Formulating minerals for the health of the urinary tract of cats

Dennis E. Jewell, PhD, Dipl. ACAN

A short history of mineral formulations in cat foods

Body composition of rats and mice

- **Protein 65% fat 25% negligible carbohydrate thus a 100 gm is approximately 485 kcal ME**
- **Calcium (Ca):** 1.5 to 2% - 0.36 g/100 kcal
- **Phosphorus (P):** 1.0 to 1.4% - 0.25 g/100 kcal
- **Calcium to Phosphorus Ratio:** 1.1 to 1.4
- **Magnesium (Mg):** approx. 0.1% - 21 mg/100 kcal

A short history of mineral formulations in cat foods

How does this relate to minerals today?

- **Selection pressure was for maximum progeny**
- **This would select for gestation and growth**
- **Today we desire to lengthen and enrich the special relationship between people and pets**

A short history of mineral formulations in cat foods

How have foods changed over the years?

- **As they were introduced, many dry foods had higher magnesium and higher urine pH, increasing struvite stone risk**

- **A reduction of dietary magnesium and return to a normal acidic 6.2 to 6.4 urinary pH resulted struvite protection and an increased risk of CaOx stone formation**

What type of stones are most prevalent?

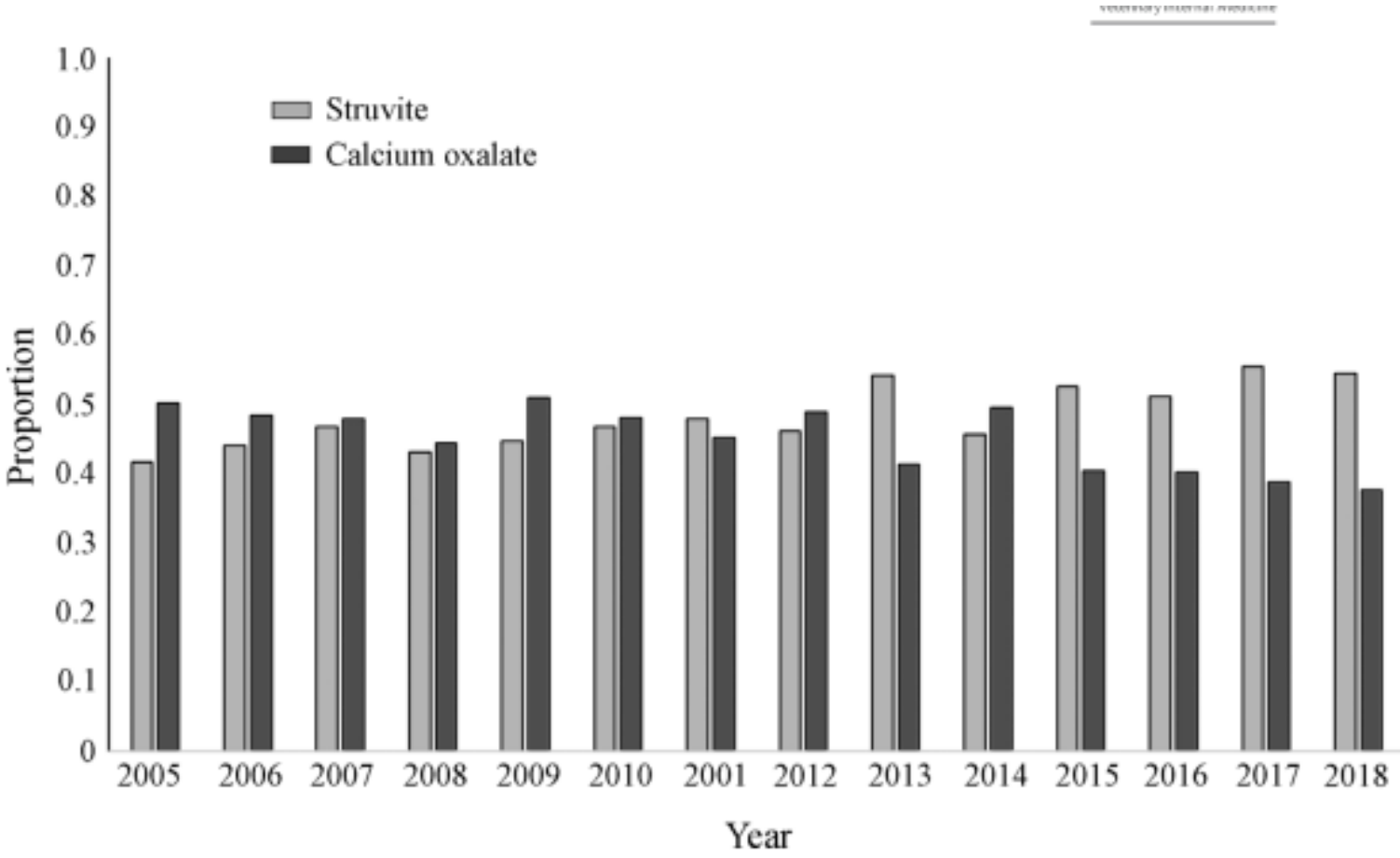
Table 1 Distribution of the different types of uroliths in cats (2006–2017) according to sex and age

Type of urolith	Frequency	Females	Males	Age groups (years)			
				<1	1–6	7–10	>10
CaOx	44 (54.3)	15 (34.1)	29 (65.9)	0	21 (47.7)	17 (38.6)	6 (13.6)
Struvite	26 (32.1)	15 (57.7)	11 (42.3)	3 (11.5)	14 (53.8)	5 (19.32)	4 (15.4)
Purines	6 (7.4)	5 (83.3)	1 (16.7)	0	5 (83.3)	1 (16.66)	0
Others*	5 (6.1)	2 (40)	3 (60)	0	3 (60)	2 (40)	0
Total	81 (100)	37 (45.7)	44 (54.3)	3 (3.7)	48 (53.1)	25 (30.9)	10 (12.3)

Data are n (%) unless otherwise indicated
*One cystine, one silica and three mixed uroliths (struvite and calcium oxalate [CaOx], ammonium urate and silica and a dried blood clot with calcium phosphate)

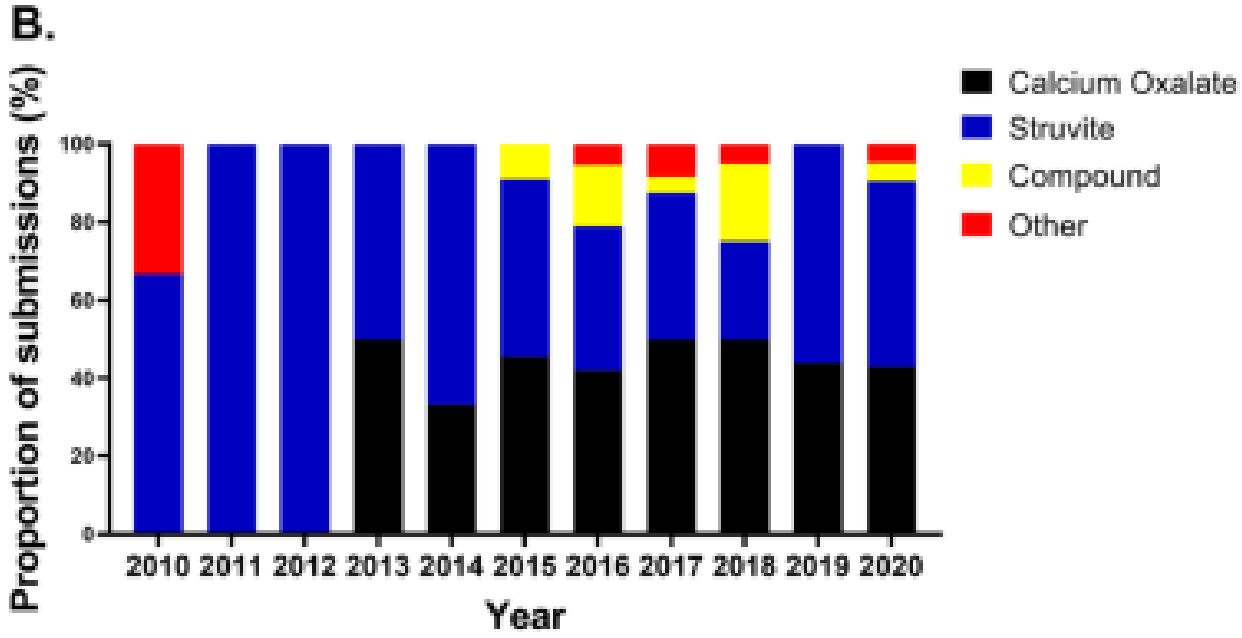
Mendoza-López, C.I., Del-Angel-Caraza, J., Aké-Chiñas, M.A., Quijano-Hernández, I.A. and Barbosa-Mireles, M.A., 2019. Epidemiology of feline urolithiasis in Mexico (2006–2017). *Journal of Feline Medicine and Surgery Open Reports*, *5*(2), p.205116919885699.

What type of stones are most prevalent?



Kopecny, L., Palm, C.A., Segev, G. and Westropp, J.L., 2021. Urolithiasis in dogs: Evaluation of trends in urolith composition and risk factors (2006-2018). *Journal of veterinary internal medicine*, *35*(3), pp.1406-1415.

What type of stones are most prevalent?



Age	Stone composition		*p*-value	OR
Age ≤ 7 years	Struvite (*n* = 40/81)	Non-struvite (*n* = 31/81)	0.007	2.87
Age > 7 years	CaOx (24/47)	Non-CaOx (23/47)	0.012	2.67

Ortega, C.J., Stavroulaki, E.M., Lawlor, A., Lulich, J. and Cuq, B., 2023. Retrospective analysis of 131 feline uroliths from the Republic of Ireland and Northern Ireland (2010-2020). *Irish Veterinary Journal*, *76*(1), p.2.

What type of stones are most prevalent?

Struvite (magnesium ammonium phosphate)

Calcium Oxalate

What do nutritional modifications change?

Solute concentration

Urine pH

Crystallization potential

What are the minerals of interest?

- Phosphorus
- Magnesium
- Calcium
- Sodium
- Potassium
- Sulfur

Why are they important?

- They form the stones (Ca, Mg & Phos)
- They change urine pH (Mg, K, and S)
- They change urine volume
- They influence inhibitors of stone formation

What is the desired outcome?

- Optimum urine solute concentration
- Urine pH controlled for the stone
- Increased inhibitory molecules
- Reduced risk of stones

Dietary solution for struvite stones is robust

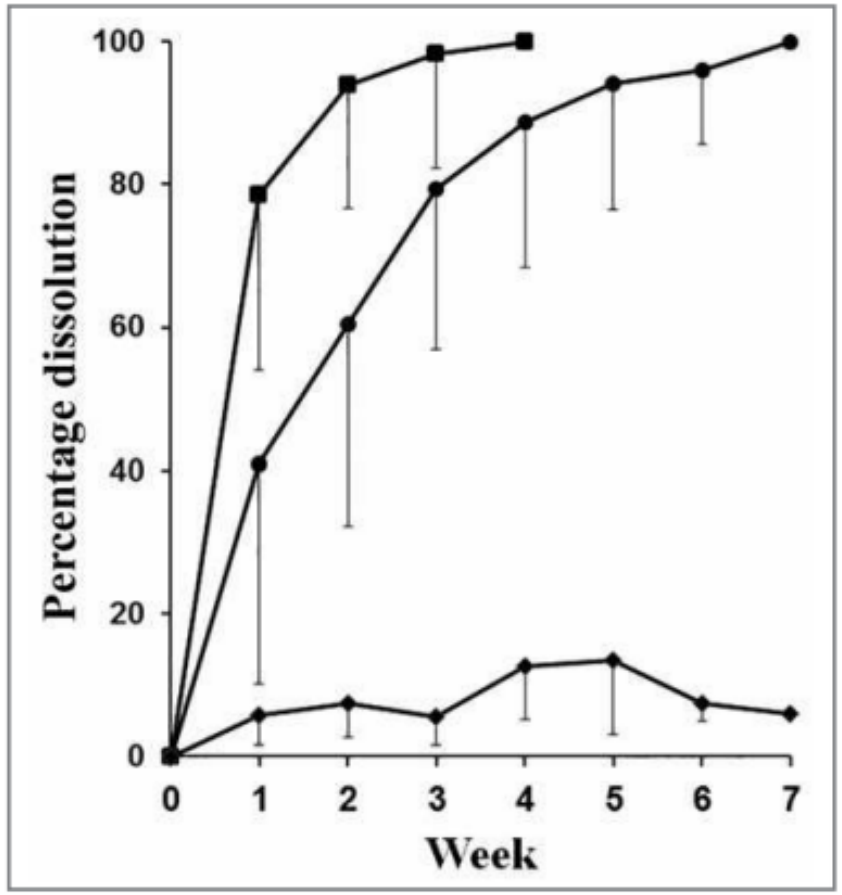


Figure 2—Mean ± SD percentage urolith dissolution by week for cats with presumed struvite uroliths that were treated with 1 of 2 commercially available, low-magnesium, urine-acidifying dry cat foods (food A, n = 16 [squares]; or food B, 16 [circles]) and 5 cats fed food B (diamonds) that had uroliths composed of 100% ammonium urate (4) or 100% calcium oxalate (1).

Urine pH was 6.1 in food A and 6.4 in food B

Dietary magnesium was the same 0.07% DMB

Food A kcal / 100 gm DMB approximately 460 ME
Food B kcal / 100 gm DMB approximately 410 MEs

Lulich, J.P., Kruger, J.M., MacLeay, J.M., Merrills, J.M., Paetau-Robinson, I., Albasan, H. and Osborne, C.A., 2013. Efficacy of two commercially available, low-magnesium, urine-acidifying dry foods for the dissolution of struvite uroliths in cats. *Journal of the American Veterinary Medical Association*, *243*(8), pp.1147-1153.

Dietary solution for struvite stones is robust

Table 1. Key parameters of the diet (dry or wet) fed

	Dry diet*	Wet diet (loaf)†
RSS-MAP	0·2	0·3
RSS-oxalate	<5	<5
Protein (g/4184 kJ)	89·4	82·1
Fat (g/4184 kJ)	40·2	59·7
Crude fibre (g/4184 kJ)	6·2	8
Na (g/4184 kJ)	3·5	2·35
P (g/4184 kJ)	2·1	1·97
Mg (g/4184 kJ)	0·2	0·2
K (g/4184 kJ)	2·7	3·2
Total *n*-3 (g/4184 kJ)	1·3	1·71
EPA:DHA	0·65	1·17
ME (kJ/kg as fed)‡	3861	938
Base excess (cation–anion balance) (4184 kJ ME)	−50·85	−39·58

RSS, relative supersaturation; MAP, magnesium ammonium phosphate; ME, metabolisable energy.
* Veterinary Diet Urinary S/O, Guelph, Ontario, Canada, Urinary High Dilution (rest of the world), Royal Canin, Aimargues, France.
† Veterinary diet Urinary S/O wet, Royal Canin, Aimargues, France.
‡ ME was measured by animal trials according to the American Association of Feed Control Officials protocol (2010).

Table 2. Time to dissolution of uroliths, age and weight of cats

	All cats (*n* 17)		Dry diet (*n* 9)		Wet diet (*n* 8)	
Variables	Median	Range	Median	Range	Median	Range
Time to dissolution (d)	18	10–56	19	10–42	16	14–55
Age (years)	5·5	2–15	6·0	2–15	5·0	3–13
Weight (kg)	6·0	3·5–11·8	6·0	4·5–7·3	6·4	3·5–11·8

Houston, D.M., Weese, H.E., Evason, M.D., Biourge, V. and van Hoek, I., 2011. A diet with a struvite relative supersaturation less than 1 is effective in dissolving struvite stones in vivo.
British journal of nutrition, *106*(S1), pp.S90-S92.

Dietary solution for struvite stones is robust

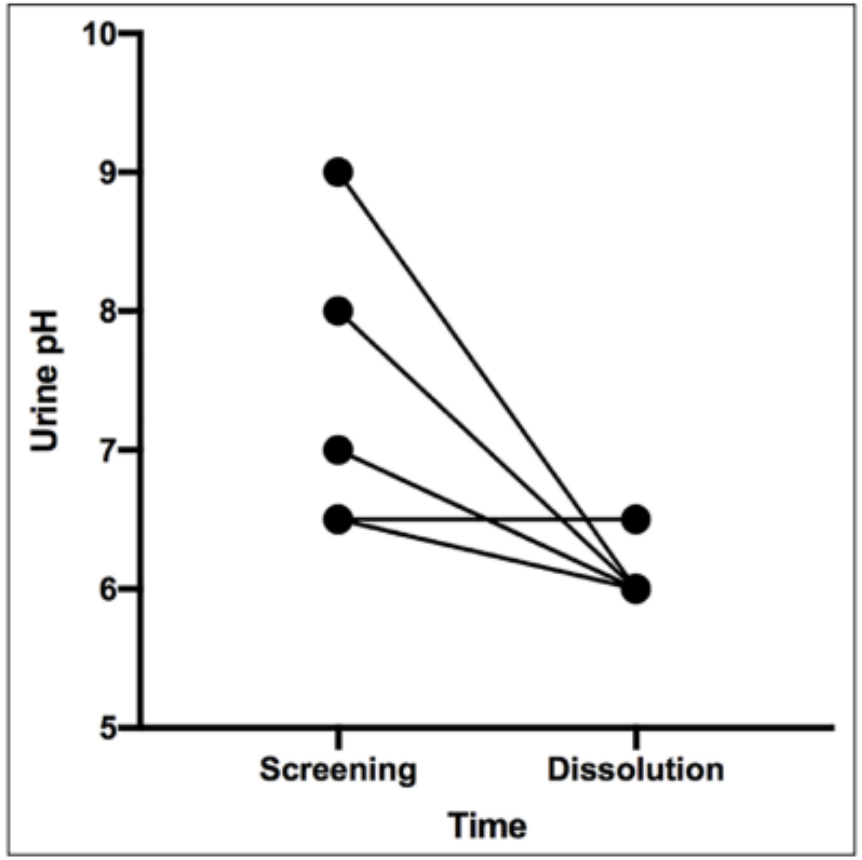


Figure 2 Urine pH at screening and at complete dissolution in seven cats for which it was available. Some of the study cats had identical pH values at screening or at dissolution. Time to dissolution varied between study cats

Urine pH was 6.0

Dietary magnesium was defined as “low” which may have used the < 25 mg /100 Kcal of AAFCO

Tefft, K.M., Byron, J.K., Hostnik, E.T., Daristotle, L., Carmella, V. and Frantz, N.Z., 2021. Effect of a struvite dissolution diet in cats with naturally occurring struvite urolithiasis. *Journal of Feline Medicine and Surgery*, *23*(4), pp.269-277.

Minerals and Calcium Oxalate Stone Formation

Excess Dietarty calcium was stated as a risk factor for CaOx stones

Table 4. POTENTIAL RISK FACTORS ASSOCIATED WITH CALCIUM OXALATE UROLITH FORMATION

Risk Factor	Etiopathologic Disorder	Pathophysiologic Mechanism
Hypercalciuria	Excess dietary calcium	Results in increased renal clearance of calcium and hypercalciuria
	Excess dietary sodium	Enhances renal excretion of calcium
	Hypercalcemia	Results in increased renal clearance of calcium and hypercalciuria
	Excess vitamin D	Augments intestinal calcium absorption and by suppressing parathyroid hormone promotes calcium excretion
	Acidosis	Promotes skeletal mobilization of calcium and inhibits renal tubular reabsorption of calcium
	Hypophosphatemia (e.g., hyperparathyroidism)	Stimulates vitamin D production, which augments intestinal calcium absorption

Carl A. Osborne, DVM, PhD, Jody P. Lulich, DVM, PhD, Rosama Thumchai, DVM, MS, PhD, LisaK. Ulrich, CVT, Lori A. Koehler, CVT, Kathleen A. Bird, CVT, and Joseph W. Bartges, DVM, PhD 1996. Feline urolithiasis: Etiology and pathophysiology. *Veterinary Clinics: Small Animal Practice*, *26*(2), pp.217-232.

Epidemiology “look back” report

- Case-Control Study
- 173 cats with CaOx uroliths, 290 cats with MAP uroliths, and 827 cats without any urinary tract diseases.
- A confounding problem is foods have attributes that move together – specifically Ca and P change together
- Urine pH – lower protects against struvite and is a risk for CaOx

- Lekcharoensuk, C., Osborne, C.A., Lulich, J.P., Pusoonthornthum, R., Kirk, C.A., Ulrich, L.K., Koehler, L.A., Carpenter, K.A. and Swanson, L.L., 2001. Association between dietary factors and calcium oxalate and magnesium ammonium phosphate urolithiasis in cats.
- *Journal of the American Veterinary Medical Association*, *219*(9), pp.1228-1237.

Data showing dietary changes associated with CaOx stones

	Control cats			Cats with CaOx uroliths		
Component	**No. of cats**	**Mean**	**SE**	**No. of cats**	**Mean**	**SE**
Protein (g/100 kcal)	827	9.42[a]	0.06	173	8.85[b]	0.14
Carbohydrate (g/100 kcal)	827	6.95[a]	0.13	173	7.84[b]	0.23
Fat (g/100 kcal)	827	4.47[a]	0.06	173	4.38[a,b]	0.10
Fiber (g/100 kcal)	826	0.72	0.04	173	0.75	0.10
Calcium (mg/kcal)	827	3.04[a]	0.03	173	2.72[b]	0.07
Phosphorus (mg/kcal)	827	2.58[a]	0.03	173	2.28[b]	0.08
Magnesium (mg/kcal)	827	0.27[a]	0.01	173	0.24[a]	0.01
Sodium (mg/kcal)	826	1.27[a]	0.02	173	1.15[a]	0.05
Potassium (mg/kcal)	819	1.82[a]	0.02	172	1.72[b]	0.03
Chloride (mg/kcal)	756	1.88[a,b]	0.03	164	1.78[a]	0.05
Moisture (%)	827	32.02[a]	1.09	173	21.44[b]	1.98
Urine acidifying potential*	763	6.28[a]	0.01	169	6.24[b]	0.01

Data showing dietary changes associated with struvite stones

Component	Control cats			Cats with MAP uroliths		
	No. of cats	Mean	SE	No. of cats	Mean	SE
Protein (g/100 kcal)	827	9.42[a]	0.06	290	9.32[a]	0.09
Carbohydrate (g/100 kcal)	827	6.95[a]	0.13	290	7.78[b]	0.21
Fat (g/100 kcal)	827	4.47[a]	0.06	290	4.09[b]	0.09
Fiber (g/100 kcal)	826	0.72	0.04	289	0.67	0.04
Calcium (mg/kcal)	827	3.04[a]	0.03	290	3.26[c]	0.05
Phosphorus (mg/kcal)	827	2.58[a]	0.03	290	2.83[c]	0.05
Magnesium (mg/kcal)	827	0.27[a]	0.01	290	0.31[b]	0.02
Sodium (mg/kcal)	826	1.27[a]	0.02	289	1.42[b]	0.04
Potassium (mg/kcal)	819	1.82[a]	0.02	285	1.91[c]	0.03
Chloride (mg/kcal)	756	1.88[a,b]	0.03	262	2.00[b]	0.05
Moisture (%)	827	32.02[a]	1.09	290	28.38[a]	1.76
Urine acidifying potential*	763	6.28[a]	0.01	262	6.35[c]	0.02

What is the effect of increasing dietary calcium on risk of CaOx stones

Table 1. Nutrient analysis of the experimental diets.

		Diet		
Analyzed composition		**A**	**B**	**C**
Dry matter	g/kg	163	174	174
Crude protein	g/kg DM	607	602	565
Crude fat	g/kg DM	274	267	245
Crude fiber	g/kg DM	2.29	2.72	3.26
Crude ash	g/kg DM	94.5	103	138
Ca	g/kg DM	12.2	18.5	27.0
P	g/kg DM	16.1	17.6	21.1
Ca:P-ratio		0.76: 1	1.05: 1	1.28: 1
Na	g/kg DM	9.72	9.69	10.7
K	g/kg DM	11.5	10.3	10.5
Mg	g/kg DM	0.90	0.93	1.12
Ox	g/kg DM	0.08	0.14	0.06
Metabolizable energy[1]	MJ/kg DM	20.6	20.3	19.2

[1]Calculated (NRC 2006).

doi:10.1371/journal.pone.0070530.t001

Passlack, N. and Zentek, J., 2013. Urinary calcium and oxalate excretion in healthy adult cats are not affected by increasing dietary levels of bone meal in a canned diet. *PLoS One*, *8*(8), p.e70530.`

What is the effect of increasing dietary calcium on risk of CaOx stones?

Table 2. Body weight (BW), feed and water intake, urine volume, urinary pH and urine composition of the cats fed a diet with 12.2 (A), 18.5 (B) and 27.0 (C) g Ca/kg DM.

	Diet A	Diet B	Diet C
* ♀ BW (kg)	4.43±1.39	4.43±1.31	4.35±1.26
Feed intake (g/kg BW/d)	65.5±14.7	59.6±15.2	64.9±13.6
Water intake (g/kg BW/d)	5.04±2.85^{ab}	5.08±2.15^{a}	4.65±3.39^{b}
* Urine volume (ml/kg BW/d)	36.2±11.7	29.5±8.92	34.7±8.02
Urinary			
* Fasting pH	6.60±0.10	6.69±0.17	6.78±0.20
Postprandial pH	6.76±0.23^{ab}	6.60±0.38^{a}	6.91±0.27^{b}
Ca (mg/l)	35.3±17.2	33.9±6.29	29.7±8.57
* P (mg/l)	1750±249	1821±226	1699±175
* Mg (mg/l)	29.2±9.52	31.6±9.78	29.6±5.60

Passlack, N. and Zentek, J., 2013. Urinary calcium and oxalate excretion in healthy adult cats are not affected by increasing dietary levels of bone meal in a canned diet. *PLoS One*, *8*(8), p.e70530.`

What is the effect of increasing dietary potassium citrate on stones?

- Increased inhibition of calcium oxalate stone formation
- Increased urinary pH (>6.5 approaching 7.0)
- Reduces relative supersaturation of CaOx

What are the urinary factors that most influence CaOx stone formation?

- Calcium ↑
- Oxalate ↑
- Citrate ↓
- Potassium ↓
- Sodium ↓

Relative supersaturation values distinguish between feline urinary and non-urinary foods and align with expected urine analytes contributions to uroliths

Elizabeth M. Morris[1]*, Allison P. McGrath[1], John Brejda[2] and Dennis E. Jewell[3]

What are the urinary factors that most influence struvite stone formation?

- pH ↑
- Magnesium ↑
- Sodium ↓
- Oxalate ↑
- Citrate ↓

Relative supersaturation values distinguish between feline urinary and non-urinary foods and align with expected urine analytes contributions to uroliths

Elizabeth M. Morris[1]*, Allison P. McGrath[1], John Brejda[2] and Dennis E. Jewell[3]

High dietary concentration of sodium decreases RSS

TABLE 1 Ingredient composition and analysed nutrient profiles of the four experimental diets

	Diet A	Diet B	Diet C	Diet D
Moisture	5.7	5.2	4.7	5.4
Crude protein	86.5	90.1	94.4	89.1
Crude fat	35.0	35.5	35.6	34.5
Total dietary fibre	15.1	19.4	26.5	16.2
Ash	13.9	15.7	17.1	20.1
Starch	66.6	61.1	59.2	66.8
Calcium	1.85	1.91	1.98	1.89
Phosphorus	1.64	1.63	1.68	1.62
Magnesium	0.16	0.17	0.16	0.17
Potassium	2.45	2.41	2.18	2.55
Sodium	0.67	1.68	2.41	3.27
Chloride	2.22	3.58	4.39	6.05
Metabolizable energy[a]	4,187	4,111	3,984	4,072

TABLE 2. Diet and water intakes, and urine composition in cats (n = 13) fed the four diets differing in sodium chloride content

	Diet A	Diet B	Diet C	Diet D	SE	*p* value
Sodium (g/1,000 kcal)	0.67	1.68	2.41	3.27		
Caloric intake (kcal/$BW^{0.71}$)	88	86	86	86	2.4	.83
Water intake (ml/kg/day)	24.5†	28.8‡	30.3‡	36.7§	1.38	<.001
Urine volume (ml/kg/day)	10.9†	13.7‡	15.5‡	19.6§	0.69	<.001
Urine specific gravity	1.067†	1.063†‡	1.061‡	1.051§	0.002	<.001
Urine pH	6.36†	6.51†	6.39†	6.27‡	0.05	<.001
CaOx RSS	3.39†	2.80‡	2.41‡	1.64§	0.25	<.001
MAP RSS	0.81†	0.83†	0.41‡	0.16§	-	<.001

Queau, Y., Bijsmans, E.S., Feugier, A. and Biourge, V.C., 2020. Increasing dietary sodium chloride promotes urine dilution and decreases struvite and calcium oxalate relative supersaturation in healthy dogs and cats. *Journal of Animal Physiology and Animal Nutrition*, *104*(5), pp.1524-1530.

High dietary concentration of potassium decreases RSS

Table 1. Ingredient composition and analyzed nutrient profiles of the experimental diets.

Analyzed Nutrient	Diet A KCl 0.6%	Diet B KCl 2.5%
Moisture	7.97	7.70
Crude protein	19.6	20.1
Crude fat	6.9	7.1
Total dietary fiber	6.3	5.8
Ash	3.2	4.2
Calcium	0.42	0.40
Phosphorus	0.39	0.40
Magnesium	0.05	0.05
Potassium	0.44	1.03
Sodium	0.24	0.23
Chloride	0.54	0.83
Metabolizable energy [a]	15.4	15.4

All nutrient contents are expressed in grams per MJ, except for moisture, which is expressed in %

Bijsmans, E., Quéau, Y. and Biourge, V., 2021. Increasing dietary potassium chloride promotes urine dilution and decreases calcium oxalate relative supersaturation in healthy dogs and cats. *Animals*, *11*(6), p.1809.

High dietary concentration of potassium decreases RSS

Variable	Diet A KCl 0.6%	Diet B KCl 2.5%	SE	*p*-Value for Diet
Caloric intake (kcal/$BW^{0.711}$)	94.9	94.4	4.7	0.892
Water intake (mL/kg/24 h)	28.5	33.8	1.6	<0.0001
Urine volume (mL/kg/24 h)	11.2	16.2	0.9	<0.0001
Urine specific gravity	1.069	1.058	0.002	<0.0001
Urine pH	5.93	5.93	0.06	0.877
CaOx RSS	3.24	2.59	0.37	0.034
MAP RSS	0.29	0.17	-	0.112

Bijsmans, E., Quéau, Y. and Biourge, V., 2021. Increasing dietary potassium chloride promotes urine dilution and decreases calcium oxalate relative supersaturation in healthy dogs and cats. *Animals*, *11*(6), p.1809.

Dietary calcium and phosphorus matters for renal health!

Excess highly available phosphorus can be detrimental to renal health

Inverse Ca/P ratios can be harmful, calcium mitigates the effects of excess phosphorus. However, excess calcium may also be detrimental

We don't have enough information to establish a safe upper limit
However, a SUL would include P availability and Ca/P ratio

Optimum (note this is my suggestion!) foods avoid excess phosphorus and have a Ca/P ratio > 1.0 and < 2.0

Dietary minerals aid in the management of renal disease

Controlled phosphorus is a part of an optimum diet
(0.11 to 0.16 g/100 kcal)

Controlled calcium is a part of the optimum diet
(0.18 to 0.23 g/100 kcal)

Calcium to Phosphorus ratio recommended between 1:1 and 1.4:1

Controlled Sodium and potassium (not elevated)

Enhanced fiber >0.5 oat beta glucan and >0.4% short chain FOS

Questions?