Stiftung Tierärztliche Hochschule Hannover
University of Veterinary Medicine Hannover, Foundation

Oral joint supplements in animal feeding

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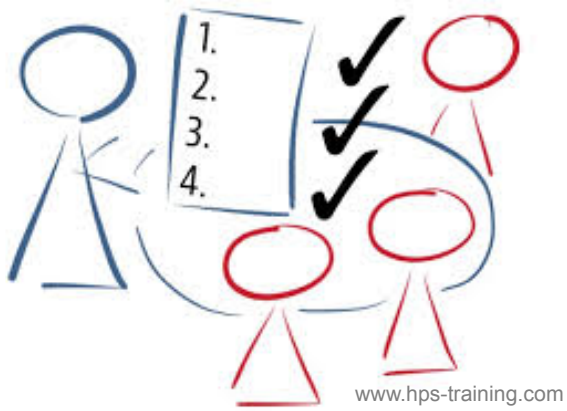
Outline

- Indications for the use of oral joint supplements in animal feeding
- Osteoarthritis (Osteoarthrosis)

- Types of oral joint supplements
- Glucosaminoglycanes, glucosamines and chondroitinsulfates
- Polyunsaturated fatty acids (n-3-fatty acids)
- Devil‘s claw (Harpagophytum procumbens)
- Willow bark (Salix species)

- Summary

- References



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Indications for the use of oral joint supplements

Horses (Geor et al. 2013; Meyer and Coenen 2014):

- Treating lame horses
- Pain management
- Preventing or delaying the development of joint problems
- Optimizing the supply of energy and nutrients of the cartilage tissue
- Supporting the activity of chondrocytes (faster healing process)
- Inhibition of inflammatory mediators

www.hundekes-online.de

Dogs (Meyer and Zentek 2013, Hazewinkel and Mott 2006):

- Treating movement disorders (often older and obese dogs)
- Preventing or delaying the development of joint problems (often in giant breeds)

Cats (Acker and Tacke 2011):

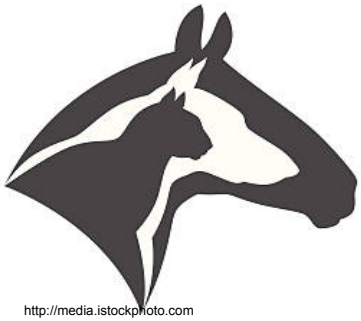
- Treatment of osteoarthritis (Slow Acting Drugs in Osteoarthritis = SADOA)

Osteoarthritis (Osteoarthrosis)

- Osteoarthritis is the single most common cause of lameness in horses (approx. 60 %; Caron and Genovese 2003; Clegg and Booth 2000)

- 25 % of American pet dogs are diagnosed with arthritis (Bland 2015), obese dogs are often affected (→ reduction of weight is the most important therapeutic approach; Meyer and Zentek 2013)

- 22 % of cats (median age: 9.5 years) and 90 % of cats older than 12 years show at least a prevalence for osteoarthritis in x-ray studies (Godfrey 2005; Hardie et al. 2002); → but, in contrast to horses and dogs: mostly primary origin



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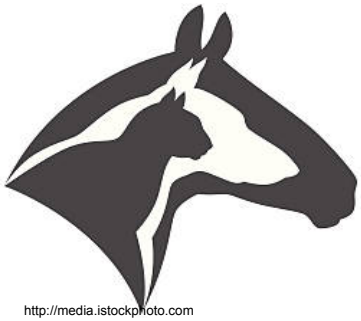
Osteoarthritis (Osteoarthrosis)

- Therapies aim at preventing further degradation while restoring function (McIlwraith 2005, Trumble 2005), analgesics are often part of the therapy
- As pets and horses are getting older nowadays, long-term treatments with minimum side effects are needed
- Oral joint supplements are a common choice of clients (Trumble 2005)
- Oral joint supplements became the most popular type of dietary supplement in horses (34 % of all equine supplements; Packaged Facts 2008) and dogs (Bland 2015)



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Osteoarthritis - Pathophysiology

- Normal conditions: Cartilage matrix is subjected to a dynamic remodeling process in which *low levels* of degradative (Il-1, TNFα, proteases) and synthetic (IGF, TGFβ, …) enzyme activities are balanced → volume of cartilage is maintained

- Osteoarthritis: matrix degrading enzymes (collagenases, gelatinases, stromelysins, other proteases) are overexpressed

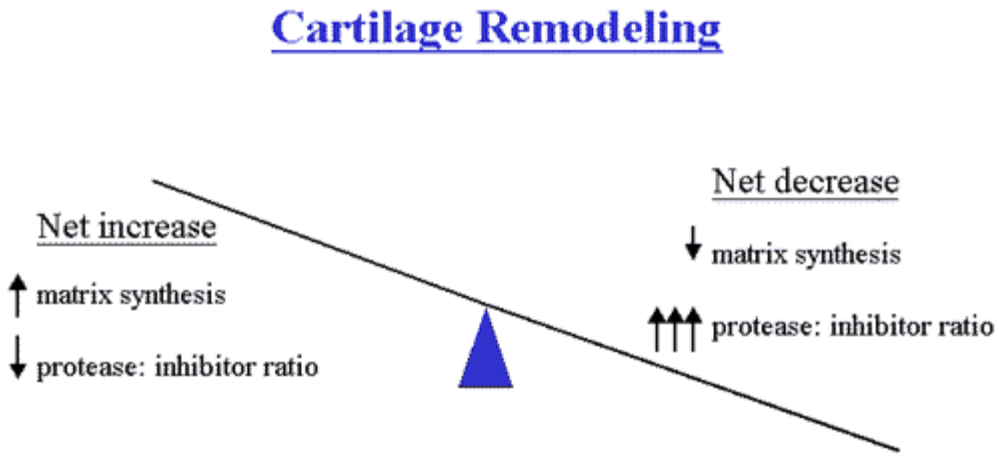

Fig: Ling and Bathon (2012)

References: Acker and Tacke (2011), Ling and Bathon (2012)

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- Changes lead (inter alia) to
  a proliferation of inflammatory cells in joint capsule and synovia,
  sensibilisation of nociceptors
  and further changes in cartilage metabolism
  (reduced content of proteoglycanes; impaired cartilage stability,
  degeneration of chondrocytes, water storage ↑, chondromalacia)

⇨ Resulting in pain!

References: Acker and Tacke (2011), Ling and Bathon (2012)

Types of oral joint supplements

… for dogs, cats and horses (Meyer and Zentek 2013, Geor et al. 2013, Meyer and Coenen 2014)

- Glucosaminoglycanes
- Chondroitinsulfates
- n-3-fatty acids (fish oil, New Zealand green-lipped mussel)
- Devil ‘s claw (Harpagophytum)
- Willow bark (Salix species)
- … or combinations

www.zechpet.de

Types of oral joint supplements - **Glucosaminoglycanes**

- Glucosamines are often fed as a precursor for glucosaminoglycanes
- Glucosamines = amino sugar
- Glucosaminoglycanes = mucopolysaccharides
- Chondroitinsulfate = subgroup of glucosaminoglycanes (sulphated, glucosamine + chondroitin, very high water binding capacity)
- Hyaluronic acid = subgroup of glucosaminoglycanes (not sulphated)

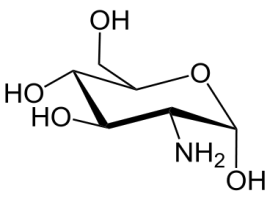


Fig. 1: Glucosamine, structural formula, www.wikimedia.org

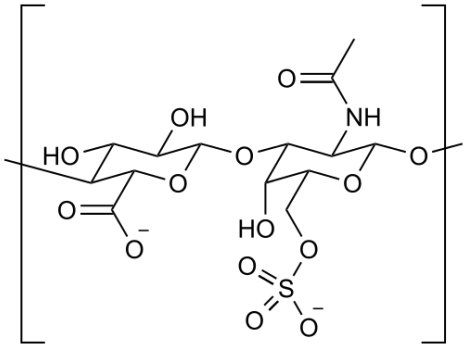


Fig. 2: Chondroitinsulfate, structural formula, www.wikimedia.org

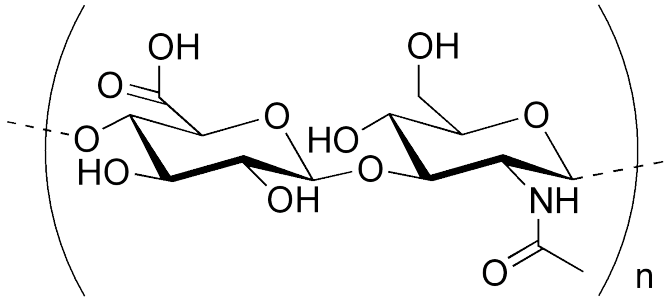


Fig. 3: Hyalorunic acid, structural formula, www.wikimedia.org

References: Meyer and Coenen (2014), Harper et al. (1984), Geor et al. 2013

Types of oral joint supplements - **Glucosaminoglycanes**

- Glucosamines: essential for the production of cartilage and synovial fluid
- Hyaluronic acid: main constituent of synovial fluid, responsible for the vicosity of the fluid
- Oral supplementation: the more glucosamines are available, the more cartilage tissue can be synthesized
- Glucosamines inhibit the release of elastases and aggrecanases
- Side effects: it has to be assumed, that an oral supplementation with glucosamines could force the insulin resistance in type 2 diabetics

References: Warzecha et al. (2006)

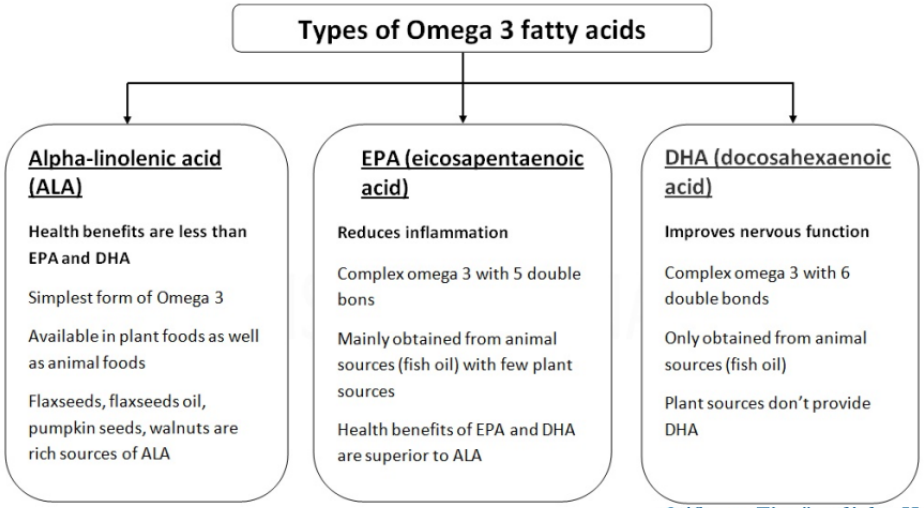
Types of oral joint supplements - **Glucosaminoglycanes**

- Horse: only low bioavailability (glucosamine: 2,5-6,1%; chondroitinsulfate: 22-32%)
- Most of glucosaminoglycanes are probably degraded fermentatively in the hindgut
- Even by intravenous application the tropism to the joints seems not to be high enough to reach effective drug concentrations (measured in vitro)
- Studies in horses show that product quality (composition, contents of glucosamines and chondroitinsulfates) can vary widely → results of studies not consistent (study design partly questionable, e.g. no control group)
- Hyaluronic acid: In a double-blinded, controlled study in horses (operated OCD) for 30 days, dietary hyaluronic acid (100 mg) led to a significant lower (less lesions) score in contrast to a placebo → mode of action is unclear!

References:
Meyer and Coenen (2014), Harper et al. (1984), Geor et al. (2013), Bergin et al. (2006)

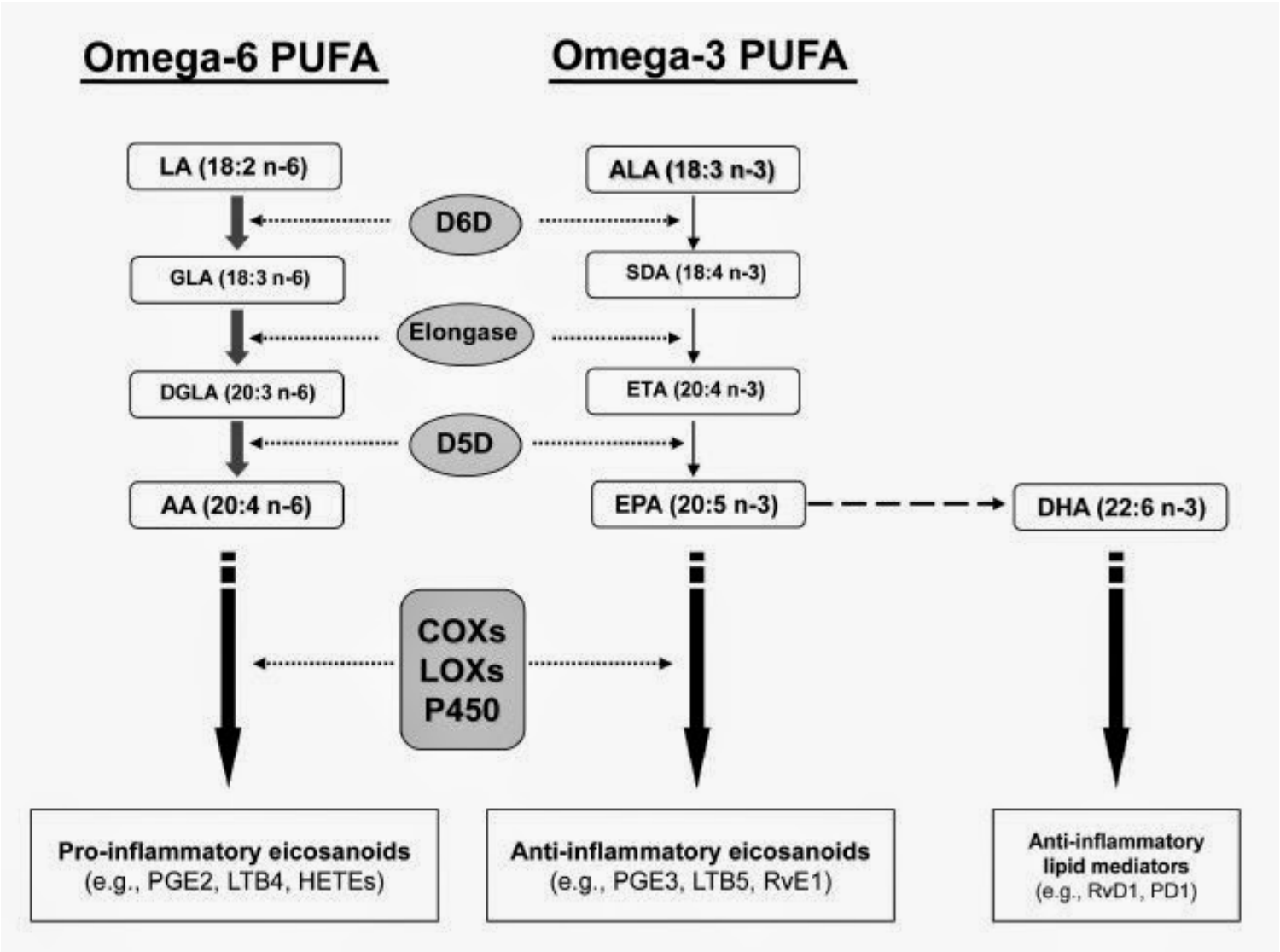
Types of oral joint supplements – n-3-fatty acids

- Fish oil, linseed oil, New Zealand green-lipped mussel, (Devil ‘s claw)
- Anti-inflammatory and analgesic characteristics (decreased production of inflammatory cytokines, arachidonic acid-derived eicosanoids and other inflammatory agents as reactive oxygen species)
- α-linolenic acid → production of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)
- Relation of n-6 : n-3 fatty acids is of special interest (for example: in human diets the ideal ratio is thought to be ~1, but in Western diets it is about 15-16.7:1!)



References:
Geor et al. (2013), Meyer and Coenen (2014), Trumble (2005), Curtis et al. (2000), Simopoulos (2002)

Types of oral joint supplements – n-3-fatty acids



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Types of oral joint supplements **– n-3-fatty acids**

- In-vitro study (bovine cartilage model): supplementation with n-3-fatty acids resulted in a decreased expression/activity of aggrecanase, MMPs, COX-2, IL-1α and tumor necrosis factor-α
- Dogs with chronic osteoarthritis, which received a test diet with fish oil omega-3 fatty acids for 3-12 weeks, carprofen dosage decreased significantly faster among dogs fed the supplemented diet than among dogs fed a control diet with low omega-3 fatty acid content
- The weight-bearing of dogs with clinical lameness could be improved by feeding a test diet for 90 days containing 3.5% fish oil omega-3 fatty acids
- In healthy adult dogs a modulation of clinical or immunological parameters (total protein content, leucocytes, red blood cell count) by a dietary supplementation of fish oil was not detectable

References: Geor et al. (2013), Meyer and Coenen (2014), Trumble (2005), Curtis et al. (2000), Fritsch et al. (2010), Roush et al. (2010), Peus (2005)

Types of oral joint supplements – Devil ‘s claw (Harpagophytum procumbens)

- Containing iridoid glycosides (glycoside harpagoside as main constituent)
- Anti-inflammatory effects by interacting with eicosanoid biosynthesis (depending on extract, sometimes even counteractive effects!)
- Limited analgesic properties
- Human studies: reduction of pain in in cases of osteoarthritis
- Several Harpagophytum products available → analgesic and antiinflammatory properties differ between these products

References: Torfs et al. (2008), Loew et al. (2001)

Types of oral joint supplements – Devil ‘s claw (Harpagophytum procumbens)

- Optimal effect in treatments lasting several weeks, no efficacy in treatment of acute pain!
- No major adverse effects reported in human studies (but: no toxicity studies!)
- No sound scientific proof for the efficacy of Harpagophytum in horses
- Authors conclude Harpagophytum might be for pain originating from (mild) degenerative joint disease, not for painful conditions such as chronic laminitis
- Fédération Équestre Internationale (FEI): substance not allowed in competition

References: Torfs et al. (2008), Loew et al. (2001)

Types of oral joint supplements – Willow bark (Salix species)

- Salicin (main ingredient): salicyl alcohol derivate, anti-inflammatory, antipyretic and analgesic properties (effects/side effects: compare with aspirin)
- Salix extract: in vitro → inhibitory effect on lipopolysaccharide(LPS)-induced release of prostaglandine E2 (PG E2), weak inhibitory effect on the production of other pro-inflammatory cytokines (tumor necrosis factor-α, IL-1β, IL-6)
- Analgesic efficacy of Salix extract on osteoarthritis in humans has been evaluated in several long-lasting clinical trials, with mostly positive (analgesic) effects
- Significant side effects in humans are minimal: allergic reactions (similar to acetylsalicylic acid allergy) occur, an effect on thrombocyte aggregation is described, long-time effects on kidney and liver are outstanding
- Studies in horses/pet animals are missing
- Fédération Équestre Internationale (FEI): substance not allowed in competition


www.zirbenherz-bett.com

References:
Torfs et al. (2008), Williamson (2001), Kammerer et al. (2005), Fiebich and Chrubasik (2004)

Summary

- As pet animals are getting older nowadays, long-term treatment of osteoarthritis (osteoarthrosis) gets more and more important
- Joint supplements are frequently used for prevention or treatment of osteoarthritis
- Commercial joint supplements differ widely in their compositions/contents of active ingredients;
  for example: a test diet for cats which resulted in a higher activity of animals with degenerative joint diseases after 9 weeks was supplemented with fish oil AND green-lipped mussel extract AND glucosamine/chondroitine sulfate (Lasceles et al. 2010)
- Oral joint supplements only have analgesic effects (if any) in long-term treatments, acute pain cannot be medicated
- The effect of the dietary use on the development of osteoarthritis is still not predictable, but published studies/case reports give hints on beneficial effects in long-term clinical or in vitro studies
- Robust models (repeatable, with control groups) are still missing in most species and for most supplements

Thank you for your attention!

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