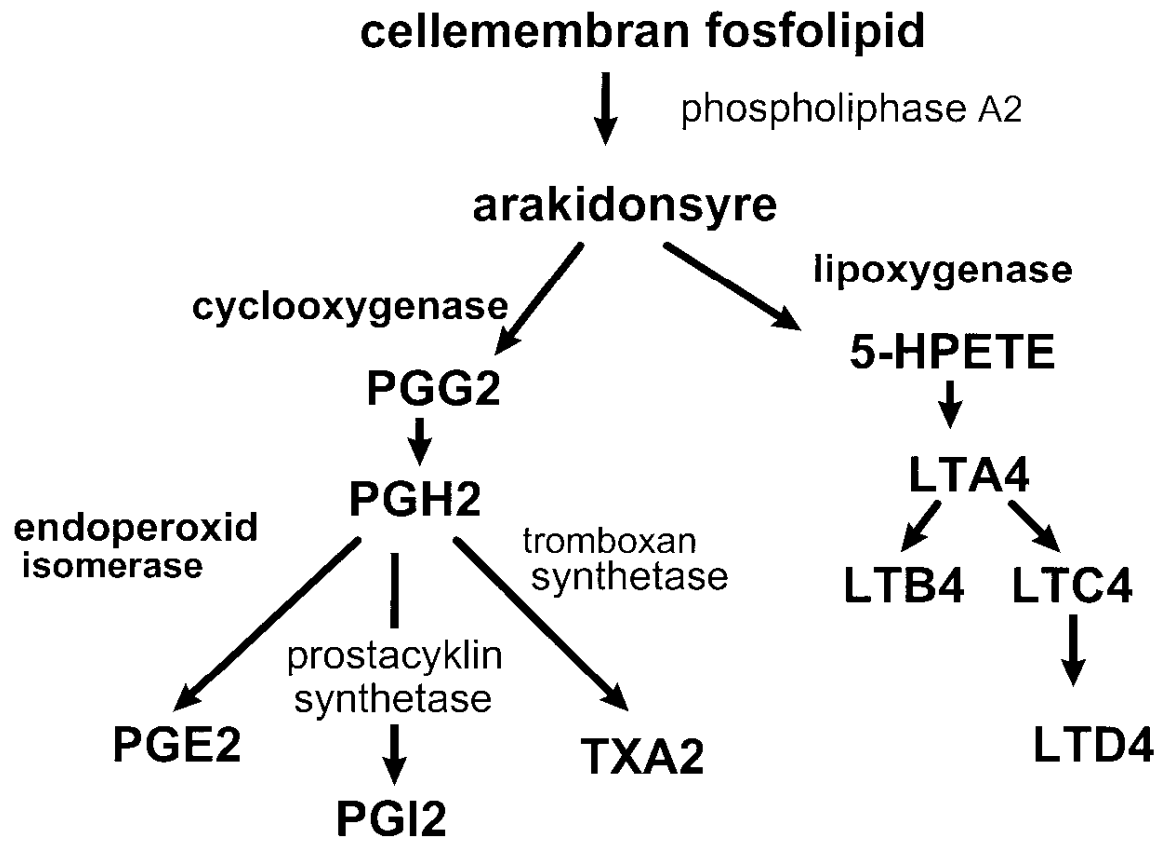


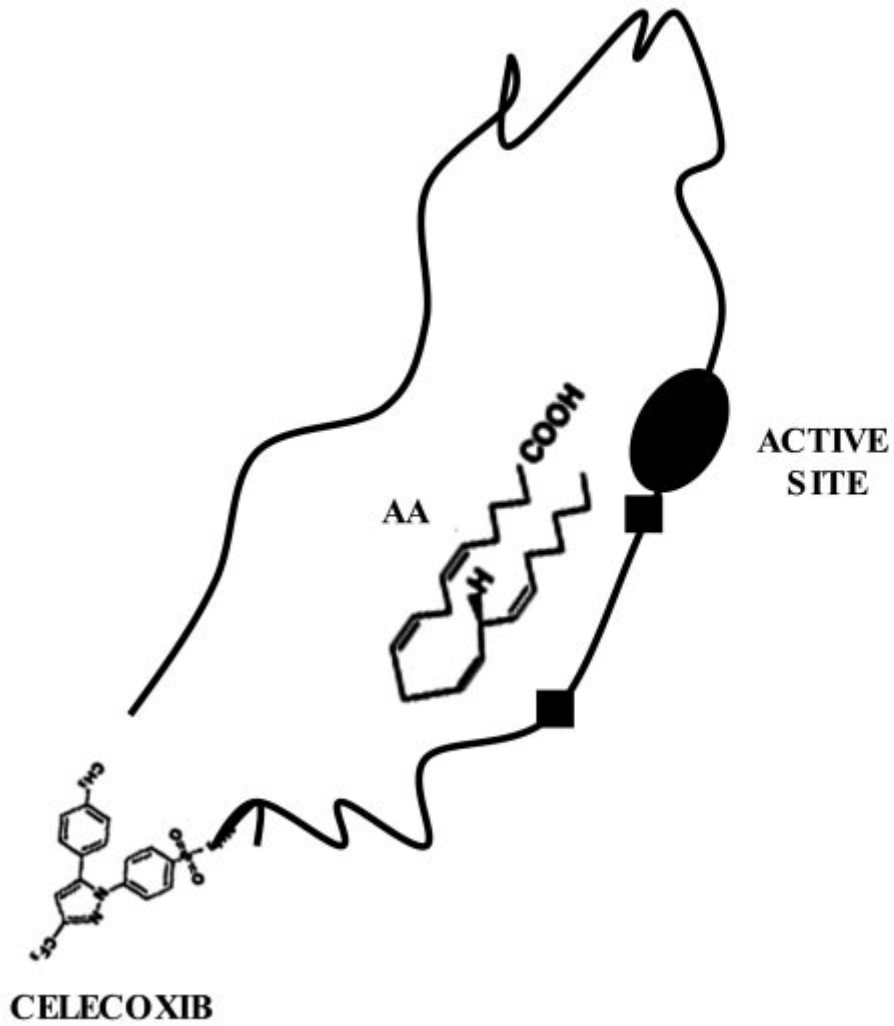
**NSAID**

**non-steroidie antiinflammatorika**

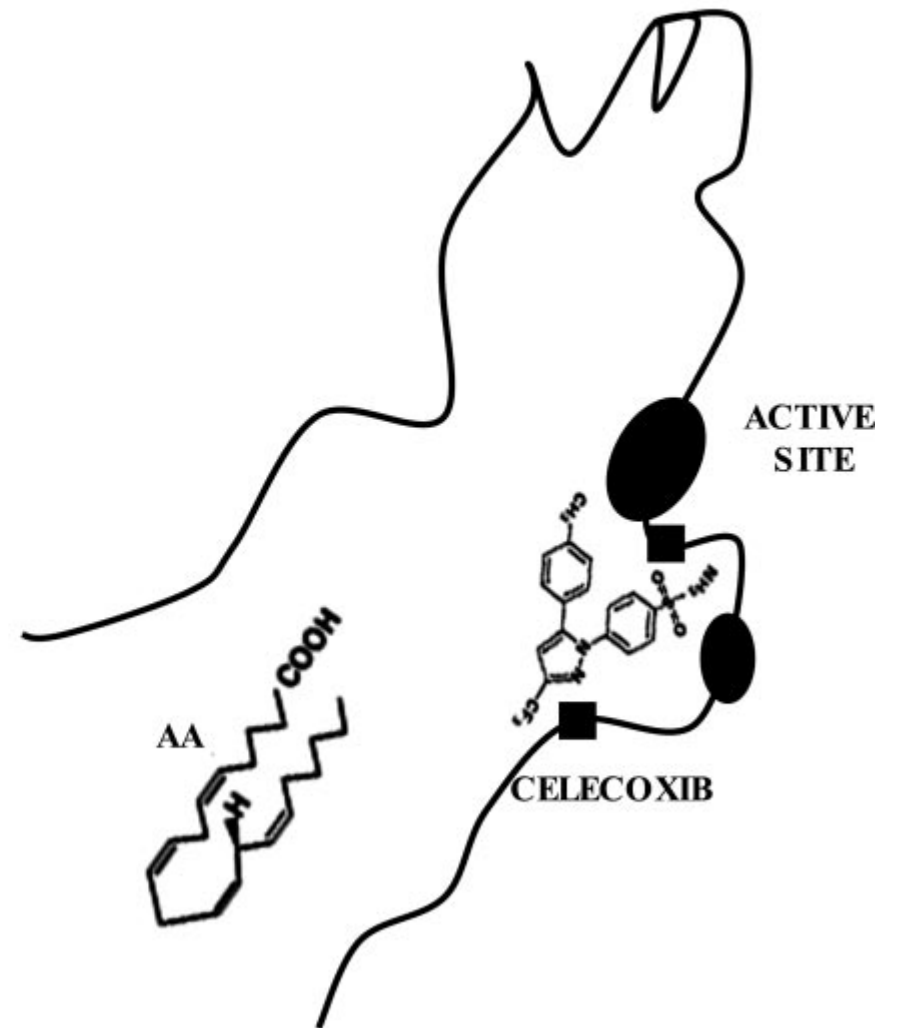


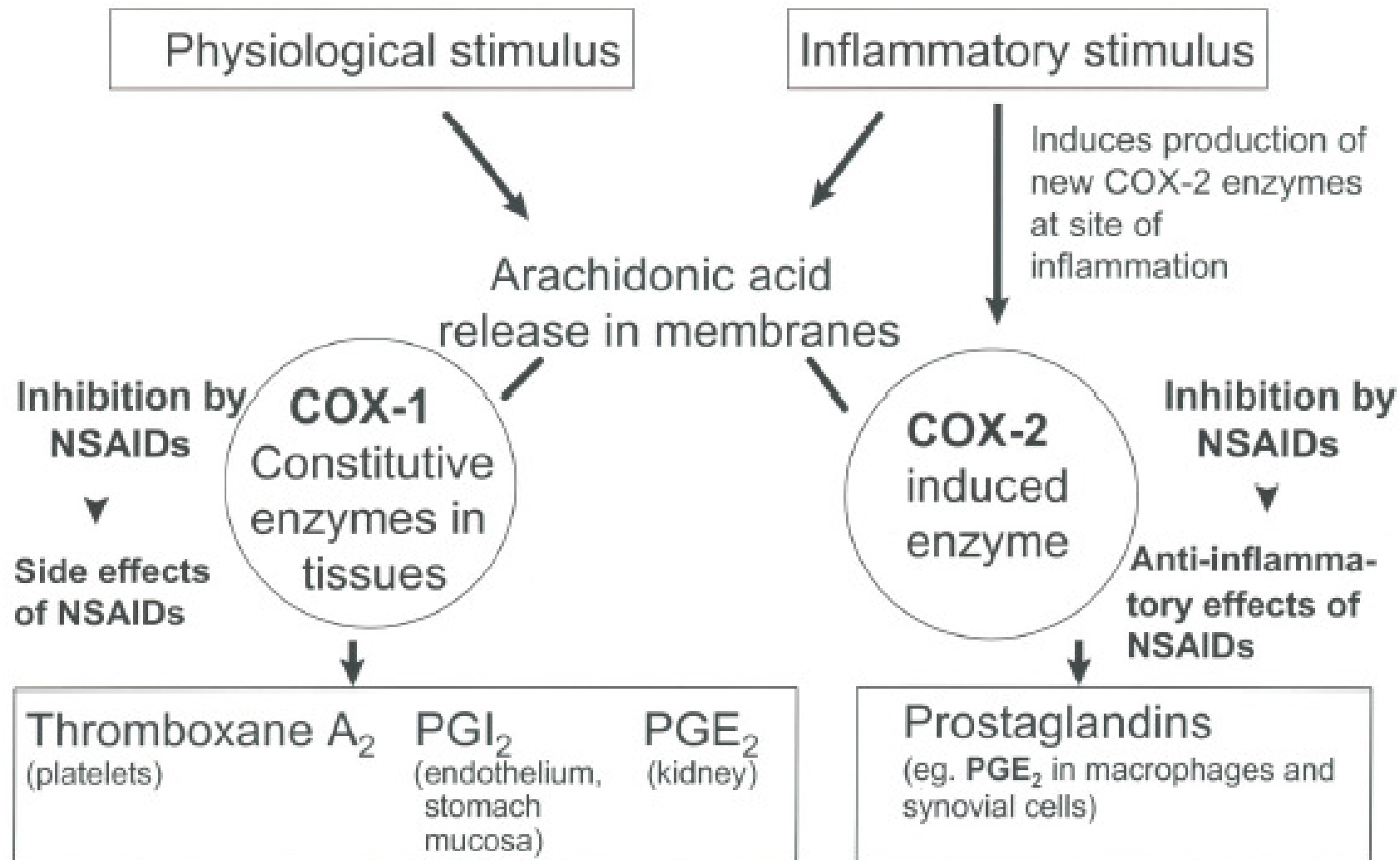
# Cyclooxygenase

## COX-1



## COX-2



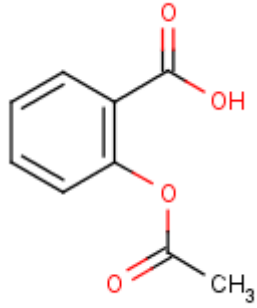


# NSAID - Veterinære præparater

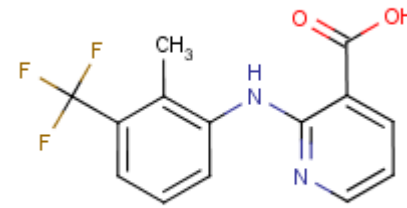
- Acetylsalicylsyre (Albyl, Magnyl)
- Phenylbutazon (Atrizin)
- Meloxicam (Metacam)
- Ketoprofen (Romefen)
- Carprofen (Rimadyl)
- Flunixin (Finadyn)
- Firocoxib (Previcox)
- Mavacoxib (Trocoxil)
- Robenacoxib (Onsior)

# COX inhibitor classification

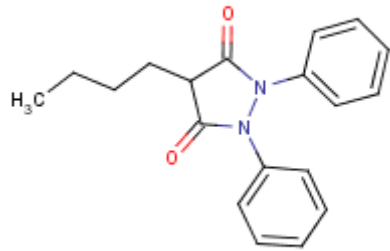
COX1	Non specific	COX2>COX1	COX2
Acetylsalicylsyre	Flunixin	Meloxicam	Firocoxib
Ketoprofen	Phenylbutazon	Carprofen	Mavacoxib
Vedaprofen			Robenacoxib



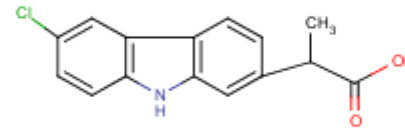
**Acetylsalicylsyre**  
carboxylsyre



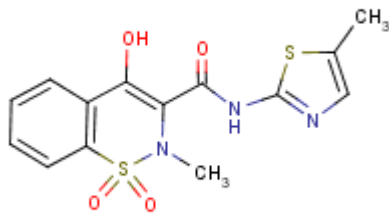
**Flunixin**  
carboxylsyre



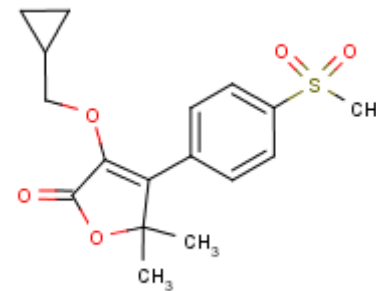
**Phenylbutazone**  
enolsyre



**Carprofen**  
carboxylsyre



**Meloxicam**  
enolsyre



**Firocoxib**  
furanone

Table 1. Pharmacodynamics of nonsteroidal anti-inflammatory drugs (NSAIDs): qualitative aspects

- Inhibition of cyclooxygenase isoforms is principal mechanism of action but some NSAIDs exert other effects at molecular levels both peripherally and centrally
- These additional effects commonly differ between drugs and may contribute to the pharmacological, toxicological and therapeutic properties of NSAIDs

Effect	Examples
Prostaglandin receptor blockade	Fenamate sub-group, e.g. meclofenamic acid
Scavenging free radicals	Phenylbutazone, piroxicam
Anti-bradykinin properties	Flunixin, ketoprofen and tolfenamic acid
Inhibition of enzyme release e.g. $\beta$ -glucuronidase	Flunixin, ketoprofen and tolfenamic acid
Inhibition of cytokine release (e.g. interleukin-6)	Carprofen
Inhibition of NF $\kappa$ B	Aspirin, carprofen, flunixin
Inhibition of 5-lipoxygenase	Tepoxalin

Table 6. Species differences in potency and potency ratios for the inhibitory effects of (COX)-1 and COX-2: human and canine enzymes

Drug	Human enzyme		
	COX-1 ( $\mu\text{M}$ )	COX-2 ( $\mu\text{M}$ )	COX1:COX-2 ratio
Aspirin	>500	>500	–
Phenylbutazone	>500	>500	–
Indomethacin	$0.06 \pm 0.03$	$2.8 \pm 1.8$	0.02
Carprofen	$54.3 \pm 24$	$17.5 \pm 10.3$	3.1
Etodolac	$130 \pm 42$	$4.5 \pm 2.2$	28
Deracoxib	$38.0 \pm 6.4$	$0.1 \pm 0.03$	380

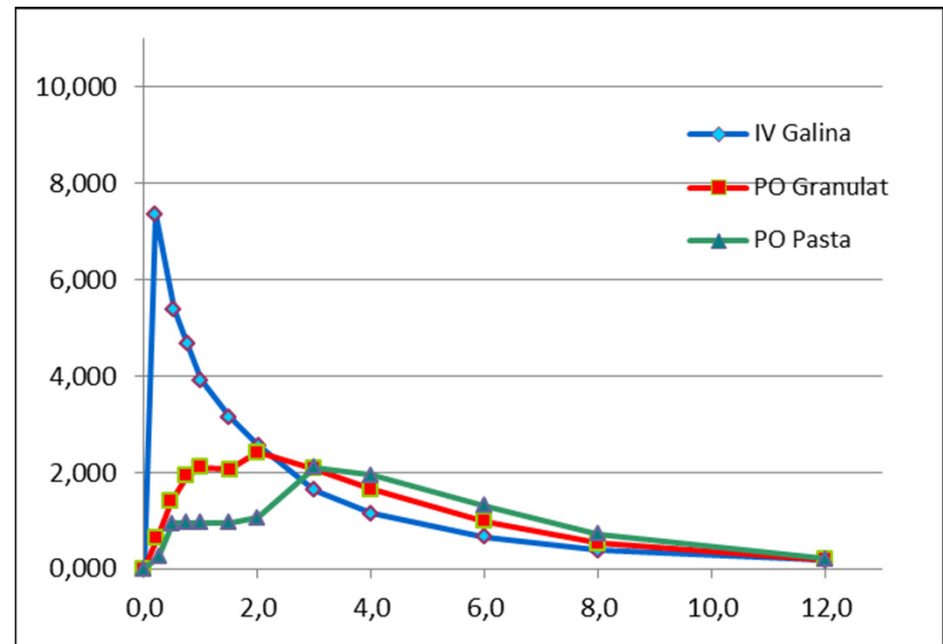
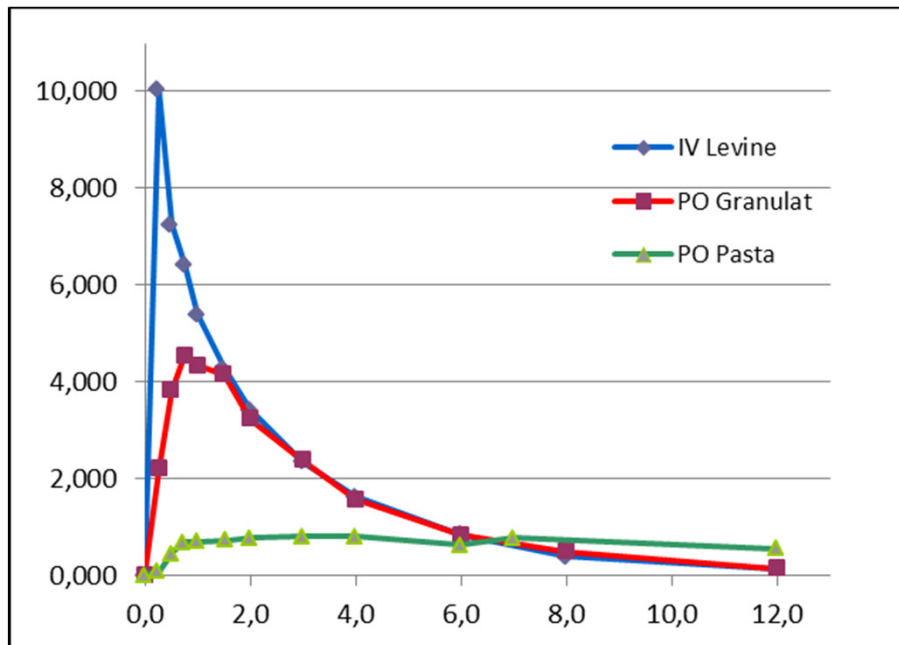
Drug	Canine enzyme		
	COX-1 ( $\mu\text{M}$ )	COX-2 ( $\mu\text{M}$ )	COX-1:COX-2 ratio
Aspirin	>500	>500	–
Phenylbutazone	>500	>500	–
Indomethacin	$0.26 \pm 0.14$	$4.4 \pm 0.04$	0.06
Carprofen	$117 \pm 68$	$1.8 \pm 1.1$	65
Etodolac	$35.1 \pm 19.6$	$10.2 \pm 0.6$	3.4
Deracoxib	$102 \pm 62$	$0.08 \pm 0.01$	1275*

# NSAID - A.D.M.E

- Svage organiske syrer
- God oral absorption
  - Bioavailability 70-100%
- Proteinbinding over 99% (undtagen salicylater)
- Vd: 0,2-0,3 L/kg
- Affinitet til inflammatorisk eksudat
  - Følger proteinerne til ødemvæsken
- Elimination
  - Metabolisering i leveren Fase I og II (metabolisering)
  - Acetylsalicylsyre og phenylbutazon har aktive metabolitter
  - Filtreres ikke i nyrerne p.g.a. proteinbinding

# Flunixin, hest

Dose: 1,1 mg/kg



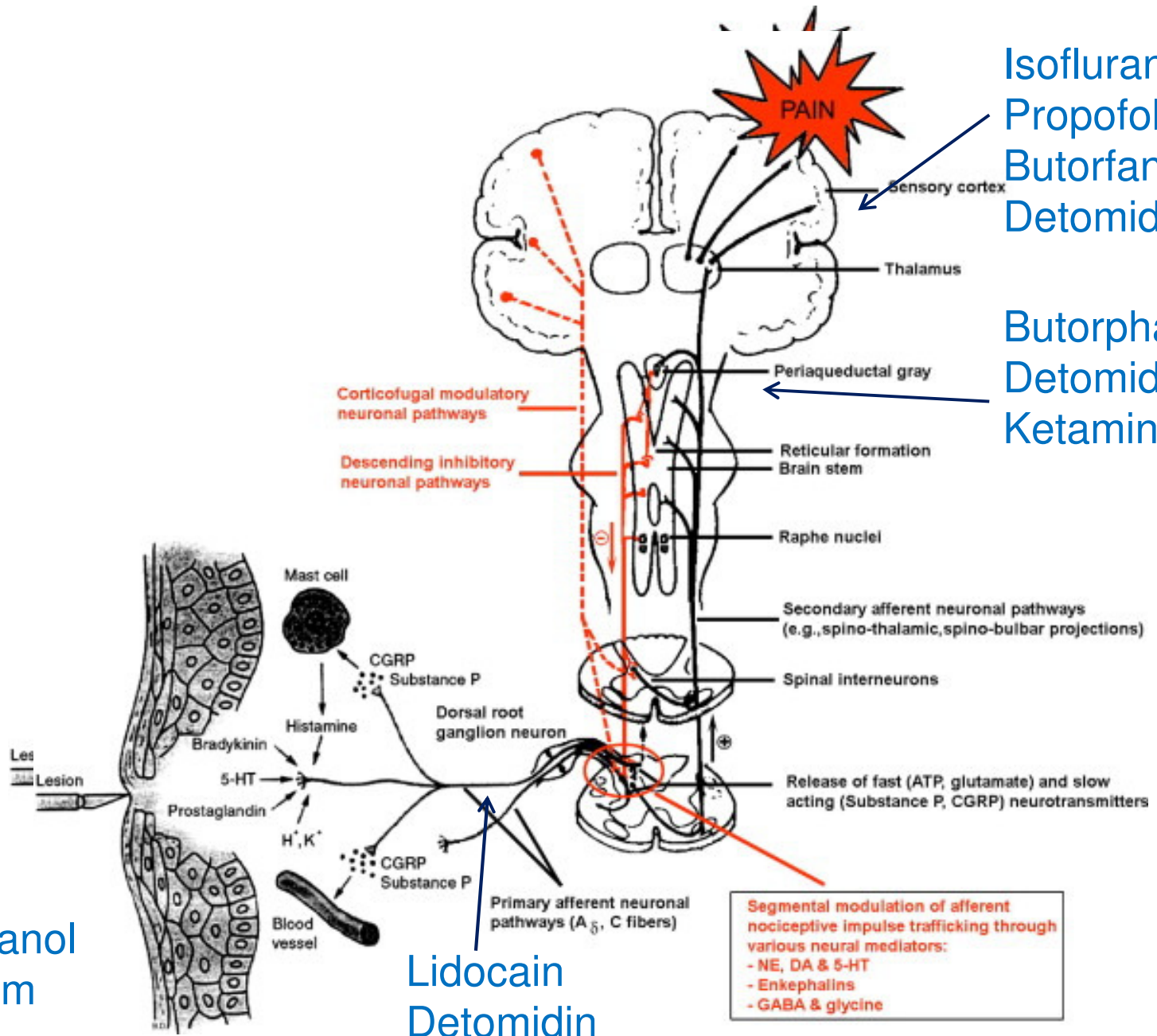
# NSAID - halveringstider (timer)

	Hund	kat	hest	kvæg	svin
acetylsalisylsyre	8,6	22-45	1-3	0,5	5,9
phenylbutazon	6	18	4	30-80	4
flunixin	3.7		1,6	3,1	
carprofen	7	15	16	37	
meloxicam	12-36	37	3	13	4
firocoxib	7,5		33		



# NSAID

- Smertebehandling
  - Mindre kirurgi
    - NSAID
    - Opioider
  - Invasiv kirurgi
    - 0 - 24 timer
      - Opioider og NSAID
    - 24 - 48 timer
      - NSAID



Isofluran  
Propofol  
Butorfanol  
Detomidin

Butorphanol  
Detomidin  
Ketamin

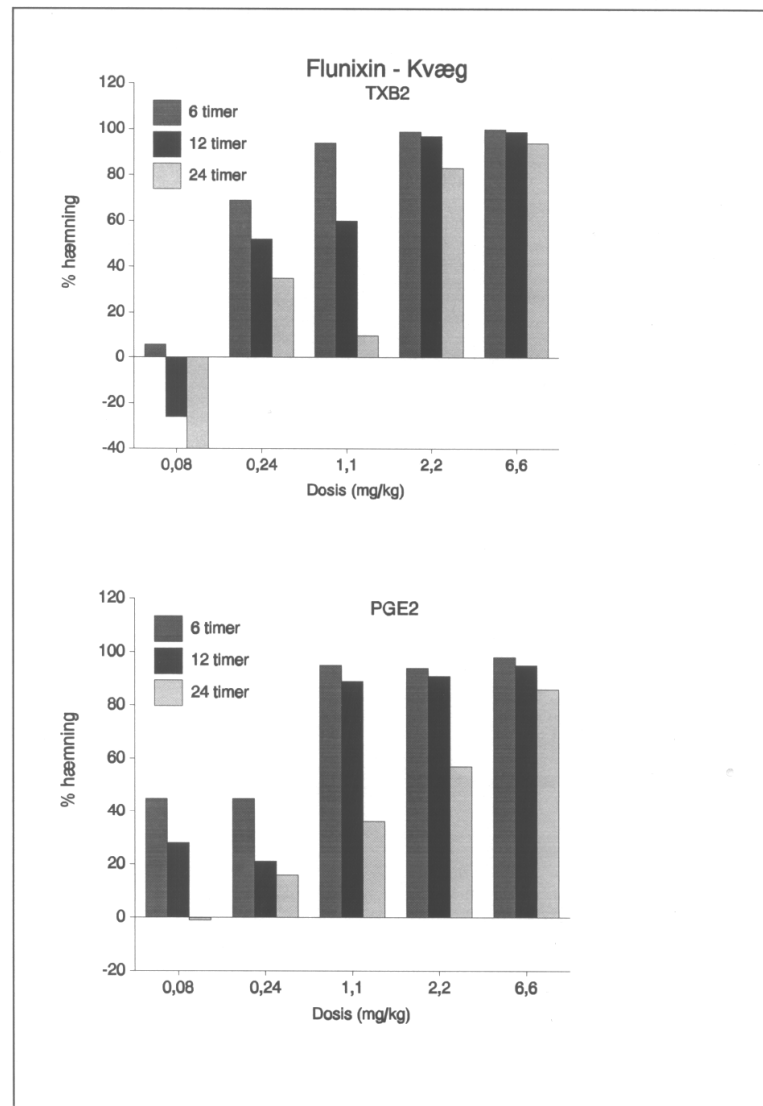
Lidocain  
Burtorphanol  
Meloxicam

Lidocain  
Detomidin

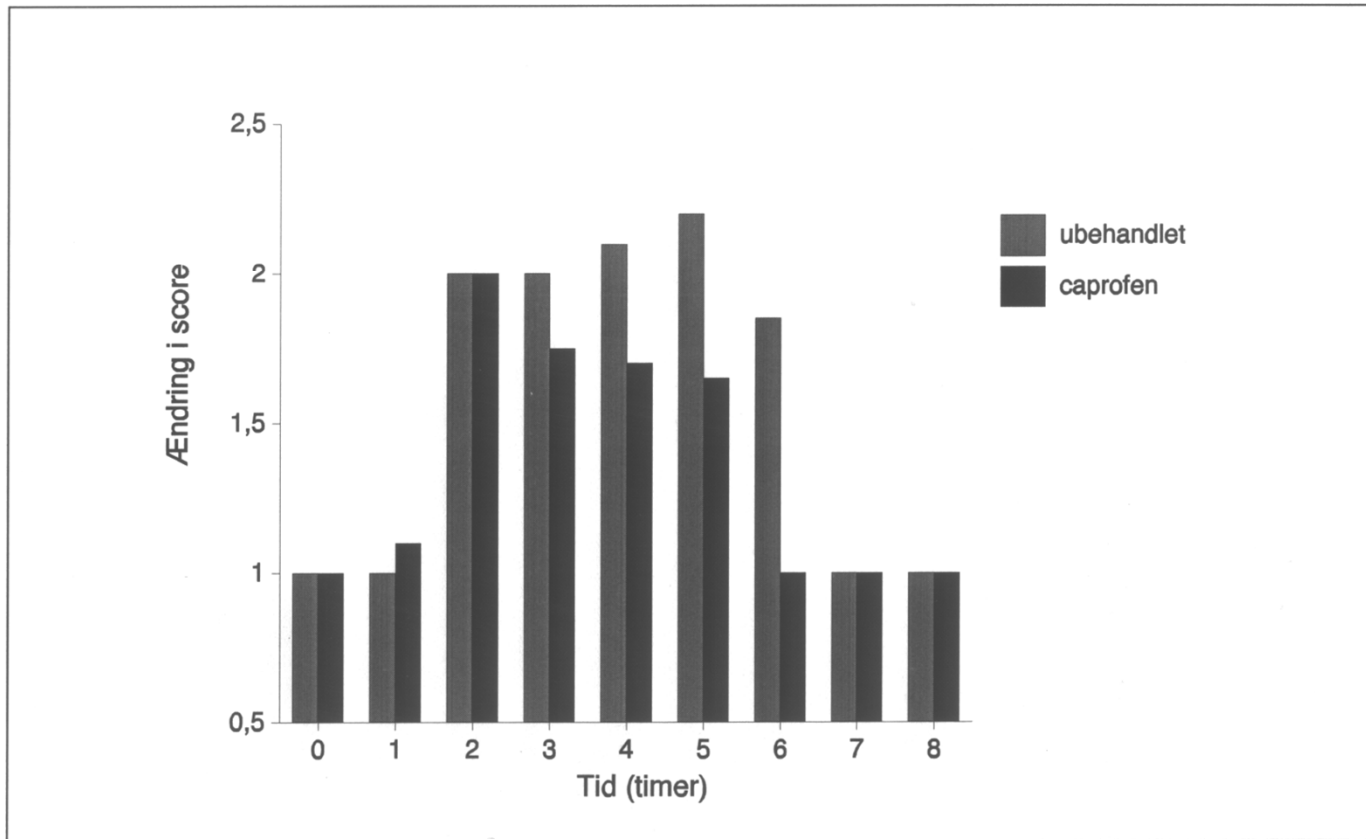
Segmental modulation of afferent nociceptive impulse trafficking through various neural mediators:  
- NE, DA & 5-HT  
- Enkephalins  
- GABA & glycine

# NSAID - Indikationer

- Aseptiske inflammationer generelt
- Kolik
- Spasmer i mave-tarmkanalen
- Viscerale smerter
- Aseptiske inflammationer i bevægeapparatet
- MMA (metritis, mastitis, agalakti)
- Pneumonier (især *Actinobacillus pleuropneumoniae*)
- Endotoksikoser
- Brandige mastitter?



**Figur 3** Inhibitorisk effekt af flunixin på TXB<sub>2</sub> i serum og PGE<sub>2</sub> i ekssudat hos kvæg. Modificeret efter Lees et al. (19)



Figur 4 Effekt af caprofen (0,7 mg/kg IV) på yverødem ved endotoksin-induceret mastitis. Modificeret efter Lohuis et al. (16).

# NSAID - Bivirkninger

- Ventrikel ulceration
- Forstyrret blodpladefunktion
  - Hæmmer koagulation
- Forstyrret nyrefunktion
  - Nedsætter renalt blood flow og GF
  - Øger virkning af ADH
  - Øger absorptionen af Cl
  - Øger K reabsorption
  - Nedsætter renin sekretion
- Forlænger drægtighed eller fødsel

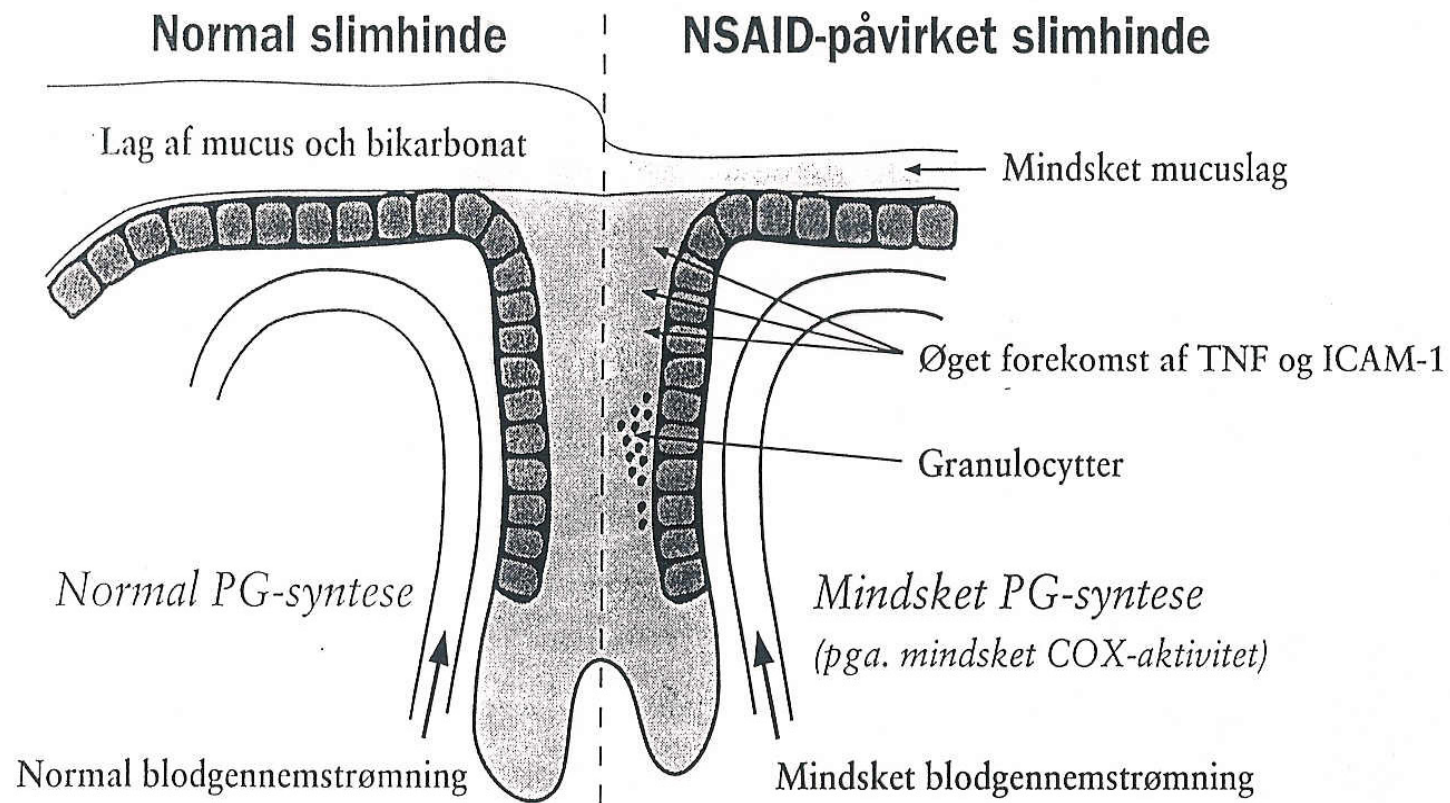
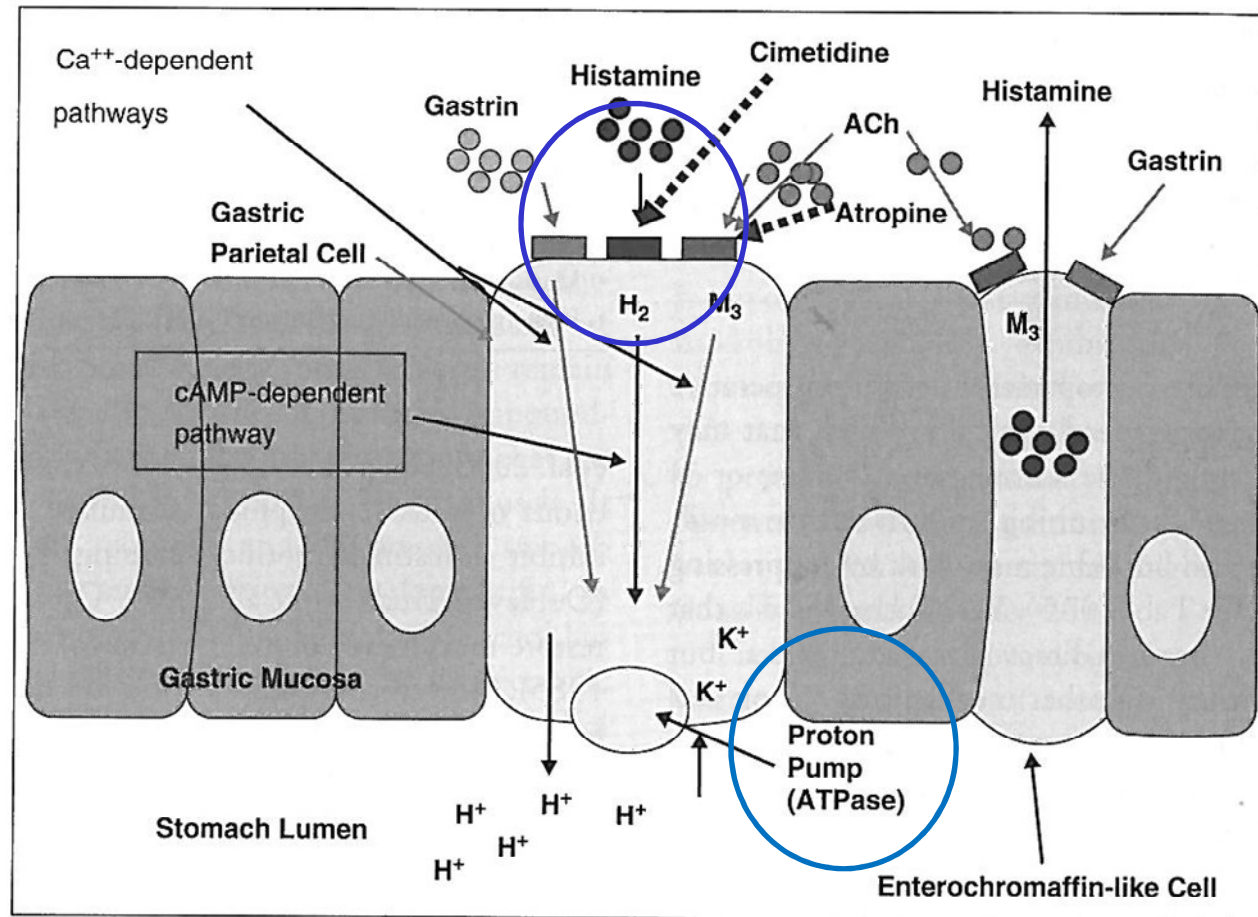


Fig. 3. Opståelse af NSAID-ulcus gennem mindsket PG-syntese. (Figuren er en videreudvikling af en illustration i "NSAID-ulcus" af Andreas Aly.)



# Meloxicam omeprazol inhibition

