your blood electrolyte levels and determine if there is any predisposition to, or any history of hyperkalemia (high blood potassium level). Do not take* KetoCitra® *if you are told by your doctor that you need to restrict the dietary intake of potassium.

- KetoCitra® is contraindicated in patients with active urinary tract infection. Do not use KetoCitra® if you have a urinary tract infection. The ability of KetoCitra® to increase urinary citrate may be attenuated by bacterial enzymatic degradation of citrate. Moreover, the rise in urinary pH resulting from taking KetoCitra® might promote further bacterial growth.
- Some people using KetoCitra® might experience stomach upset, diarrhea, constipation, or stomach pain. These side effects are more likely to happen in first-time users or when very high serving sizes are used. First-time users should start with half the recommended serving size and only increase the serving size after tolerance is established. Taking KetoCitra® with meals is recommended.
- KetoCitra® is not recommended for use by pregnant or nursing women unless recommended by your physician.
- Use of KetoCitra® may impact how some drugs are metabolized. Talk to your doctor about all medications you are taking prior to beginning use of the product.
- Allergens: KetoCitra® is free from all 8 major food allergens, (milk, eggs, fish, crustacean shellfish, tree nuts, peanuts, wheat and soybeans), confirmed by a combination of direct finished product testing for gluten, dairy and soy for each batch and rigorous sanitization, storage, and scheduling procedures designed to eliminate cross contamination on shared equipment. These processes are performed in an FDA-registered facility in accordance with strict current Good Manufacturing Practices (cGMPs) and are independently verified by a qualified third-party auditor and certifier.
- Not to be used as sole-source nutrition.

Tamper Evident: Do not use if safety seal is missing or broken or if package is damaged or open.

Storage: Keep container with dry powder tightly closed in a cool, dry place. The powder attracts moisture from the air. Container contains a packet of desiccant to prevent clumping by moisture. Please keep the desiccant packet in the container for the entire time. Do not eat the desiccant.

References

1. **Carney EF**. Ketosis slows the progression of PKD. *Nat Rev Nephrol* 16: 1–1, 2020. doi: 10.1038/s41581-019-0226-4.
2. **Cassina L**, **Chiaravalli M**, **Boletta A**. Increased mitochondrial fragmentation in polycystic kidney disease acts as a modifier of disease progression. *FASEB J* 34: 6493–6507, 2020. doi: https://doi.org/10.1096/fj.201901739RR.
3. **Chiaravalli M**, **Rowe I**, **Mannella V**, **Quilici G**, **Canu T**, **Bianchi V**, **Gurgone A**, **Antunes S**, **D'Adamo P**, **Esposito A**, **Musco G**, **Boletta A**. 2-Deoxy-d-Glucose Ameliorates PKD Progression. *J Am Soc Nephrol* 27: 1958–69, 2016. doi: 10.1681/ASN.2015030231.
4. **Hallows KR**, **Althouse AD**, **Li H**, **Saitta B**, **Abebe KZ**, **Bae KT**, **Miskulin DC**, **Perrone RD**, **Seliger SL**, **Watnick TJ**. Association of Baseline Urinary Metabolic Biomarkers with ADPKD Severity in TAME-PKD Clinical Trial Participants. *Kidney360* published on March 11, 2021: 1–30, 2021. doi: 10.34067/KID.0005962020.
5. **Lin CC**, **Kurashige M**, **Liu Y**, **Terabayashi T**, **Ishimoto Y**, **Wang T**, **Choudhary V**, **Hobbs R**, **Liu LK**, **Lee PH**, **Outeda P**, **Zhou F**, **Restifo NP**, **Watnick T**, **Kawano H**, **Horie S**, **Prinz W**, **Xu H**, **Menezes LF**, **Germino GG**. A cleavage product of Polycystin-1 is a mitochondrial matrix protein that affects mitochondria morphology and function when heterologously expressed. *Sci Rep* 8: 2743, 2018. doi: 10.1038/s41598-018-20856-6.
6. **Magistroni R**, **Boletta A**. Defective glycolysis and the use of 2-deoxy-D-glucose in polycystic kidney disease: from animal models to humans. *J Nephrol* 30: 511–519, 2017. doi: 10.1007/s40620-017-0395-9.
7. **Nowak KL**, **Hopp K**. Metabolic Reprogramming in Autosomal Dominant Polycystic Kidney Disease: Evidence and Therapeutic Potential. *Clin J Am Soc Nephrol* 15(4): 577–584, 2020. doi: 10.2215/CJN.13291019.
8. **Padovano V**, **Kuo IY**, **Stavola LK**, **Aerni HR**, **Flaherty BJ**, **Chapin HC**, **Ma M**, **Somlo S**, **Boletta A**, **Ehrlich BE**, **Rinehart J**, **Caplan MJ**. The polycystins are modulated by cellular oxygen-sensing pathways and regulate mitochondrial function. *Mol Biol Cell* 28: 261–269, 2017. doi: 10.1091/mbc.E16-08-0597.
9. **Padovano V**, **Podrini C**, **Boletta A**, **Caplan MJ**. Metabolism and mitochondria in polycystic kidney disease research and therapy. *Nat Rev Nephrol* 14(11): 678–687, 2018. doi: 10.1038/s41581-018-0051-1.
10. **Podrini C**, **Rowe I**, **Pagliarini R**, **Costa ASH**, **Chiaravalli M**, **Di Meo I**, **Kim H**, **Distefano G**, **Tiranti V**, **Qian F**, **di Bernardo D**, **Frezza C**, **Boletta A**. Dissection of metabolic reprogramming in polycystic kidney disease reveals coordinated rewiring of bioenergetic pathways. *Commun Biol* 1: 194, 2018. doi: 10.1038/s42003-018-0200-x.
11. **Riwanto M**, **Kapoor S**, **Rodriguez D**, **Edenhofer I**, **Segerer S**, **Wuthrich RP**. Inhibition of Aerobic Glycolysis Attenuates Disease Progression in Polycystic Kidney Disease. *PLoS One* 11: e0146654, 2016. doi: 10.1371/journal.pone.0146654.
12. **Rowe I**, **Boletta A**. Defective metabolism in polycystic kidney disease: potential for therapy and open questions. *Nephrol Dial Transpl* 29: 1480–6, 2014. doi: 10.1093/ndt/gft521.
13. **Rowe I**, **Chiaravalli M**, **Mannella V**, **Ulisse V**, **Quilici G**, **Pema M**, **Song XW**, **Xu H**, **Mari S**, **Qian F**, **Pei Y**, **Musco G**, **Boletta A**. Defective glucose metabolism in polycystic kidney disease identifies a new therapeutic strategy. *Nat Med* 19: 488–93, 2013. doi: 10.1038/nm.3092.
14. **Sas KM**, **Yin H**, **Fitzgibbon WR**, **Baicu CF**, **Zile MR**, **Steele SL**, **Amria M**, **Saigusa T**, **Funk J**, **Bunni MA**, **Siegal GP**, **Siroky BJ**, **Bissler JJ**, **Bell PD**. Hyperglycemia in the absence of cilia accelerates cystogenesis and induces

renal damage. *Am J Physiol Ren Physiol* 309: F79-87, 2015. doi: 10.1152/ajprenal.00652.2014.

15. **Torres JA**, **Kruger SL**, **Broderick C**, **Amarlkhagva T**, **Agrawal S**, **Dodam JR**, **Mrug M**, **Lyons LA**, **Weimbs T**. Ketosis Ameliorates Renal Cyst Growth in Polycystic Kidney Disease. *Cell Metab* 30: 1007-1023.e5, 2019. doi: 10.1016/j.cmet.2019.09.012.

16. **Allison SJ**. Crystal deposition aids cystogenesis. *Nat Rev Nephrol* 15: 730–730, 2019. doi: 10.1038/s41581-019-0215-7.

17. **Blijdorp CJ**, **Severs D**, **Musterd-Bhaggoe UM**, **Gansevoort RT**, **Zietse R**, **Hoorn EJ**, **DIPAK Consortium**. Serum bicarbonate is associated with kidney outcomes in autosomal dominant polycystic kidney disease. *Nephrol Dial Transplant* , 2020. doi: 10.1093/ndt/gfaa283.

18. **Errasti P**, **Manrique J**, **Lavilla J**, **Rossich E**, **Hernandez A**, **Pujante D**, **Ndarabu A**, **Garcia N**, **Purroy A**. Autosomal-dominant polycystic kidney disease: high prevalence of graft loss for death-related malignancies and cardiovascular risk factors. *Transpl Proc* 35: 1717–9, 2003. doi: 10.1016/s0041-1345(03)00619-5.

19. **Grampsas SA**, **Chandhoke PS**, **Fan J**, **Glass MA**, **Townsend R**, **Johnson AM**, **Gabow P**. Anatomic and metabolic risk factors for nephrolithiasis in patients with autosomal dominant polycystic kidney disease. *Am J Kidney Dis* 36: 53–7, 2000. doi: 10.1053/ajkd.2000.8266.

20. **Kocyigit I**, **Yilmaz MI**, **Orscelik O**, **Sipahioglu MH**, **Unal A**, **Eroglu E**, **Kalay N**, **Tokgoz B**, **Axelsson J**, **Oymak O**. Serum uric acid levels and endothelial dysfunction in patients with autosomal dominant polycystic kidney disease. *Nephron Clin Pr* 123: 157–64, 2013. doi: 10.1159/000353730.

21. **Levine E**, **Grantham JJ**. Calcified renal stones and cyst calcifications in autosomal dominant polycystic kidney disease: clinical and CT study in 84 patients. *AJR Am J Roentgenol* 159: 77–81, 1992. doi: 10.2214/ajr.159.1.1609726.

22. **Mejias E**, **Navas J**, **Lluberes R**, **Martinez-Maldonado M**. Hyperuricemia, gout, and autosomal dominant polycystic kidney disease. *Am J Med Sci* 297: 145–8, 1989. doi: https://doi.org/10.1097/00000441-198903000-00002.

23. **Nishiura JL**, **Neves RF**, **Eloi SR**, **Cintra SM**, **Ajzen SA**, **Heilberg IP**. Evaluation of nephrolithiasis in autosomal dominant polycystic kidney disease patients. *Clin J Am Soc Nephrol* 4: 838–44, 2009. doi: 10.2215/CJN.03100608.

24. **Panizo N**, **Goicoechea M**, **Garcia de Vinuesa S**, **Arroyo D**, **Yuste C**, **Rincon A**, **Verdalles U**, **Ruiz-Caro C**, **Quiroga B**, **Luno J**. Chronic kidney disease progression in patients with autosomal dominant polycystic kidney disease. *Nefrologia* 32: 197–205, 2012. doi: 10.3265/Nefrologia.pre2011.Dec.11177.

25. **Torres JA**, **Rezaei M**, **Broderick C**, **Lin L**, **Wang X**, **Hoppe B**, **Cowley BD**, **Savica V**, **Torres VE**, **Khan S**, **Holmes RP**, **Mrug M**, **Weimbs T**. Crystal deposition triggers tubule dilation that accelerates cystogenesis in polycystic kidney disease. *J Clin Invest* 129: 4506–4522, 2019. doi: 10.1172/JCI128503.

26. **Torres VE**, **Erickson SB**, **Smith LH**, **Wilson DM**, **Hattery RR**, **Segura JW**. The association of nephrolithiasis and autosomal dominant polycystic kidney disease. *Am J Kidney Dis* 11: 318–25, 1988. doi: 10.1016/S0272-6386(88)80137-9.

27. **Torres VE**, **Wilson DM**, **Hattery RR**, **Segura JW**. Renal stone disease in autosomal dominant polycystic kidney disease. *Am J Kidney Dis* 22: 513–9, 1993. doi: 10.1016/S0272-6386(12)80922-X.

28. **Nowak KL**, **You Z**, **Gitomer B**, **Brosnahan G**, **Torres VE**, **Chapman AB**, **Perrone RD**, **Steinman TI**, **Abebe KZ**, **Rahbari-Oskoui FF**, **Yu ASL**, **Harris PC**, **Bae KT**, **Hogan M**, **Miskulin D**, **Chonchol M**. Overweight and Obesity Are Predictors of Progression in Early Autosomal Dominant Polycystic Kidney Disease. *J Am Soc Nephrol* 29: 571–578, 2018. doi: 10.1681/ASN.2017070819.

29. **Reed B**, **Helal I**, **McFann K**, **Wang W**, **Yan XD**, **Schrier RW**. The impact of type II diabetes mellitus in patients with autosomal dominant polycystic kidney disease. *Nephrol Dial Transpl* 27: 2862–5, 2012. doi: 10.1093/ndt/gfr744.

30. **Hutchison AJ**, **Wilkie M**. Use of magnesium as a drug in chronic kidney disease. *Clin Kidney J* 5: i62–i70, 2012. doi: 10.1093/ndtplus/sfr168.

31. **Lemann J**, **Pleuss JA**, **Worcester EM**, **Hornick L**, **Schrab D**, **Hoffmann RG**. Urinary oxalate excretion increases with body size and decreases with increasing dietary calcium intake among healthy adults. *Kidney Int* 49: 200–8, 1996. doi: 10.1038/ki.1996.27.

32. **von Unruh GE**, **Voss S**, **Sauerbruch T**, **Hesse A**. Dependence of oxalate absorption on the daily calcium intake. *J Am Soc Nephrol* 15: 1567–73, 2004. doi: 10.1097/01.asn.0000127864.26968.7f.

33. **Desroches S**, **Lapointe A**, **Ratté S**, **Gravel K**, **Légaré F**, **Turcotte S**. Interventions to enhance adherence to dietary advice for preventing and managing chronic diseases in adults. *Cochrane Database Syst Rev* : CD008722, 2013. doi: 10.1002/14651858.CD008722.pub2.

34. **Jensen NJ**, **Wodschow HZ**, **Nilsson M**, **Rungby J**. Effects of Ketone Bodies on Brain Metabolism and Function in Neurodegenerative Diseases. *Int J Mol Sci* 21: 8767, 2020. doi: 10.3390/ijms21228767.

35. **Rusek M**, **Pluta R**, **Ułamek-Kozioł M**, **Czuczwar SJ**. Ketogenic Diet in Alzheimer's Disease. *Int J Mol Sci* 20, 2019. doi: 10.3390/ijms20163892.

36. **Schlundt DG**, **Rea MR**, **Kline SS**, **Pichert JW**. Situational obstacles to dietary adherence for adults with diabetes. *J Am Diet Assoc* 94: 874–879, 1994. doi: 10.1016/0002-8223(94)92367-1.

37. **Sherman AM**, **Bowen DJ**, **Vitolins M**, **Perri MG**, **Rosal MC**, **Sevick MA**, **Ockene JK**. Dietary Adherence: Characteristics and Interventions. *Control Clin Trials* 21: S206–S211, 2000. doi: 10.1016/S0197-2456(00)00080-5.

38. **Włodarek D**. Role of Ketogenic Diets in Neurodegenerative Diseases (Alzheimer's Disease and Parkinson's Disease). *Nutrients* 11, 2019. doi: 10.3390/nu11010169.

39. **Kang David E.**, **Sur Roger L.**, **Haleblian George E.**, **Fitzsimons Nicholas J.**, **Borawski Kristy M.**, **Preminger Glenn M.** Long-Term Lemonade Based Dietary Manipulation in Patients With Hypocitraturic Nephrolithiasis. *J Urol* 177: 1358–1362, 2007. doi: 10.1016/j.juro.2006.11.058.

40. **Seltzer MA**, **Low RK**, **McDonald M**, **Shami GS**, **Stoller ML**. Dietary manipulation with lemonade to treat hypocitraturic calcium nephrolithiasis. *J Urol* 156: 907–9, 1996. doi: 10.1016/S0022-5347(01)65659-3.

41. **Holmes RP**, **Knight J**, **Assimos DG**. Lowering urinary oxalate excretion to decrease calcium oxalate stone disease. *Urolithiasis* 44: 27–32, 2016. doi: 10.1007/s00240-015-0839-4.

42. **Minisola S**, **Rossi W**, **Pacitti MT**, **Scarnecchia L**, **Bigi F**, **Carnevale V**, **Mazzuoli G**. Studies on citrate metabolism in normal subjects and kidney stone patients. *Miner Electrolyte Metab* 15: 303–308, 1989. doi: PMID: 2811789.

43. **Zuckerman JM**, **Assimos DG**. Hypocitraturia: Pathophysiology and Medical Management. *Rev Urol* 11: 134–144, 2009. doi: 10.3909/riu0424].

44. **Chebib FT**, **Torres VE**. Recent Advances in the Management of Autosomal Dominant Polycystic Kidney Disease. *Clin J Am Soc Nephrol* 13(11): 1765–1776, 2018. doi: 10.2215/CJN.03960318.

45. **Kramers BJ**, **Koorevaar IW**, **Drenth JPH**, **Fijter JW de**, **Neto AG**, **Peters DJM**, **Vart P**, **Wetzels JF**, **Zietse R**, **Gansevoort RT**, **Meijer E**. Salt, but not protein intake, is associated with accelerated disease progression in autosomal dominant polycystic kidney disease. *Kidney Int* 98: 989–998, 2020. doi: 10.1016/j.kint.2020.04.053.

46. **Carlson JL**, **Erickson JM**, **Lloyd BB**, **Slavin JL**. Health Effects and Sources of Prebiotic Dietary Fiber. *Curr Dev Nutr* 2, 2018. doi: 10.1093/cdn/nzy005.

47. **Neri-Numa IA**, **Pastore GM**. Novel insights into prebiotic properties on human health: A review. *Food Res Int* 131: 108973, 2020. doi: 10.1016/j.foodres.2019.108973.

48. **Peters RJB**, **Oomen AG**, **Bemmel G van**, **Vliet L van**, **Undas AK**, **Munniks S**, **Bleys RLAW**, **Tromp PC**, **Brand W**, **Lee M van der**. Silicon dioxide and titanium dioxide particles found in human tissues. *Nanotoxicology* 14: 420–432, 2020. doi: 10.1080/17435390.2020.1718232.

49. **Villota R**, **Hawkes JG**, **Cochrane H**. Food applications and the toxicological and nutritional implications of amorphous silicon dioxide. *C R C Crit Rev Food Sci Nutr* 23: 289–321, 1986. doi: 10.1080/10408398609527428.

50. **Younes M**, **Aggett P**, **Aguilar F**, **Crebelli R**, **Dusemund B**, **Filipič M**, **Frutos MJ**, **Galtier P**, **Gott D**, **Gundert-Remy U**, **Kuhnle GG**, **Leblanc J-C**, **Lillegaard IT**, **Moldeus P**, **Mortensen A**, **Oskarsson A**, **Stankovic I**, **Waalkens-Berendsen I**, **Woutersen RA**, **Wright M**, **Boon P**, **Chrysafidis D**, **Gürtler R**, **Mosesso P**, **Parent-Massin D**, **Tobback P**, **Kovalkovicova N**, **Rincon AM**, **Tard A**, **Lambré C**. Re-evaluation of silicon dioxide (E 551) as a food additive. *EFSA J* 16: e05088, 2018. doi: https://doi.org/10.2903/j.efsa.2018.5088.