Upregulation of β-Catenin, Ki67 and VEGF gene expression level following treatment of date palm fruit fraction in hypoxic cardiomyocyte–BMMSC co-culture

Nur Fariha Mohd Manzor[1], Nurul Farihah Samsudin[1], Noraziah Nordin[1], Siva Gowri Pathmanathan[2], Marlini Muhamad[1], Hayati Abdul Rahman[2]

[1]Department of Medical Sciences I, Faculty of Medicine and Health Sciences, Universiti Sains Islam Malaysia, 71800 Bandar Baru Nilai, Negeri Sembilan, Malaysia, [2]Department of Medical Sciences II, Faculty of Medicine and Health Sciences, Universiti Sains Islam Malaysia, 71800 Bandar Baru Nilai, Negeri Sembilan, Malaysia

ABSTRACT

Introduction: Date palm fruit is rich in bioactive compounds with regenerative properties. An aqueous extract was fractionated using solid-phase extraction, and Fraction D (FD) was identified based on its ability to enhance BMMSC proliferation (MTT assay). FD was then evaluated for its angiogenic paracrine potential. Materials and Methods: BMMSCs were co-cultured for 24 h with hypoxia-injured cardiomyocytes in four conditions: (i) basal medium (negative control), (ii) complete growth medium with 10% FBS (positive control), (iii) 10% FBS supplemented with FD, and (iv) 2% FBS supplemented with FD. BMMSCs were harvested for total RNA extraction, cDNA synthesis, and quantitative PCR (qPCR) analysis of β-catenin, Ki67, and VEGF gene expression. Pairwise statistical comparisons between groups were performed using the Mann–Whitney test ($p < 0.05$). **Results:** Gene expression analysis revealed no significant changes in β-catenin among groups. However, Ki-67, a proliferation marker, was markedly upregulated in BMMSCs co-cultured with 2% FBS + FD compared to both the control and 10% FBS groups ($p < 0.05$). Similarly, VEGF-A expression was significantly elevated in the 10% FBS + FD group relative to control and 10% FBS, while the 2% FBS + FD group showed reduced VEGF-A expression ($p < 0.05$). These findings suggest that Fraction D supplementation enhances BMMSC proliferative capacity and paracrine pro-angiogenic signalling under optimized culture conditions. **Conclusion:** Supplementation with date palm Fraction D enhances BMMSC functional activity by promoting proliferation (Ki-67 upregulation) and paracrine pro-angiogenic signalling (VEGF-A induction). These findings highlight its potential as a regenerative agent to support stem cell-mediated cardiac repair.

Keywords: Ajwa date palm fruit, proliferation, angiogenesis, mesenchymal stem cells, hypoxic cellular model