DIPEPTIDYL-PEPTIDASE IV (DPP IV/CD26) AFFECTS THE WOUND HEALING PROCESS IN A STREPTOZOTOCIN-INDUCED DIABETES MODEL IN MICE

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ABSTRACTS

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BS01

Natural flavonols of plant origin as novel carbon monoxide releasing molecules

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Keywords: CO release, Dehydrosilybin, natural flavonols, Quercetin

INTRODUCTION: Carbon monoxide (CO) is a gasotransmitter studied for its potential therapeutic applications. Photoactivatable CO releasing molecules (photoCORMs) including synthetic flavone scaffold-containing molecules are used to deliver CO to the target cells and tissues. Naturally occurring flavonoids of plant origin are an important part of a human diet with beneficial effects on many physiological processes, however, whether they are capable of CO release upon photoexcitation is unknown. Our objective was to investigate the ability to release CO from synthetic and natural flavonoids after photoexcitation and its biological consequences.
METHODS: HepG2 and HepaRG cell lines were used to measure cytotoxicity of synthetic flavonol, quercetin and dehydrosilybin with/without white light-irradiation using MTT assay. CO release was quantitated by GC-RGA. Biological effects of CO release were studied by Western blotting (β-catenin, β-actin), GC/MS (Krebs cycle intermediates) and FACS (cell cycle).
RESULTS: Quercetin and dehydrosilybin release CO upon white light irradiation with different rates-dehydrosilybin fastest, followed by synthetic flavonol and quercetin at concentrations of 400 μM. CO release from synthetic flavonol significantly decreased cell metabolism, β-catenin protein expression and slowed cell cycle progression. All flavonols show significant toxicity at concentrations of 400 μM upon white light irradiation.
CONCLUSION: We discovered that natural flavonols quercetin and dehydrosilybin are effective photoCORMs with dehydrosilybin as most potent CO releaser. CO production from flavonols affects cell metabolism and proliferation which might contribute to an anti-cancer effect of these molecules.

BS02

DIPEPTIDYL-PEPTIDASE IV (DPP IV/CD26) AFFECTS THE WOUND HEALING PROCESS IN A STREPTOZOTOCIN-INDUCED DIABETES MODEL IN MICE

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Keywords: diabetes mellitus, DPP IV/CD26, hyperglycemia, wound healing

INTRODUCTION/OBJECTIVES: Diabetes mellitus is a metabolic disorder with multiple etiology, characterised by chronic hyperglycemia with disturbances of metabolism of carbohydrates, fats and proteins. It results from defects in insulin secretion, action or both. Dipeptidyl-peptidase IV/CD26 (DPP IV/CD26) molecule is known to be involved in an array of physiological and pathological processes, in the regulation of glycaemia as well. A variety of complications caused by diabetes can cause hospitalizations. DPP IV/CD26 inhibitors can be used to treat diabetes mellitus. The aim of this research was to investigate the processes of wound healing in conditions of CD26 deficiency in experimental hyperglycaemia.
MATERIALS AND METHODS: In this experiment two strains of mice were used, wild type and CD26-deficient mice. Experimental diabetes was induced using a solution of streptozotocine in citrate buffer (50mg/kg, i.p.) during five days. Serum samples as well as pancreas, cutaneous (control) tissue and wound tissue were analyzed. Pathohistological, immunohistochemical and immunobiochemical analyses were performed on wound samples and control skin. Serum samples were analysed for DPP IV/CD26 activity and concentration of target angiogenic factors.
RESULTS: Results of this study revealed that DPP IV/CD26 has an important role in the regulation of blood glucose concentration. Inactivation of DPP IV/CD26 improves the state associated with hyperglycemia. The process of cutaneous wound healing is improved in conditions of CD26 deficiency.
CONCLUSION: The inhibition of DPP IV/CD26 has positive effects on the wound healing process in hyperglycemia. DPP IV/CD26 inhibition can be suggested as a therapeutic option for treatment of diabetes mellitus and its complications like delayed wound healing.