Undenatured type II collagen mitigates inflammation and cartilage degeneration in healthy untrained Labrador retrievers after exercise

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Introduction

Undenatured type II collagen (UC-II®) is a glycoprotein from chicken sternum cartilage that shows promise in the reduction of exercise-associated pain and lameness in canines[1]. Exercise can cause microtrauma in the tissue and joints of dogs, resulting in a cycle of inflammation and discomfort even in healthy dogs[2]. The objective of this trial was to evaluate the effect and etiology of undenatured type II collagen supplementation on inflammation and cartilage degeneration after exercise in untrained, healthy dogs.

Materials and Methods

Animals and Housing

- 40 healthy Labrador retrievers (20m/20f; 5-12yrs) selected from colony of Labrador retrievers at Four Rivers Kennel.
- All dogs housed in temperature controlled individual kennels overnight and aired outside in social groups for appx 6hrs daily.
- All dogs fed the same standard kennel diet.
- Water was provided *ad libitum* via automatic waterers.

Diet and Treatments

- All dogs fed the same standard kennel diet once daily in the morning.
- All dogs sorted into two treatment groups based on age, sex body weight, and genetic lineage.
- Twenty dogs from undenatured type II collagen group received 40mg UC-II® (10mg Collagen Type II/Min. 3% Undenatured Type II Collagen; Lonza Consumer Health, Inc) in capsule form once daily by mouth.
- Twenty dogs from placebo group received 40mg maltodextrin in capsule form once daily by mouth.

Study Design

- Three-week trial to evaluate the effectiveness and safety of undenatured type II collagen on the mediation of inflammation and joint pain during and after exercise.
- After a two-week acclimation and loading period, each dog performed a 4.66km endurance run. The dogs ran freely in groups alongside an all-terrain vehicle in the bush and were free to stop, swim, etc.
- Activity during the run was quantified via Actical® accelerometer collars and Garmin® GPS collar data.
- Blood samples were collected via jugular venipuncture at baseline (prior to loading), 1h pre-run, and 24-hours post-run.
- Interleukin-6 targeted as a marker of inflammation and analyzed via commercially available ELISA kit (Abcam, Cambridge, MA).
- Cartilage oligomeric matrix protein (COMP) targeted as a marker of cartilage degeneration and analyzed via commercially available ELISA kit (MyBiosource, San Diego, CA).
- Hematological analysis targeted as a marker of inflammation and analyzed via in-house automatic analyzer (Abaxis HM5).

Results and Discussion

- Interleukin-6 (Figure 1): IL-6 was significantly lower in undenatured type II collagen dogs compared to placebo at 24h post-run ($p<0.01$). Undenatured type II collagen dogs also had a significant decrease in IL-6 pre to 24h post-run ($p=0.03$), compared to placebo dogs with no significant change ($p=0.16$). These results indicate lower levels of inflammation after exercise in undenatured type II collagen dogs.
- Cartilage Oligomeric Matrix Protein (Figure 2): COMP was significantly lower in undenatured type II collagen dogs at 24h post-run compared to pre-run ($p=0.02$), compared to placebo dogs having no significant differences between timepoints ($p=0.24$). These results indicate decreased levels of cartilage degeneration after exercise in undenatured type II collagen dogs.
- Neutrophil/Lymphocyte Ratio (Figure 3): At both 1h pre- and 24h post-run undenatured type II collagen dogs had no significant increases in neutrophil:lymphocyte ratio (NLR; inflammatory marker), but P dogs had significantly higher NLR compared to baseline ($p=0.01$). NLR was also significantly lower in undenatured type II collagen supplemented dogs compared to P dogs at pre-run ($p<0.01$). These results indicate lower levels of inflammation in undenatured type II collagen dogs.
- Activity: Undenatured type II collagen males had significantly higher activity per kilometer compared to placebo males ($p<0.05$). These results indicate increased activity intensity in undenatured type II collagen male dogs.
- Undenatured type II collagen dogs had significantly lower white blood cell counts after supplementation compared to P dogs ($p<0.05$) (Table 1).

Figure 1

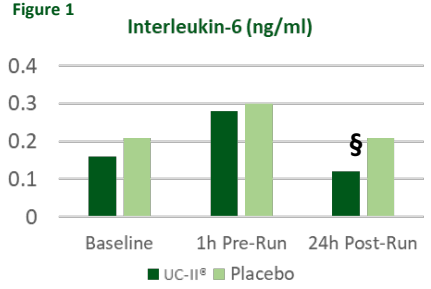


Figure 2

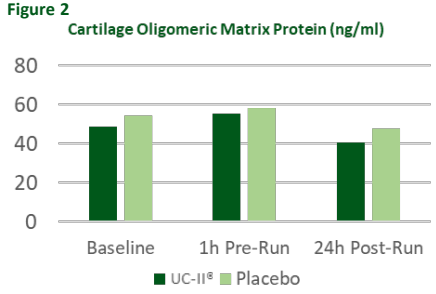


Figure 3 Neutrophil/Lymphocyte Ratio

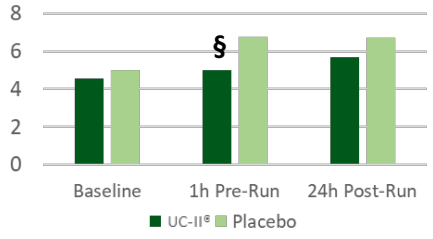
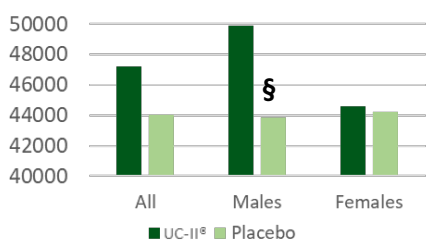


Figure 4 Activity per Kilometer



§ Significant difference between groups ($p<0.05$)

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Table 1. Comparison of biomarker and hematology values in UCII vs placebo Labrador retrievers.

Test	Group	Sex	Time Point			SEM	P-value
			Baseline	1h Pre-Run	24h Post-Run		
White blood cells, 10^9/l	UC-II®	All	9.43^{b}	10.88^{ab}	11.61^{a}	0.43	0.003
	Placebo	All	9.25^{b}	11.24^{a}	10.86^{a}	0.31	<0.001
	UC-II®	Male	9.00^{b}	10.88^{ab}	11.63^{a}	0.65	0.022
	Placebo	Male	9.86^{b}	12.00^{a}	11.86^{a}	0.52	0.011
	UC-II®	Female	9.87	10.88	11.59*	0.59	0.142
	Placebo	Female	8.63^{b}	10.48^{a}	9.86^{ab}*	0.37	0.005
Monocytes, 10^9/l	UC-II®	All	0.45	0.52	0.53	0.05	0.471
	Placebo	All	0.41^{b}	0.58^{a}	0.54^{ab}	0.04	0.024
	UC-II®	Male	0.40	0.48	0.56	0.07	0.267
	Placebo	Male	0.36	0.60	0.55	0.07	0.049
	UC-II®	Female	0.51	0.57	0.51	0.07	0.794
	Placebo	Female	0.45	0.56	0.53	0.06	0.441
Neutrophils, 10^9/l	UC-II®	All	7.17^{b}	8.38^{ab}	9.25^{a}	0.39	0.001
	Placebo	All	7.12^{b}	8.99^{a}	8.72^{a}	0.31	<0.001
	UC-II®	Male	6.90^{b}	8.47^{ab}	9.25^{a}	0.59	0.028
	Placebo	Male	7.47^{b}	9.51^{a}	9.65^{a}	0.54	0.013
	UC-II®	Female	7.44^{b}	8.30^{ab}	9.25^{a}*	0.51	0.060
	Placebo	Female	6.77^{b}	8.47^{a}	7.79^{ab}*	0.30	0.002
Eosinophils, 10^9/l	UC-II®	All	0.12^{ab}	0.17^{a}	0.09^{b}	0.02	0.049
	Placebo	All	0.16	0.18	0.16	0.03	0.878
	UC-II®	Male	0.09*	0.19	0.10	0.03	0.078
	Placebo	Male	0.22*	0.26	0.22	0.06	0.840
	UC-II®	Female	0.15	0.15	0.08	0.03	0.163
	Placebo	Female	0.11	0.10	0.10	0.02	0.898
Basophils, 10^9/l	UC-II®	All	0.05^{ab}	0.07^{a}	0.04^{b}	0.01	0.037
	Placebo	All	0.07	0.07	0.06	0.01	0.951
	UC-II®	Male	0.03^{b}‡	0.08^{a}	0.04^{ab}‡	0.01	0.025
	Placebo	Male	0.08‡	0.08	0.08‡	0.01	0.956
	UC-II®	Female	0.07	0.07	0.05	0.01	0.315
	Placebo	Female	0.06	0.05	0.04	0.01	0.760

^{abc} Within rows, means not connected by a common letter are considered significantly different over time.
‡ Within columns, significant difference between groups ($p<0.01$).
* Within columns, significant difference between groups ($p<0.05$).

Conclusions

In summary, untrained Labrador retrievers supplemented with undenatured type II collagen had decreased inflammation and cartilage degeneration compared to non-supplemented dogs after exercise.

References

[1] D'Altilio M., Peal A., Alvey M., Simms C., Curtsinger A., Gupta R.C., Canerdy T.D., and Goad J.T. (2007) Therapeutic Efficacy and Safety of Undenatured Type II Collagen Singly or in Combination with Glucosamine and Chondroitin in Arthritic Dogs. *Toxicol Mech Methods,* 17, 189-196.

[2] Pearson W., Pezzali J.G., Donadelli R.A., Wagner A., and Buff P. (2020) The Time Course of Inflammatory Biomarkers Following a One-Hour Exercise Bout in Canines: A Pilot Study. *Animals*, 10(3), 486.