

# Protease Supplementation Improves Muscle Function after Eccentric Exercise

THOMAS W. BUFORD, MATTHEW B. COOKE, LIZ L. REDD, GEOFFREY M. HUDSON, BRIAN D. SHELMADINE, and DARRYN S. WILLOUGHBY

*Exercise and Biochemical Nutrition Laboratory, Baylor University, Waco, TX*

## ABSTRACT

BUFORD, T. W., M. B. COOKE, L. L. REDD, G. M. HUDSON, B. D. SHELMADINE, and D. S. WILLOUGHBY. Protease Supplementation Improves Muscle Function after Eccentric Exercise. *Med. Sci. Sports Exerc.*, Vol. 41, No. 10, pp. 1908–1914, 2009. Protease supplementation has been purported to reduce the damaging effects of eccentric exercise and accelerate recovery of muscle function, possibly by regulating inflammation. **Purpose:** To determine the effectiveness of protease supplementation in attenuating

**“These enzymes are critically involved in numerous physiological processes ranging from the digestion of food particles to highly regulated systems such as blood clotting or immunological function...”**

**“The results of the present study indicate that 21 d of dietary supplementation with orally ingested proteases significantly improves muscle function...”**

**“...reductions in circulating IL-6 and IL-12 in the protease group may have contributed reduced muscle inflammation and thus improved muscle force.”**

**E**ccentric exercise involving lengthening muscle contraction is a common component of many sports and activities. These events are associated with muscle damage and increased inflammation, which can lead to the typical disruptions in muscle function that occur after exercise. This damage, such as Z-line streaming (16), and as myofibrillar leakage of proteins, such as creatine kinase (CK), lactate dehydrogenase (LDH), and aspartate aminotransferase (AST), are components of the inflammatory response to muscle damage. In addition to the mechanically induced damage, an inflammatory response to the muscle damage is also typically mounted by the immune system and is generally characterized by an increase in circulating leukocytes, including leukotrienes and prostaglandins (18). These events are associated with muscle damage and increased inflammation, which can lead to the typical disruptions in muscle function that occur after exercise.

**“This result not only indicates a potential beneficial effect on health but also seems to support the hypothesis that protease supplementation may reduce inflammation by inhibiting the arachidonic acid cascade...”**

**“Our data also led us to speculate that it remains possible that inhibition of the arachidonic acid pathway plays a role because of the significant repression of COX2 in the protease group...”**

Address for correspondence: Darryn S. Willoughby, Ph.D., Department of Health, Human Performance, and Nutrition Laboratory, Baylor University, Waco, TX. E-mail: Darryn\_Willoughby@baylor.edu  
Submitted for consideration August 2008  
Accepted for publication March 2009.

**“By far our most intriguing finding is the increase in circulating eosinophils and basophils in the protease group...”**

0195-9131/09/4110-1908/0  
MEDICINE & SCIENCE IN SPORTS & EXERCISE®  
Copyright © 2009 by the American College of Sports Medicine  
DOI: 10.1249/MSS.0b013e3181a518f0

challenge to muscle as it induces increases in serum cortisol and muscle damage. In addition to the mechanically induced damage, an inflammatory response to the muscle damage is also typically mounted by the immune system and is generally characterized by an increase in circulating leukocytes, including leukotrienes and prostaglandins (18). These events are associated with muscle damage and increased inflammation, which can lead to the typical disruptions in muscle function that occur after exercise. In addition to the mechanically induced damage, an inflammatory response to the muscle damage is also typically mounted by the immune system and is generally characterized by an increase in circulating leukocytes, including leukotrienes and prostaglandins (18). These events are associated with muscle damage and increased inflammation, which can lead to the typical disruptions in muscle function that occur after exercise. At present, it is unclear whether muscle repair process (17,29,33), other data indicate that muscle force decrements after exercise cannot be fully explained by mechanical damage and are correlated with inflammatory cell invasion (14,19). Much interest in developing practical interventions to reduce muscle inflammation after muscle

## REFERENCES

1. ACSM, ed. *ACSM's Guidelines for Exercise Testing and Prescription*. Baltimore, MD: Lippincott Williams & Wilkins; 2006. 366 pp.
2. Allen DL, Teitelbaum DH, Kurachi K. Growth factor stimulation of matrix metalloproteinase expression and myoblast migration and invasion *in vitro*. *Am J Physiol Cell Physiol*. 2003;284(4):C805–15.
3. Armstrong RB. Initial events in exercise-induced muscular injury. *Med Sci Sports Exerc*. 1990;22(4):429–35.
4. Armstrong RB, Ogilvie RW, Schwane JA. Eccentric exercise-induced injury to rat skeletal muscle. *J Appl Physiol*. 1983;54(1):80–93.
5. Arnold L, Henry A, Poron F, et al. Inflammatory monocytes recruited after skeletal muscle injury switch into antiinflammatory macrophages to support myogenesis. *J Exp Med*. 2007;204(5):1057–69.
6. Beck TW, Housh TJ, Johnson GO, et al. Effects of a protease supplement on eccentric exercise-induced markers of delayed-onset muscle soreness and muscle damage. *J Strength Cond Res*. 2007;21(3):661–7.
7. Cannon JG, Fielding RA, Fiatarone MA, Orencole SF, Dinarello CA, Evans WJ. Increased interleukin 1 beta in human skeletal muscle after exercise. *Am J Physiol*. 1989;257(2):R451–5.
8. Chiquet M. Regulation of extracellular matrix gene expression by mechanical stress. *Matrix Biol*. 1999;18(5):417–26.
9. Cirelli MG. Clinical experience with bromelains in proteolytic enzyme therapy of inflammation and edema. *Med Times*. 1964;92:919–22.
10. Clarkson PM, Byrnes WC, McCormick KM, Turcotte LP, White JS. Muscle soreness and serum creatine kinase activity following isometric, eccentric, and concentric exercise. *Int J Sports Med*. 1986;7(3):152–5.
11. Clarkson PM, Nosaka K, Braun B. Muscle function after exercise-induced muscle damage and rapid adaptation. *Med Sci Sports Exerc*. 1992;24(5):512–20.
12. Ebbeling CB, Clarkson PM. Exercise-induced muscle damage and adaptation. *Sports Med*. 1989;7(4):207–34.
13. Eston RG, Finney S, Baker S, Baltzopoulos V. Muscle tenderness and peak torque changes after downhill running following a prior bout of isokinetic eccentric exercise. *J Sports Sci*. 1996;14(4):291–9.
14. Faulkner JA, Brooks SV, Opitck JA. Injury to skeletal muscle fibers during contractions: conditions of occurrence and prevention. *Phys Ther*. 1993;73(12):911–21.
15. Fielding RA, Frontera WR, Hughes VA, Fisher EC, Evans WJ. The reproducibility of the Bruce protocol exercise test for the determination of aerobic capacity in older women. *Med Sci Sports Exerc*. 1997;29(8):1109–13.
16. Friden J, Sjöström M, Ekblom B. Myofibrillar damage following intense eccentric exercise in man. *Int J Sports Med*. 1983;4(3):170–6.
17. Huard J, Li Y, Fu FH. Muscle injuries and repair: current trends in research. *J Bone Joint Surg Am*. 2002;84A(5):822–32.
18. Louis E, Raue U, Yang Y, Jemiolo B, Trappe S. Time course of proteolytic, cytokine, and myostatin gene expression after acute exercise in human skeletal muscle. *J Appl Physiol*. 2007;103(5):1744–51.
19. MacIntyre DL, Reid WD, Lyster DM, Szasz IJ, McKenzie DC. Presence of WBC, decreased strength, and delayed soreness in muscle after eccentric exercise. *J Appl Physiol*. 1996;80(3):1006–13.
20. Mackey AL, Donnelly AE, Turpeenniemi-Hujanen T, Roper HP. Skeletal muscle collagen content in humans after high-force eccentric contractions. *J Appl Physiol*. 2004;97(1):197–203.
21. Malm C, Nyberg P, Engström M, et al. Immunological changes in human skeletal muscle and blood after eccentric exercise and multiple biopsies. *J Physiol*. 2000;529(1):243–62.
22. Malm C, Sjödin TL, Sjöberg B, et al. Leukocytes, cytokines, growth factors and hormones in human skeletal muscle and blood after uphill or downhill running. *J Physiol*. 2004;556(3):983–1000.
23. Miller PC, Bailey SP, Barnes ME, Derr SJ, Hall EE. The effects of protease supplementation on skeletal muscle function and DOMS following downhill running. *J Sports Sci*. 2004;22(4):365–72.
24. Newham DJ, McPhail G, Mills KR, Edwards RH. Ultrastructural changes after concentric and eccentric contractions of human muscle. *J Neurol Sci*. 1983;61(1):109–22.
25. Nishimura T, Nakamura K, Kishioka Y, Kato-Mori Y, Wakamatsu J, Hattori A. Inhibition of matrix metalloproteinases suppresses the migration of skeletal muscle cells. *J Muscle Res Cell Motil*. 2008;29(1):37–44.
26. Peterson JM, Trappe TA, Mylona E, et al. Ibuprofen and acetaminophen: effect on muscle inflammation after eccentric exercise. *Med Sci Sports Exerc*. 2003;35(6):892–6.
27. Round JM, Jones DA, Cambridge G. Cellular infiltrates in human skeletal muscle: exercise induced damage as a model for inflammatory muscle disease? *J Neurol Sci*. 1987;82(1–3):1–11.
28. Satchek JM, Milbury PE, Cannon JG, Roubenoff R, Blumberg JB. Effect of vitamin E and eccentric exercise on selected biomarkers of oxidative stress in young and elderly men. *Free Radic Biol Med*. 2003;34(12):1575–88.
29. Shireman PK, Contreras-Shannon V, Ochoa O, Karia BP, Michalek JE, McManus LM. MCP-1 deficiency causes altered inflammation with impaired skeletal muscle regeneration. *J Leukoc Biol*. 2007;81(3):775–85.
30. Smith LL. Acute inflammation: the underlying mechanism in delayed onset muscle soreness? *Med Sci Sports Exerc*. 1991;23(5):542–51.
31. Smyth RD, Moss JN, Brennan R, Harris JC, Martin GJ. Biochemical studies on the resolution of experimental inflammations in animals treated with bromelain. *Exp Med Surg*. 1967;25(1):229–35.
32. Soricter S, Mair J, Koller A, et al. Skeletal troponin I as a marker of exercise-induced muscle damage. *J Appl Physiol*. 1997;83(4):1076–82.
33. Tidball JG. Inflammatory cell response to acute muscle injury. *Med Sci Sports Exerc*. 1995;27(7):1022–32.
34. Tidball JG. Inflammatory processes in muscle injury and repair. *Am J Physiol Regul Integr Comp Physiol*. 2005;288(2):R345–53.
35. Trappe TA, Fluckey JD, White F, Lambert CP, Evans WJ. Skeletal muscle PGF(2)(alpha) and PGE(2) in response to eccentric resistance exercise: influence of ibuprofen acetaminophen. *J Clin Endocrinol Metab*. 2001;86(10):5067–70.
36. Vellini M, Desideri D, Milanese A, et al. Possible involvement of eicosanoids in the pharmacological action of bromelain. *Arznei-mittelforschung*. 1986;36(1):110–2.
37. Warren GL, Hulderman T, Mishra D, et al. Chemokine receptor CCR2 involvement in skeletal muscle regeneration. *FASEB J*. 2005;19(3):413–5.
38. Warren GL, O'Farrell L, Summan M, et al. Role of CC chemokines in skeletal muscle functional restoration after injury. *Am J Physiol Cell Physiol*. 2004;286(5):C1031–6.
39. Weinheimer EM, Jemiolo B, Carroll CC, et al. Resistance exercise and cyclooxygenase (COX) expression in human skeletal muscle: implications for COX-inhibiting drugs and protein synthesis. *Am J Physiol Regul Integr Comp Physiol*. 2007;292(6):R2241–8.
40. Woolf RM, Snow JW, Walker JH, Broadbent TR. Resolution of an artificially induced hematoma and the influence of a proteolytic enzyme. *J Trauma*. 1965;5:491–4.