Life Sci. 2004 May 21;75(1):11-9.

Dietary myo-inositol hexaphosphate prevents dystrophic calcifications in soft tissues: a pilot study in Wistar rats.

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Abstract

Myo-inositol hexaphosphate (InsP6) is an abundant component of plant seeds. It is also found in significant levels in blood and mammalian tissues, but they are totally dependent on their dietary intake. In the present paper, we describe studies on the effect of InsP6 on a model of dystrophic calcification, which was chemically induced by subcutaneous injection of a 0.1% KMnO4 solution. Male Wistar rats were randomly divided into four groups for treatment over 31 days. A: animals consuming a purified diet in which InsP6 was absent but to which 1% of InsP6 (as sodium salt) was added. In this group, the InsP6 plasma levels (0.393 +/- 0.013 microM) were similar to those observed in rats consuming a standard diet. B: animals consuming only the purified diet in which InsP6 was absent. In this case the InsP6 plasma levels decreased (0.026 +/- 0.006 microM); C: animals consuming the same purified diet as group B but received daily subcutaneous injections of 50 microg kg(-1) etidronate during the last 14 days. In this case the InsP6 plasma levels were also very low (0.025 +/- 0.007 microM); D: animals consuming the same diet as group B but a 6% of carob germ (InsP6 rich product) was added. The InsP6 plasma levels (0.363 +/- 0.035 microM) were also similar to those observed in rats consuming a standard diet. After 21 days plaque formation was induced. Calcification plaques were allowed to proceed for 10 days, after which the plaque material present was excised, dried and weighed. It was found that the presence of myo-inositol hexaphosphate (phytate) in plasma at normal concentrations (0.3-0.4 microM) clearly inhibited the development of dystrophic calcifications in soft tissues. These results demonstrates that myo-inositol hexaphosphate acts as an inhibitor of calcium salt crystallization.

Biofactors. 2000;11(3):171-7.

Phytate prevents tissue calcifications in female rats.

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Abstract

The AIN-76 A, a purified rodent diet, has a propensity to cause kidney calcifications in female rats which is not observed with non-purified rodent diets, suggesting a nutritional factor that avoids these calcifications. One candidate is phytate, which inhibits crystallisation of calcium salts and is practically absent in purified diets. Therefore, the effects on calcification of kidney tissue of phytate addition to the AIN-76 A diet using female Wistar rats were studied. The rats were assigned to three groups: AIN-76 A, AIN-76 A + 1% phytate and standard nonpurified chow. Urinary phytate of the AIN-76 A fed group was undetectable. Urinary phytate of AIN-76 A + 1% phytate and standard fed groups did not differ and was significantly higher than in the AIN-76 A group. The concentrations of calcium and phosphorus in kidneys were greater in the AIN-76 A group than in AIN-76 A + 1% phytate and standard groups. Only rats of the AIN-76 A group displayed mineral deposits at the corticomedullary junction. These findings demonstrated that the absence of phytate in the AIN-76 A diet is one of the causes of renal calcification in female rats.

Br J Dermatol. 2005 May;152(5):1022-5.

Study of a myo-inositol hexaphosphate-based cream to prevent dystrophic calcinosis cutis.

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Abstract

BACKGROUND: Calcinosis cutis is a disorder caused by abnormal deposits of calcium phosphate in the skin and is observed in diverse disorders. Myo-inositol hexaphosphate (InsP(6)) is a diet-dependent molecule found in all mammalian fluids and tissues, which exhibits an extraordinary capacity as a crystallization inhibitor of calcium salts.

OBJECTIVES: To establish the effects of topically administered InsP(6) cream on artificially provoked dystrophic calcifications in soft tissues.

METHODS: Fourteen male Wistar rats were randomly assigned into two groups: control and treated groups. Rats were fed with an InsP(6)-free or phytate diet. Plaque formation was induced by subcutaneous injection of 0.1% KMnO(4) solution. From 4 days before plaque induction to the end of the experiment, control rats were treated topically with a standard cream, whereas treated rats were treated with the same cream with 2% InsP(6) or phytate (as sodium salt). Calcification of plaques was allowed to proceed for 10 days. InsP(6) in urine was determined. The plaques were excised and weighed.

RESULTS: It was found that when InsP(6) was administered topically through a moisturizing cream (2% InsP(6)-rich), the plaque size and weight were notably and significantly reduced compared with the control group (1.6 +/- 1.1 mg InsP(6)-treated, 26.7 +/- 3.0 mg control). The InsP(6) urinary levels for animals treated with the InsP(6)-enriched cream were considerably and significantly higher than those found in animals treated topically with the cream without InsP(6) (16.96 +/- 4.32 mg L(-1) InsP(6)-treated, 0.06 +/- 0.03 mg L(-1) control).

CONCLUSIONS: This demonstrates the important capacity of InsP(6) as a crystallization inhibitor and also demonstrates that it is possible to propose topical use as a new InsP(6) administration route.

Front Biosci. 2005 Jan 1;10:799-802. Print 2005 Jan 1.

Absorption of myo-inositol hexakisphosphate (InsP6) through the skin: study of the matrix effects. mechanism of phytate topical absorption.

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Source

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Abstract

Myo-inositol hexakisphosphate (InsP6, phytate) is a molecule to which diverse beneficial properties have been attributed. Some of these properties are related to its dermatological use as discolouring agent, on preventing calcinosis cutis or due to its important role on premature aging. Other studies also seem to demonstrate a capacity of InsP6 to inhibit skin cancer. In this paper, the effect of the vehicle of topical administration of phytate is studied, using four groups of male Wistar rats (n = 6) fed with an InsP6 defficient diet and treated with a hydrophyl gel or an O/W moisturizing cream with two different concentrations of InsP6. Due to the correlation between InsP6 absorption and its urinary excretion, these last values were used to evaluate this process. It was found that phytate was absorbed through the skin using both a gel or a cream, demonstrating that its absorption is independent on the matrix used for topical treatment. However, urinary InsP6 values were slightly higher when using the gel, but in all cases values were much higher than those found with oral InsP6 treatment, due to the formation of insoluble species in the gastrointestinal tract when InsP6 is administered orally.

Arthritis Res Ther. 2010;12(2):R56. Epub 2010 Mar 30.

Calcium deposition in osteoarthritic meniscus and meniscal cell culture.

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Abstract

INTRODUCTION: Calcium crystals exist in the knee joint fluid of up to 65% of osteoarthritis (OA) patients and the presence of these calcium crystals correlates with the radiographic evidence of hyaline cartilaginous degeneration. This study sought to examine calcium deposition in OA meniscus and to investigate OA meniscal cell-mediated calcium deposition. The hypothesis was that OA meniscal cells may play a role in pathological meniscal calcification.

METHODS: Studies were approved by our human subjects Institutional Review Board. Menisci were collected during joint replacement surgeries for OA patients and during limb amputation surgeries for osteosarcoma patients. Calcium deposits in menisci were examined by alizarin red staining. Expression of genes involved in biomineralization in OA meniscal cells was examined by microarray and real-time RT-PCR. Cell-mediated calcium deposition in monolayer culture of meniscal cells was examined using an ATP-induced (45)calcium deposition assay.

RESULTS: Calcium depositions were detected in OA menisci but not in normal menisci. The expression of several genes involved in biomineralization including ENPP1 and ANKH was upregulated in OA meniscal cells. Consistently, ATP-induced calcium deposition in the monolayer culture of OA meniscal cells was much higher than that in the monolayer culture of control meniscal cells.

CONCLUSIONS: Calcium deposition is common in OA menisci. OA meniscal cells calcify more readily than normal meniscal cells. Pathological meniscal calcification, which may alter the biomechanical properties of the knee meniscus, is potentially an important contributory factor to OA.

Arthritis Rheum. 2009 Sep;60(9):2694-703.

Calcification of articular cartilage in human osteoarthritis.

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Abstract

OBJECTIVE: Hypertrophic chondrocyte differentiation is a key step in endochondral ossification that produces basic calcium phosphates (BCPs). Although chondrocyte hypertrophy has been associated with osteoarthritis (OA), chondrocalcinosis has been considered an irregular event and linked mainly to calcium pyrophosphate dihydrate (CPPD) deposition. The aim of this study was to determine the prevalence and composition of calcium crystals in human OA and analyze their relationship to disease severity and markers of chondrocyte hypertrophy.

METHODS: One hundred twenty patients with end-stage OA undergoing total knee replacement were prospectively evaluated. Cartilage calcification was studied by conventional x-ray radiography, digital-contact radiography (DCR), field-emission scanning electron microscopy (FE-SEM), and synovial fluid analysis. Cartilage calcification findings were correlated with scores of knee function as well as histologic changes and chondrocyte hypertrophy as analyzed in vitro.

RESULTS: DCR revealed mineralization in all cartilage specimens. Its extent correlated significantly with the Hospital for Special Surgery knee score but not with age. FE-SEM analysis showed that BCPs, rather than CPPD, were the prominent minerals. On histologic analysis, it was observed that mineralization correlated with the expression of type X collagen, a marker of chondrocyte hypertrophy. Moreover, there was a strong correlation between the extent of mineralization in vivo and the ability of chondrocytes to produce BCPs in vitro. The induction of hypertrophy in healthy human chondrocytes resulted in a prominent mineralization of the extracellular matrix.

CONCLUSION: These results indicate that mineralization of articular cartilage by BCP is an indissociable process of OA and does not characterize a specific subset of the disease, which has important consequences in the development of therapeutic strategies for patients with OA

Osteoarthritis Cartilage. 2009 Oct;17(10):1333-40. Epub 2009 May 7.

Contribution of calcium-containing crystals to cartilage degradation and synovial inflammation in osteoarthritis.

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Abstract

OBJECTIVES: The role of calcium phosphate and pyrophosphate crystals in osteoarthritis (OA) is unclear: are they a symptom of the damage that occurs to the joint or a key intermediate in the progression of inflammation and joint damage that occurs in OA? The proinflammatory and catabolic response of synthetic calcium phosphate and pyrophosphate crystals and crystals extracted from human osteoarthritic knee cartilage has been investigated. The crystal forms eliciting a response have been characterised allowing a comparison of the biological effects of synthetic and native calcium crystals on human osteoarthritic chondrocytes and synoviocytes to be carried out.

METHODS: Calcium phosphate and pyrophosphate crystals were synthesised in vitro and their crystal forms characterised by X-ray powder diffraction (XRPD). The inorganic crystalline material present in human osteoarthritic cartilage was extracted and its structural composition elucidated by XRPD. These crystals were applied to human primary osteoarthritic chondrocytes and synoviocytes and the production of proinflammatory and catabolic mediators measured.

RESULTS: The crystals extracted from human osteoarthritic knee cartilage were identified as consisting of a mixture of monoclinic and triclinic calcium pyrophosphate dihydrate (m-CPPD and t-CPPD). These crystals elicited an inflammatory and catabolic response in human primary osteoarthritic chondrocytes and synoviocytes as measured by an increase in nitric oxide (NO), matrix metalloproteinase 13 (MMP-13) and prostaglandin E2 (PGE(2)) production. NO, MMP-13 and PGE(2) production was also increased when the synthetic calcium hydrogen phosphate dihydrate (DCPD) and calcium pyrophosphate hydrates were applied to the cells.

CONCLUSIONS: Crystals extracted from human osteoarthritic knee cartilage induce the production of proinflammatory and catabolic mediators (NO, MMP-13 and PGE(2)) in human primary chondrocytes and synoviocytes. Synthetic calcium phosphate and pyrophosphate crystals elicit a similar response in those cells. Our findings suggest that these crystals could contribute to cartilage degradation and synovitis in OA.

Curr Opin Rheumatol. 2011 Mar;23(2):170-3.

Crystals, inflammation, and osteoarthritis.

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Abstract

PURPOSE OF REVIEW:
Calcium pyrophosphate dihydrate (CPPD) and basic calcium phosphate (BCP) crystals are common components of osteoarthritic joint fluids and tissues. Why these crystals form and how they contribute to joint damage in osteoarthritis remain unclear. With renewed interest in inflammation as a key component of osteoarthritis the role of calcium-containing crystals in this common disease warrants re-examination.
RECENT FINDINGS:
There is ample evidence supporting a pathogenic role for inflammation in osteoarthritis, and the innate immune system likely participates in this inflammatory process. Recent work reinforces the almost universal existence of calcium-containing crystals in tissues from patients with end-stage osteoarthritis. Calcium-containing crystals may contribute to inflammation in osteoarthritis tissues through their direct interactions with components of the innate immune system, as well as by inducing or amplifying other inflammatory signals.
SUMMARY:
There is increasing evidence that calcium-containing crystals contribute to osteoarthritis and their inflammatory properties may mediate detrimental effects through innate immunity signals. Calcium-containing crystals may thus represent important therapeutic targets in osteoarthritis

J Med Food. 2008 Dec;11(4):747-52.

Phytate (myo-inositol hexaphosphate) and risk factors for osteoporosis.

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Abstract

Several risk factors seem to play a role in the development of osteoporosis. Phytate is a naturally occurring compound that is ingested in significant amounts by those with diets rich in whole grains. The aim of this study was to evaluate phytate consumption as a risk factor in osteoporosis. In a first group of 1,473 volunteer subjects, bone mineral density was determined by means of dual radiological absorptiometry in the calcaneus. In a second group of 433 subjects (used for validation of results obtained for the first group), bone mineral density was determined in the lumbar column and the neck of the femur. Subjects were individually interviewed about selected osteoporosis risk factors. Dietary information related to phytate consumption was acquired by questionnaires conducted on two different occasions, the second between 2 and 3 months after performing the first one. One-way analysis of variance or Student's t test was used to determine statistical differences between groups. Bone mineral density increased with increasing phytate consumption. Multivariate linear regression analysis indicated that body weight and low phytate consumption were the risk factors with greatest influence on bone mineral density. Phytate consumption had a protective effect against osteoporosis, suggesting that low phytate consumption should be considered an osteoporosis risk factor.