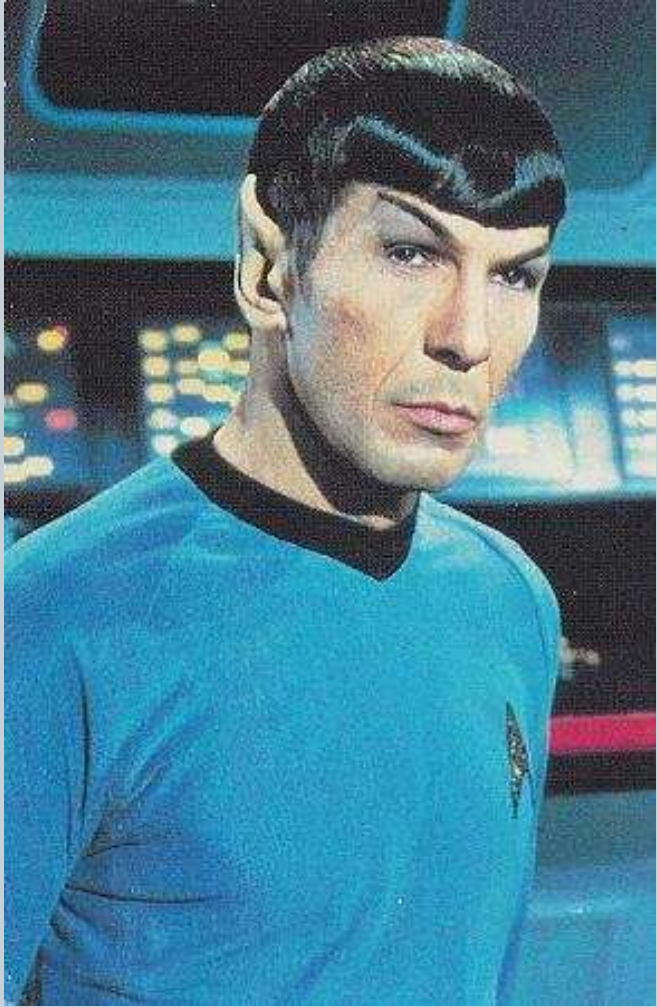


La démarche de la médecine factuelle (médecine basée sur les preuves, ou EBM des anglo-saxons) appliquée aux nutraceutiques vétérinaires



**Prof JM Vandeweerd,
DMV, MSc, PhD, Cert Equine Surgery, Dipl ECVS
Université de Namur (UNamur), Belgique**

Dr Spock?



Dr Benjamin Spock

Dr Spock

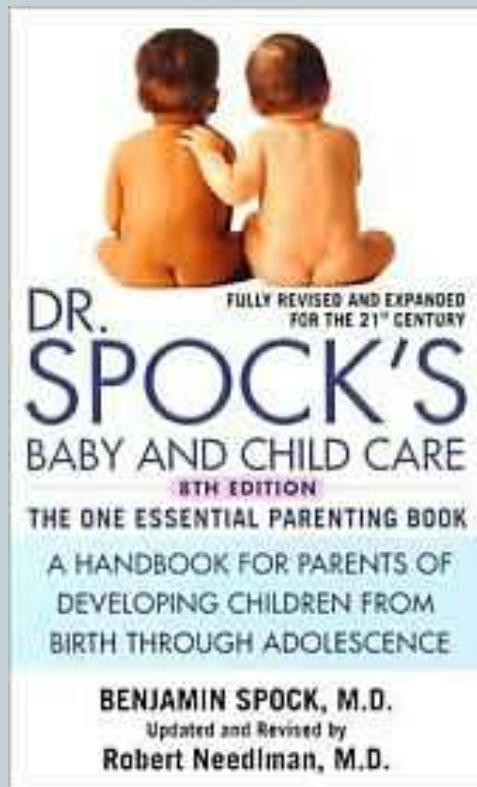
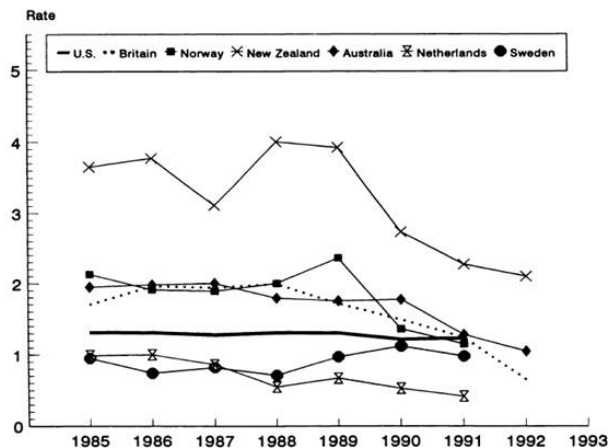


Fig 1. Postneonatal sudden infant death syndrome (SIDS) rates in the United States and selected other countries, 1985-1992. These rates are calculated as the number of SIDS deaths, >27 days and <1 year of age, per 1000 live births. The 1992 SIDS rates are provisional.



American Academy of Pediatrics (1992)

En 2000: 80 % des enfants dorment sur le dos,
incidence de la mort subite est réduite de 40 %

1946: « The common sense book of baby »
1958: « Bébés doivent dormir sur le ventre »



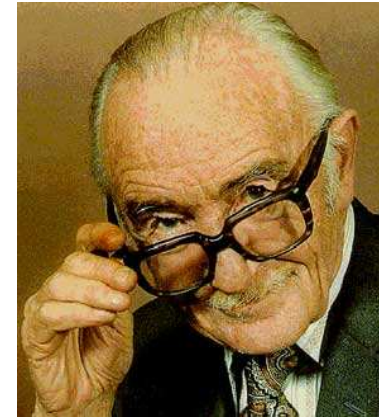
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Archie Cochrane



David Sackett



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L' EBM (Evidence Based Medicine) réfère
à l'utilisation consciente et explicite
des meilleures preuves scientifiques du moment
pour prendre une décision

Au cours de ce processus, le clinicien doit associer au mieux
son expertise personnelle
avec les meilleurs éléments de preuve extérieurs

(Sackett et al, 1996

Evidence based medicine: what it is and what it isn't)

« Médecine Basée sur la Preuve »
« Médecine factuelle »
« Meilleures Données Acquisées de la Science »



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4 étapes

1. Poser la question
2. Recherche documentaire
3. Validité interne?
4. Validité externe?





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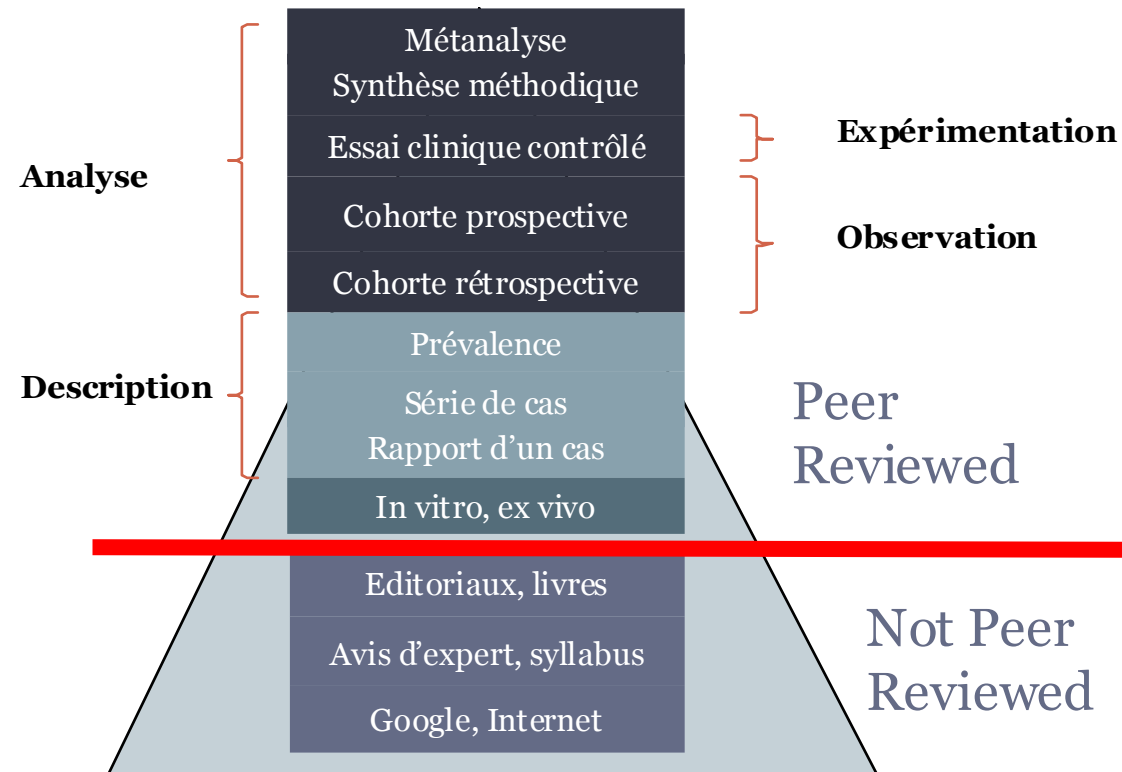
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● Etape 3: évaluer la validité interne





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The Veterinary Journal 191 (2012) 28–34



Contents lists available at ScienceDirect

The Veterinary Journal

journal homepage: www.elsevier.com/locate/tvj



Review

Is evidence-based medicine so evident in veterinary research and practice?
History, obstacles and perspectives

Jean-Michel Vandeweerd ^{a,*}, Nathalie Kirschvink ^a, Peter Clegg ^b, Sandrine Vandenput ^c, Pascal Gustin ^d,
Claude Saegeman ^e

Understanding Veterinary Practitioners' Decision- Making Process: Implications for Veterinary Medical Education

Jean-Michel E.F. Vandeweerd ■ Solène Vandeweerd ■ Catherine Gustin ■
Geneviève Keesemaecker ■ Carole Cambier ■ Peter Clegg ■ Claude Saegeman ■
Ayulu A. Reda ■ Philippe Perrenoud ■ Pascal Gustin

J Vet Med Educ. 2012;39(2):142-51.



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⌘ Appel à

- Collègues: 64.0 %
- Spécialistes: 85.0 %
- Laboratoires: 86.0 %
- Internet: 68.0 %

⌘ Ressources

- PubMed : 2.5 % (19 % capables de consulter une base de donnée)
- EBM?: 19.5 %
- Anglais?: 56.0 %
- Littérature scientifique francophone: 54.0 %
- Littérature anglaise: 6.0 %

⌘ Pas le temps...



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How Can Veterinarians Base Their Medical Decisions on the Best Available Scientific Evidence?

Jean-Michel Vandeweerd, DMV, MS^{a,*}, Peter Clegg, VetMB, MA, PhD^b,
Sébastien Buczinski, Dr Vét, DÉS, MSc^c

Vet Clin Food Anim 28 (2012) 1–11
doi:10.1016/j.cvfa.2011.12.001

vetfood.theclinics.com

Using Systematic Reviews to Critically Appraise the Scientific Information for the Bovine Veterinarian

Jean-Michel Vandeweerd, DMV, MS^{a,*}, Peter Clegg, VetMB, MA, PhD^b,
V. Hougardy, BSc^c, Sébastien Buczinski, Dr Vét, DÉS, MSc^d

Vet Clin Food Anim 28 (2012) 13–21
doi:10.1016/j.cvfa.2011.12.002

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Synthèse narrative	Synthèse méthodique	Méta-analyse
Avis d'un spécialiste	Avis de plusieurs spécialistes	Avis de plusieurs spécialistes
Recherche exhaustive de la littérature pas garantie	Recherche exhaustive de la littérature garantie : requête, nombre d'articles trouvés, critères de choix des articles précisés, grille	Synthèse méthodique + statistiques
Peer reviewing pas garanti	Peer reviewing	Peer reviewing



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- **Nutraceutique**



- capsules, pilules, liquides, poudres, gélules.
- en Europe, pas d'obligation légale pour être commercialisé
- mise sur le marché sans aucune étude scientifique approfondie



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Review

J Vet Intern Med 2012;26:448–456

Systematic Review of Efficacy of Nutraceuticals to Alleviate Clinical Signs of Osteoarthritis

J.-M. Vandeweerdt, C. Coisnon, P. Clegg, C. Cambier, A. Pierson, F. Hontoir, C. Saegerman,
P. Gustin, and S. Buczinski



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PubMed

[“Dietary Supplements” OR “Fish Oils” OR “Chondroitin”
OR “Glucosamine”] AND [“Osteoarthritis” OR “Joint
Diseases”] AND [“Dogs” OR “Cats” OR “Horses”]

CAB Abstract, Google Scholar

[“Nutraceuticals” OR “Dietary Supplements” OR “Fish Oils”]
AND [“Osteoarthritis” OR “Joint Diseases”] AND [“Dogs”
OR “Cats” OR “Horses”]

[Trials] AND [“Dogs” OR “Cats” OR “Horses”] AND
[“Osteoarthritis” OR “Joint Diseases”]

Gingerich and Strobel, 2003

Sanderson et al, 2009

Richardson and Loinaz, 2007

Pearson and Lindinger, 2009



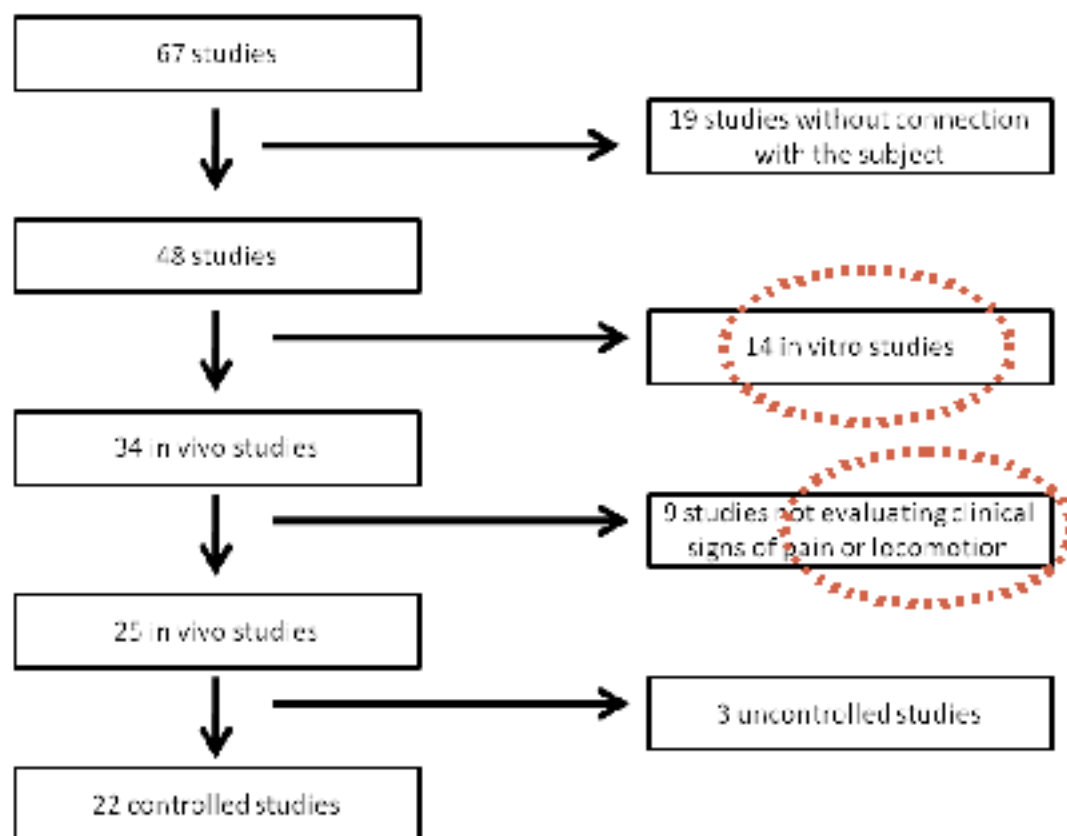
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1. O3FA, omega-3 fatty acids;
2. GLMP, green lipped mussel powder;
3. P54FP, Indian and Javanese turmeric;
4. ASU, avocado and soybean unsaponifiable;
5. GLU, glucosamine;
6. CS, chondroitin sulfate;
7. UC-II, undenatured type II collagen;
8. GH, gelatine hydrolysate β G, β -1,3/1,6 glucans ;
9. SMPC, special milk protein concentrate;
10. AOV, amino acids, oligo-element and vitamins;
11. HCA, hydroxycitric acid;
12. MA, myristoleic acid ;
13. MSM, methylsulfonylmethane





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Titre et résumé (2 %)
Introduction (2 %)
Matériel et méthodes (48 %)
<i>Design (3 %)</i>
<i>Participants (8 %)</i>
<i>Interventions (7 %)</i>
<i>Résultats (6 %)</i>
<i>Taille de l'échantillon (3 %)</i>
<i>Randomisation (7 %)</i>
<i>Dissimulation (2 %)</i>
<i>Implementation (1 %)</i>
<i>Aveuglement (4 %)</i>
<i>Placebo (2 %)</i>
<i>Méthodes statistiques (5 %)</i>
Résultats (30 %)
<i>Flux des participants (8%)</i>
<i>Recrutement (3 %)</i>
<i>Baseline data (8 %)</i>
<i>Intention de traiter (3 %)</i>
<i>Description des résultats (3 %)</i>
<i>Analyses (3 %)</i>
<i>Effets secondaires (2 %)</i>
Discussion (15 %)
<i>Faiblesses (5%)</i>
<i>Application possible (5%)</i>
<i>Interprétation (5%)</i>
Financement, conflit d'intérêt (3 %)



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Gupta et al. 2009 ¹ , Keegan et al. 2007 ² , Kawcak et al. 2007 ³ , Verde et al. 2006 ⁴ , Clayton et al. 2002 ⁵ , Beynen et al. 2010 ⁶ , Beynen et al. 2010 ⁷ , Fritsch et al. 2010 ⁸ , Fritsch et al. 2010 ⁹ , Roush et al. 2010 ¹⁰ , Roush et al. 2010 ¹¹ , Peal et al. 2007 ¹² , McCarthy et al. 2007 ¹³ , Pollard et al. 2005 ¹⁴ , Blejer et al. 2002 ¹⁵ , Bul et al. 2001 ¹⁶ , Dobenecker et al. 2002 ¹⁷ , Moreau et al. 2003 ¹⁸ , Depierre et al. 2005 ¹⁹ , Gingerich et al. 2003 ²⁰ , Innes et al. 2003 ²¹ , Lascelles et al. 2010 ²²																						
Study ID	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
N	25	35	16	10	8	46	60	177	131	127	38	25	35	81	96	31	58	68	15	35	54	40
Horse						Dog						Cat										
Title and summary (2/100)																						
Title and abstract: identification of the study design in the title is present (1%); structured summary of trial design, methods, results, and conclusions is provided (1%)																						
0	2	1	1	1	2	2	1	1	1	1	1	2	1	0	1	0	1	1	2	2	1	
Introduction (2/100)																						
Background and objectives: scientific background and explanation of rationale are explained (1%); specific objectives or hypotheses are explained (1%)																						
2	2	2	2	2	2	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	
Material and methods (48/100)																						
Trial design: the trial is controlled (1) and allocation ratio is described (1%); reference is made to an ethical protocol (1%)																						
2	1	3	2	2	2	2	3	3	2	2	2	3	3	2	2	2	3	3	1	2	2	
Participants: eligibility criteria for participants (2%), settings, locations where the data were collected (2%), inclusion criteria (2%), exclusion criteria (2%), are detailed																						
6	6	4	2	4	2	2	8	8	8	8	2	6	8	2	4	4	8	6	6	8	8	
Interventions: the interventions for each group are described with sufficient details to allow replication (5%) and no additional treatment is allowed (2%)																						
7	7	7	7	7	5	5	5	7	7	5	5	5	5	5	5	5	7	7	5	7	7	
Outcomes: subjective outcome measures are used and accurately described (2%); semi-objective measures are used (2%); objective outcome measures are used (2%)																						
4	4	4	4	5	4	4	4	4	6	4	1	4	4	2	4	2	6	4	4	6	6	
Sample size: how the sample size was determined is reported (3%)																						
0	0	0	0	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	3	3	
Randomisation: allocation is randomized (2%); method used to generate the random allocation sequence is described (4%); details of restriction are reported (1%)																						
0	2	0	2	4	2	2	5	5	3	2	2	6	2	2	3	2	6	2	2	2	2	
Allocation concealment: mechanism used to implement the random allocation sequence and to conceal the sequence until intervention is described (2%)																						
0	0	0	0	0	0	0	2	2	0	0	0	0	0	0	0	0	0	0	0	0	2	0
Implementation: it is reported who generated the random allocation sequence, who enrolled participants, and who assigned participants to the interventions (1%)																						
0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
Blinding: blinding is present (2%) with description of who was blinded after assignment to interventions and how blinding was performed (2%)																						
0	2	2	2	2	3	3	4	2	2	2	2	2	2	2	2	2	2	2	2	2	2	
Placebo: a placebo was used (2%)																						
2	2	2	2	2	2	2	0	0	0	0	2	0	2	0	0	2	2	0	2	2	2	
Statistical methods: statistical methods are accurately described (5%)																						
5	5	5	5	3	3	3	5	5	5	5	1	5	5	2	5	0	5	5	5	5	5	
Results (30/100)																						
Flow of participants: the numbers of participants who were eligible, included or excluded, randomly assigned, received intended treatment, lost to follow up and analysed for the primary outcome are described (2%) in a flow chart or table (2%); reasons are explained (2%) and less than 20 % of patients are lost to follow up (2%)																						
0	5	0	0	0	4	4	8	4	2	4	0	6	6	0	0	6	6	0	4	6	6	
Recruitment: dates defining the periods of recruitment and follow-up are reported (3%)																						
0	0	0	0	0	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	0	
Baseline data: a table showing baseline demographic characteristics for each group is presented with treated and control groups similar at the start of the trial (8%)																						
0	0	0	0	8	8	8	8	8	8	8	0	8	0	0	0	0	0	0	8	8	8	
Subjects analyzed: it is reported whether the results were analyzed by intention to treat or Per Protocol (3%)																						
0	0	0	0	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	3	0	
Results: results for each group were accurately described (3%)																						
3	3	3	3	3	1	1	3	3	3	3	1	3	3	3	3	2	3	3	3	3	3	
Analyses: results of any analyses are explained (2%); the effect size and clinical significance are reported (1%)																						
2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1	2	2	2	3	3	
Risks: all important harms or unintended effects in each group are adequately explained (2%)																						
2	0	0	1	0	0	0	2	2	2	0	0	0	2	0	0	0	1	0	2	1	2	
Discussion (16/100)																						
Limitations: trial limitations, sources of potential bias, imprecision, and, if relevant, multiplicity of analyses, are addressed (5%)																						
2	5	5	2	1	2	2	2	2	2	4	0	5	2	1	4	3	3	4	5	5	4	
Generalisability: generalisability (external validity, applicability) of the trial findings is discussed (5%)																						
0	3	3	4	0	0	0	0	0	0	0	0	3	2	0	3	2	3	3	2	5	4	
Interpretation: interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence, are provided (5%)																						
3	3	5	3	0	2	2	3	3	3	4	1	3	2	1	4	3	4	5	3	5	3	
Additional information (3/100)																						
Funding: funding sources and their supports for major phenomena or findings are mentioned and sources of conflicts of interest are declared (2%)																						
1	1	1	0	1	0	0	1	0	0	0	1	1	1	1	1	0	1	1	1	1	1	
Quality	41	55	49	44	48	48	74	68	57	59	34	67	58	27	44	40	66	44	63	63	74	
Lo	In	In	Lo	In	In	In	Hi	Hi	In	In	Lo	Hi	In	Lo	Lo	Lo	Hi	Lo	Hi	Hi	Hi	



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48	46	74	68	57	59	24	67	58	27	44	40	65	44	63	83
In	In	Hi	Hi	In	In	Lo	Hi	In	Lo	Lo	Lo	Hi	Lo	Hi	Hi



Fritsch D., Allen T.A., Dodd C.E., et al. Dose-titration effects of fish oil in osteoarthritis dogs. J Vet Intern Med 2010;24:1020-1026.

Fritsch D.A., Allen T.A., et al. A multicenter study of the effects of dietary supplementation with fish oil omega-3 fatty acids on carprofen dosage in dogs with osteoarthritis. J Am Vet Med Assoc 2010;236:535-539.

Roush JK, Dodd CE, Fritsch DA, et al. Multicenter veterinary practice assessment of the effects of omega-3 fatty acids on osteoarthritis in dogs. J Am Vet Med Assoc 2010;236: 59-66.

Roush JK, Cross AR, Renberg WC, et al. Evaluation of the effects of dietary supplementation with fish oil omega-3 fatty acids on weight bearing in dogs with osteoarthritis. J Am Vet Med Assoc 2010;236:67-73.

Faible qualité et quantité;
manque de mesures objectives, taille de l'effet, conflit d'intérêt?



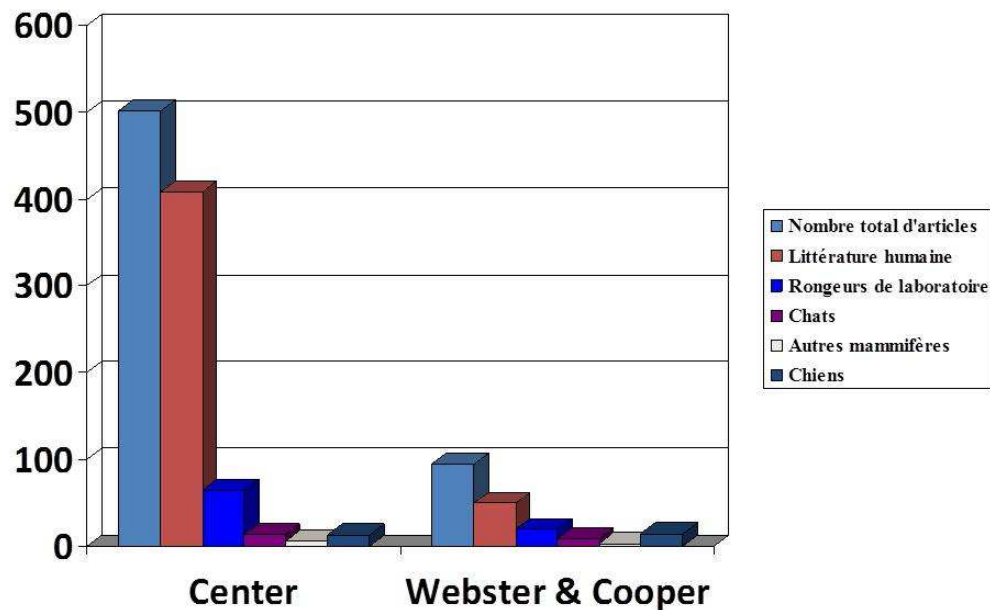
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Nutraceuticals in canine liver disease: a tricky search for clinical evidence. Vandeweerd JM, Masselot A, Cambier C, Clegg P, Gustin P. Vet Clinics of North America Small Animals, 2013, In press.



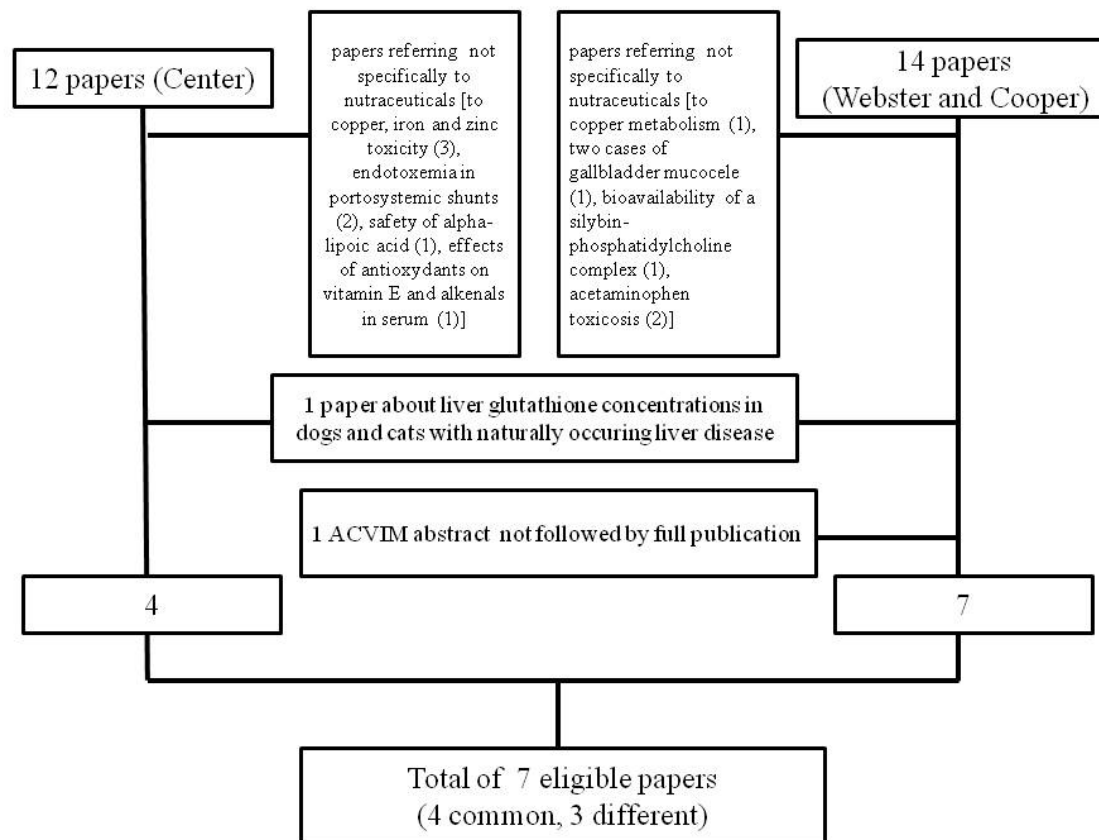
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Title	Authors	Date	Journal	Study design
Use of ursodeoxycholic acids in a dog with chronic hepatitis: effects on serum hepatic tests and endogenous bile acid composition	Meyer DJ, Thompson MB, Senior DF.	1997	J Vet Intern Med	Single case report
S-adenosylmethionine treatment of Tylenol toxicity in a dog	Wallace K, Center SA, Hickford F, et al.	2002	J Am Anim Hosp Assoc	Single case report
Protection by silibinin against <i>Amanita phalloides</i> intoxication in beagles	Vogel G, Tuchweber B, Trost W, et al.	1984	Toxicol Appl Pharmacol	Experimental in vivo trial (induced hepatotoxicosis)
Verification of the hepatoprotective and therapeutic effects of sylibinin in experimental liver injury with tetrachloromethane in dogs	Paulova J, Dvorak M, Kolouch F, Nanova L, Janeckova L.	1990	Vet med (Praha)	Experimental in vivo trial (induced hepatotoxicosis)
Improvement of portal flow and hepatic microcirculatory tissue flow with N-acetylcysteine in dogs with obstructive jaundice produced by bile duct ligation	Kigawa H, Nakano K, Kumada, et al.	2000	Eur J Surg	Experimental in vivo trial (induced hepatopathy)
Short-term effects of N-acetylcysteine and ischemic preconditioning in a canine model of hepatic ischemia-reperfusion injury	Baumann J, Ghosh S, Szakmany T, et al.	2008	Eur Surg Res	Experimental in vivo trial (induced hepatopathy)
Evaluation of the influence of S-adenosylmethionine on systemic and hepatic effects of prednisolone in dogs	Center SA, Warner KL, McCabe J, et al.	2005	Am J Vet Res	Experimental in vivo trial (induced hepatopathy)
Propective randomized clinical trial assessing the efficacy of denamarin for prevention of CCNU-Induced hepatopathy in tumor-bearing dogs	Skorupski, Hammond, Irish et al.	2011	J Vet Intern Med	Experimental in vivo trial (hepatopathy associated to the use of CCNU)



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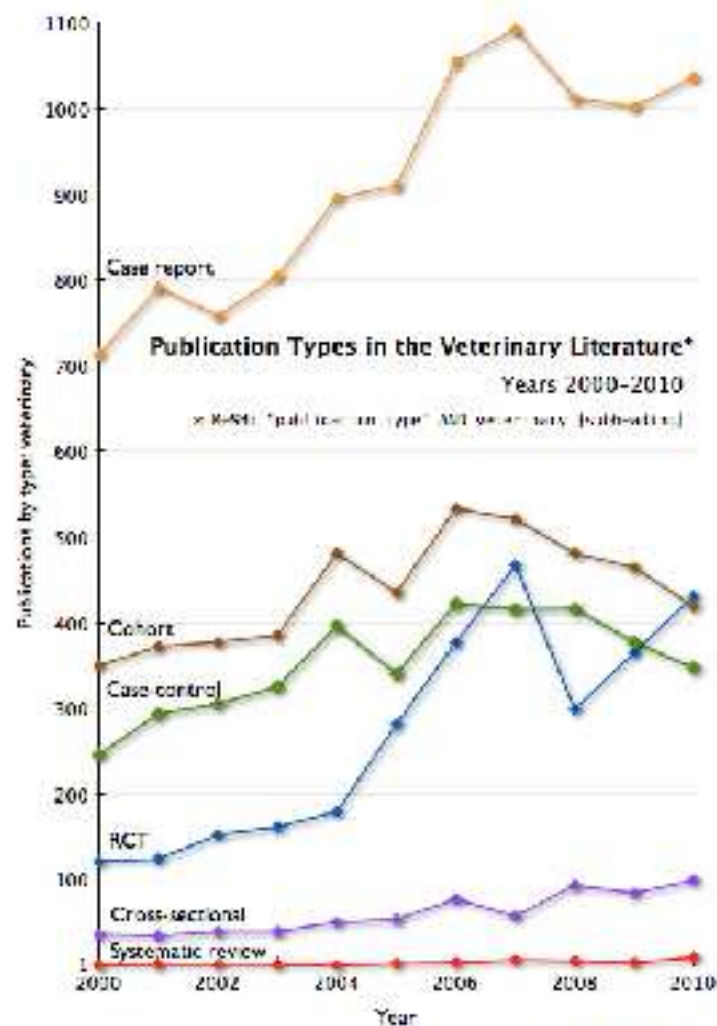
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- (1): faibles qualité et quantité des publications



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- (1): faibles qualité et quantité des publications
- (2): connaissance de l'épidémiologie clinique





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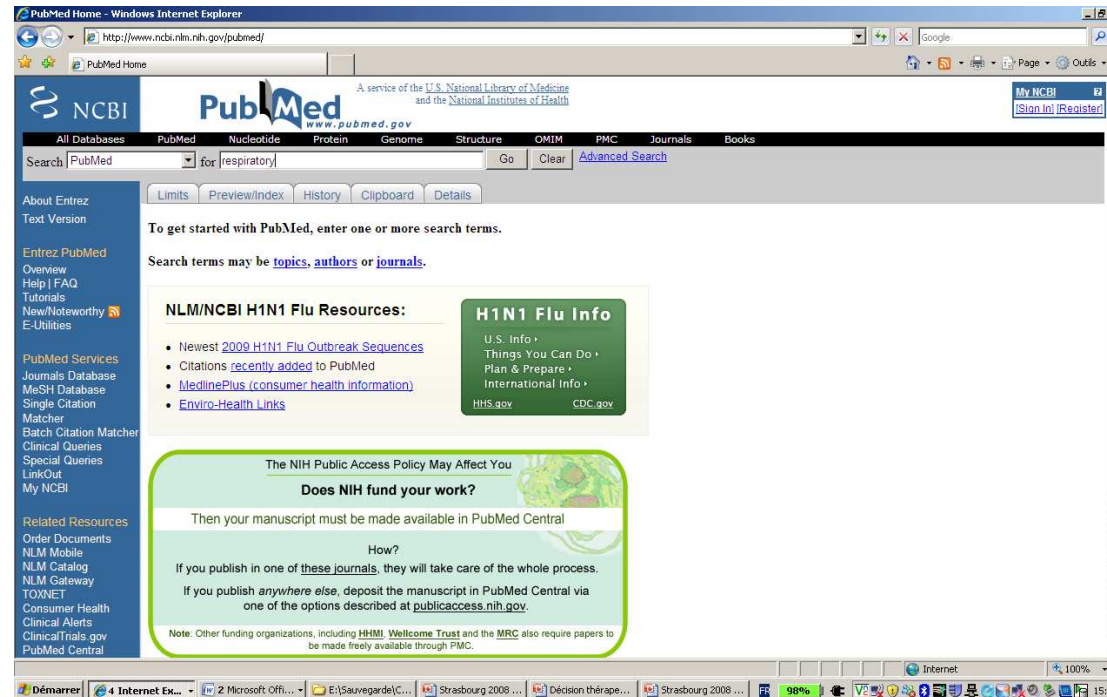
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- (1): faibles qualité et quantité des publications
- (2): connaissance de l'épidémiologie clinique
- (3): manque d'accès aux bases de données et articles





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- (1): faibles qualité et quantité des publications
- (2): connaissance de l'épidémiologie clinique
- (3): manque d'accès aux bases de données
- (4): manque de temps entre les consultations





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vétérinaire

Synthèse méthodique
appliquée aux
nutraceutiques

Ostéoarticulaires
Hépatiques

Perspectives

- (1): faibles qualité et quantité des publications; taille des échantillons; instruments de mesure objectifs
 - (2): connaissance de l'épidémiologie clinique
 - (3): manque d'accès aux bases de données
 - (4): manque de temps entre les consultations
-
- (1): standards de publication; adapter le niveau d'évidence aux réalités de la médecine vétérinaire; intégrer les praticiens

Evidence-Based Practice? An Evolution Is Necessary for Bovine Practitioners, Teachers, and Researchers

Jean-Michel Vandeweerd, DMV, MS^{a,*}, Pascal Gustin, DMV, PhD^b,
Sébastien Buczinski, Dr Vét, DÉS, MSc^c

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 - (2): formation en EBM



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 - Systematic reviews
 - Critically Appraised Topics
 - Structured Abstracts



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- Transparency
- Accountability

MERCI



Questions



- Niveaux de preuve
- N of 1
- Cochrane
- Action H
- Action OA
- EBM Med VT

**NIVEAUX DE
PREUVE
OXFORD**

La Table des niveaux de preuves du Centre d'Evidence-Based Medicine d'Oxford (version 2011)

Question	Etape 1 (Niveau 1*)	Etape 2 (Niveau 2*)	Etape 3 (Niveau 3*)	Etape 4 (Niveau 4*)	Etape 5 (Niveau 5)
Quelle est la fréquence du problème ?	Etude récente et locale sur des échantillons aléatoires (ou recensement)	Revue systématique d'études dont les conditions sont proches mais non identiques aux conditions locales**	Etude locale sur des échantillons non aléatoires**	Série de cas**	/
Le diagnostic ou le test de contrôle est-il exact ? (Diagnostic)	Revue systématique d'études transversales menées en aveugle et utilisant un standard de référence appliqué de manière constante	Etude transversale menée en aveugle et utilisant un standard de référence appliqué de manière constante	Série de cas à recrutement non consécutif ; étude transversale sans standard de référence appliqué de manière constante **	Etude cas-témoins ; étude avec un standard de référence non-indépendant ou de faible qualité **	Raisonnement déductif basé sur la pathophysiologie
Que se passera-t-il si aucun traitement n'est appliqué ? (Pronostic)	Revue systématique d'études de cohortes où les patients sont inclus au début de leur maladie (<i>inception cohort</i>)	Etude de cohorte où les patients sont inclus au début de leur maladie (<i>inception cohort</i>)	Etude de cohorte ; considération du groupe contrôle (non traité) dans un essai contrôlé randomisé	Série de cas ; étude cas-témoins ; étude de cohorte pronostique de pauvre qualité **	/
Cette intervention est-elle bénéfique ? (Bénéfices du traitement)	Revue systématique d'essais contrôlés randomisés ou d'essais de taille 1 (<i>n-of-1 trials</i>)	Essai contrôlé randomisé ; étude d'observation avec effet majeur	Etude de cohorte non randomisée**	Série de cas ; étude cas-témoins ; étude contrôlée pour laquelle la collecte des données du groupe contrôle a précédé celle du groupe étudié**	Raisonnement déductif basé sur la pathophysiologie
Quels sont les effets indésirables fréquents ? (Effets indésirables du traitement)	Revue systématique d'essais contrôlés randomisés ; revue systématique d'études cas-témoins recrutés dans la population d'une étude de cohorte ; revue systématique d'essais de taille 1 (<i>n-of-1 trials</i>) ; revue systématique d'études d'observation avec un effet majeur	Essai contrôlé randomisé ; (exceptionnellement) étude d'observation avec effet majeur	Etude de cohorte contrôlée non randomisée (surveillance post-commercialisation) à condition qu'il y ait un nombre suffisant de patients par rapport à la fréquence de l'événement (pour les effets à long terme, la durée du suivi doit être suffisante)**	Série de cas ; étude cas-témoins ; étude contrôlée pour laquelle la collecte des données du groupe contrôle a précédé celle du groupe étudié**	Raisonnement déductif basé sur la pathophysiologie
Quels sont les effets indésirables rares ? (Effets indésirables du traitement)	Revue systématique d'essais contrôlés randomisés ou d'essais de taille 1 (<i>n-of-1 trials</i>)	Essai contrôlé randomisé ; (exceptionnellement) étude d'observation avec effet majeur			
Ce test (détection précoce) en vaut-il la peine ? (Dépistage)	Revue systématique d'essais contrôlés randomisés	Essai contrôlé randomisé	Etude de cohorte contrôlée non randomisée**	Série de cas ; étude cas-témoins ; étude contrôlée pour laquelle la collecte des données du groupe contrôle a précédé celle du groupe étudié**	Raisonnement déductif basé sur la pathophysiologie

* Le niveau de preuve d'une étude peut être rétrogradé sur base des faiblesses intrinsèques de l'étude, d'imprécisions, du caractère indirect de la preuve, à cause de l'incohérence entre études, ou à cause de la taille de l'effet absolu qui est très petit ; le niveau de preuve peut être mieux classé si la taille de l'effet est grande ou très grande.

** Une revue systématique est généralement meilleure qu'une étude individuelle.

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N OF 1



- N of 1
- Expérimentation sur 1 patient
- Randomisation ttm ou placebo (cross over)
- P ex 3 cycles de comparaisons: 3 cycles de 4 semaines (2 sem placebo et 2 semaines traitement)
- Pro:
 - Pas besoin de groupe témoin
 - Bon lien avec la causalité
 - Utile sur des maladies chroniques (Mahon and Andreas)
 - Augmente la connaissance de leur problème, la participation à leur traitement
 - Tendances actuelles: génôme pour prévoir la réaction au médicament; limites dues à des sous-groupes (clustering); partager la décision avec le patient
- Cons
 - Manque d'expérience intellectuelle et administrative des cliniciens
 - Les patients parfois ont tendance à continuer leur traitement habituel malgré les preuves



- Guyatt GH, Sackett D, Taylor DW, et al. Determining optimal therapy — randomised trials in individual patients. N Engl J Med. 1986;314:889–892
- Mahon J, Andreas L, Donner A, Wood T. Randomised study of *n*-of-1 trials versus clinical practice. BMJ. 1996;312:1069–1074.

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Obstacles

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- En médecine humaine
 - Kernic, 2000: « Muddling through in a parallel track universe »
 - Veldhuis et al, 1998; Deliberate departures from good general practice?
 - Freeman and Sweeney, 2001. Why general practitioners do not implement evidence: qualitative study ?
 - > être gentil (42 %), prévenir un conflit (30 %), résultats scientifiques stressent le patient, ...c'est quand même le patient qui choisit

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2. [Antioxidant supplements for prevention of mortality in healthy participants and patients with various diseases](#) (34)
3. [Glucosamine for osteoarthritis](#) (31)
4. [Statins for the primary prevention of cardiovascular disease](#) (31)
5. [Pain management for women in labour – an overview](#) (30)
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7. [Breathing exercises for asthma](#) (27)
8. [Cranberries for preventing urinary tract infections](#) (24)
9. [Interventions for preventing obesity in children](#) (24)
10. [Intrapartum antibiotics for known maternal Group B streptococcal colonization](#) (21)
11. [Nebulized hypertonic saline solution for acute bronchiolitis in infants](#) (21)
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14. [Early skin-to-skin contact for mothers and their healthy newborn infants](#) (19)
15. [A comparison of multifocal and monofocal intraocular lens implants used in cataract surgery](#) (17)
16. [Can nicotine replacement therapy \(NRT\) help people quit smoking](#) (16)
17. [Exercise for depression](#) (16)
18. [Exercise for improving balance in older people](#) (16)

Have your say!
'Your views on The Cochrane Library: survey'

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Vitamin C for preventing and treating the common cold

Have your say!

'Your views on *The Cochrane Library*: survey'

Hemilä H, Chalker E, Douglas B

Published Online: March 17, 2010

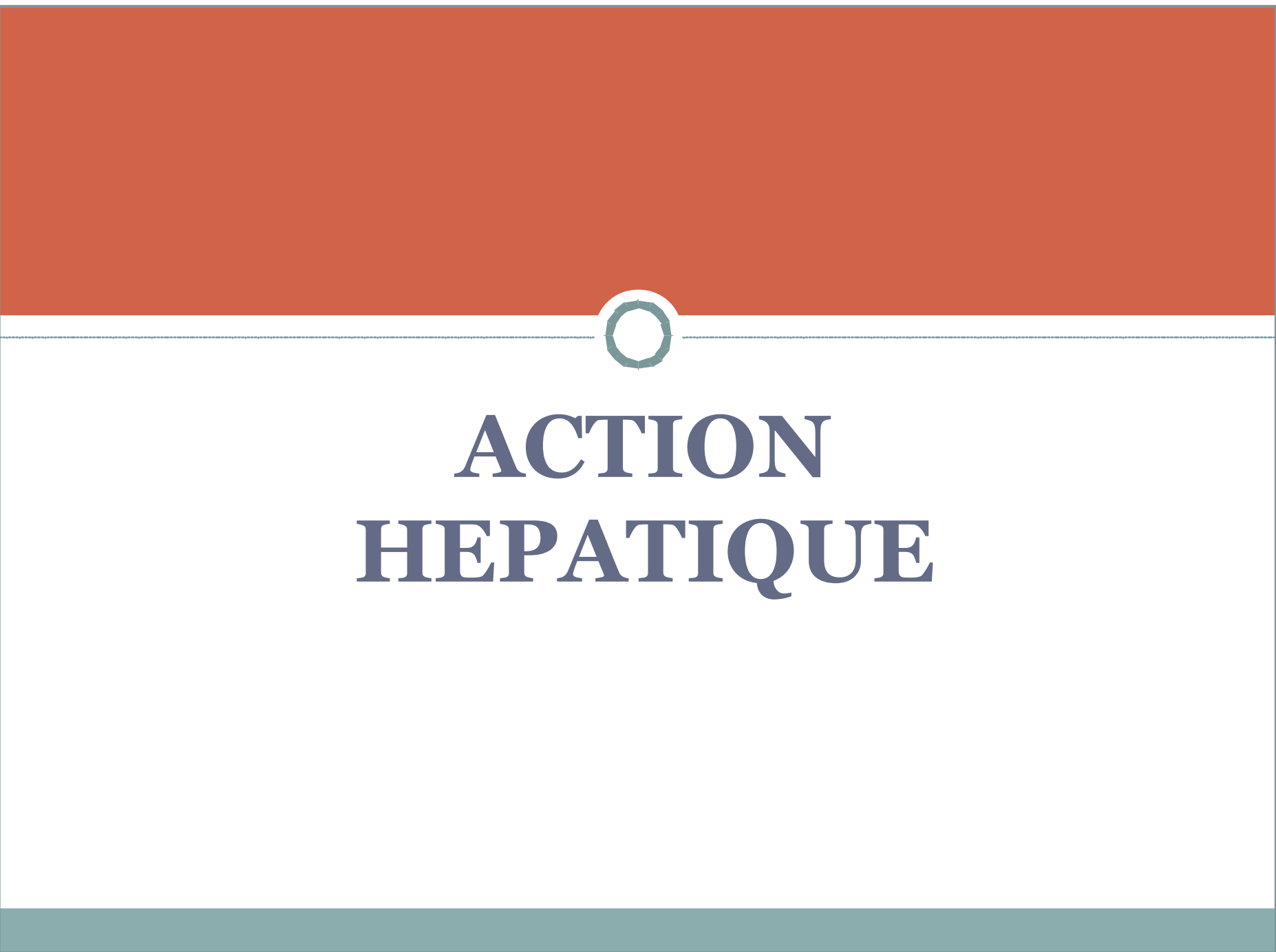
The term 'the common cold' does not denote a precisely defined disease, yet the characteristics of this illness are familiar to most people. It is a major cause of visits to a doctor in Western countries and of absenteeism from work and school. It is usually caused by respiratory viruses for which antibiotics are useless. Other potential treatment options are of substantial public health interest.

Since vitamin C was isolated in the 1930s it has been proposed for respiratory infections. It became particularly popular in the 1970s when Nobel laureate Linus Pauling concluded from earlier placebo-controlled trials that vitamin C would prevent and alleviate the common cold. Over two dozen new trials were undertaken thereafter. Vitamin C has been widely sold and used as both a preventive and therapeutic agent.

This review is restricted to placebo-controlled trials testing 0.2 g per day or more of vitamin C. Regular ingestion of vitamin C had no effect on common cold incidence in the ordinary population. However, it had a modest but consistent effect in reducing the duration and severity of common cold symptoms. In five trials with participants exposed to short periods of extreme physical stress (including marathon runners and skiers) vitamin C halved the common cold risk.

Trials of high doses of vitamin C administered therapeutically, starting after the onset of symptoms, showed no consistent effect on either duration or severity of common cold symptoms. However, only a few therapeutic trials have been carried out, and none have examined children, although the effect of prophylactic vitamin C has been greater in children. One large trial with adults reported equivocal benefit from an 8 g therapeutic dose at the onset of symptoms, and two trials using five-day supplementation reported benefit. More trials are necessary to settle the possible role of therapeutic vitamin C, meaning administration immediately after the onset of symptoms.

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ACTION HEPATIQUE



Vet Clin Small Anim
34 (2004) 67–172

THE VETERINARY
CLINICS
Small Animal Practice

Metabolic, antioxidant, nutraceutical,
probiotic, and herbal therapies relating to
the management of hepatobiliary disorders

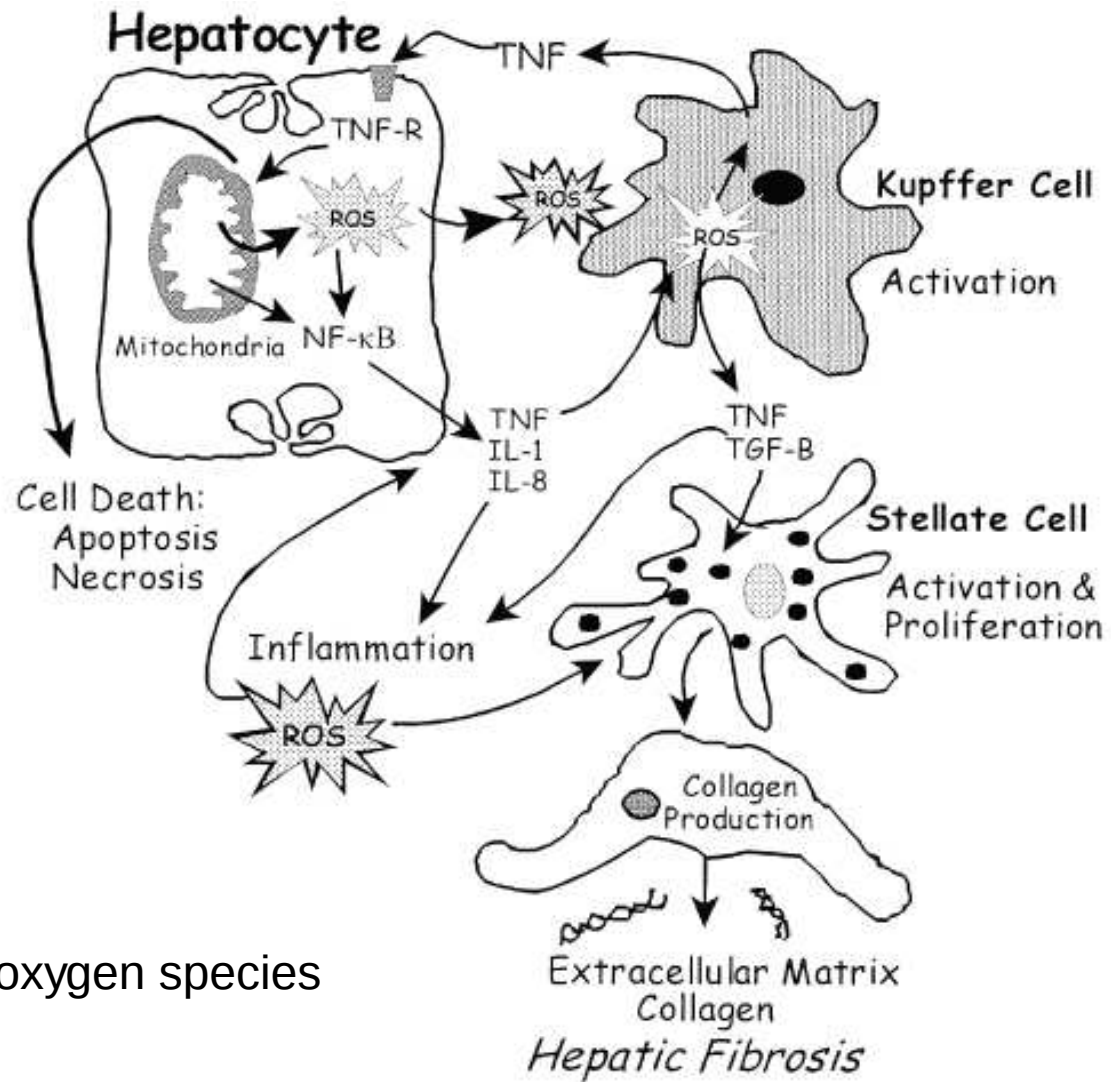
Sharon A. Center, DVM

College of Veterinary Medicine, Cornell University, Ithaca, NY 14853, USA

Therapeutic Use of Cytoprotective Agents in Canine and Feline Hepatobiliary Disease

Cynthia R.L. Webster, DVM^a, Johanna Cooper, DVM^{b,*}

tions. With the popularity of so-called evidence-based medicine, an expression used by clinician–scientists looking for proof that treatment surpasses the placebo effect (causing no harm), many clinicians are searching for data that justify the use of novel products. Evidence-based data are complicated; recently even the use of a placebo control group was called into question [1]. Many nutraceutical, conditionally essential nutrients and botanical extracts have been proposed as useful in the management of liver disease. The most studied of these are addressed in terms of proposed mechanisms of action, benefits, hazards, and safe dosing recommendations allowed by current information. While this is an area of soft science, it is important to keep an open and tolerant mind, considering that many major treatment discoveries were in fact serendipitous accidents. Consider, for example, the realization by Western medicine that the ancient Asian custom of using bear bile in the treatment of liver disease provides ursodeoxycholic acid (UDCA), now known to provide a number of diverse and important therapeutic benefits in cholestatic and necroinflammatory liver disease.



reactive oxygen species
(ROS)

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- Hépatocyte idéalement situé pour souffrir (intestin, circulation)
- Enhanced mitochondrial ROS, production can result from exposure to a number of biologic mediators, drugs, toxins, and conditions (eg, tumor necrosis factor- α [TNF- α], bile, acids, ischemia–reperfusion injury)
- Cell redox balance, influences normal cell function through effects on gene expression and transcription factors. Oxidative stress is known to (1) upregulate production of inflammatory cytokines, chemokines, and adhesion molecules; (2) increase expression and binding of Fas-L; (3) induce survival genes (ie, NF- κ B) that can block TNF- α –initiated apoptosis; and (4) induce MPT directly. Mitochondrial permeability transition (MPT), a process that precedes organelle/cell suicide.
- Depending on the extent and nature of oxidative stress, cell death can result from apoptosis or necrosis. The latter is favored by high-level oxidant exposure.
- inhibiting inflammation and fibrosis, initiation of apoptosis, and by preemptively protecting against oxidant injury to ensure full ability to maintain an appropriate redox balance.
- While pathomechanisms of liver injury and fibrosis are multifactorial, nearly all involve collateral oxidative/peroxidative damage of cell and organelle membranes, proteins, and enzymes
- Oxidative stress is defined as an imbalance between oxidant and antioxidant systems (such as an excess of reactive oxygen species [ROS] or a deficiency in antioxidants) in the cell which leads to tissue damage



- The liver is also home to a large population of macrophages, the Kupffer cells, which stand poised and ready for activation with subsequent release of inflammatory and toxic cytokines. These cytokines, particularly tumor necrosis factor alpha (TNF- α), can augment and perpetuate liver injury.¹ Additionally, the liver contains a population of vitamin A–storing stellate cells that can transform during liver injury (under the influence of another cytokine, transforming growth factor beta [TGF- β]) into extracellular matrix–producing myofibroblasts that lead to hepatic fibrosis
- Given this hostile environment, hepatocytes have developed several ways to protect themselves from harm. These protections include enzymatic (catalase, superoxide dismutase [SOD], and glutathione [GSH] peroxidase and transferase) and nonenzymatic (GSH, vitamin E, ascorbate) defense mechanisms.^{2,3} Hepatocytes also respond to toxic insults by initiating intracellular prosurvival signaling pathways. These pathways are controlled by hormones (eg, glucagon) and growth factors (eg,
- hepatocyte growth factor), and work through the modulation of survival kinases.⁴ Many medicinal, nutraceutical, and botanic extracts have cytoprotective properties in the liver.^{3–12} These agents enhance natural defense mechanisms to inhibit inflammation and fibrosis, prevent apoptosis, or protect against oxidant injury by maintenance of an appropriate redox balance.

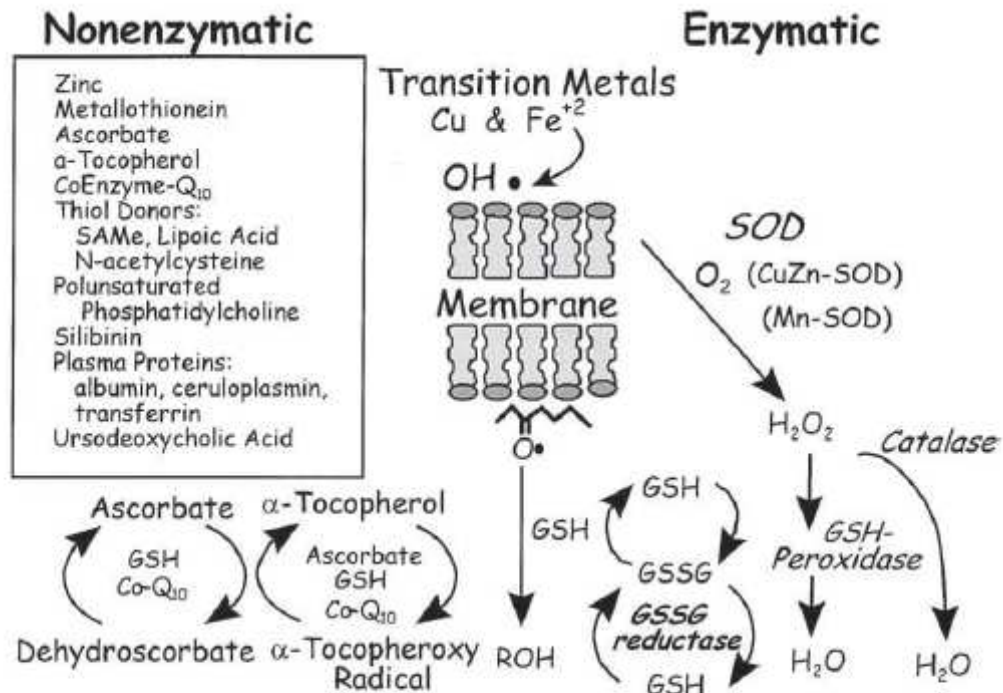


Fig. 3. Important antioxidant mechanisms for the liver (natural and therapeutic) depicted as nonenzymatic (molecular) antioxidants and enzymatic antioxidants (*italicized*), as discussed in the text. In the center of the diagram a cartoon depicts a biologic membrane with hydrophilic polarity indicated by the oval structures and lipid tails (paired polyunsaturated fatty acids in the hydrophobic portion). Note the reappearing and important contributions made by GSH.



- Many important biological processes involve redox reactions.
- **Cellular respiration**, for instance, is the oxidation of glucose ($C_6H_{12}O_6$) to CO_2 and the reduction of oxygen to water. The summary equation for cell respiration is:
$$C_6H_{12}O_6 + 6 O_2 \rightarrow 6 CO_2 + 6 H_2O$$
- The process of cell respiration also depends heavily on the reduction of NAD^+ to NADH and the reverse reaction (the oxidation of NADH to NAD^+). Photosynthesis and Cellular respiration are complementary but photosynthesis is not the reverse of the redox reaction in cell respiration:
- $6 CO_2 + 6 H_2O + \text{light energy} \rightarrow C_6H_{12}O_6 + 6 O_2$ Biological energy is frequently stored and released by means of redox reactions. Photosynthesis involves the reduction of carbon dioxide into sugars and the oxidation of **water** into molecular **oxygen**. The reverse reaction, respiration, oxidizes sugars to produce carbon dioxide and water. As intermediate steps, the reduced carbon compounds are used to reduce **nicotinamide adenine dinucleotide** (NAD^+), which then contributes to the creation of a **proton gradient**, which drives the synthesis of **adenosine triphosphate** (ATP) and is maintained by the reduction of oxygen. In animal cells, mitochondria perform similar functions. See *Membrane potential* article.
- **Free radical** reactions are redox reactions that occur as a part of **homeostasis** and killing microorganisms, where an electron detaches from a molecule and then reattaches almost instantaneously. Free radicals are a part of redox molecules and can become harmful to the human body if they do not reattach to the redox molecule or an antioxidant. Unsatisfied free radicals can spur the mutation of cells they encounter and are thus causes of cancer.
- The term **redox state** is often used to describe the balance of $NAD^+/NADH$ and $NADP^+/NADPH$ in a biological system such as a cell or organ. The redox state is reflected in the balance of several sets of metabolites (e.g., lactate and pyruvate, **beta-hydroxybutyrate** and **acetoacetate**), whose interconversion is dependent on these ratios. An abnormal redox state can develop in a variety of deleterious situations, such as hypoxia, shock, and **sepsis**. Redox signaling involves the control of cellular processes by redox processes.
- Redox proteins and their genes must be co-located for redox regulation according to the CoRR hypothesis for the function of DNA in mitochondria and chloroplasts.



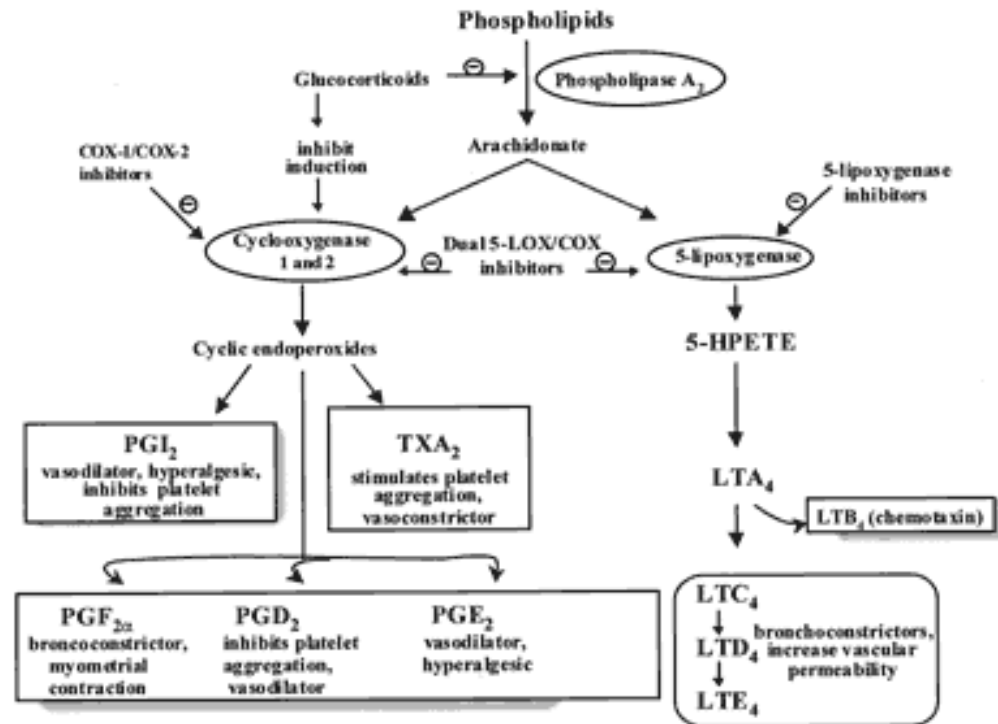
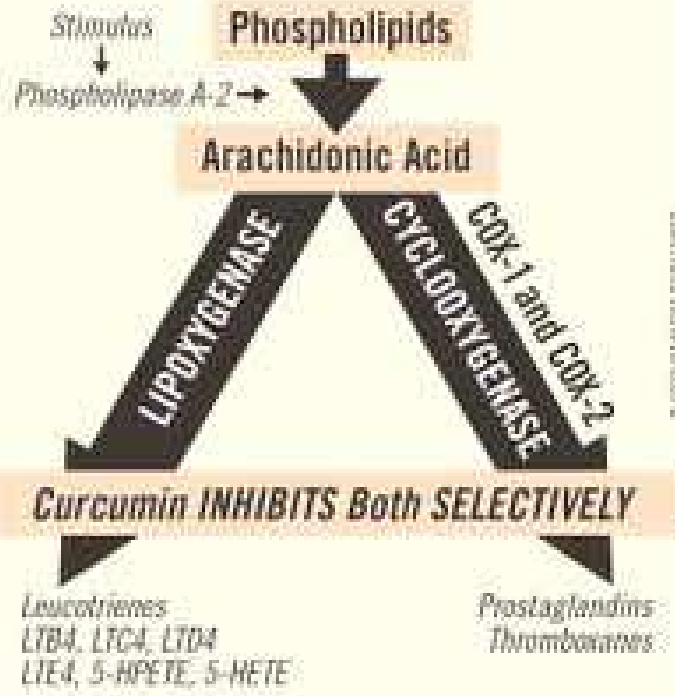
ACTION OA

Supplement	Mode of action
O3FA	O3FA may lower arachidonic acid concentrations and alter the production of eicosanoids to less inflammatory forms ²⁸ ; it may reduce the expression of cartilage degrading enzymes, cyclooxygenase-2, and inflammation-inducible cytokines. ²⁹
GLMP	GLMP has been shown to contain a unique O3FA, eicosatetraenoic acid, which appears to act as dual inhibitor of arachidonic acid oxygenation by both the cyclooxygenase and lipoxygenase pathways. ³⁰
P54FP	P54FP, an extract of Indian and Javanese turmeric, contains a mixture of active ingredients including curcuminoids and essential oils and has been reported to possess anti-inflammatory properties. ³¹
ASU	ASU has shown, in vitro, positive effect on both the inflammatory cascade and structural components of articular cartilage matrix. ^{32,33}
GLU and CS	There are indications that they provide prophylactic protection against synovitis ³⁴ , they retard the degenerative process synergistically ³⁵ and they modulate the metabolism of articular cartilage. ³⁶
UC II	In humans, UC-II would reduce immune-mediated damage to joint cartilage, thereby improving joint mobility and flexibility in rheumatoid arthritis. ³⁷
GH	There are indications that the amino acids in GH stimulate the synthesis of collagen in human cartilage. ³⁸
β G	Feeding of β G in pigs reduces the plasma concentrations of the proinflammatory cytokines, IL-6 and TNF α and raises the concentration of the anti-inflammatory cytokine, IL-10. ³⁹
SMPC	It is speculated that SMPC contains natural factors that inhibit inflammation by suppressing neutrophil emigration from the vascular space, possibly by restricting extravasation through tight junctions. ⁴⁰
AOV, HCA, MA, MSM	Their effect has been evaluated without real explanation of their hypothetical mechanism of action in OA by the investigators.

O3FA, omega-3 fatty acids; GLMP, green lipped mussel powder; P54FP, Indian and Javanese turmeric; ASU, avocado and soybean unsaponifiable; GLU, glucosamine; CS, chondroitin sulfate; UC-II, undenatured type II collagen; GH, gelatine hydrolysate β G, β -1,3/1,6 glucans ; SMPC, special milk protein concentrate; AOV, amino acids, oligo-element and vitamins; HCA, hydroxycitric acid; MA, myristoleic acid ; MSM, methylsulfonylmethane.

The Arachidonic Acid Cascade

Curcumin Inhibits Pain and Inflammation and Supports Homeostasis



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 - The case against alternative medicine. *Canadian Veterinary Journal* 41, 769-772.
- (Bertone, 2001; Ramey and Rollin, 2001; Roen, 2001; Milstein, 2002; Ramey, 2002; Jacobs, 2004; Lumeij, 2004; Milstein, 2005)



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- Olivry et al., 2001; 2003
 - Evidence-based veterinary dermatology: A systematic review of the pharmacotherapy of canine atopic dermatitis. Veterinary Dermatology 14, 121-146.



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- Cockcroft and Holmes, 2003
 - Handbook of Evidence-based Veterinary Medicine, Blackwell Publishing, Oxford, UK, pp. 154-181.
- Après 2003...



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En Belgique et en France?

- 2004 Commission EBM à l'AVEF
- Séries d'articles dans Pratique Vétérinaire Equine, Le Point Vétérinaire, Le journal des GTV (2005 à 2011)
- Congrès: AVEF, AVF, AFVAC, GTV
- Formation continue: recherche documentaire et EBM
- Livre: Vandeweerd, J.M., Saegerman, C. 2009. Guide pratique de médecine factuelle vétérinaire. Les éditions du point vétérinaire, Paris, France

