CLINICAL STUDY REFERENCES: Calcium & Bone Health
(HYDROXYAPATITE, CITRATE & MALATE, IPRIFLAVONE)

Familiarizing oneself with relevant scientific research is critical to understanding nutritional supplements at a deeper level. Clinical studies on supplement ingredients can be accessed in many ways, from visiting a local University library to using an online database such as PubMed. (See last page to learn more about using the PubMed database.) Some useful studies on ingredients related to calcium and bone health are noted below.

### MICROCRYSTALLINE CALCIUM HYDROXYAPATITE

- **Age and Ageing 1973 Nov;2(4):230-4**
  - The Effect of Whole-Bone Extract on 47 Ca Absorption In the Elderly.
  - Windsor AC, Misra DP, Loudon JM, Staddon GE
  - Department of Geriatric Medicine, Bristol General Hospital

- **Am J Clin Nutr 1982 36;426-430**
  - Vitamin D, hydroxyapatite, and calcium gluconate in treatment of cortical bone thinning in postmenopausal women with primary biliary cirrhosis.
  - Epstein O, Kato Y, Dick R, Sherlock S

- **Osteoporos Int 1995 Jan;5(1):30-4**
  - Comparison of the treatment effects of ossein-hydroxyapatite compound and calcium carbonate in osteoporotic females.
  - Ruegsegger P, Keller A, Dambacher MA
  - Institute for Biomedical Engineering, University and Federal Institute of Technology, Zurich, Switzerland

- **Curr Med Res Opin 1984;8(10):734-42**
  - Clinical trial of microcrystalline hydroxyapatite compound (‘Ossopan’) in the prevention of osteoporosis due to corticosteroid therapy.
  - Pines A, Raafat H, Lynn AH, Whittington J
  - Hertford County Hospital and East Herts Hospital, Hertford, and Advisory Services (Clinical and General) Ltd, London, England

- **British Medical Journal 1978 Oct 21;2(6145):1124**
  - Microcrystalline calcium hydroxyapatite compound in corticosteroid-treated rheumatoid patients: a controlled study.
  - Nilsen KH, Jayson MI, Dixon AST
  - Department of Medicine, University of Bristol, and Royal Nations Hospital for Rheumatic Diseases, Bath

### CALCIUM CITRATE, MALATE & OTHER SALTS

- **Am J Clin Nutr 1990 Dec;9(6):583-7**
  - Superior calcium absorption from calcium citrate than calcium carbonate using external forearm counting.
  - Harvey JA, Kenny P, Poindexter J, Pak CY
  - Center for Mineral Metabolism and Clinical Research, University of Texas Southwestern Medical Center, Dallas 75235.

- **Am J Ther 1999 Nov;6(6):313-21**
  - Meta-analysis of calcium bioavailability: a comparison of calcium citrate with calcium carbonate.
  - Sakhaee K, Bhuket T, Adams-Huet B, Rao DS
  - University of Texas Southwestern Medical School, Center for Mineral Metabolism and Clinical Research, Dallas, TX

- **J Clin Endocrinol Metab 1985 Aug;61(2):301-3**
  - Calcium bioavailability from calcium carbonate and calcium citrate.
  - Nicar MJ, Pak CY

  - Comparison of the effects of calcium loading with calcium citrate or calcium carbonate on bone turnover in postmenopausal women.
  - Center on Aging, MC-5215, University of Connecticut Health Center, Farmington, CT 06030-5215, US.

- **Osteoporos Int 1996;6(4):314-9**
  - The effect of a short course of calcium and vitamin D on bone turnover in older women.
  - Prestwood KM, Pannullo AM, Kenny AM, Pilbeam CC, Raisz LG
  - Travelers Center on Aging, University of Connecticut Health Center, Farmington 06030-5215, USA
(CALCIUM CITRATE, MALATE & OTHER SALTS CONT’D)

A controlled trial of the effect of calcium supplementation on bone density in postmenopausal women.
Dawson-Hughes B, Dallal GE, Krall EA, Sadowski L, Sahyoun N, Tannenbaum S
U.S. Department of Agriculture Human Nutrition Research Center on Aging at Tufts University, Boston, MA 02111.

J Nutr 1994 Jul;124(7):1060-4
Spinal bone loss in postmenopausal women supplemented with calcium and trace minerals.
Strause L, Saltman P, Smith KT, Bracker M, Andon MB
Department of Biology, University of California at San Diego, La Jolla 92093

Absorption of calcium fumarate salts is equivalent to other calcium salts when measured in the rat model.
Weaver CM, Martin BR, Costa NM, Saleeb FZ, Huth PJ
Department of Foods and Nutrition, Purdue University, 1264 Stone Hall, West Lafayette, Indiana 47907-1264, USA.

Osteoporos Int 1993 Sep;3(5):271-5
Acute biochemical variations induced by four different calcium salts in healthy male volunteers.
Reginster JY, Denis D, Bartsch V, Deroisy R, Zegels B, Franchimont P
Centre Universitaire d’Investigation du Metabolisme Osseux et du Cartilage Articulaire, University of Liege, Belgium

(IPRIFLAVONE CONT’D)

Calcif Tissue Int 1997;61 Suppl 1:S23-7
Efficacy of ipriflavone in established osteoporosis and long-term safety.
Agnusdei D, Bufalino L
Institute of Internal Medicine and Medical Pathology, University of Siena, Italy

Ipriflavone: an important bone-building isoflavone.
Head KA

Lack of any estrogenic effect of ipriflavone in postmenopausal women.
Melis GB, Paoletti AM, Cagnacci A, Bufalino L, Spinetti A, Gambacciani M, Fioretti P
Istituto di Ginec. Ostetrica e Fisiopatologia della Riproduzione Umana, Un. of Cagliari, Italy.

Menopause 1999 Fall;6(3):233-41
Isoflavones and postmenopausal bone health: a viable alternative to estrogen therapy?
Scheiber MD, Rebar RW
Department of Obstetrics and Gynecology, University of Cincinnati College of Medicine, Ohio

Bone density changes in postmenopausal women with the administration of ipriflavone alone or in association with low-dose estrogen replacement therapy.
de Aloysio D, Gambacciani M, Altieri P, et al.
Dept. of Obst. and Gyn., U of Bologna, Italy

Ipriflavone.
Kitatani K, Morii H
Osaka City University Medical School, Second Department of Internal Medicine, Japan

Alternative therapies for menopause.
Kass-Annese B
Department of Obstetrics and Gynecology, Harbor UCLA Medical Center, Torrance, CA

J Endocrinol Invest 1993 May;16(5):333-7
Effects of ipriflavone administration on bone mass & metabolism in ovariectomized women.
Istituto di Clinica Ostetrica e Ginecologica, Un. di Pisa, Italy

Maturitas 1997 Sep;28(1):75-81
Effects of combined low dose of the isoflavone derivative ipriflavone and estrogen replacement on bone mineral density and metabolism in postmenopausal women.
Dept. of Obstetrics and Gynecology, Univ. of Pisa, Italy

Calcif Tissue Int 1997;61(7):19-22
Effect of chronic treatment with ipriflavone in postmenopausal women with low bone mass.
Gennari C, Adami S, Agnusdei D, et al.
Internal Med and Med. Path. Inst., U of Siena, Policlinico “Le Scotte”, Siena, Italy

Effect of ipriflavone on bone in elderly hemiplegic stroke patients with hypovitaminosis D.
Department of Neurology, Futase Social Insurance Hospital, Izuka, Japan
**TIPS & GUIDELINES FOR USING PUBMED**

**PubMed is an online research database.** It provides access to literally millions of clinical studies that have been published in selected scientific journals. The PubMed database is part of the National Library of Medicine at the National Institutes of Health.

To research a topic on PubMed, go to: www.pubmed.com. Doing this will redirect you to the site’s actual URL: www.ncbi.nlm.nih.gov/entrez/query.fcgi?DB=pubmed. (You may also type the actual URL into your browser – it’s just more complicated. Save the page as a bookmark to avoid this step in the future.)

Once on the PubMed site, find the search bar near the top of the page and enter the keywords you desire. Hit the Go button to the right of the search bar (or your “return” key) to bring up studies in the database that are relevant to your search.

**TIPS FOR SUCCESSFUL SEARCHING**

- **Narrow down your search by entering more than one keyword or phrase.**
- **Surround phrases with quotation marks.** (Example: instead of calcium citrate, type “calcium citrate.”)
- **Use commas or the word AND in upper case letters to separate multiple keywords or phrases.** (Example: instead of calcium citrate bone, type in “calcium citrate” AND bone.)
- **To find a specific study whose authors or title are known, include one or more last names of the authors and a few choice words from the title as keywords.** (Note: This is the easiest way to pull up the studies noted in Pioneer’s Clinical Study References.)

**VIEWING ABSTRACTS VS SUMMARIES**

When you hit “Go,” studies will be displayed in what is called summary form. The summary only provides journal name & volume number, date of publication, author names and title - the same points noted in these clinical reference pages. For information about the study’s results and conclusions, you will want to view an abstract of the study - a paragraph describing a study’s objective, procedure and findings.*

- **To view a single abstract,** click on the authors’ names (appearing in blue) in the summary.
- **To view several abstracts,** click in the boxes located to the left of the summaries. Then select “Abstract” from the pull down Display menu (located below the left side of the search bar, under the folder icons).
- **To view additional studies on the same topic,** click on the words “Related Articles” (appearing in blue) located to the right of each study summary or abstract.

*Note: Not all studies on PubMed are available as abstracts, but it is sometimes possible to find the abstract – even the full text – elsewhere on line by entering the title or author in a search engine, such as Google or Dogpile.