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# Nitric oxide restores impaired healing in normoglycaemic diabetic rats.

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## Abstract

### OBJECTIVE:

Hyperglycaemia impairs wound healing. However, little is known about the underlying cellular mechanisms that lead to diminished wound repair in insulin-controlled and non-insulin-controlled diabetes. This study investigated the role of endogenous and exogenous nitric oxide on incisional wound healing in diabetic rats.

### METHOD:

Groups of 10 wild-typeWistar control rats - 10 genetically diabetic BioBreeding rats and 10 genetically diabetic BioBreeding rats treated with subcutaneous insulin implants to render them normoglycaemic - underwent dorsal skin incision followed by subcutaneous insertion of polyvinyl alcohol sponges. The rats were sacrificed 10 days later to determine the wound-breaking strength and reparative collagen deposition. Nitric oxide, an important mediator in diabetic wound healing and collagen synthesis, was measured in wound fluid. Wound-derived fibroblasts were tested for ex vivo synthesis of nitric oxide and collagen. Exogenous nitric oxide was used for the therapeutic interventions.

### RESULTS:

Wound-breaking strength and wound collagen deposition were significantly impaired in the hyperglycaemic diabetic animals ($p<0.01$). Wound nitric-oxide synthesis and ex vivo wound fibroblast nitric-oxide production were reduced in the hyperglycaemic rats ($p<0.01$). Insulin treatment partially reversed some of the effects of hyperglycaemia on wound repair ($p<0.05$). Exogenous nitric oxide further restored wound mechanical strength, collagen deposition and fibroblast collagen synthesis ($p<0.01$) in insulin-treated (normoglycaemic) diabetic animals.

### CONCLUSION:

Wound healing is impaired in hyperglycaemic and normoglycaemic diabetic rats. This is reflected in impaired wound fibroblast nitric-oxide synthesis. Used in combination with insulin, exogenous nitric oxide further improves healing outcomes, making it a potential target for therapeutic intervention in insulin-treated normoglycaemic diabetes.