Bone cell-independent benefits of raloxifene on the skeleton: A novel mechanism for improving bone material properties

Bone cell-independent benefits of raloxifene on the skeleton: A novel mechanism for improving bone material properties

Gallant, Maxime A. ; Brown, Drew M. ; Hammond, Max ; Wallace, Joseph M. ; Du, Jiang ; Deymier-Black, Alix C. ; Almer, Jonathan D. ; Stock, Stuart R. ; Allen, Matthew R. ; Burr, David B.

Permanent Link: http://hdl.handle.net/1805/3906
Date: 2014
Keywords: mechanical testing ; raloxifene ; toughness ; water ; bone loss
Cite As: Gallant MA, Brown DM, Hammond M, Wallace JM, Du J, Deymier-Black AC, Almer JD, Stock SR, Allen MR, Burr DB. Bone cell-independent benefits of raloxifene on the skeleton: A novel mechanism for improving bone material properties. Bone. 2014 Apr;61:191–200. doi:10.1016/j.bone.2014.01.009

Sponsorship: The authors would like to thank Dr. Paul K. Hansma (Department of Physics, University of California, Santa Barbara), for suggesting the soaking technique and Dr. John Okasinski, Advanced Photon Source, for helping collect the WAXS data. Raloxifene was kindly provided by Eli Lilly (Indianapolis, IN, USA) under a Material Transfer Agreement to D.B.B. Eli Lilly was not involved in the study design, analyses or interpretation of the results. We are grateful to Dr. Susan J. Gunst for sharing dog tissue. Use of the Advanced Photon Source was supported by the US Department of Energy, Office of Science, Office of Basic Energy Sciences, under Contract No. DE-AC02-06CH11357. This work was supported by NIH grants to D.B.B. and M.R.A.

Abstract:

Raloxifene is an FDA approved agent used to treat bone loss and decrease fracture risk. In clinical trials and animal studies, raloxifene reduces fracture risk and improves bone mechanical properties, but the mechanisms of action remain unclear because these benefits occur largely independent of changes to bone mass. Using a novel experimental approach, machined bone beams, both from mature male canine and human male donors, were depleted of living cells and then exposed to raloxifene ex vivo. Our data show that ex vivo exposure of non-viable bone to raloxifene improves intrinsic toughness, both in canine and human cortical bone beams tested by 4-point bending. These effects are cell-independent and appear to be mediated by an increase in matrix bound water, assessed using basic gravimetric weighing and sophisticated ultrashort echo time magnetic resonance imaging. The hydroxyl groups (-OH) on raloxifene were shown to be important in both the water and toughness increases. Wide and small angle x-ray scattering patterns during 4-pt bending show that raloxifene alters the transfer of load between the collagen matrix and the mineral crystals, placing lower strains on the mineral, and allowing greater overall deformation prior to failure. Collectively, these findings provide a possible mechanistic explanation for the therapeutic effect of raloxifene and more importantly identify a cell-independent mechanism that can be utilized for novel pharmacological approaches for enhancing bone strength.

Description:

Authors' accepted manuscript. Bone Biology Laboratory http://www.iupui.edu/~bonelab/ Department of Anatomy and Cell Biology Indiana University School of Medicine Department of Biomedical Engineering IUPUI

This item appears in the following Collection(s)

- Department of Anatomy and Cell Biology Works (/handle/1805/4108)
- Department of Biomedical Engineering Works (/handle/1805/4002)

 Show Statistical Information (#)

My Account

- Login
- Register

Statistics

- Most Popular Items
- Statistics by Country
- Most Popular Authors