LEHVOSS Nutrition

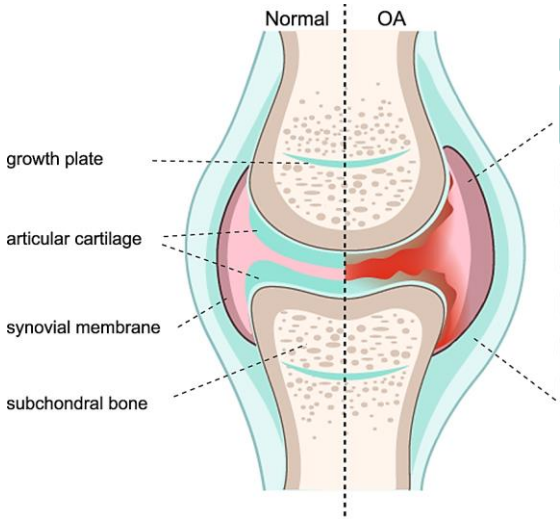
Univestin™ + AmLexin™

Synergistic Approach for Optimal Joint Care

Common Symptoms Experienced In Osteoarthritis (OA)

- **Pain:** Affected joints might hurt during or after movement.
- **Stiffness:** Joint stiffness might be most noticeable upon awakening or after being inactive.
- **Tenderness:** Your joint might feel tender when you apply light pressure to or near it.
- **Loss of flexibility:** You might not be able to move your joint through its full range of motion.
- **Grating sensation:** You might feel a grating sensation when you use the joint, and you might hear popping or crackling.
- **Bone spurs:** These extra bits of bone, which feel like hard lumps, can form around the affected joint.
- **Swelling/Edema/Inflammation:** This might be caused by soft tissue inflammation around the joint.

Osteoarthritis (OA): Underlying Malfunctions In Joints



- joint pain
- loss of chondrocytes
  articular cartilage erosion
- synovial hyperplasia
- abnormal angiogenesis
- synovial inflammation
- subchondroal bone disturbance
- ligaments and tendons instability
- joint stiffness

Due to loss of **articular cartilage**.

Breakage of cartilage components causes **Inflammation.**

Promoted by **inflammation due to cartilage degradation and loss of chondrocytes**.

Stimulated by inflammation.

Increased levels of proinflammatory biomarkers - **IL-6, IL-1β, TNFα, MMP-3 and MMP-13.**

Overexpression of inflammatory cytokines lead to subchondral disturbances.

Articular cartilage loss resulting from injury, overuse or repeating a movement over time. Contributes to osteoarthritis.

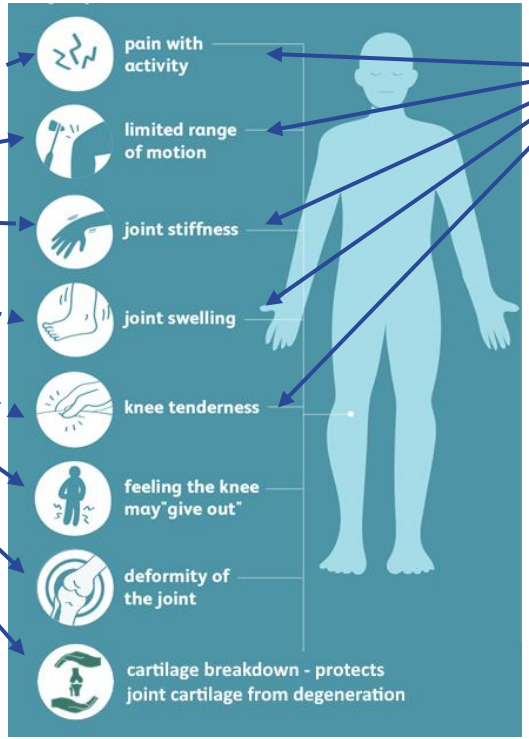
Results in reduced range of motion and physical function.

Synergistic Approach For Optimal Joint Care

According to Research:

AMLEXIN™

Helps improve



Univestin®

Helps improve

Structural Integrity

Symptom Relief

Pain associated with OA

- The most common symptom of OA is pain and associated stiffness in the affected joint which tends to worsen with joint movement.

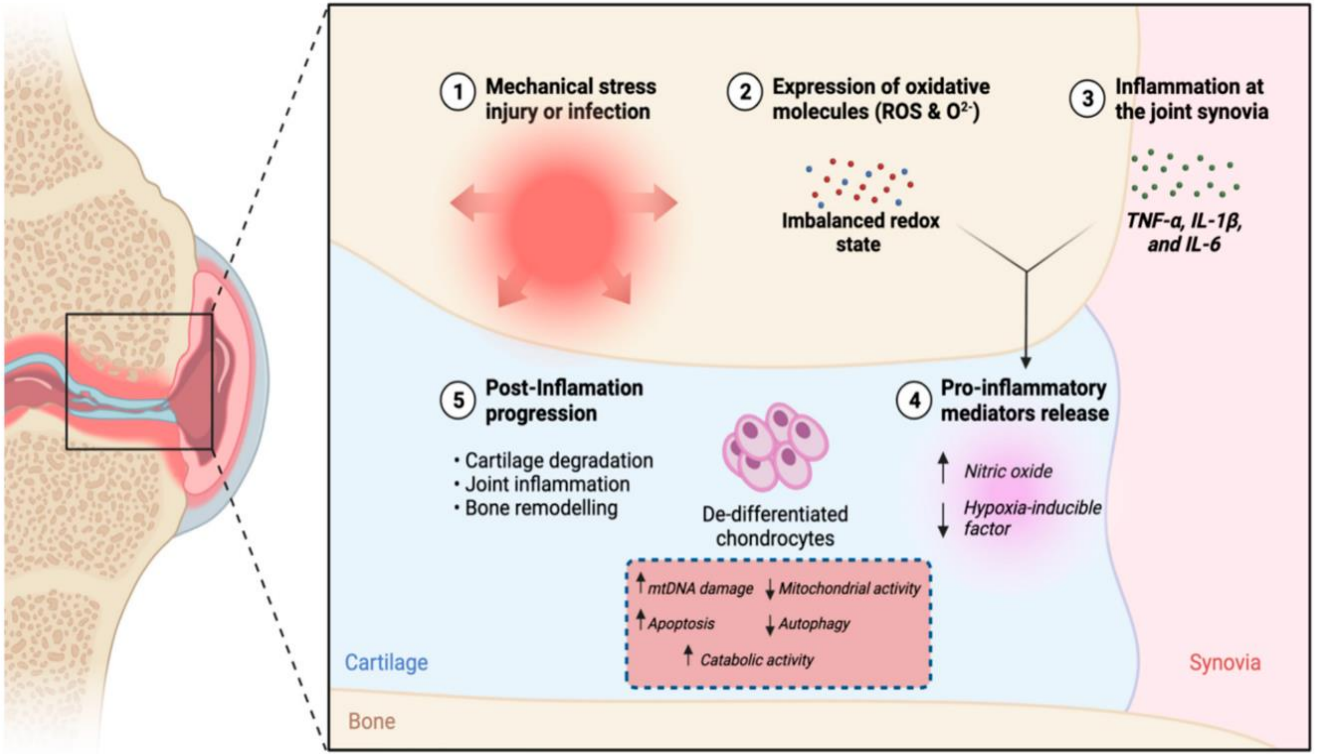
- The **WOMAC** is a **valid and reliable** outcome measure in patients with OA.

- **WOMAC OA index - quantifies pain severity, joint stiffness and range of motion.**

Higher the score = Higher the pain severity

Oxidative Stress in Osteoarthritis: The mechanism behind

- **Superoxide anion** is the most potent free oxygen radical (**ROS**), released during **cartilage wear & tear** and in OA.
- Superoxide release **results** in **inflammation, tissue damage and pain**.
- Cartilage degradation in turn releases more superoxide, setting up a **vicious cycle**.



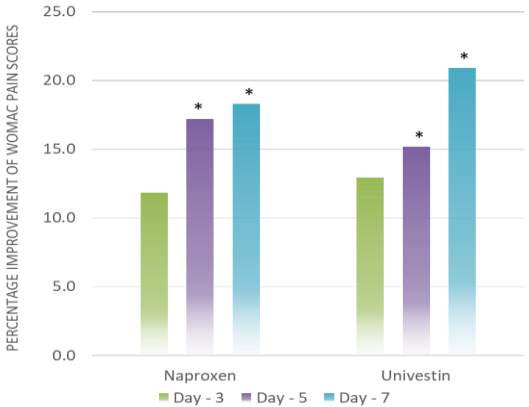
Oxidative Stress in Osteoarthritis: AmLexin™ Potent Antioxidant Activity

	Superoxide Anion
AmLexin™	**12066**
Univestin™	4767
Ginkgo Extract (24% flavonoids)	6768
Resveratrol	266
Citrus Bioflavonoids (20%)	0

Against the most powerful ROS – the “Superoxide Anion”.

Pain in Osteoarthritis: Univestin™ and AmLexin™ Scientific Evidence

Univestin™ results in **effective pain relief**, in as early as **5 days**.



Fast acting, effectively alleviates pain with activity - hard activity.

AmLexin™ led to **51% reduction in WOMAC pain scores over 12 weeks.**

Combination Effect

AmLexin™ has a potent antioxidant effects against superoxide anions and Univestin™ has powerful pain-relieving and anti-inflammatory qualities.

Combining Univestin™ and AmLexin™ potentially boost the pain relief effects.

Combining with Univestin™ and AmLexin™ potentially boost pain relief

OA - Associated Pain	Univestin™	AmLexin™	Reference
Acute pain relief	✓✓	-	Arjmandi *et al.*
Chronic pain relief	✓✓	✓✓	Kalman *et al.*, Sampalis *et al.*

TABLE 1: Percentage changes in pain sensitivity for MIA- Induced rats treated with AmLexin™, Univestin™ and their combination.

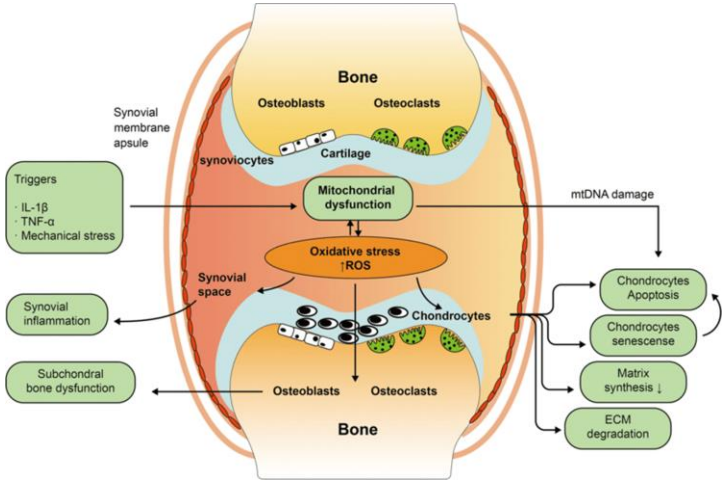
Group	Dose (mg/kg)	*N*	Wk 1	Wk 2	Wk 3	Wk 4	Wk 5
% increase							
MIA	10	10	44.9†	45.4†	47.7†	46.5†	47.1†
% inhibition							
Diclofenac	10	10	49.6†	34.5†	34.3†	35.5†	34.9†
AmLexin™	400	10	21.1*	28.3*	33.0†	37.0†	38.0†
Ü■Ⱡś ℓč■™	250	10	35.5†	33.8†	38.1†	43.3†	45.9†
Composition‡	650	10	59.6†	64.6†	70.7†	69.9†	70.3†

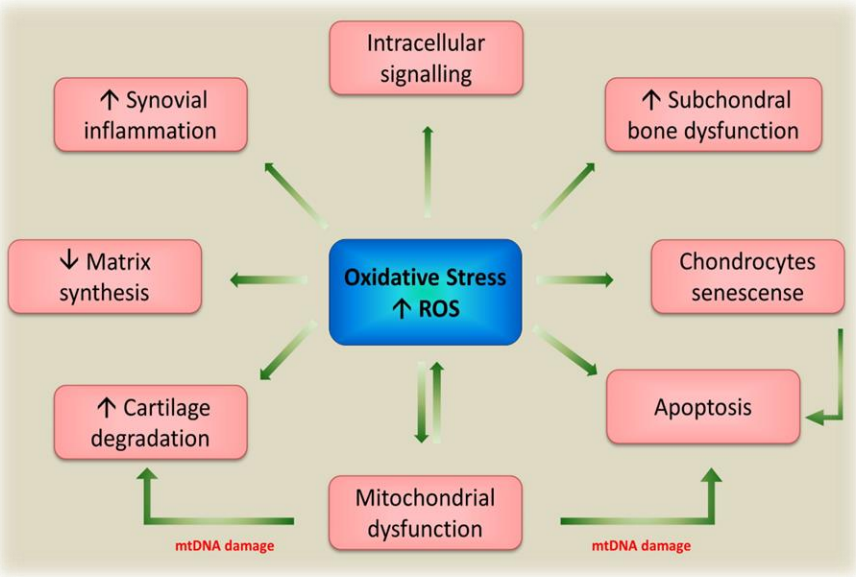
*$P \leq 0.00001$ verses MIA; †$P \leq 0.000001$ verses MIA or normal control; % increase = ((mean normal control − mean MIA)/mean normal control) ∗ 100; % inhibition = ((mean treatment − mean MIA)/(mean normal control − mean MIA)) ∗ 100. ‡Composition: AmLexin™ + Univestin™

Stiffness in Osteoarthritis

- Joint inflammation and oxidative stress are **directly associated with OA progression.**

- Joint stiffness might be **most noticeable upon waking up or after being inactive.**

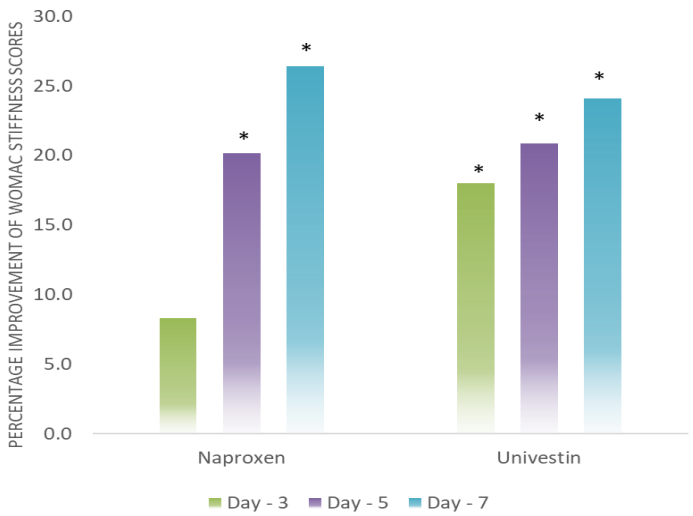




Stiffness in Osteoarthritis

Univestin®

Significant reduction in joint stiffness **within 3 days of use of Univestin™.**



AMLEXIN™

45% reduction in WOMAC stiffness scores.

Remember:

AmLexin™ has highest ORAC value for Superoxide Anion (ORAC: 12066).

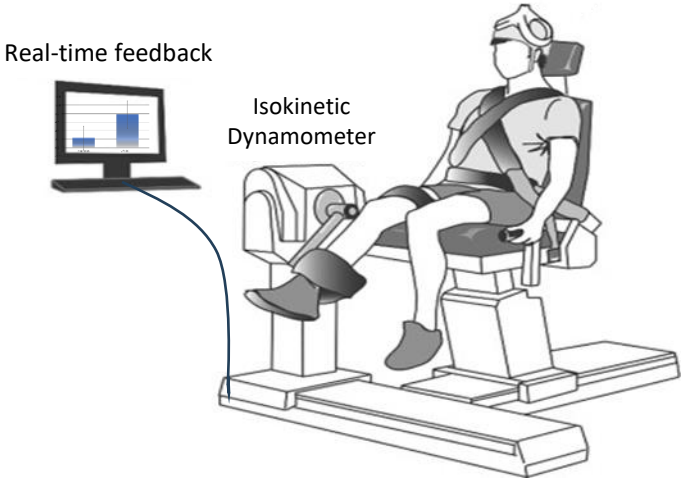
Stiffness in Osteoarthritis

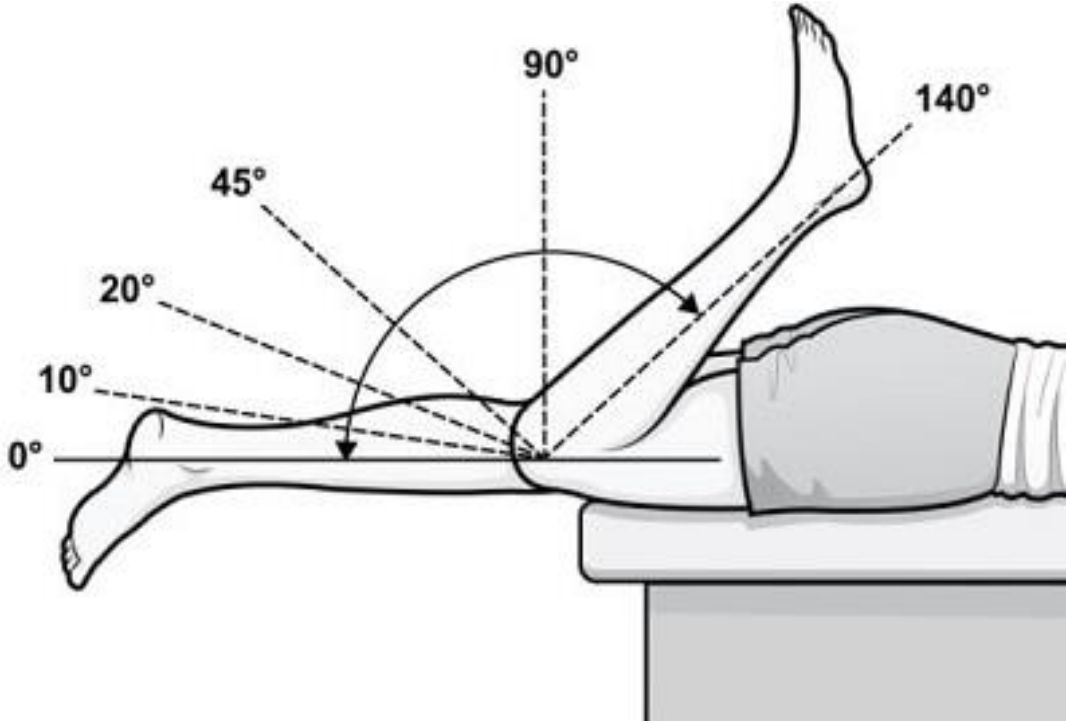
Stiffness	Univestin™	AmLexin™	References
Relief from joint stiffness	✓✓	✓✓	Arjmandi *et al.*, Kalman *et al.*
Increased Reactive oxygen species (ROS)	✓✓	✓✓	Yimam *et al.*

Loss of function and flexibility in Osteoarthritis

Meaning:

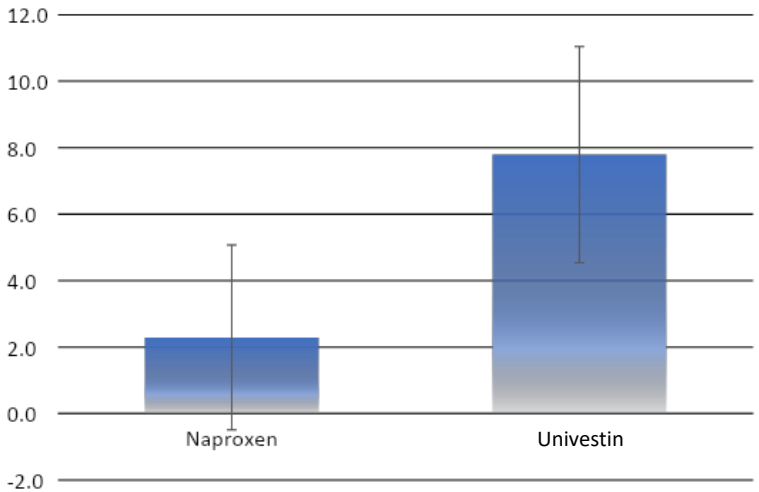
- **Not being able** to move the joint through its full **range of motion**.





Loss of flexibility in Osteoarthritis: Univestin™ and AmLexin™ Benefits

Univestin™ significantly improves range of motion.

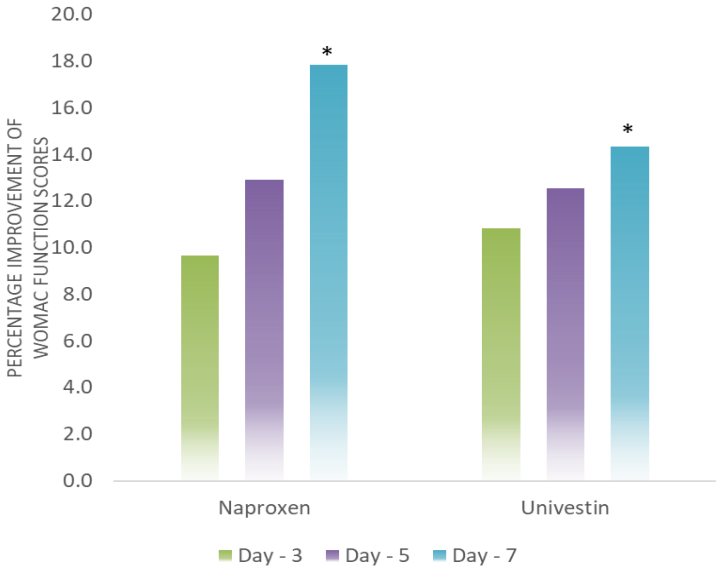


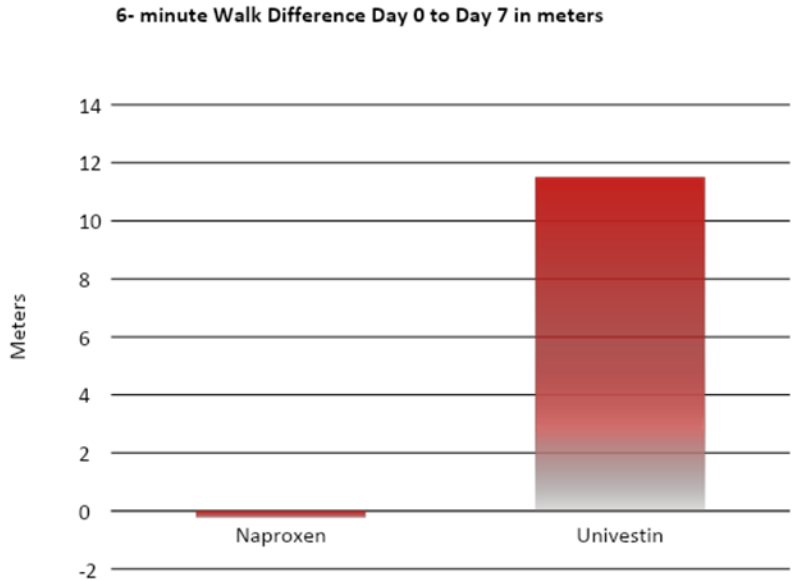
Extension change from baseline to day 84	1.65 ± 2.43 (43) 0 (−1–10) $p < 0.001$*
Flexion change from baseline to day 84	−8.3 ± 7.1 (43) −8 (−25–8) $p < 0.001$*

*Significant: $p \leq 0.05$.

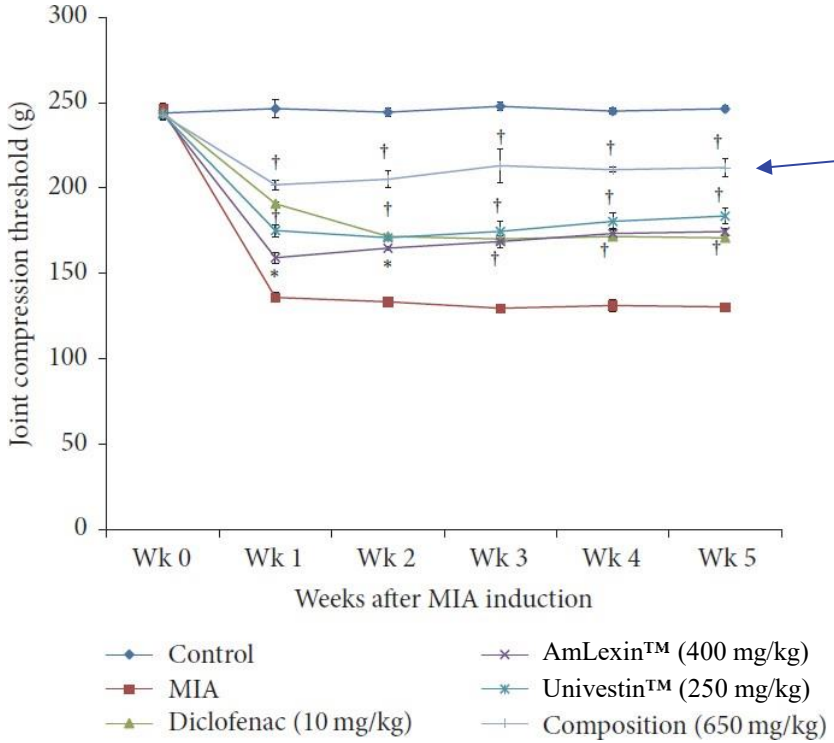
Loss of function in Osteoarthritis: Univestin™ Benefits

- **Improved joint function within 7 days of use of Univestin™**





Joint Compression: Univestin™ and AmLexin™ Benefits



Combining Univestin™ with AmLexin™ potentiates joint function.

Conclusion

Univestin™ + AmLexin™ combined potentially enhanced the joint compression threshold in rats.

Yimam M et al. (2017) Cartilage Protection and Analgesic Activity of a Botanical Composition Comprised of Morus alba, Scutellaria baicalensis, and Acacia catechu, Evid Based Complement Alternat Med. 2017 Aug 20;2017:7059068. doi: 10.1155/2017/7059068

Joint function and Range of Motion(RoM)

Joint Function and Flexibility	Univestin™	AmLexin™	References
Improved joint function and RoM	✓✓	✓	Arjmandi *et al.*, Kalman *et al.*, Yimam *et al.*

COX/LOX inhibition for Quelling Inflammation: Concerns

Non selective COX inhibition leads to gastric disturbances due to COX-1 inhibition while selective COX-2 inhibition may cause cardiac side effects.

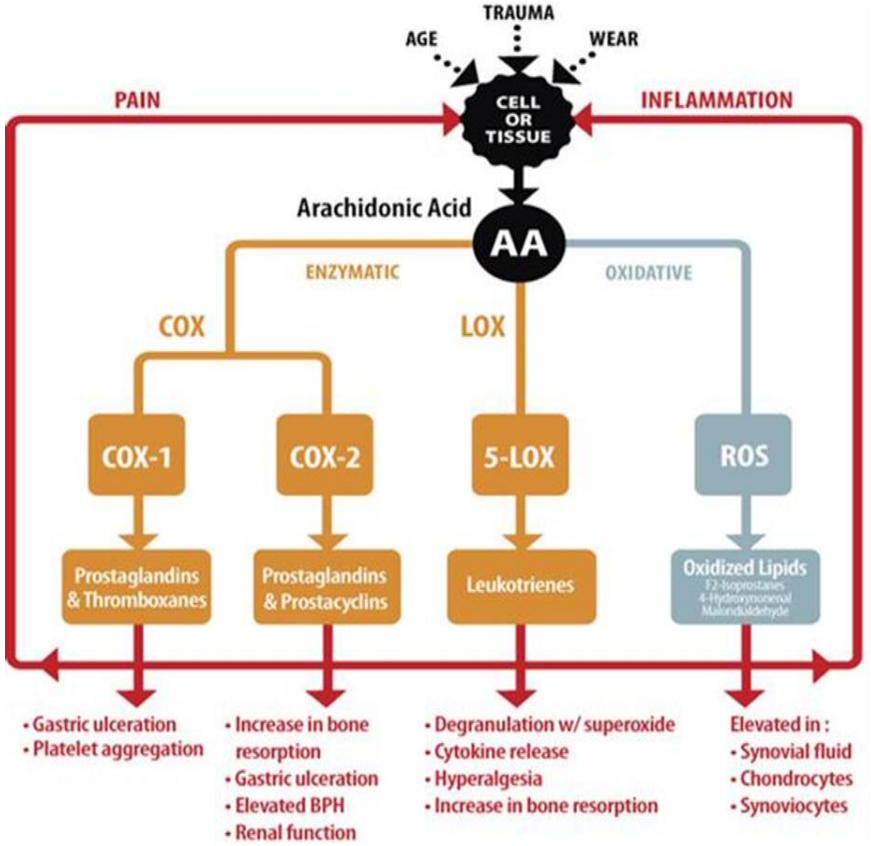
Blocking the COX pathway(s) shunts more AA metabolism down the 5-LOX path ⇒ ↑ **highly chemotactic and inflammatory leukotrienes.**

These effects are mediated through LTB4 which is:

- Associated with **increased production of the pro-inflammatory cytokines.**
- Shown to **stimulate osteoclastic bone resorption.**
- Detected at **high levels** in the walls of **NSAID induced gastric ulcers.**

Joint Swelling and Inflammation: Univestin™ and AmLexin™ Synergy

Univestin™ and AmLexin™ demonstrate dual **COX and LOX** inhibition of systemic inflammation and reduce **ROS** enabling a holistic control of **all four** AA metabolism **pathways**.



Burnett et al., (2007) A medicinal extract of Scutellaria baicalensis and Acacia catechu acts as a dual inhibitor of cyclooxygenase and 5-lipoxygenase to reduce inflammation, J Med Food. 10(3):442-51.

Yimam et al., (2016), UP1306, a Botanical Composition with Analgesic and Anti-inflammatory Effect, Pharmacognosy Res. 2016 Jul-Sep;8(3):186-92.

Counters swelling and inflammation by ‘Dual Mechanism’

Swelling and Inflammation	Univestin™	AmLexin™	References
COX-1 & COX-2 inhibition	✓✓✓	✓	Burnett *et al.*, Yimam *et al.*
5-LOX inhibition	✓	✓✓✓	

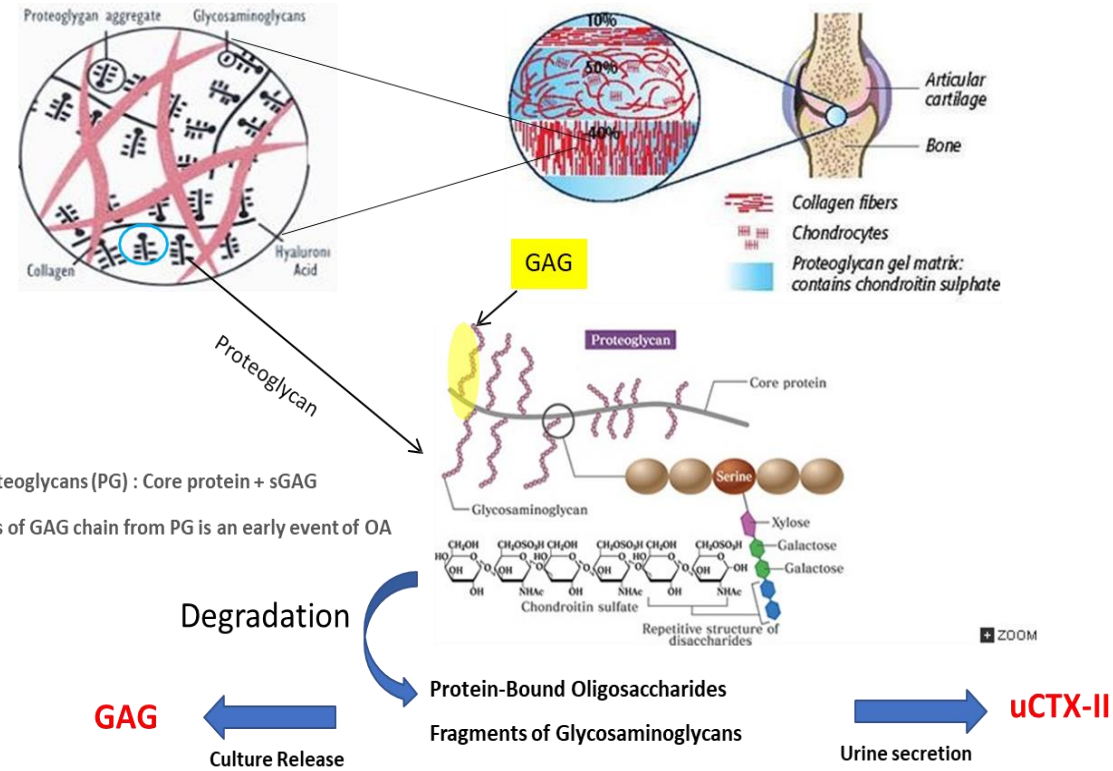
Joint Swelling and Inflammation: Univestin™ and AmLexin™ Synergy

The Double Advantage of Combining Univestin™ + AmLexin™:

Univestin™ and **AmLexin™** tackle the **pro-inflammatory biomarkers (IL-6, 1β, TNFα)** while **AmLexin™** further reduces **proteolytic enzymes (MMP3 and MMP13)** - both of these are involved in inflammation and articular cartilage degradation.

		Univestin™	AmLexin™
Pro-inflammatory Biomarkers Suppression	**IL-6**	✓	✓✓✓
	IL-1β	✓	✓✓✓
	TNFα	✓	✓✓✓
Cartilage Degradation Biomarkers Suppression	**MMP3**	-	✓✓
	MMP13	-	✓✓

Joint Cartilage Degradation in Osteoarthritis



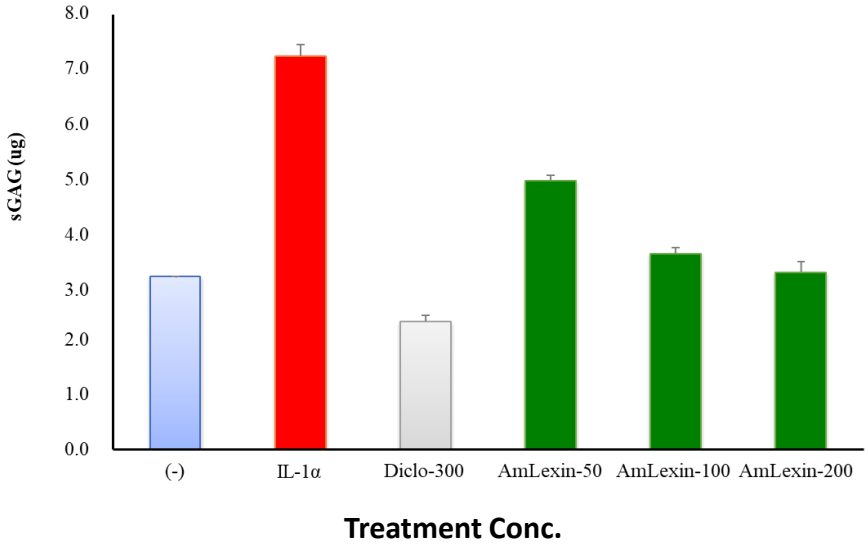
- Proteoglycans (PG) : Core protein + sGAG
- Loss of GAG chain from PG is an early event of OA

GAG and uCTX-II:

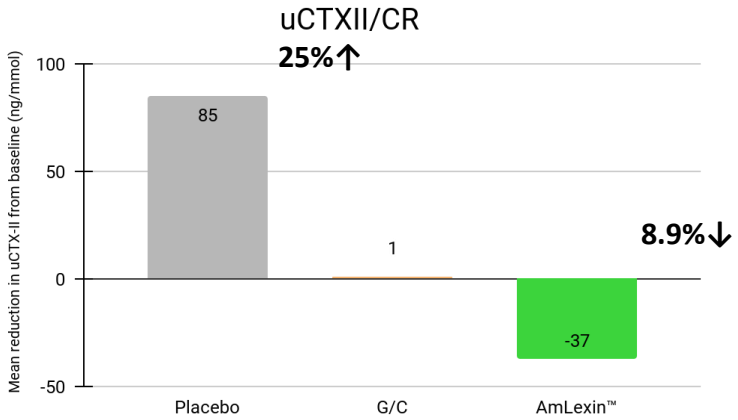
Two main biomarkers for joint cartilage degradation.

Joint Cartilage Degradation in Osteoarthritis: AmLexin™ Benefits on Cartilage Degradation

- AmLexin™ reduced IL-1α **mediated degradation of Glycosaminoglycans (GAG)** from proteoglycan of joint cartilage.



- AmLexin™ significantly **reduces uCTX-II levels** over placebo in subjects with knee osteoarthritis.



Synergistic effect of Univestin™ + AmLexin™ on Cartilage Protection

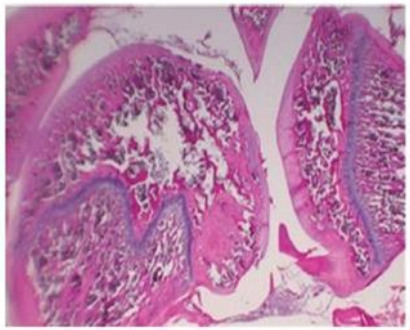
- Injection of **Mono-IodoAcetate (MIA)** into rats' femorotibial joint triggers limb pain and progressive cartilage degradation, establishing an **osteoarthritis (OA) model akin to human OA.**

- *In vivo*, **AmLexin™ + Univestin™** treated rats exhibit marked **preservation of articular structure**, evidenced by histopathological findings (image on next slide).

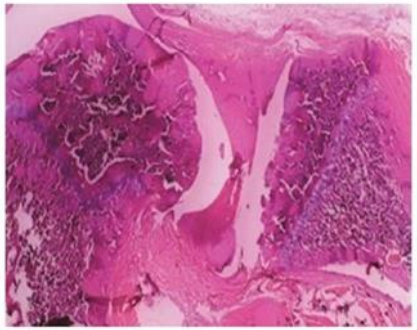
- **In contrast, diclofenac failed to significantly protect cartilage**, highlighting NSAIDs' limitation in OA treatment, mainly offering symptomatic relief without disease-modifying effects.

Yimam M et al. (2017) Cartilage Protection and Analgesic Activity of a Botanical Composition Comprised of Morus alba, Scutellaria baicalensis, and Acacia catechu, Evid Based Complement Alternat Med. 2017 Aug 20;2017:7059068. doi: 10.1155/2017/7059068

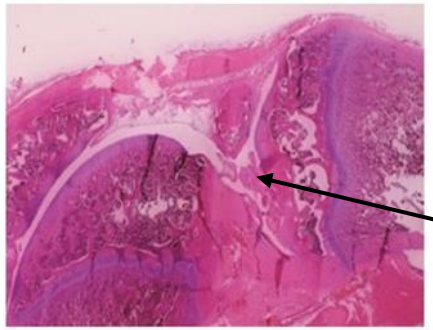
Synergistic effect of Univestin™ + AmLexin™ on Cartilage Protection



Normal control

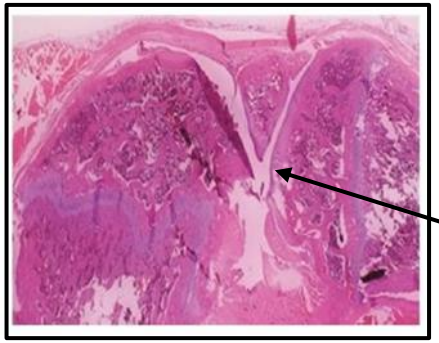


MIA control



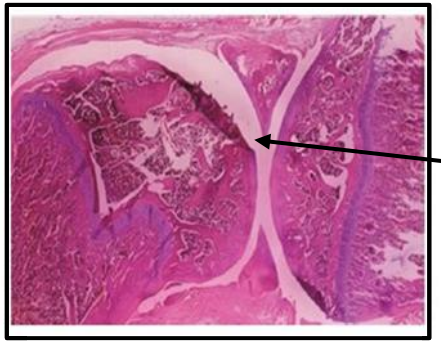
MIA diclofenac (10 mg/kg)

Failed to protect cartilage



Preserved articular cartilage

MIA + AmLexin™ (400 mg/kg)



Preserved articular cartilage much more effectively

MIA + Combination

Chondroprotection: AmLexin™ Benefits

Parameters of joint degradation	Univestin™	AmLexin™	References
Glycosaminoglycans (GAG)	-	✓✓	Kalman *et al.*, Yimam *et al.*
Increased uCTX-II	-	✓✓	

Take Away: Synergy 1 + 1 = 11

- According to Research, **the combination of Univestin™ and AmLexin™** shows to provide **greater pain relief and cartilage protection.**

- This combination also shows to **reduce associated symptoms** by enhancing the anti-inflammatory and analgesic action of Univestin™ with the cartilage degradation support from AmLexin™.

Alleviation of OA Signs and Symptoms	Univestin™	AmLexin™
Pain	✓✓✓	✓
Stiffness	✓✓✓	✓✓
Swelling and Inflammation	✓✓✓	✓
Range of Motion	✓✓✓	✓
Joint Cartilage Degradation	✓	✓✓✓
ROS - Superoxide Anion	✓	✓✓✓

The Complete Optimal Joint Care Solution

AMLEXIN™

+

Univestin®

Talk to the experts

Find here your sales representative in Europe

For details about our ingredients register to our digital platform:

WEBAPP

Visit our website lehvoss-nutrition.com

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