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Effects of Resveratrol, Piceatannol and Quercetin in an Equine Cartilage Explant Model for Potential Use in Treating Osteoarthritis

Purba Islam

School of Veterinary Medicine and Science

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Abstract

Currently there are no disease-modifying osteoarthritis drugs (DMOADs) available and the treatment for osteoarthritis (OA) is still based on minimising symptoms. Commonly used drugs for OA have health hazards from long and short term use and has led to patients using alternatives therapies such as nutraceuticals.

In this study, three natural phenols (resveratrol, piceatannol and quercetin) were compared with commonly used drugs used for treating OA; phenylbutazone (Non-steroidal anti-inflammatory drug, NSAID) and prednisolone (corticosteroid) and a nitric oxide inhibitor (S-ethylisothiourea) in an IL-1β stimulated equine cartilage explant culture. Treatments at 100 µg/ml were assessed for their ability to inhibit inflammatory markers present in OA (nitric oxide, PGE_2, glycosaminoglycan, cell viability). Resveratrol, piceatannol and quercetin showed close to 100% nitric oxide inhibition similar to S-ethylisothiourea. Piceatannol was the only treatment which showed significant glycosaminoglycan inhibition. Cell viabilities for fresh cartilage, cultured control cartilage, piceatannol (in the presence of IL-1β) and resveratrol (in the presence of IL-1β) treated cartilage were 83.9 ± 0.98 %, 76.8 ± 2.59 %, 78.8 ± 3.57 % and 63.1 ± 4.35 % respectively.

In dose-response IL-1β stimulated cartilage explant studies, piceatannol and quercetin significantly inhibited nitric oxide at a concentration range of 1-300 µg/ml, whereas for resveratrol it was 10-300 µg/ml. Effective inhibition of GAG breakdown for resveratrol and quercetin was in a range of 10-30 µg/ml in the stimulated cartilage explant. The IC_{50} for inhibition by piceatannol of GAG breakdown was 2 µg/ml. Inhibition of PGE_2 production appeared to be obscured by the vehicle (1% DMSO) used to dissolve the phenols.

This study suggests that nitric oxide is not playing a major role in GAG breakdown and cell death in the stimulated equine cartilage explant. Moreover, in this study, it was observed that GAG breakdown does not appear to initiate cell death at least at the early stages of an OA-like condition.

Resveratrol, piceatannol and quercetin may be potential DMOAD candidates to treat OA. Further studies on their beneficial effects, especially *in vivo*,

should be compared against novel OA-modulators (such as GLPG1972) which are currently in clinical trials as they may offer a far cheaper therapeutic alternative.