Cobre para cães: Estaremos fornecendo em excesso?

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Por que existe a suspeita de excesso de cobre em alimentos comerciais?

Introdução

Acredita-se que tenha ocorrido aumento da incidência de hepatite crônica associada ao cobre em cães nos últimos 15-20 anos

Aumento das concentrações hepáticas de cobre em cães ao longo do tempo

O início desse aumento parece ter coincidido com uma mudança no tipo de cobre utilizado no *premix* adicionado a alimentos comerciais para cães

Tendência de mercado parecem ter exacerbado o aumento dessa incidência: alimentos formulados com um alto teor de ingredientes de origem animal (ex. dietas evolutivas) e alimentos compostos por vegetais com alto teor de cobre (ex. batata-doce)

AVMA
American Veterinary Medical Association
Journals

Viewpoint

Is it time to reconsider current guidelines for copper content in commercial dog foods?

Sharon A. Center DVM
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David C. Twedt DVM
Joseph J. Wakshlag DVM, PhD
Penny J. Watson VetMD
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2021

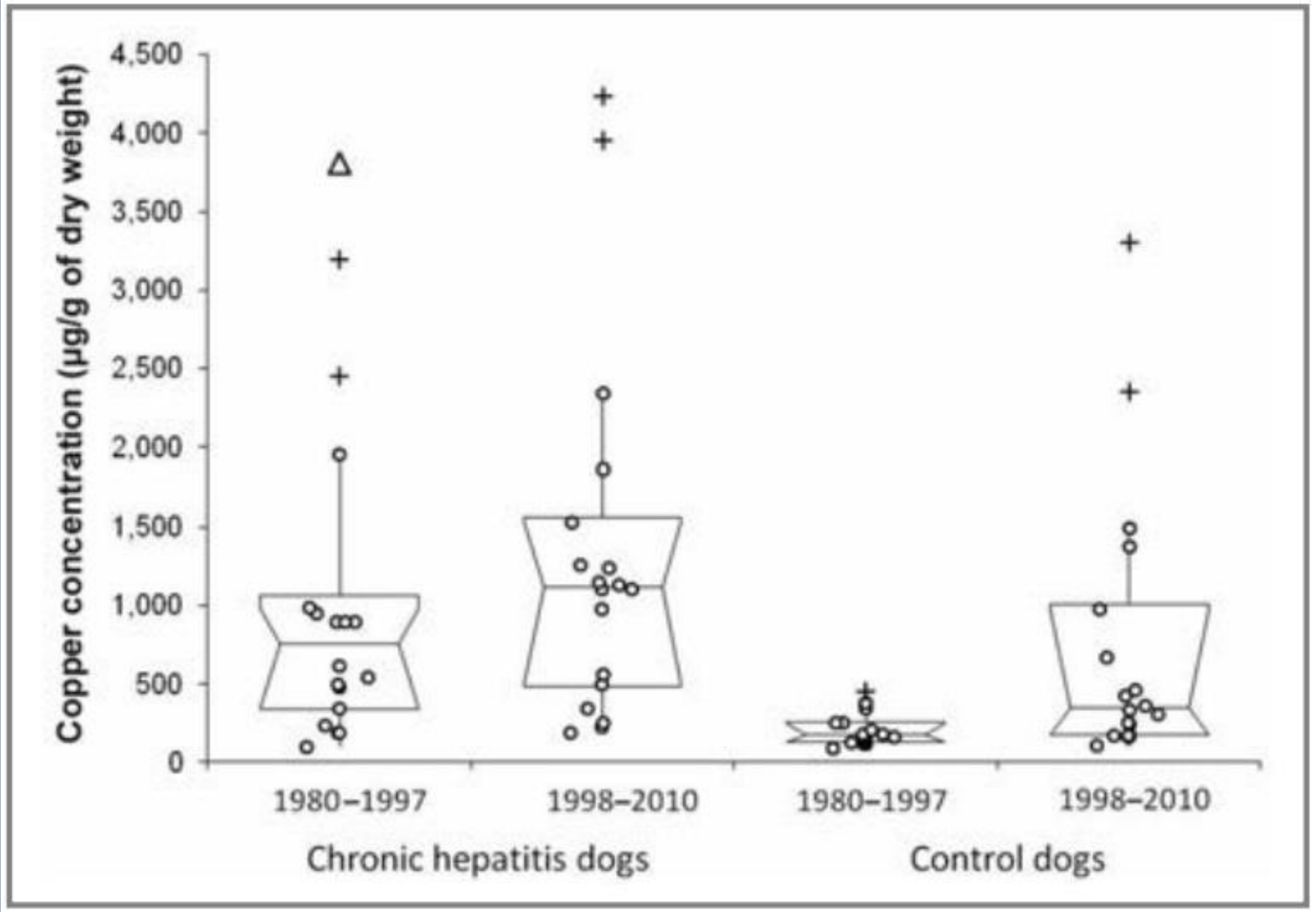
Algumas informações científicas

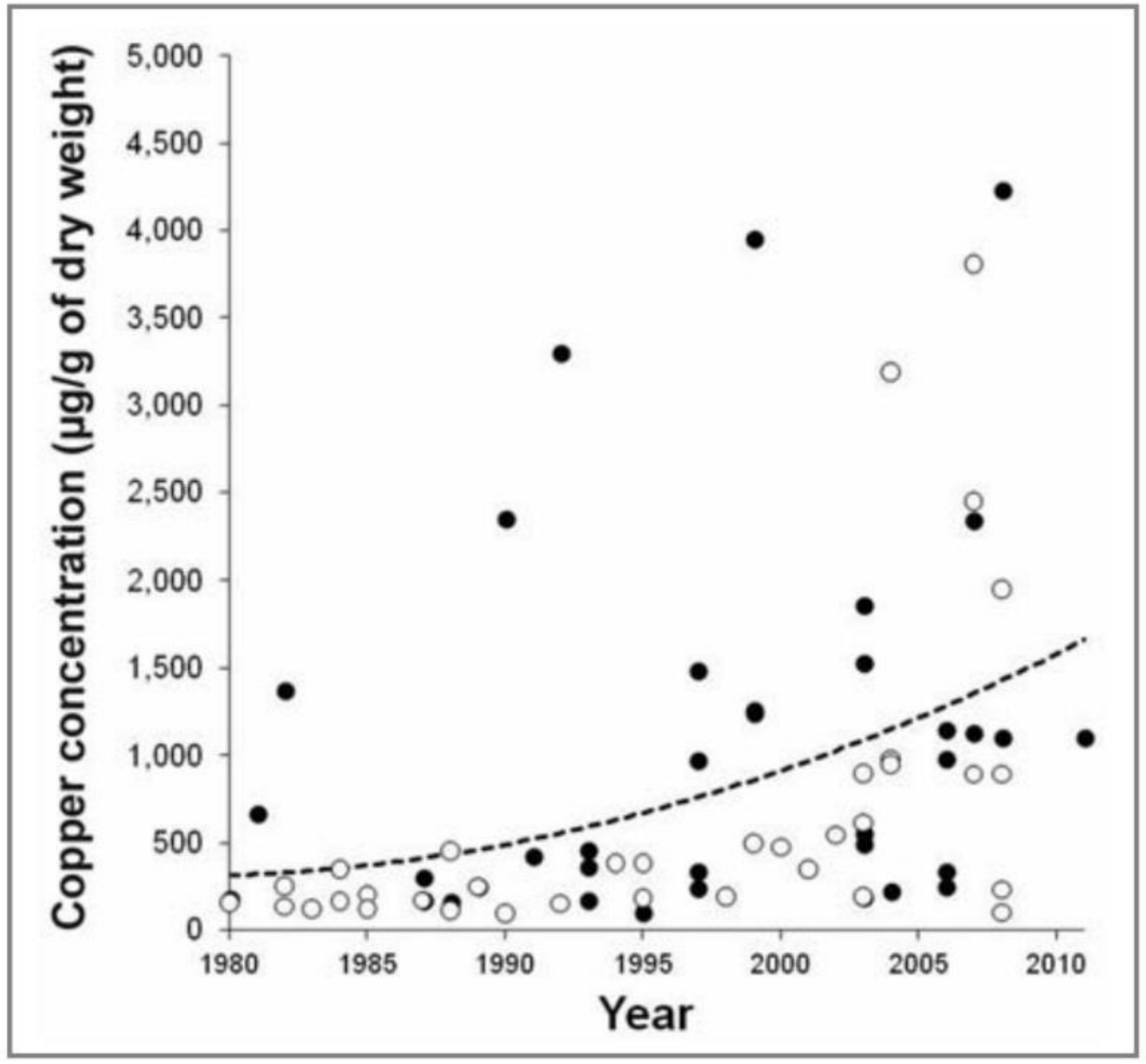
SMALL ANIMALS/ EXOTIC

Hepatic copper concentrations in Labrador Retrievers with and without chronic hepatitis: 72 cases (1980–2010)

Andrea N. Johnston, DVM; Sharon A. Center, DVM; Sean P. McDonough, DVM, PhD; Joseph J. Wakshlag, DVM, PhD; Karen L. Warner

2013





Algumas informações científicas

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WILEY Journal of Veterinary Internal Medicine Open Access

ACVIM American College of Veterinary Internal Medicine

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STANDARD ARTICLE

Hepatic copper concentrations in 546 dogs (1982–2015)

Jaimie M. Strickland DVM[1] | John P. Buchweitz PhD[1] | Rebecca C. Smedley DVM, MS, DACVP[2] | Katherine J. Olstad DVM, DACVP[1#] | Ryan S. Schultz DVM[3#] | N. Bari Oliver DVM, PhD, DACVIM[3] | Daniel K. Langlois DVM, DACVIM[3]

TABLE 2 Proportion of dogs with $[Cu]_H$ exceeding 300 μg/g, 400 μg/g, and 1000 μg/g

		1982–1988	1989–1996	1997–2007	2009–2015[a]
NPB	>300 μg/g	27.5% (25/91)**	N/A	N/A	49.1% (52/106)**
	>400 μg/g	19.8% (18/91)	N/A	N/A	30.2% (32/106)
	>1,000 μg/g	4.4% (4/91)	N/A	N/A	5.7% (6/106)
PB	>300 μg/g	48.2% (41/85)**	N/A	N/A	71.4% (75/105)**
	>400 μg/g	38.8% (33/85)**	N/A	N/A	61.0% (64/105)**
	>1,000 μg/g	10.6% (9/85)***	N/A	N/A	31.4% (33/105)***
LR	>300 μg/g	34.6% (9/26)	36.7% (11/30)***	73.5% (75/102)***	71.0% (71/100)
	>400 μg/g	23.1% (6/26)	29.4% (10/30)*	56.9% (58/102)*	60.0% (60/100)
	>1,000 μg/g	0% (0/26)	3.3% (1/30)*	19.6% (20/102)*	30.0% (30/100)

The percentage of dogs with hepatic copper concentrations >300 μg/g, > 400 μg/g, and > 1000 μg/g for the various breed groupings are presented. The actual number of dogs are in parentheses. LR, Labrador Retrievers; N/A, not available; NPB, non-predisposed breeds; PB, predisposed breeds.

[a] For Labrador Retrievers only, this grouping consisted of the years 2008–2015, not 2009–2015, to allow a more even distribution of cases in the latter 2 periods.

Statistical comparisons were made within each row of data using Fisher exact testing.

*$P < .05$ **$P < .01$ ***$P < .001$

TABLE 3 Hepatic copper concentrations in dogs with and without hepatitis

		1982–1988	2009–2015	P-value
PB dogs	Non-hepatitis	249.2 μg/g (154.8–429.0)	381.6 μg/g (250.3–763.5)	.004
		n = 40	n = 66	
	Hepatitis	404.2 μg/g (191.4–821.1)	1274.0 μg/g (563.0–1773.0)	< .001
		n = 45	n = 39	
NPB dogs	Non-hepatitis	170.0 μg/g (104.3–310.3)	262.5 μg/g (166.0–398.8)	.013
		n = 64	n = 84	
	Hepatitis	181.1 μg/g (129.8–346.1)	542.2 μg/g (270.3–862.3)	.004
		n = 27	n = 22	

Median (IQR) hepatic copper concentrations (μg/g) for both predisposed breed (PB) and non-predisposed breed (NPB) dogs are presented when further stratified by the presence or absence of hepatitis. In the PB population, hepatic copper concentrations were greater in the 2009–2015 period as compared to the 1982–1988 period in both dogs with and without hepatitis. In the NPB population, dogs with hepatitis in the 2009–2015 period also had greater concentrations than dogs with hepatitis in the 1982–1988. The difference in copper concentrations in the 1982–1988 and 2009–2015 periods in NPB dogs without hepatitis was not significant when corrected for multiple comparisons ($P = 0.013$).

Algumas informações científicas

Received: 18 February 2018 | Revised: 5 July 2018 | Accepted: 26 July 2018
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WILEY Journal of Veterinary Internal Medicine Open Access
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STANDARD ARTICLE

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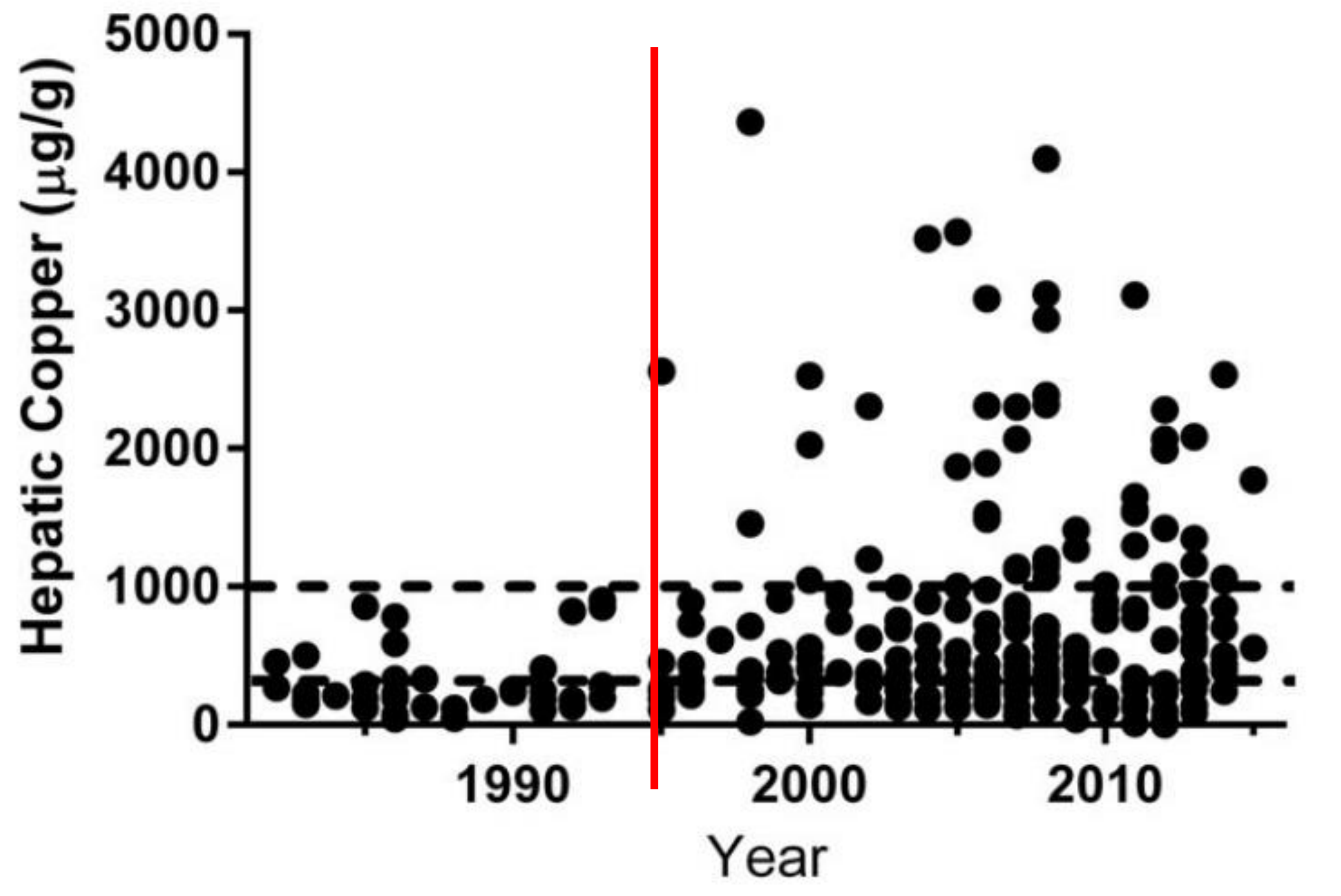
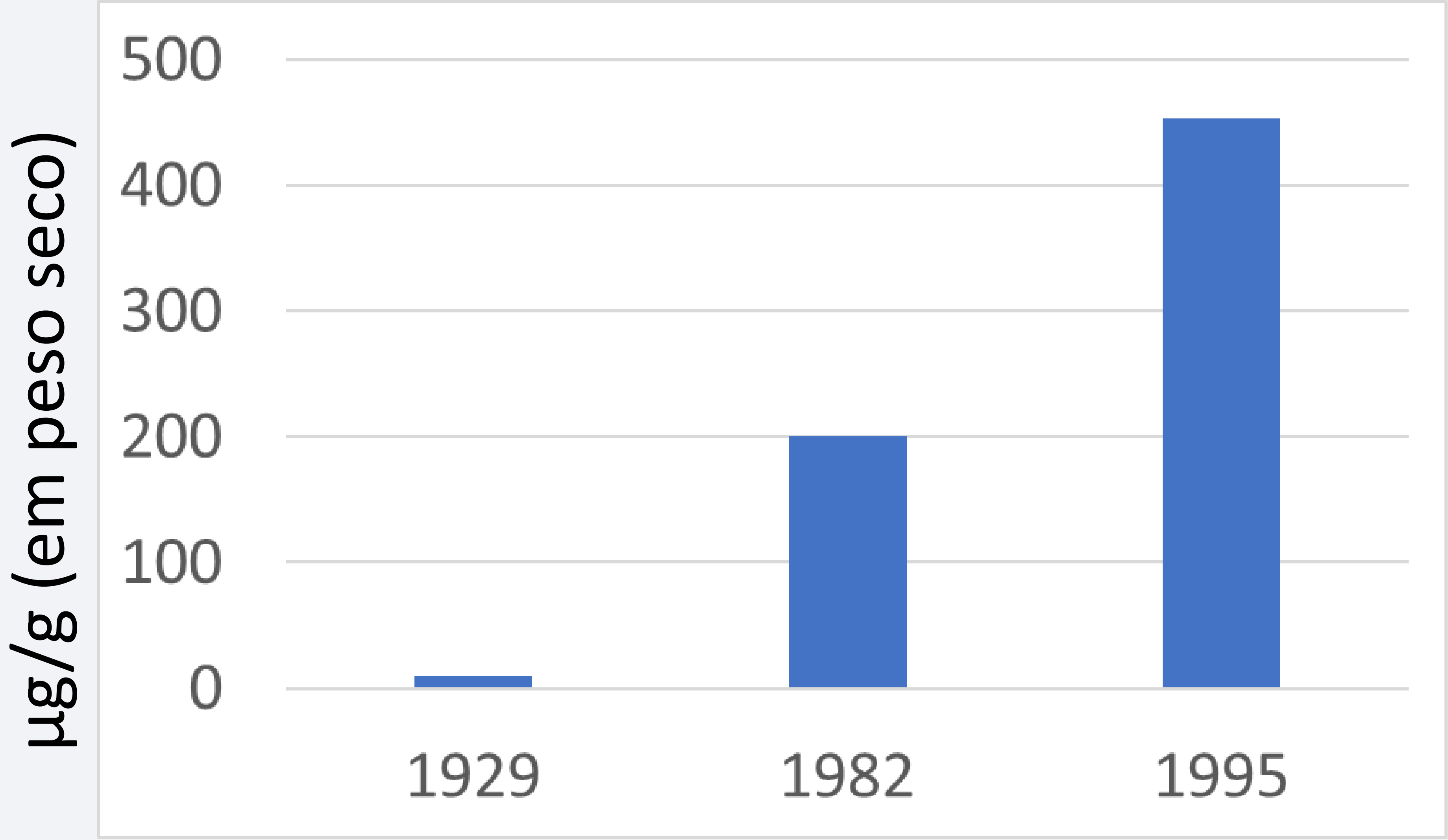


FIGURE 1 Scatterplot of hepatic copper concentrations (µg/g) in Labrador Retrievers from 1982–2015. Black circles represent individual data points. Dashed lines represent hepatic copper concentrations of 300 µg/g and 1000 µg/g. It should be noted that copper concentrations exceeding 1000 µg/g were observed in approximately 25% of Labrador Retrievers undergoing hepatic tissue sampling beginning in the mid to late 1990s

Algumas informações científicas

Concentrações hepáticas médias de cobre em cães ao longo do tempo



Flinn and Inouye, 1929; Meyer and Eggreet, 1932; Beck, 1956; Gumbrell, 1972; Sternlieb et al., 1977; Ludwig et al., 1980; Keen et al., 1981; Hunt et al., 1986; Thornburg et al., 1986; Zentek and Meyer, 1991; Su et al., 1982; Johnston et al., 2013

Suspeita-se que o conteúdo de cobre de vários alimentos comerciais para cães seja superior à necessidade biológica e, até mesmo, exceda a tolerância desses animais

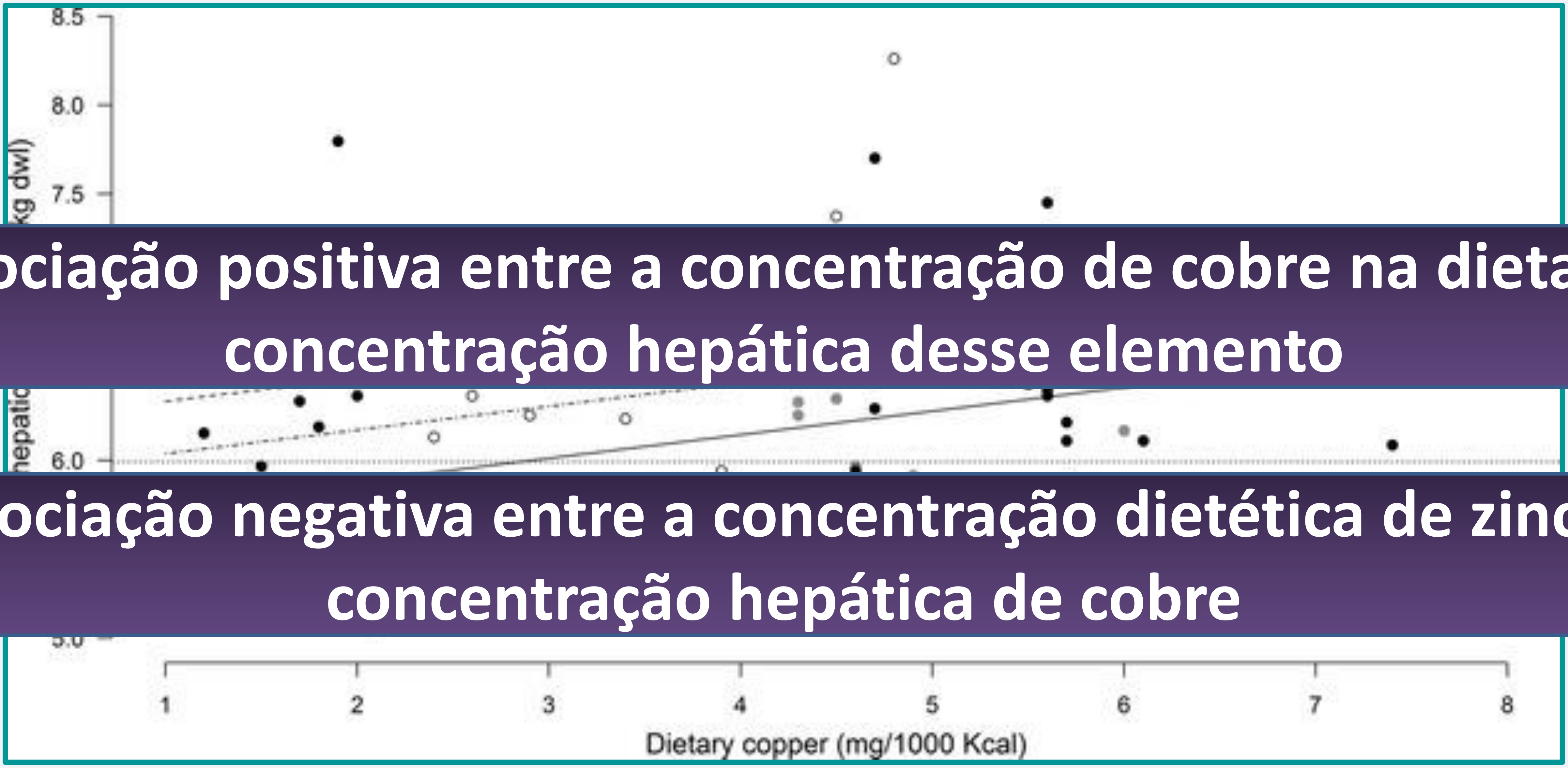
Thornburg, 2000; Hoffmann et al., 2009; Fieten et al., 2012; Gagné et al., 2013; Johnston et al., 2013; Strickland et al., 2018; Center et al., 2021

Associação entre concentrações dietéticas e hepáticas de cobre

J Vet Intern Med 2012

Association of Dietary Copper and Zinc Levels with Hepatic Copper and Zinc Concentration in Labrador Retrievers

H. Fieten, B.D. Hooijer-Nouwens, V.C. Biourge, P.A.J. Leegwater, A.L. Watson, T.S.G.A.M. van den Ingh, and J. Rothuizen



Associação positiva entre a concentração de cobre na dieta e a concentração hepática desse elemento

Associação negativa entre a concentração dietética de zinco e concentração hepática de cobre

Linha tracejada: valor ajustado para uma dieta com teor de zinco de 30 mg/1.000 kcal

Linha pontilhada: valor ajustado para uma dieta com teor de zinco de 50 mg/1.000 kcal

contínua: valores …os para uma dieta com …de zinco de 70 mg/1.000 kcal

Concentrações de cobre em alimentos comerciais

Received: 9 January 2019 | Accepted: 14 February 2019
DOI: 10.1111/jvim.15467

CONSENSUS STATEMENT

Journal of Veterinary Internal Medicine Open Access
ACVIM American College of Veterinary Internal Medicine

Consensus Statements of the American College of Veterinary Internal Medicine (ACVIM) provide the veterinary community with up-to-date information on the pathophysiology, diagnosis, and treatment of clinically important animal diseases. The ACVIM Board of Regents oversees selection of relevant topics, identification of panel members with the expertise to draft the statements, and other aspects of assuring the integrity of the process. The statements are derived from evidence-based medicine whenever possible and the panel offers interpretive comments when such evidence is inadequate or contradictory. A draft is prepared by the panel, followed by solicitation of input by the ACVIM membership which may be incorporated into the statement. It is then submitted to the Journal of Veterinary Internal Medicine, where it is edited prior to publication. The authors are solely responsible for the content of the statements.

ACVIM consensus statement on the diagnosis and treatment of chronic hepatitis in dogs

Cynthia R. L. Webster[1] | Sharon A. Center[2] | John M. Cullen[3] |
Dominique G. Penninck[1] | Keith P. Richter[4] | David C. Twedt[5] | Penny J. Watson[6]

TABLE 3 Dietary copper minimum allowances and copper content of dog foods

	NRC[a] minimum	AAFCO[b] minimum	Average dog food	Hepatic diets[c]
Copper concentration (mg/kg DM/d)	6[d]	7.3[e]	~15-25	~4.9

Abbreviations: AAFCO, Association of American Food Control Officials; DM, dry matter; NRC, National Research Council.

Environ Sci Pollut Res
DOI 10.1007/s11356-017-8541-4

CrossMark

ECOTOXICOLOGY AND TOXICOLOGY: PROBLEMS AND DECISIONS

Trace element measurement for assessment of dog food safety

Elisabete A. De Nadai Fernandes[1] · Camila Elias[1] · Márcio Arruda Bacchi[1] · Peter Bode[2]

2017

Table 1 Minimum and maximum values (mg/kg) of chemical elements measured in adult dog foods ($n = 63$) and puppy dog foods ($n = 32$)

	Adult		Puppy			Adult		Puppy	
	Min	Max	Min	Max		Min	Max	Min	M
Al	<21	11,900	49	8500	I	0.9	14	0.7	[illegible]
As	<0.13	0.43	<0.14	0.56	La	<0.02	3.32	<0.02	[illegible]
Br	2.05	16.90	3.10	15.42	Mn	6.0	111	16	149
Cd	<1.1	<2.4	<1.1	<2.4	Rb	5.67	25.04	6.50	[illegible]
Co	0.08	0.82	0.08	0.75	Sb	<0.01	5.04	<0.01	[illegible]
Cr	<0.20	4.33	<0.20	8.27	Sc	0.01	1.41	0.01	[illegible]
Cs	0.02	0.17	0.02	0.19	Ti	<9.0	2300	<9.0	[illegible]
Cu	9.0	60	15	64	U	<0.13	2.25	<0.13	[illegible]
Fe	177	862	198	675	V	<0.17	4.88	<0.12	3.24
Hg	<0.05	<0.10	<0.05	<0.10	Zn	44	554	46	614

Results expressed in dry mass

Recomendação FEDIAF (2021): 7,2-8,3 mg/kg

Limite legal FEDIAF (2021): 28 mg/kg

Talanta 108 (2013) 157–164

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Talanta

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ELSEVIER

talanta

Multivariate optimization of an analytical method for the analysis of dog and cat foods by ICP OES

Silvânio Silvério Lopes da Costa [a,b], Ana Cristina Lima Pereira [a], Elisangela Andrade Passos [a], José do Patrocínio Hora Alves [a,c], Carlos Alexandre Borges Garcia [a], Rennan Geovanny Oliveira Araujo [a,*]

Table 7

Concentrations of Al, Ba, Ca, Cu, Fe, K, Mg, Mn, P, S, Sr, and Zn determined in dog foods by ICP OES, and minimum and maximum concentrations permitted by regulatory agencies.

Food	Moisture (%)	Flavor	Al/mg kg^{-1}	Ba/mg kg^{-1}	Ca/g kg^{-1}	Cu/mg kg^{-1}	Fe/mg kg^{-1}	K/g kg^{-1}	Mg/g kg^{-1}	Mn/mg kg^{-1}	P/g kg^{-1}	S/g		
Dog food (1)	10	Meat and bones	236 ± 6	25.1 ± 1.7	2.3 ± 0.2	15.5 ± 1.7	606 ± 13	1.3 ± 0.2	0.33 ± 0.03	92.3 ± 3.6	2.4 ± 0.2	0.3		
Dog food (2)	8	Meat and vegetables	2835 ± 8	24.6 ± 3.7	2.5 ± 0.1	26.5 ± 0.4	421 ± 13	1.2 ± 0.05	0.23 ± 0.01	13.7 ± 4.3	2.2 ± 0.1	0.52 ± 0.004	21,1 ± 1.2	106 ± 5
Dog food (3)	9	Meat	45.5 ± 6.4	24.2 ± 1.1	2.4 ± 0.3	17.4 ± 0.3	337 ± 7	1.0 ± 0.02	0.25 ± 0.01	93.2 ± 4.6	2.2 ± 0.2	0.38		
Dog food (4)	8	Meat and vegetables	475 ± 10	21.5 ± 4.0	2.7 ± 0.3	22.2 ± 0.8	147 ± 7	1.0 ± 0.1	0.14 ± 0.01	6.5 ± 1.0	2.2 ± 0.2	0.4		
Dog food (5)	10	Cereals	54.0 ± 5.7	7.1 ± 0.8	1.6 ± 0.2	34.1 ± 3.2	595 ± 8	1.1 ± 0.2	0.16 ± 0.02	149 ± 12	2.3 ± 0.2	0.7		
Minimum allowable concentration			***	***	6.0[a]	7.3[a]	80.0[a]	6.0[a]	0.4[a]	5.0[a]	5.0[a] 0.6[b]	***		
Maximum allowable concentration			***	***	25.0[a] 2.4[B]	250[a]	3000[a]	***	3.0[a]	***	16.0[a]	***		

[a] Values established by AAFCO.
[b] Values established by MAPA.

Recomendação FEDIAF (2021): 7,2-8,3 mg/kg

Limite legal FEDIAF (2021): 28 mg/kg

Journal of Consumer Protection and Food Safety
https://doi.org/10.1007/s00003-018-1178-5

Journal of Consumer Protection and Food Safety
Journal für Verbraucherschutz und Lebensmittelsicherheit

RESEARCH ARTICLE

CrossMark

Risk assessment of 22 chemical elements in dry and canned pet foods

Ana Carolina Cavalheiro Paulelli[1] · Airton Cunha Martins Jr[1] · Eloísa Silva de Paula[1,2] · Juliana Maria Oliveira Souza[1] · Maria Fernanda Hornos Carneiro[1] · Fernando Barbosa Júnior[1] · Bruno Lemos Batista[1,3]

2018

Table 1 Levels (mean ± SD (min–max)) of essential elements in pet food (dry and canned) and their respective recommended concentration

Element	Dry food		Canned food		Minimum recommended[a]	Maximum limit[a]
	Dog	Cat	Dog	Cat		
Fe (mg/kg)	362 ± 42.6 (223–680)	384 ± 102 (149–535)	910 ± 544 (380–2032)**	896 ± 618 (254–1913)**	D: 36[b]/40[a] C: 80[a,b]	D/C: 1420[b]
Zn (mg/kg)	133 ± 8.79 (125–142)	167 ± 64 (91.5–351)	235 ± 66 (125–316)**	158 ± 67 (92–254)	D: 72[b]/ 80[a] C: 75[a,b]	NA
Mn (mg/kg)	37.8 ± 7.86 (29.9–45.7)*	25.9 ± 12.5 (4.3–44.9)	23.2 ± 12.8 (5.8–39.8)	37.3 ± 16.1 (14.3–60)	D: 5.0[a]/ 5.8[b] C: 5.0[b]/ 7.6[a]	D/C: 170[b]
Cu (mg/kg)	15.8 ± 1.19 (14.6–17)	16.5 ± 3.8 (7.7–20.9)	25.7 ± 15.4 (10.0–45.6)**	20.1 ± 12.0 (8.5–41.3)	D: 7.2[b]/ 7.3[a] C: 5.0[a,b]	C: 28[b]
Rb (mg/kg)	11.5 ± 0.87 (10.6–12.3)	10.3 ± 2.3 (5.8–12.8)	14.0 ± 1.5 (12.1–16.2)	8.9 ± 4.2 (3.1–15.1)	NA	NA
Mo (mg/kg)	0.87 ± 0.06 (0.319–1.69)	0.88 ± 0.38 (0.38–1.6)	1.1 ± 0.25 (0.79–1.4)	0.80 ± 0.3 (0.45–1.2)	NA	NA
Se (mg/kg)	0.56 ± 0.05 (0.51–0.61)	0.74 ± 0.36 (0.34–1.8)	1.5 ± 0.19 (1.2–1.8)**	1.2 ± 0.43 (0.58–1.9)**	D: 0.30[b]/ 0.35[a] C: 0.3[a,b]	D: 0.5[b]/2.0[a] C: 0.57[b]
V (mg/kg)	0.38 ± 0.05 (0.33–0.43)	0.27 ± 0.19 (0.10–0.77)	0.37 ± 0.16 (0.25–0.69)	0.3 ± 0.07 (0.17–0.46)	NA	NA
Cr (mg/kg)	5.1 ± 0.4 (4.7–5.5)	5.1 ± 0.4 (4.3–5.9)	6.1 ± 0.4 (5.3–6.7)	5.1 ± 0.7 (3.8–6.0)	NA	NA
Co (mg/kg)	0.14 ± 0.02 (0.12–0.16)	0.13 ± 0.06 (0.053–0.308)	0.12 ± 0.08 (0.06–0.29)	0.1 ± 0.05 (0.04–0.2)	NA	NA
Mg (g/kg)	1.6 ± 0.13 (0.58–7.2)**	1.5 ± 0.57 (0.61–2.4)*	0.68 ± 0.11 (0.51–0.87)	0.74 ± 0.20 (0.54–1.1)	D: 0.6[a]/ 0.7[b] C: 0.4[a,b]	NA
Ca (g/kg)	14.1 ± 1.2 (5.6–31.7)**	15.6 ± 7.5 (7.0–36.8)**	6.8 ± 2.9 (2.5–10.7)	7.0 ± 2.4 (3.6–12.0)	D: 5.0[a,b] C: 6.0[a,b]	D: 25[b]/18[a]
P (g/kg)	15.8 ± 5.1 (7.1–33.3)*	18.9 ± 7.2 (9.7–36.5)*	13.9 ± 2.9 (8.8–19.0)	13.6 ± 3.1 (9.6–19.3)	D: 4.0[a,b] C: 5.0[a,b]	D: 16.0[a,b]

D dog, *C* cat, *NA* not available

*p < 0.05, **p < 0.01. Asterisks indicate differences when comparing the levels of the elements obtained in canned versus dry food and vice versa

[a]AAFCO (2003)

[b]FEDIAF (2011)

Recomendação FEDIAF (2021): 7,2-8,3 mg/kg

Limite legal FEDIAF (2021): 28 mg/kg

SCIENTIFIC REPORTS

OPEN

Mineral analysis of complete dog and cat foods in the UK and compliance with European guidelines

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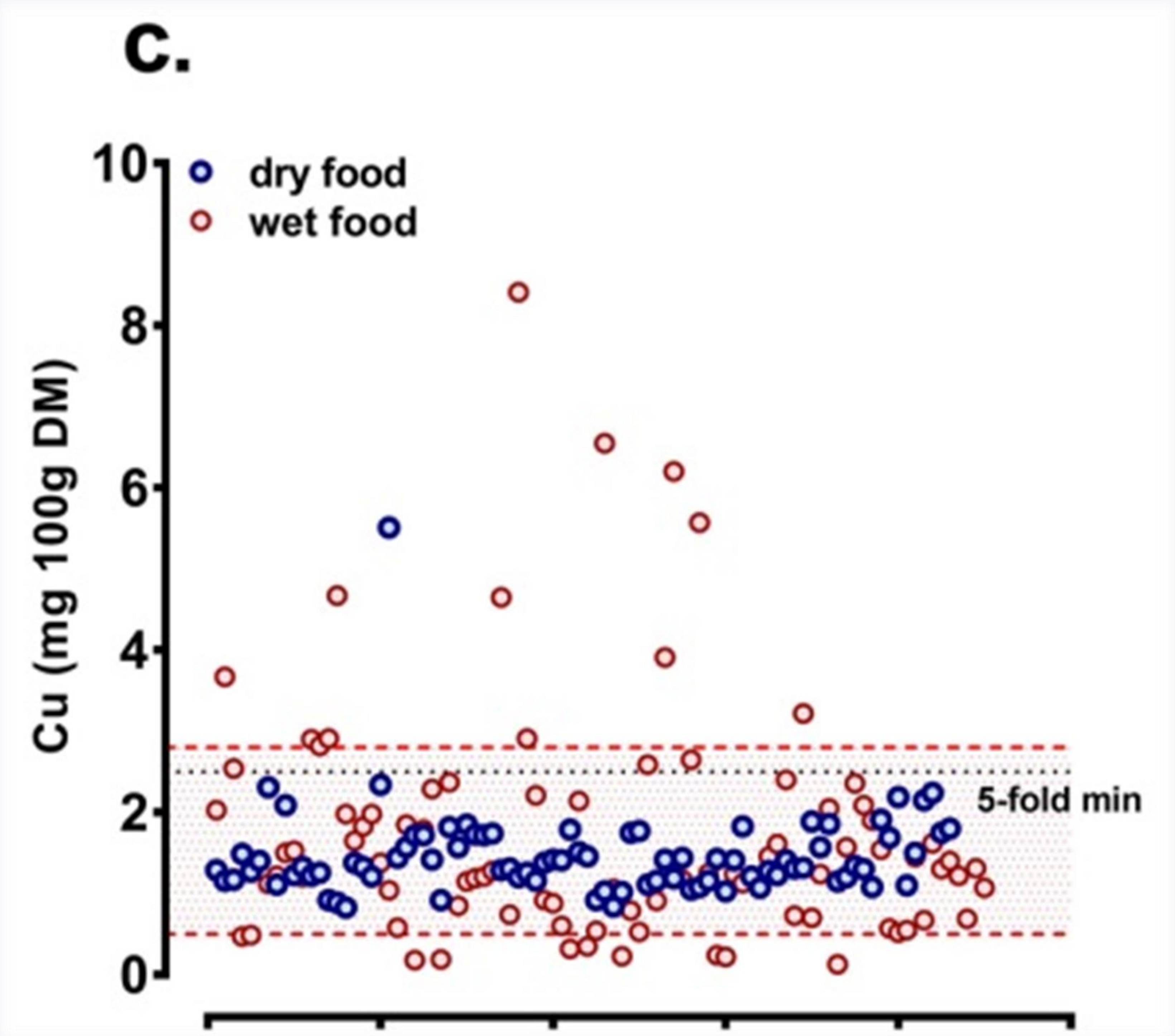
M. Davies[1,2], R. Alborough[1], L. Jones[1], C. Davis[1], C. Williams[1] & D. S. Gardner[1]



Maiores concentrações em alimentos para gatos

Table 1. Copper and zinc concentrations (mg/kg DM) in commercial dog and cat food, and comparison with the legal limit values of European Union legislation (Regulation 1831/2003/EC).

	Dog foods		Cat foods	
	Copper	Zinc	Copper	Zinc
Limite legal (mg/kg)	28	227	28	227
Mean ± SD	23.05 ± 13.67	182.12 ± 76.21	26.32 ± 19.50	173.54 ± 78.00
minimum - maximum	0- 103,65	53,4 - 322,56	0 - 87,44	21,15 - 349,35
Coefficient of variation	0,59	0,42	0,74	0,45
% above the legal limit (n)	20,83 (15)	26,39 (19)	28,57 (8)	14,29 (4)
% samples with detection (n)	97,22 (70)	100 (72)	89,29 (25)	100 (28)

Legenda: SD= standard deviation.

Table 2- Comparison of copper and zinc conce... s for dogs and cats.

Element	Dry dog foods	SEM	Dry cat ... s	SEM	*P*
Copper	24.0047	0.6273	33.7996	1.5538	<0.0001
Zinc	182.57	1.73	195.08	3.7329	0.0027

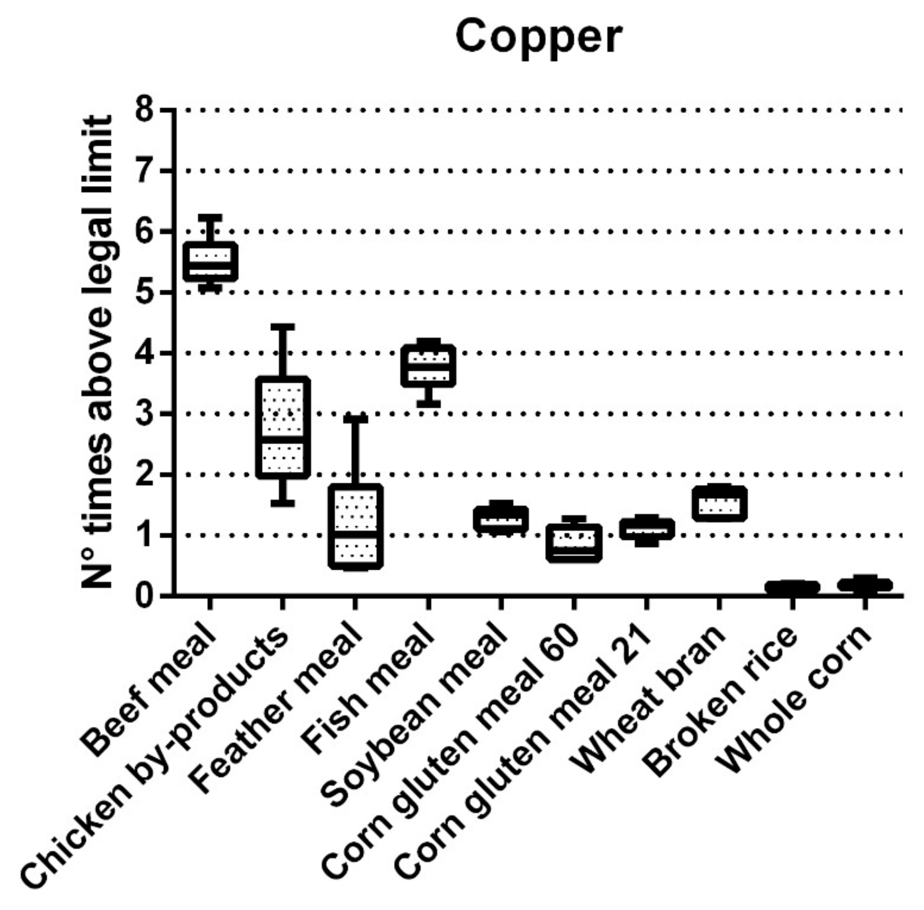
Legend: SEM: standard error of mean; P=probability of significance

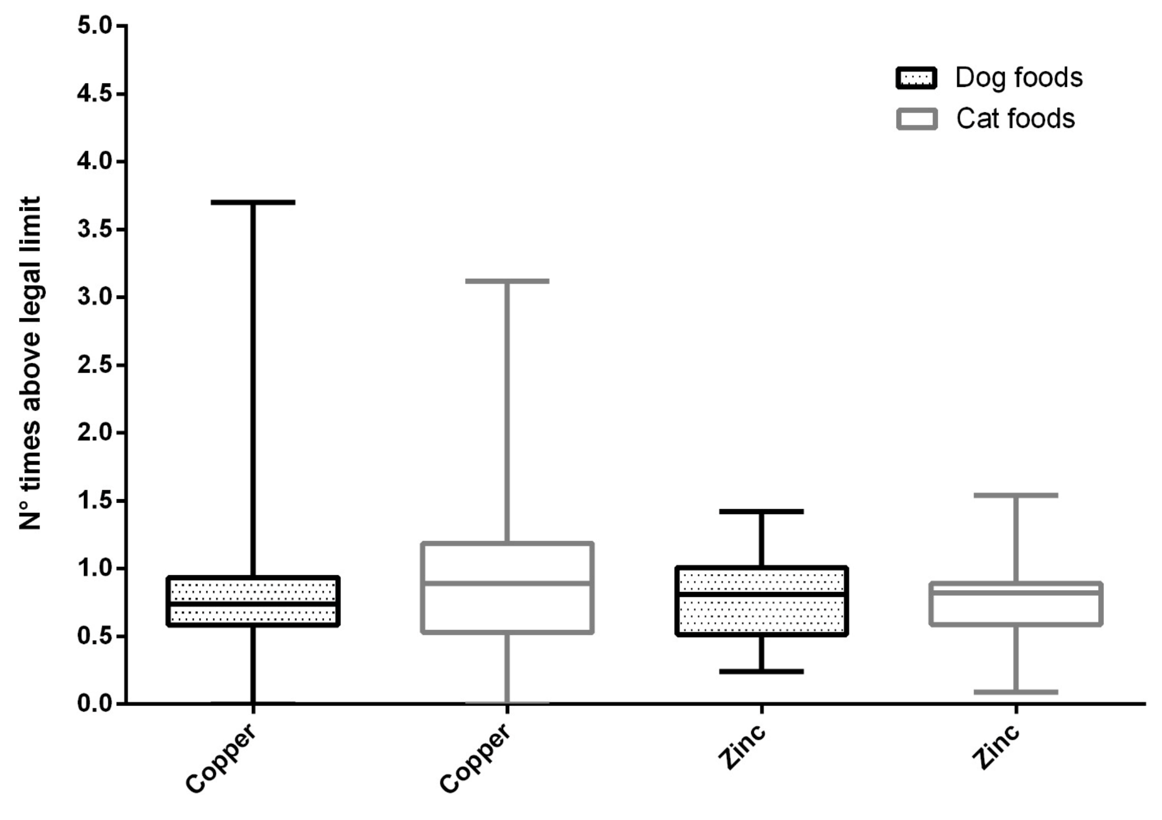
Table 4- Comparison of copper and zinc concentrations (mg/kg) between the different categories of dry dog foods.

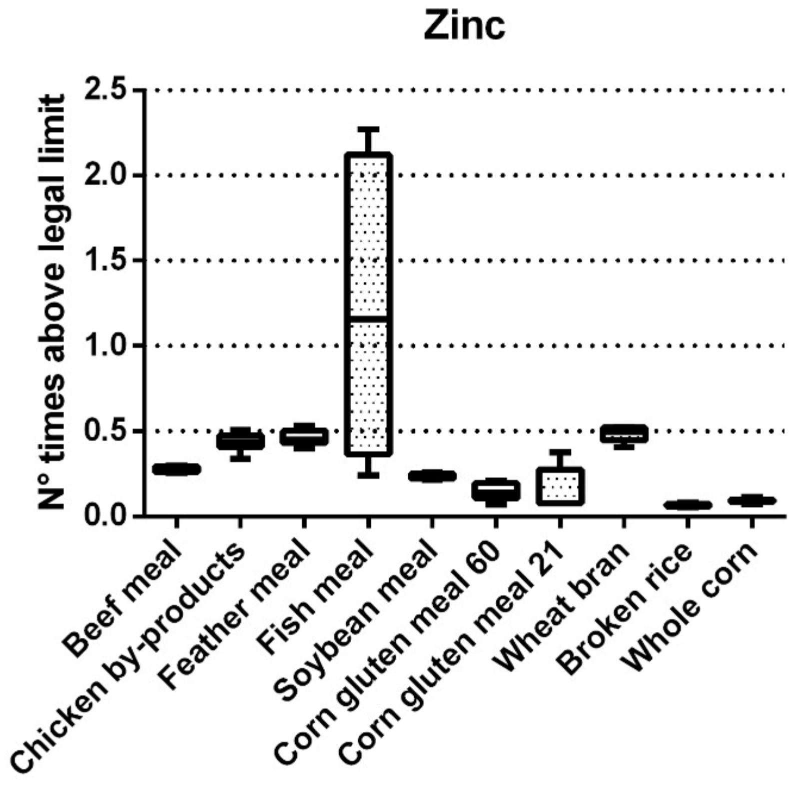
Element	Standard	SEM	Premium	SEM	Super premium	SEM	*P*
Copper	17.0288 [c]	0.9726	23.9083 [b]	1.0196	30.4325 [a]	1.2335	<0.0001
Zinc	134.67 [c]	2.7353	182.12 [b]	2.8139	226.18 [a]	3.3629	<0.0001

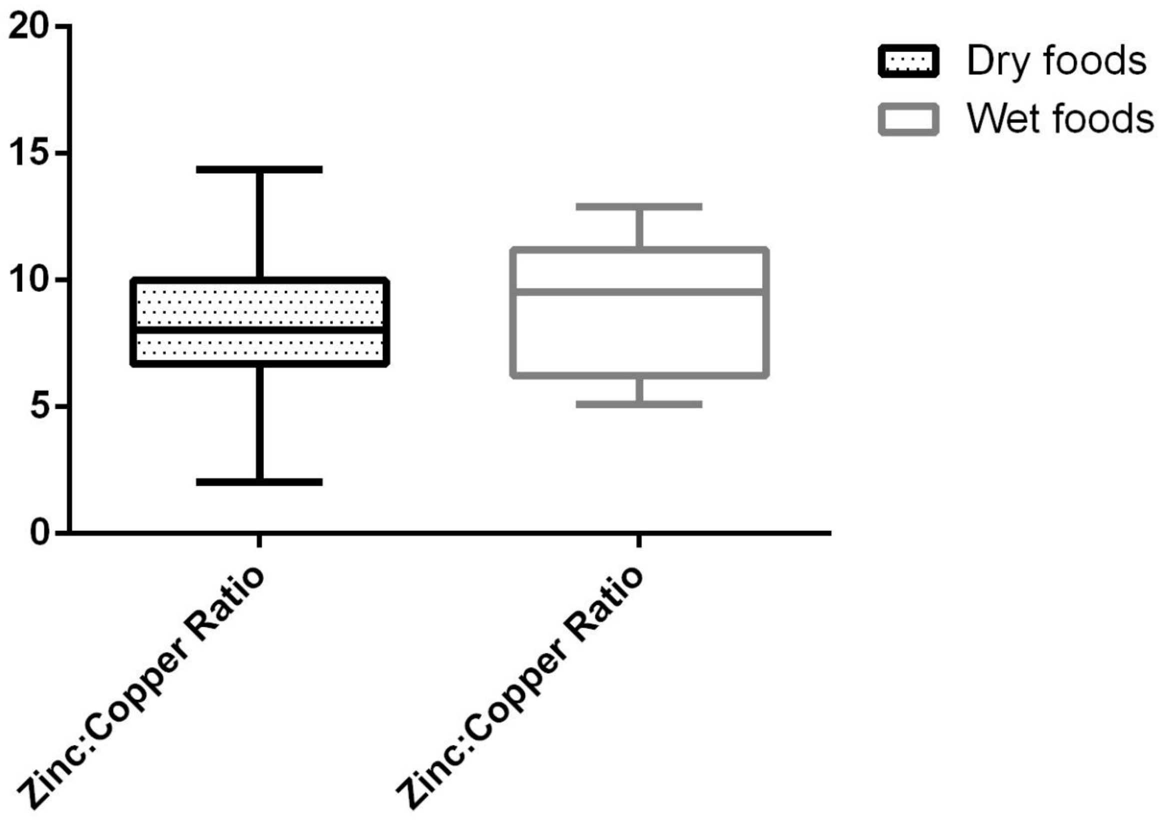
Legend: SEM: standard error of mean; P=probability of significance; [a-b] Averages followed by different letters on the lines differ (P<0,05).

Zafalon et al. (2020)







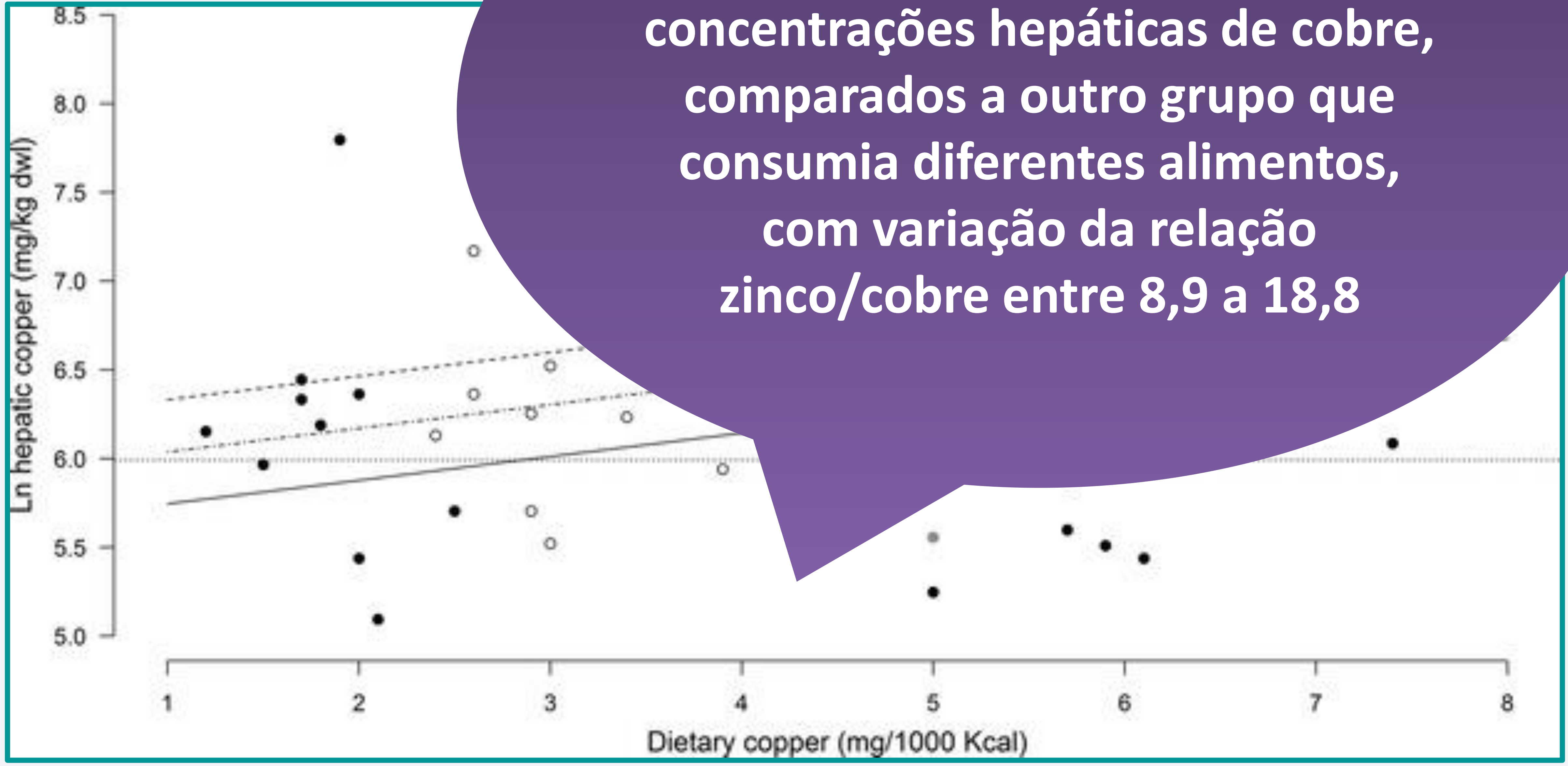


Zafalon et al. (2020)

J Vet Intern Med 2012

Association of Dietary Copper and Zi... with Hepatic
Copper and Zinc Concen... ...ers

H. Fieten, B.D. Hooijer-N...
T.S...



Relação zinco/cobre de 32,5 - apresentaram menores concentrações hepáticas de cobre, comparados a outro grupo que consumia diferentes alimentos, com variação da relação zinco/cobre entre 8,9 a 18,8

Table 8- Copper and zinc concentrations (mg/kg) in mineral supplements.

Element	Sodium chloride 1	Sodium chloride 2	Potassium chloride 1	Potassium chloride 2	Calcium carbonate	Dicalcium phosphate
Copper	<0.05	<0.05	<0.05	<0.05	16.62	505.19
Zinc	<0.05	<0.05	<0.05	<0.05	2.51	100.23

Zafalon et al. (2020)

Fatores que contribuem para altas concentrações de cobre nos alimentos

- Utilização de grande quantidade de ingredientes com alto teor de cobre
- Poluição ambiental
- Aditivos
- Adição de cobre sem levar em consideração o teor já existe nos ingredientes

Viewpoint

Is it time to reconsider current guidelines for copper content in commercial dog foods?

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Unfortunately, the true copper content of a pet food cannot be reliably ascertained simply by reading the food label. It appears that many manufacturers include premixes to ensure that their diets comply with AAFCO's minimum nutrient content recommendations; however, they may do so without taking into account native copper already in the baseline diet. Also, even if the copper content is referenced on a food label, the wide bioavailability of copper from natural ingredients complicates determining the true copper intake.

Hepatite crônica associada ao cobre

Lesão tóxica mais comum

mation on the pathophysiology, diagnosis, and treatment of clinically important animal diseases. The ACVIM Board of Regents oversees selection

Pode se desenvolver em qualquer raça, incluindo raças mistas, mas o Bedlington Terrier (BT), dálmata, Labrador Retriever (LR), Doberman Pinscher e West Highland White Terrier são mais predispostos

O acúmulo hepático de Cu anormal resulta da excreção hepática alterada de Cu na bile, ingestão excessiva de Cu ou ambas

Quando o Cu excede a capacidade de transporte nos hepatócitos e a capacidade de ligação a outras moléculas, o Cu livre causa estresse oxidativo, levando à degeneração hepatocelular e morte celular com inflamação hepática aguda ou crônica ou ambas

Excreção alterada de Cu pode estar associada a mutações genéticas nas proteínas transportadoras de Cu no fígado

TABLE 2 Factors implicated in the etiology of chronic hepatitis (CH) in dogs and the consensus panel's opinion on the relative strength of evidence (strong, moderate, or weak) based on both the scientific literature and clinical experience

Etiology	Evidence	References
Immune	Moderate-strong	(see Table 5)
Toxic		
Copper	Strong	Many (6–46)
Metabolic		
Protoporphyria	Moderate (but rare)	Kroeze (47)
alpha-1-anti-trypsin	Weak	Sevelius (48)
Infectious		
Leptospirosis	Moderate	Bishop (49) Adamus (50) McKallum (51)
Leishmaniasis	Moderate-strong	Gonzalez (52) Rallis (53)
Rickettsial	Weak	Egenvall (54) Mylonakis (55) Frank (56) Harrus (57) Nair (58) Hildebrandt (59) De Castro (60)
Mycobacteria	Moderate	Campora (61) Martinho (62) Naughton (63) Turinelli (64) Rocha (65)
Histoplasmosis	Moderate	Chapman (66) Bromel (67)
Protozoal (Neospora, Sarcocystis, Toxoplasma)	Moderate	Allison (68) Dubey (69) Fry (70) Hoon-Hanks (71) Magana (72) Dubey (73)
Bartonella	Weak	Gillepsie (74) Saunders (75)
Viral	Negligible	Bexfield (76) Boomkins (77) Rakich (78) Van der Laan (79)

Ainda mais preocupante em raças predispostas à HAC





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www.elsevier.com/locate/jhep

The ubiquitously expressed MURR1 protein is absent in canine copper toxicosis

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© 1999 Oxford University Press Human Molecular Genetics, 1999, Vol. 8, No. 3 501–507

Genetic mapping of the copper toxicosis locus in Bedlington terriers to dog chromosome 10, in a region syntenic to human chromosome region 2p13–p16

Bart J. A. van de Sluis, Matthew Breen[3], Manoj Nanji[4], Monique van Wolferen[1], Pieter de Jong[5], Matthew M. Binns[3], Peter L. Pearson, Jeroen Kuipers[2], Jan Rothuizen[1], Diane W. Cox[4], Cisca Wijmenga* and Bernard A. van Oost[1]

SHORT COMMUNICATIONS

Copper-induced hepatitis in an Anatolian shepherd dog

J. T. BOSJE, T. S. G. A. M. VAN DEN INGH, A. FENNEMA, J. ROTHUIZEN

Received: 19 September 2018 | Accepted: 14 May 2019
DOI: 10.1111/jvim.15536
Journal of Veterinary Internal Medicine ACVIM Open Access

STANDARD ARTICLE

Association of the canine *ATP7A* and *ATP7B* with hepatic copper accumulation in Dobermann dogs

Xiaoyan Wu[1] | Paul J. J. Mandigers[1] | Adrian L. Watson[2] | Ted S. G. A. M. van den Ingh[3] | Peter A. J. Leegwater[1] | Hille Fieten[1]

© 2002 Oxford University Press Human Molecular Genetics, 2002, Vol. 11, No. 2 165–173

Identification of a new copper metabolism gene by positional cloning in a purebred dog population

Bart van de Sluis, Jan Rothuizen[1], Peter L. Pearson, Bernard A. van Oost[1] and Cisca Wijmenga*

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Case Report Rapport de cas

Copper-associated hepatitis in a Pembroke Welsh corgi

Jean Rifkin, Matthew D. Miller

Human Genetics (2019) 138:541–546
https://doi.org/10.1007/s00439-019-02010-y

ORIGINAL INVESTIGATION

Predicting copper toxicosis: relationship between the ATP7A and ATP7B gene mutations and hepatic copper quantification in dogs

Sharon Pindar[1] · Christina Ramirez[2]

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© Springer-Verlag GmbH Germany, part of Springer Nature 2019

J Vet Intern Med 2002;16:665–668

Copper-Associated Liver Disease in Dalmatians: A Review of 10 Dogs (1998–2001)

Craig B. Webb, David C. Twedt, and Denny J. Meyer

Received: 27 July 2022 | Revised: 25 February 2023 | Accepted: 2 March 2023
DOI: 10.1002/vetr.2832
VetRecord

ORIGINAL RESEARCH

Copper toxicosis in Bedlington terriers is associated with multiple independent genetic variants

Susan Haywood[1] | June Swinburne[2] | Ellen Schofield[3] | Fernando Constantino-Casas[4] | Penny Watson[4]

Vet. Pathol. 27:81–88 (1990)

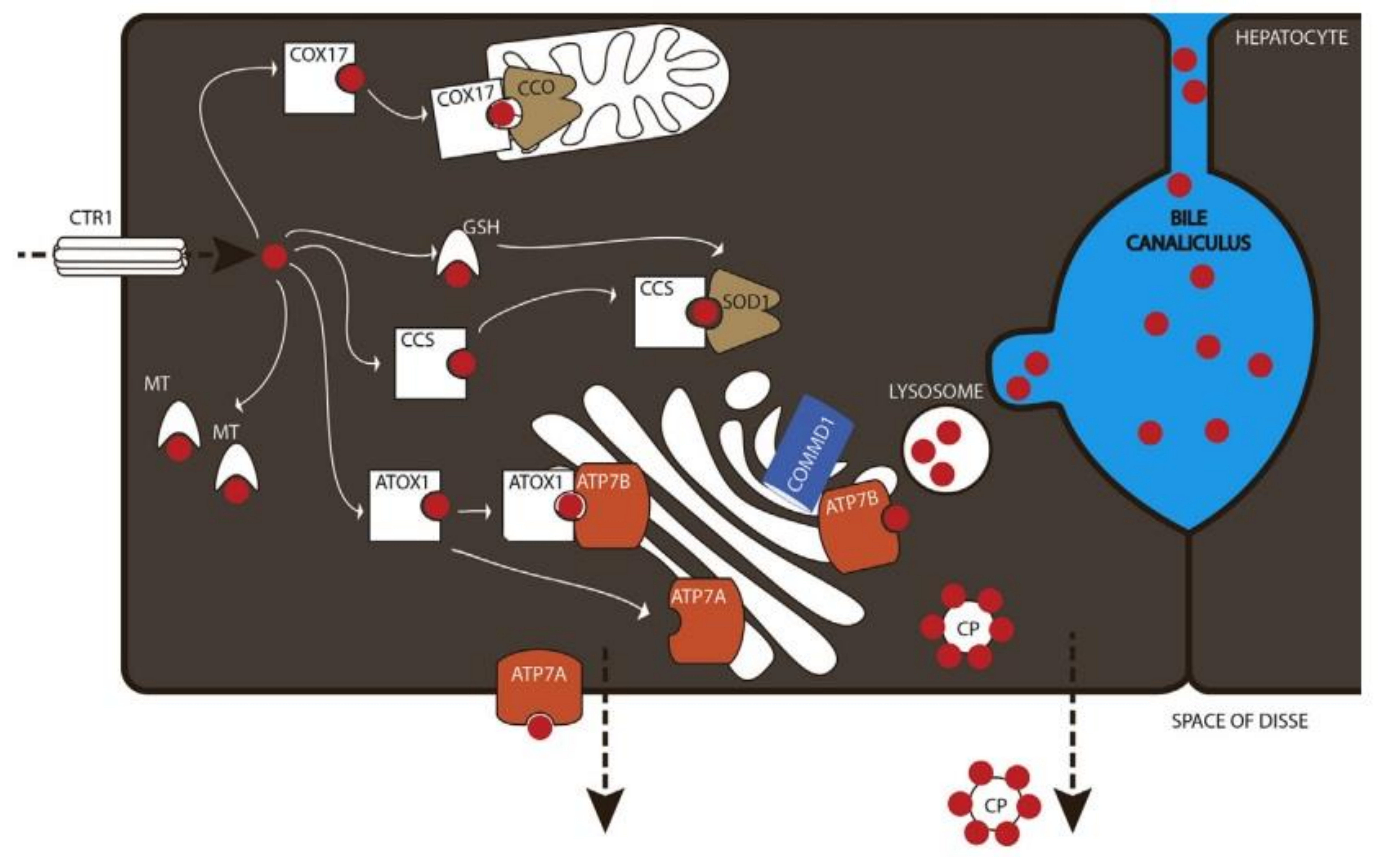
Hepatic Copper Concentrations in Purebred and Mixed-breed Dogs

L. P. THORNBURG, G. ROTTINGHAUS, M. MCGOWAN, K. KUPKA, S. CRAWFORD, AND S. FORBES

Vet. Pathol. 25:408–414 (1988)

Hepatitis and Copper Accumulation in Skye Terriers

S. HAYWOOD, H. C. RUTGERS, AND M. K. CHRISTIAN
Department of Veterinary Pathology and Small Animal Hospital, University of Liverpool, Liverpool; and Chester Road, Kelsall, Cheshire, UK


HEPATOCYTE
COX17
COX17
CCO
CTR1
GSH
BILE
CANALICULUS
CCS
CCS
SOD1
MT
MT
LYSOSOME
COMMD1
ATOX1
ATOX1
ATP7B
ATP7B
ATP7A
ATP7A
CP
SPACE OF DISSE
CP

Recomendações de cobre para cães

Mudanças das recomendações para adição de cobre em alimentos

Czarnecki-Maulden et al. (1993)

Óxido de cobre (1,7 ou 4,7 mg/1.000 kcal)

Redução nas concentrações séricas de cobre e hemoglobina em 16 semanas

Sulfato de cobre (1,9 mg/1.000 kcal)

Não desenvolvimento de anemia

Sulfato de cobre (2,7 mg/1.000 kcal) → Sem diminuição nas concentrações séricas de cobre

Valores extrapolados da necessidade de cadelas gestantes e lactantes >> ingestão recomendada para manutenção estimada em 0,1 mg Cu/kg PC/dia (0,2 mg/kg $PC^{0,75}$/dia) , assumindo uma biodisponibilidade de Cu de 30% (Meyer, 1984; Meyer et al., 1985)

TABLE 15-5 (continued)

Nutrient	Minimal Requirement									...nit		
	Amt./ kg DM (≡4,000 kcal)[a]	Amt./ 1,000 kcal ME[b]	... BW								...nt./ ...,000 kcal ME[b]	Amt./ kg $BW^{0.75}$
Sodium (mg)	300	75	9.85									
Potassium (g)												
Chloride (mg)				1,200						23.5 g		
Iron (mg)[g]				30			30	7.5	1.0			
Copper (mg)[g]				6		0.2	6	1.5	0.2			
Zinc (mg)				60	15	2.0	60	15	2.0			
Manganese (mg)				4.8	1.2	0.16	4.8	1.2	0.16			
Selenium (μg)				350	87.5	11.8	350	87.5	11.8			
Iodine (μg)	700	175	23.6				880	220	29.6	≥ 4 mg		
Vitamins												
Vitamin A (RE)[h]				1,212	303	40	1,515	379	50	64,000[h]	16,000[h]	2,099[h]
Cholecalciferol (μg)[i]				11.0	2.75	0.36	13.8	3.4	0.45	80	20	2.6
Vitamin E (α-tocopherol) (mg)[j]				24	6.0	0.8	30	7.5	1.0			
Vitamin K (Menadione) (mg)[k]				1.3	0.33	0.043	1.63	0.41	0.054			
Thiamin (mg)				1.8	0.45	0.059	2.25	0.56	0.074			
Riboflavin (mg)	4.2	1.05	0.138				5.25	1.3	0.171			
Pyridoxine (mg)				1.2	0.30	0.04	1.5	0.375	0.049			
Niacin (mg)				13.6	3.4	0.45	17.0	4.25	0.57			
Pantothenic Acid (mg)				12	3.0	0.39	15	3.75	0.49			
Cobalamin (μg)				28	7	0.92	35	8.75	1.15			
Folic Acid (μg)				216	54	7.1	270	67.5	8.9			
Biotin[l]												
Choline (mg)				1,360	340	45	1,700	425	56			

NRC (2006)

TABLE III-3$_b$.

Recommended nutrient levels for complete dog food
Unit per 1000 kcal of metabolisable energy (ME)

Nutrient	UNIT	Minimum Recommended Level				Maximum
		Adult based on MER of		Early Growth (< 14 weeks) & Reproduction	Late Growth (≥ 14 weeks)	(L) = EU legal limit (given only on DM basis, see table III-3$_a$) (N) = nutritional
		95 kcal/kg$^{0.75}$	110 kcal/kg$^{0.75}$			
Trace elements*						
Copper*	mg	2.08	1.80	2.75	2.75	(L)
Iodine*	mg	0.30	0.26	0.38	0.38	(L)
Iron*	mg	10.40	9.00	22.00	22.00	(L)
Manganese	mg	1.67	1.44	1.40	1.40	(L)
Selenium* (wet diets)	µg	67.50	57.50	100.00	100.00	(L)
Selenium* (dry diets)	µg	55.00	45.00	100.00	100.00	(L)
Zinc*	mg	20.80	18.00	25.00	25.00	(L)

Determinação das necessidades dietéticas

Necessidade de nutriente: menor quantidade (absorvida ou consumida) necessária para manutenção das funções biológicas e da saúde ideal (OMS, 1988)

Estudos de balanço metabólico: impraticáveis por inúmeras variáveis

Ensaios de alimentação: também são difíceis de serem executados

Observações epidemiológicas

Abordagem atual proposta

Center et al. (2021)

Limite superior de tolerabilidade

Não estabelecido para cães

Abordagem atual:

- Informações atuais poderiam ser utilizadas para definição
- Alteração da recomendação para o teor de cobre biodisponível em alimentos para cães para o que era recomendado antes de 1997

Center et al. (2021)

Resumo das evidências para reconsiderar as recomendações dietéticas de cobre para cães

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Viewpoint

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2021

A incidência de HAC parece que aumentou após novas diretrizes para o teor de cobre em alimentos para cães em 1997

Aumento das concentrações hepáticas de cobre ao longo desse tempo

HAC pode ser tratada com sucesso em cães através de quelação de cobre, seguida de restrição desse mineral ao longo da vida

Em estudos com Labrador Retrievers, as observações clínicas dos autores sugerem que a alimentação a longo prazo de dietas com restrição de cobre (0,04 a 0,07 mg/kg/d) é segura para cães saudáveis e cães com alterações hepáticas

A recomendação atual da AAFCO de cobre para cães é 1,83 mg/1.000 kcal equivale a uma ingestão de cobre de aproximadamente 0,067 mg/kg/d para um cão de médio ou grande porte >> aproximadamente 1,7 a 1,8 vezes a ingestão de cobre através de dietas com restrição deste mineral, consideradas seguras a longo prazo

A insuficiência generalizada de cobre não foi reconhecida clinicamente antes do desenvolvimento de novas diretrizes dietéticas de cobre em 1997

Conclusões

- Há evidências de que vários alimentos comerciais apresentam teores excessivos de cobre
- As próprias recomendações mínimas de ingestão têm sido questionadas
- Acredita-se que as recomendações atuais são altas e podem exceder o limite superior de tolerabilidade para alguns cães
- Tem sido abordado que as recomendações de cobre sejam reconsideradas e que se considere o estabelecimento de um limite superior de tolerabilidade
- Acredita-se que isso reduziria a incidência de hepatopatia associada ao cobre em cães

Obrigado!

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