INTRODUCTION: IL-1β activates reactive oxygen species (ROS) production, release of MMPs and chondrocyte apoptosis which leads to matrix breakdown and osteoarthritis. The ROS generating NADPH oxidase 4 (Nox4) could play a central role in this pathway (Grange et al, 2006). Nox4 activity is regulated by heme oxygenase-1 (HO-1) (Rousset et al, in preparation).

Potential targets of CA on C-20/A4 chondrocytes

1- Nox4 Activity
Effects of CA and its components were assessed after 96h incubation on Nox4 activity with the tetracycline inducible HEK293 TRex_NoX4 cells (Serrander et al, 2007).

CA displays an indirect antioxidant effect dependant on Copper and Ginger

2- MMP secretion
Impact of CA and its components on IL-1β induced proMMP1 and ADAMTS5 secretion by C-20/A4 chondrocytes. Western blot densitometry is normalized to BSA.

CA decreases ADAMTS5 secretion via GS and MMP1 secretion via Copper and Ginger

3- Apoptosis
Impact of 96h incubation with CA and its components on IL-1β-induced caspase 3 activation on the C-20/A4 chondrocyte cell line.

CA and GS reduce IL-1β-induced caspase 3 activation

4- HO-1 expression
Impact of CA and its components on HO-1 expression by C-20/A4 chondrocytes after 96h incubation. CoPp is the positive control of HO-1 induction.

CA and GS increase HO-1 expression

CONCLUSION: In this study we provided experimental evidences that glucosamine sulfate decreases ADAMTS5 expression and apoptosis in the IL-1β stimulated C-20/A4 chondrocytes. In addition, ginger root and copper sulfate decrease the Nox4 regulated proMMP1 expression. Molecular mechanisms could imply a downregulation of Nox4 activity by the antioxidant protein HO-1. These findings emphasize in vitro the potential beneficial effects of Cuivramine in osteoarthritis.

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