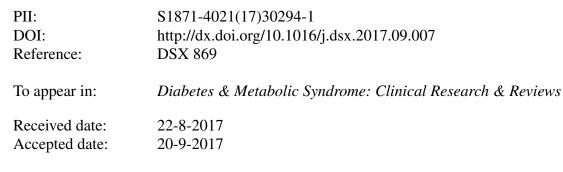
## Accepted Manuscript

Title: Platelet rich plasma and growth factors cocktails for diabetic foot ulcers treatment: state of art developments and future prospects

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## Platelet rich plasma and growth factors cocktails for diabetic foot ulcers treatment: state of art developments and future prospects

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**Abstract:** Current advances in diabetic foot ulcers (DFU) treatment are discussed. Normal and pathological wound healing process are observed and the role of growth factors (GFs) is elucidated. Current techniques involving GFs and platelet rich plasma (PRP) are compared. Up-to-date research suggests that treatment with single growth factor (GF) could be insufficient and not encompassing all pathological changes in DFU bed. Efficiency of PRP is rather controversial and lacks evidence. Thus the use of cocktail of particular GFs is suggested. Pro et contra of each approach are discussed.

Keywords: growth factors, diabetic foot ulcer, platelet rich plasma, growth factors cocktail, diabetes

### **1. Introduction**

Diabetes mellitus (also referred to as diabetes) is a highly-frequent and fast-spreading disease in the world. According to International Diabetes Federation, 415 million adults (1 of 11) have diabetes. About 15 % of them suffer from diabetic foot ulcers (DFU) which can lead to severe consequences if no appropriate treatment is provided. More than 88 % of lower limb amputations are caused by diabetic foot ulcers complicated by necrosis [1], gangrene and osteomyelitis [2, 3], because ulcers are highly susceptible to infections [3]. These wounds are mostly chronic and are caused by several factors that result in different pathways of DFU formation. Peripheral neuropathy hampers ability to feel pain and affect muscles involved in moving thus callus is likely to appear. Patient's awareness of wounding is decreased and ulcer can easily develop if no adequate treatment is provided [4]. Diabetic angiopathy causes peripheral vascular disease and hampers perfusion on macrovascular level [5, 6]. Often ulcers with vascular insufficiency need revascularization by angiosurgery, thrombolysis and bypass surgery [4]. In contrast, neuropathic ulcers could be treated medically [7]. Also structural and functional changes of microcirculation occur that lead to ischemia and changes in the metabolism of cells corrupting normal wound healing mechanism. Other common reasons for ulcers are foot deformity, high plantar pressures, peripheral oedema, and external trauma, the latter one could cause DFU [2].

Thus it is important to diagnose the disease at early stages and provide effective management to avoid dramatic consequences. Current standard of care for DFUs starts with assessment for vascular disease, skin, soft tissue or bone infection and neuropathy [8]. Conventional techniques for DFU treatment include debridement of the wound and offloading [9]. Debridement aims at removing all devitalized tissues, including callus, necrotic, and infected tissue, and leaving only healthy one and effectively

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