Glucosamine Oral Bioavailability and Plasma Pharmacokinetics after Increasing Doses of Crystalline Glucosamine Sulfate in Man

Stefano Persiani, PhD*, Enrico Roda, MD†, Lucio C. Rovati, MD*, Marcello Locatelli, PhD‡, Giampaolo Giacovelli, PhD*, Aldo Roda, PhD‡

*Clinical Pharmacology Department, Rotta Research Laboratorium/Rottapharm, Monza, *Italy*, †Department of Digestive Diseases, Metabolism and Infective Diseases, S. Orsola-Malpighi Hospital, University of Bologna, School of Medicine, Bologna, *Italy*, ‡Department of Pharmaceutical Sciences, University of Bologna, School of Pharmacy, Bologna, *Italy*

PURPOSE

Pharmacokinetic data on glucosamine are scant, limiting the understanding of glucosamine sulfate mechanism of action in support of its treatment effects in osteoarthritis. This study investigated the oral pharmacokinetics and dose-proportionality of glucosamine after administration of the patented crystalline glucosamine sulfate in man.

METHODS

Twelve healthy volunteers received three consecutive once-daily oral administrations of glucosamine sulfate soluble powder at the doses of 750, 1500, and 3000 mg, in an open, randomised, cross-over fashion. Glucosamine was determined in plasma collected up to 48 h after the last dose by a validated Liquid Chromatography method with Mass Spectrometry detection. Pharmacokinetic parameters were calculated at a steady state.

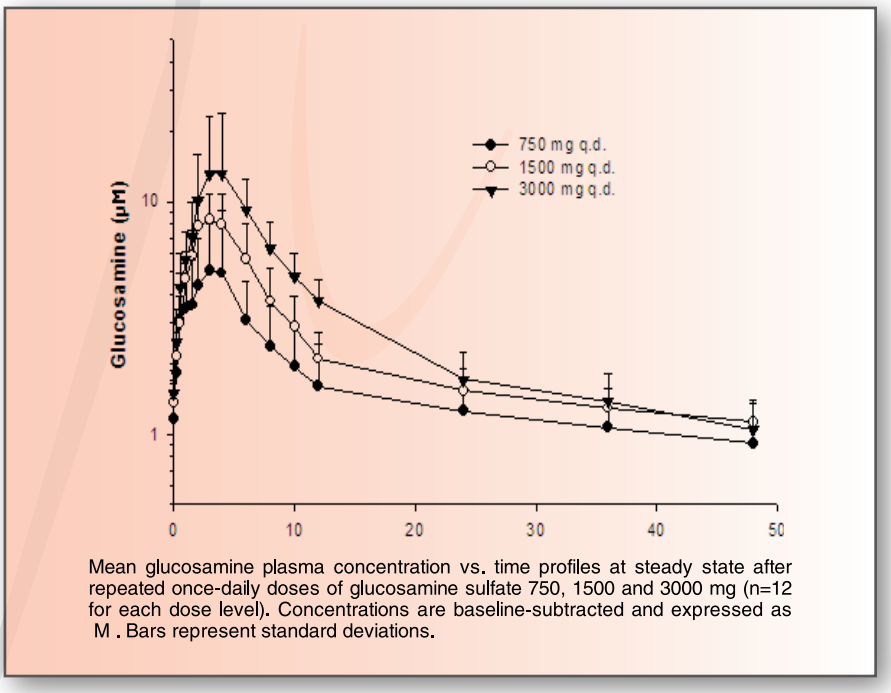
RESULTS

Endogenous plasma levels of glucosamine were detected (10.4-204 ng/ml, with low intra-subject variability). Glucosamine was rapidly absorbed after oral administration and its pharmacokinetics were linear in the dose range 750-1500 mg, but not at 3000 mg, where the plasma concentration-time profiles were less than expected based on dose proportionality. Plasma levels increased over 30-folds from baseline and peaked at about 10 μM with the standard 1500 mg once-daily dosage. Glucosamine distributed to extravascular compartments and its plasma concentrations were still above baseline up to the last collection time. Glucosamine elimination half-life was only tentatively estimated to average 15 h.

CONCLUSIONS

Glucosamine is bioavailable after oral administration of crystalline glucosamine sulfate, persists in circulation, and its pharmacokinetics support once-daily dosage. Steady state peak concentrations at the therapeutic dose of 1500 mg were in line with those found to be effective in selected in vitro mechanistic studies. This is the only glucosamine formulation for which pharmacokinetic, efficacy and safety data are now available.

OsteoArthritis and Cartilage (2005) 13, 1041-1049



Mean glucosamine plasma concentration vs. time profiles at steady state after repeated once-daily doses of glucosamine sulfate 750, 1500 and 3000 mg (n=12 for each dose level). Concentrations are baseline-subtracted and expressed as M . Bars represent standard deviations.